International Journal of Drug Policy 74 (2019) 152–159

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research Paper

The effect of cannabis laws on opioid use

Jamie L. Flexon[a,*], Lisa Stolzenberg[b], Stewart J. D'Alessio[c]

[a] Department of Criminology and Criminal Justice, Green School of International and Public Affairs, Florida International University, Modesto A. Maidique Campus, 11200 SW 8th Street, PCA-366A, Miami, FL 33199, USA
[b] Department of Criminology and Criminal Justice, Green School of International and Public Affairs, Florida International University, Modesto A. Maidique Campus, 11200 SW 8th Street, PCA-253A, Miami, FL 33199, USA
[c] Department of Criminology and Criminal Justice, Green School of International and Public Affairs. Florida International University, Modesto A. Maidique Campus, 11200 SW 8th Street, PCA-263B, Miami, FL 33199, USA

ARTICLE INFO

Keywords:
Medical Marijuana Laws
Opioids
Chronic pain management
Cannabis

ABSTRACT

Background: Many Americans rely on opioids at varying dosages to help ameliorate their suffering. However, empirical evidence is mounting that opioids are ineffective at controlling non-cancer related chronic pain, and many argue the strategies meant to relieve patient suffering are contributing to the growing opioid epidemic. Concurrently, several states now allow the use of medical cannabis to treat a variety of medical conditions, including chronic pain. Needing more exploration is the impact of cannabis laws on general opioid reliance and whether chronic pain sufferers are opting to use cannabis medicinally instead of opioids.
Methods: This study investigates the effect of Medical Marijuana Laws (MML)s on opioid use and misuse controlling for a number of relevant factors using data from several years of the National Survey on Drug Use and Health and multivariate logistic regression and longitudinal analysis strategies.
Results: Results provide evidence that MMLs may be effective at reducing opioid reliance as survey respondents living in states with medical cannabis legislation are much less apt to report using opioid analgesics than people living in states without such laws, net other factors. Results further indicate that the presence of medicinal cannabis legislation appears to have no influence over opioid misuse.
Conclusion: MMLs may ultimately serve to attenuate the consequences of opioid overreliance.

Background

While numbers vary, it is estimated that up to 116 million Americans suffer from chronic pain (Institute of Medicine, 2011; Reuben et al., 2015), with concentration in the older adult population (> 40%) (Johannes, Le, Zhou, Johnston & Dworkin, 2010; Volkow & McLellan, 2016). Of this group, an estimated 5 to 8 million Americans needing long-term pain management (Reuben et al., 2015), or roughly between 8% to 30%, rely on opioids at varying dosage levels (Nuckols et al., 2014). Although opioids were originally reserved for patients with cancer-related pain, post-operative pain, and for patients needing palliative care, state medical boards over the past two decades have eased laws regulating the granting of opioid prescriptions. This loosening of opioid prescription laws has contributed to a dramatic rise in the public's use of opioids making it the most often prescribed analgesic in the U.S. (Volkow & McLellan, 2016). To illustrate, the issuance of opioid prescriptions increased from 76 million in 1991 to 219 million by 2011 (Reuben et al., 2015), and by 2014, 245 million prescriptions for opioids were dispensed from U.S. pharmacies not accounting for refills (National Institute on Drug Abuse, 2015; Volkow & McLellen, 2016). This trend clearly parallels the movement by the medical community to manage chronic pain and lessen patient suffering. Further contributing to the widespread use of opioids is that there are few alternatives to deal with chronic pain, the recognition that patients have an endemic right to pain relief, advocacy by support organizations to use opioids, and the aggressive marketing by pharmaceutical companies (Manchikanti et al., 2012; Volkow & McLellan, 2016).

Reliance on opioids is not without detriment. Opioid use has an associated cost of $560–635 billion in reduced work productivity, sick time, medication expenses, and medical care (Institute of Medicine, 2011; Reuben et al., 2015). Hospital visits for problematic opioid use are now quite common. Between the years of 2005 to 2014, opioid related emergency room visits increased 117% and associated

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
* Corresponding author.
E-mail addresses: flexonj@fiu.edu (J.L. Flexon), stolzenb@fiu.edu (L. Stolzenberg), dalessi@fiu.edu (S.J. D'Alessio).

https://doi.org/10.1016/j.drugpo.2019.09.013

hospital stays increased by 76% (Mallow, Belk, Topmiller & Strassels, 2018). Deaths attributable to prescription opioid overdose rose from 3442 in 1999 to 17,029 in 2017, and drug overdose deaths from any opioid use rose from 8048 to 47,600 during the same time period (National Institute on Drug Abuse, 2019). Recent projections indicate that opioid overdoses will worsen with an annual number of deaths reaching approximately 82,000 by 2025, yielding a total of over 700,000 projected deaths between 2016 and 2025 (Chen et al., 2019). It is striking that 80% of these deaths were attributable to illicit use, and problematically these researchers only found modest impact on these projections from alterations in prescribing behaviour, such as strategies meant to prevent prescription opioid misuse. Alarmingly, ".. opioid analgesics are now responsible for more deaths than the number of deaths from both suicide and motor vehicle crashes, or deaths from cocaine and heroin combined" (Manchikanti et al., 2012, p. ES9). Contributing to the problem is a belief among the public that prescription drugs are safer to misuse than illicit drugs along with a related tendency to use opioids with other drugs such as benzodiazepines (Nuckols et al., 2014). Both of these behaviours, and others, may be in response to inadequate pain control and can ultimately contribute to increased morbidity and mortality.

The widespread reliance on opioids to manage patient suffering appears to be nested in tradition, clinical experience, and anecdotal observations rather than on sound, empirically-based evidence (Manchikanti et al., 2012). There is no corroboration of a long-term benefit in either chronic pain or function stemming from treatment with opioids, but rather increased harms including problematic substance use, opioid use disorder, overdose, and motor vehicle injury are quite possible (Dowell, Haegerich & Chou, 2016). To illustrate, a comprehensive review of the extant literature undertaken by Martell et al. (2007) not only failed to discern any indication that opioid use mollified chronic back pain, but there was also evidence of significant substance use disorder along with aberrant medication-taking behaviours in as high as 24% of the opioid patients. Further, the Center for Disease Control (CDC) reports that alternative therapies in the forms of nonpharmacologic (e.g., exercise) and nonopioid therapy (e.g., NSAIDS, acetaminophen) have been shown to cause less harm and show more efficacy in pain management, and the new recommendation is that nonopioid treatment is preferred for chronic pain.

While mounting evidence suggests that opioids are ineffective as a means to control chronic, non-cancer related pain, as well as being linked to a myriad of issues associated with opioid use disorder (Dowell et al., 2016), many states are enacting Medical Marijuana Laws (MMLs; also referred to herein as medical cannabis laws or medical cannabis legislation) for the treatment of various medical complaints, including chronic pain. Against this backdrop, patients may seek out this alternative to manage their discomfort and increase their quality of life as it may be more effective at pain control than opioids (Abrams, Couey, Shade, Kelly & Benowitz, 2011; Hill, 2015; Reiman, Welty & Solomon, 2017). As early evidence for pain control attributable to medicinal cannabis accrues, this shift away from opioids may occur along with its associated threats such as overdose, drug interactions and death (Boehnke, Gangopadhyay, Clauw & Haffajee, 2019). Hence, the legal availability of cannabis may serve to diminish the consequences of opioid reliance as it might serve as a better alternative to treat chronic pain.

Despite cannabis' widespread acceptance and usage (Center for Behavioral Health Statistics & Quality, 2016a) and as more states enact MMLs, studies are only emerging that examine the efficacy of cannabis as a tool for pain management (e.g., Abrams et al., 2011; Boehnke, Litinas & Clauw, 2016; Carroon, Mischley & Sexton, 2017; Lucas, 2012; Lucas & Walsh, 2017; Piper et al., 2017; Reiman et al., 2017). This research supports the notion that cannabis and its derivatives may have potential as an important adjunct to other pain medications or serve as a primary analgesic. For example, a review of several high-quality studies supported the use of cannabis as an analgesic for the treatment of chronic pain, neuropathic pain, and spasticity stemming from multiple sclerosis (Hill, 2015), and vaporized cannabis served to augment the effects of opioids in such a manner that pain was significantly decreased (Abrams et al., 2011). The researchers concluded that the combination of cannabis with lower doses of opioids may be a more effective strategy in treating pain than opioids alone while avoiding opioid's dose dependent side effects. Others have reached similar conclusions regarding the perceived effectiveness of cannabis and preference among patients (e.g., Boehnke et al., 2016, 2019; Burns & Ineck, 2006; Hill, 2015; Lau et al., 2015; Lucas, 2012; Reiman et al., 2017). Recently, Reiman et al. (2017) surveyed patients concerning their cannabis and opioid use with patients reporting significant improvement in pain with cannabis, less side effects than opioid analgesics, and an ability to reduce opioid dosage. Hence, patient reports continue to demonstrate a preference for cannabis over opioids for perceived pain control.

Work examining the general qualifying conditions for medicinal cannabis and treatment efficacy also complement the above findings. Boehnke et al. (2019) report that, "Chronic pain is currently and historically the most common qualifying condition reported by medical cannabis patients (64.9% in 2016). Of all patient-reported qualifying conditions, 85.5% had either substantial or conclusive evidence of therapeutic efficacy" (p. 295). This is important as it elucidates that a significant proportion of medical cannabis users are relying on the drug for pain management, which should have a substantial impact on diminishing opioid use and associated consequences.

Though beyond the scope of the current inquiry, it is interesting that evidence also points to daily cannabis use improving outcomes for opioid agonist treatment (OAT; Socias et al., 2018). The research demonstrated that at least daily cannabis use was associated with a corollary increase in OAT retention of about 21% compared to those with less cannabis use (Socias et al., 2018). Such findings point to another avenue for which opioid reliance and consequences may be diminished through the use of cannabis. Taken together, these above studies demonstrate a possible and promising role for cannabis in medical management of conditions that may influence the consequences of the opioid epidemic through displacement.

Although Tetrahydrocannabinol (THC), the primary psychoactive constituent of cannabis, is not inferior to opioids for pain management, concern has been raised regarding the potential side effects of cannabis use such as mental cloudiness and sedation, substance use disorder, lung related illness, among others (e.g., Häuser, Finnerup & Moore, 2018; Kroenke & Cheville, 2017). Nonetheless, cannabis is not, at least yet, associated with the same problematic substance use profile of opioids, and there is not a known risk for death associated with cannabis overdose (Walker & Huang, 2002). Given these recent findings and concerns, further research into the efficacy and risks of cannabis as a line of therapy for chronic pain is certainly warranted, particularly as more states enact MMLs.

In tandem with the above, there is a dearth of research investigating the effect of MMLs on opioid use generally, but recent studies have examined the impact of MMLs on opioid associated overdose and other related behaviours (e.g., Bachhuber, Saloner, Cunningham & Barry, 2015; Powell, Pacula & Jacobson, 2018; Wen, Hockenberry & Cummings, 2015). While informational, these studies are novel and not directly comparable. For example, while one study reported fewer opioid overdoses in MML states suggesting a shift in use toward cannabis (Bachhuber et al., 2015), another dispelled the idea of displacement by showing that MMLs had little effect on the misusing or the illegal use of opioids (Wen et al., 2015). Problematically, both studies severely limited the pool of users who may be replacing opioid analgesics for cannabis. This situation is especially troublesome because most people receiving opioids for the long-term do not misuse or experience an overdose (Kroenke & Cheville, 2017). Other studies examining the impact of MMLs on opioid displacement also vet limited samples (Bradford & Bradford, 2016, 2017; Wen & Hockenberry, 2018).

The above clearly illustrates the need for research that discerns whether MMLs are impacting the use of opioids among the population and not solely among misusers and those having overdosed. As noted above, research does suggest that people are replacing opioids with cannabis (Boehnke et al., 2016; ; Corroon et al., 2017; Lucas & Walsh, 2017; Piper et al., 2017; Reiman et al., 2017). However, more research is warranted that examines whether a shift away from opioid analgesics toward medical cannabis is occurring among a more comprehensive population as statutes liberate its use for pain management.

Aim

With the increasing availability of medical cannabis to pain sufferers and with research showing that cannabis may be effective at controlling pain (Abrams et al., 2011; Hill, 2015), the current study sought to vet whether it is plausible that chronic pain sufferers may be opting to use medical cannabis instead of opioids for pain relief. The present approach investigated this proposition using several analytic strategies among a more general population by evaluating whether the presence of a MML influences opioid use and misuse, net a myriad of controls.

Methods

Data

The current study uses 2015, 2016, and 2017 data drawn from the National Survey on Drug Use and Health (NSDUH; Center for Behavioral Health Statistics & Quality, 2016b). The National Survey on Drug Use and Health is a nationally representative sample of the U.S. population that is conducted by the Substance Abuse and Mental Health Services Administration. The survey is uniquely suited to address these issues because it contains information on opioid pain reliever use among the population along with individual demographic characteristics of the respondent. The National Survey on Drug Use and Health is available online at https://www.datafiles.samhsa.gov/. Only adults ages 18 and older are included because state cannabis laws typically have a minimum age of 18. The age restriction in these laws is rooted in research showing that cannabis use, beginning at a young age, can amplify one's risk of use and dependence on cannabis and other illicit substances (e.g., Chen, Storr & Anthony, 2009). Cannabis can also have a serious impact on cognitive function, affecting both memory and the intelligence quotient (Hassunah & McIntosh, 2016). A total 120,764 respondents are included in the analysis examining years 2015 through 2017 of the survey.

It is important to emphasize upfront that data on prescription opioid use rather than only misuse was added in 2015 and available for the years 2015 through 2017 of the survey. The definition of misuse was also modified during this time period (for more information see Center for Behavioral Health Statistics & Quality, 2016c).

Measures

Dependent variables

Two dependent variables are analyzed in this study. The first dependent variable is pain reliever use, which records whether the respondent used any prescription pain reliever during the past year. Prescription pain relievers include only prescription opioid analgesics: hydrocodone, oxycodone, propoxyphene, tramadol, extended-release tramadol, codeine pills, morphine, extended-release morphine, fentanyl, buprenorphine, oxymorphone, extended-release oxymorphone, hydromorphone, extended-release hydromorphone, and methadone. The survey screens for brand name and generic versions of these drugs. Any use of prescription drugs is defined as the use of one's own prescription medication as directed by a medical doctor. The second dependent variable, pain reliever misuse, measures whether the respondent misused any prescription opioid pain reliever during the past year. Misuse of prescription drugs is defined as any (opioid) pain reliever use not directed by a medical doctor, including use without a prescription of one's own medication, drug use in greater amounts, frequency, and duration than prescribed, or any use not supervised by a medical doctor. Both dependent variables are dummy coded.

Independent variables

The theoretically relevant independent variable in the analysis is MML state, which is a dummy coded variable that indicates whether a survey respondent lived in a state that legally allowed the use of cannabis for medical purposes at the time of the interview. For the present analysis, MML state is coded as 1 if the respondent lived in a state that had a law allowing the use of cannabis for medical reasons on or before the interview date. MML state is coded as 0 if (a) the respondent was in a state that did not have a law allowing the use of cannabis for medical reasons at any time during the survey year; or (b) the respondent was in a state where a law allowing the use of cannabis for medical reasons went into effect during the survey year but after the interview date. It is important to note that because individual states could not be specifically identified in the data, we are unable to determine the length of time that the MMLs were in effect and whether MML states also enacted recreational cannabis laws. There remains a possibility that opioid use would be more greatly affected in states with both medical and recreational cannabis laws. Additionally, it may take a year or more for cannabis to become available to the public through distribution centers in states with newly enacted MMLs. While these issues are relevant omissions in the main analysis, a state-level supplemental analysis was conducted to help mitigate some of these concerns and includes a measure for the presence of a recreational cannabis law.

In addition to the MML state variable, several control variables were incorporated into the analyses to avoid basing conclusions on spurious or suppressed relationships, as well as to control for survey year. The variables for survey year are added to account for any time-related effects not accounted for in the model and should account for issues related to overlapping MML and annual retrospective accounting of opioid use by year. Variables previously used by researchers were analyzed to facilitate replication and comparability (e.g., Wen et al., 2015). These variables include age, which is coded as a dummy set with 65 and older serving as the reference group, sex, race/ethnicity, self-reported health, cigarette smoking, health insurance, family income, county metro status, marital status, education, and employment. Also included are variables measuring levels of cannabis use during the past year. The means and standard deviations for all variables are reported in Table 1.

Analytic method

Multivariate logistic regression was used to ascertain the influence of the MML state and the control variables on the two dependent variables using SPSS, version 25 (IBM Corp., 2017). When values are indicated in the text, they represent the percent change in the log odds transformation using the following formula: percent change in the Odds Ratio = $(e^{\beta} - 1)$*100. Multicollinearity diagnostics were performed and revealed no problems.

The .001 rather than the .01 or .05 level of significance is the criterion used for identifying a salient association between an independent variable and each of the dependent variables because of the large sample size analyzed. When a large number of people are surveyed, relatively small differences in the probability of pain reliever use and pain reliever misuse among the independent variables may turn out to be statistically significant. Consequently, when evaluating a variable's influence on the likelihood of pain reliever use and misuse, emphasis should be placed on the direction and magnitude of the variable's impact in each of the equations.

Table 1
Description of variables included in the study (N = 120,764).

	MML state (N = 64,524)		Non-MML state (N = 56,240)	
	Mean	S.D.	Mean	S.D.
Pain reliever use (past year)	0.28	0.45	0.32	0.46
Pain reliever misuse (past year)	0.06	0.23	0.06	0.23
Age: 65 or older (ref.)				
18	0.04	0.20	0.04	0.20
19	0.04	0.19	0.04	0.19
20	0.04	0.19	0.04	0.19
21	0.04	0.19	0.04	0.20
22–23	0.08	0.27	0.08	0.28
24–25	0.09	0.28	0.09	0.28
26–29	0.09	0.29	0.09	0.29
30–34	0.11	0.32	0.11	0.32
35–49	0.26	0.44	0.26	0.44
50–64	0.12	0.33	0.12	0.32
Male	0.47	0.50	0.46	0.50
Cannabis use (past year): no use (ref.)				
1–11 days	0.06	0.24	0.05	0.21
12–49 days	0.04	0.19	0.03	0.17
50–99 days	0.02	0.14	0.02	0.13
100–299 days	0.06	0.23	0.04	0.20
300–365 days	0.05	0.22	0.03	0.18
Race/ethnicity: non-Hispanic white (ref.)				
Non-Hispanic black	0.11	0.31	0.16	0.36
Non-Hispanic Asian	0.07	0.25	0.03	0.16
Hispanic	0.21	0.41	0.14	0.35
Self-reported health: scale (1 = excellent, 5 = poor)	20.27	0.98	2.31	1.00
Cigarette smoking: non-smoker (ref.)				
Non-daily smoker	0.10	0.30	0.11	0.31
Daily smoker	0.12	0.32	0.15	0.36
Health insurance	0.91	0.29	0.86	0.35
Family income: ≥200% FPL (ref.)				
Living <100% FPL	0.18	0.38	0.20	0.40
Living 100–200% FPL	0.21	0.40	0.23	0.42
County metro status: non-metro (ref.)				
Living in large metro	0.54	0.50	0.34	0.47
Living in small metro	0.31	0.46	0.40	0.49
Marital status: married (ref.)				
Widowed	0.03	0.17	0.03	0.18
Divorced/separated	0.10	0.30	0.12	0.32
Never married	0.46	0.50	0.42	0.49
Education: college graduate (ref.)				
Less than high school	0.13	0.33	0.14	0.35
High school graduate	0.25	0.43	0.28	0.45
Some college	0.33	0.47	0.34	0.47
Employment: full-time employed (ref.)				
Part-time employed	0.16	0.37	0.15	0.36
Unemployed	0.06	0.24	0.06	0.24
Not in labor force	0.25	0.44	0.27	0.44
Study year: 2015 (ref.)				
2016	0.31	0.46	0.35	0.48
2017	0.38	0.49	0.27	0.44

Results

Prescription opioid pain reliever use

Table 2 reports the results of the two logistic regression equations estimating the influence of the MML state and control variables on the likelihood of pain reliever use and misuse. The findings for opioid use in Table 2 show a statistically discernible relationship between the dummy coded MML state variable and the likelihood that a survey respondent will properly use an opioid pain reliever. The coefficient for the MML variable is statistically significant and is in the negative direction indicating that living in a state with a MML lowers the log odds of an opioid pain reliever being used by about 9.7%, net the effects of the other independent variables included the equation (Table 2).

Table 2
Logistic regression analysis predicting pain reliever use and misuse (N = 120,764).

	Pain reliever use			Pain reliever misuse		
	B	S.E.	Exp(B)	B	S.E.	Exp(B)
MML state	−0.102*	0.014	0.903	−0.088	0.028	0.916
Age 18	−0.141	0.047	0.868	0.997*	0.116	2.709
Age 19	−0.208*	0.048	0.812	1.092*	0.115	2.982
Age 20	−0.316*	0.047	0.729	1.119*	0.113	3.062
Age 21	−0.252*	0.046	0.777	1.189*	0.112	3.285
Age 22–23	−0.161*	0.037	0.851	1.150*	0.104	3.159
Age 24–25	−0.093	0.036	0.911	1.219*	0.102	3.385
Age 26–29	−0.045	0.034	0.956	1.197*	0.102	3.311
Age 30–34	0.013	0.032	1.014	1.204*	0.099	3.334
Age 35–49	0.037	0.028	1.038	1.022*	0.095	2.778
Age 50–64	0.097*	0.029	1.101	0.658*	0.101	1.931
Male	−0.343*	0.014	0.709	0.072	0.027	1.075
Cannabis use 1–11 days	0.104*	0.029	1.109	1.034*	0.047	2.811
Cannabis use 12–49 days	0.126*	0.037	1.134	1.354*	0.052	3.874
Cannabis use 50–99 days	0.162*	0.048	1.176	1.429*	0.063	4.176
Cannabis use 100–299 days	0.042	0.031	1.043	1.484*	0.042	4.409
Cannabis use 300–365 days	−0.045	0.035	0.956	1.747*	0.043	5.739
Non-Hispanic black	0.068*	0.020	1.071	−0.367*	0.043	0.693
Non-Hispanic Asian	−0.609*	0.036	0.544	−0.653*	0.093	0.520
Hispanic	−0.232*	0.020	0.793	−0.085	0.038	0.918
Self-reported health	0.293*	0.007	1.341	0.211*	0.014	1.234
Non-daily smoker	0.157*	0.022	1.170	0.589*	0.036	1.803
Daily smoker	0.277*	0.020	1.319	0.757*	0.035	2.133
Health insurance	0.338*	0.023	1.402	0.038	0.039	1.039
Living <100% FPL	0.021	0.020	1.021	−0.060	0.038	0.942
Living 100–200% FPL	0.004	0.018	1.004	−0.031	0.034	0.969
Living in large metro	−0.007	0.019	0.993	0.070	0.038	1.073
Living in small metro	0.036	0.018	1.037	0.039	0.038	1.040
Widowed	−0.111	0.038	0.895	0.277	0.095	1.319
Divorced/separated	0.109*	0.021	1.115	0.155*	0.048	1.168
Never married	−0.156*	0.018	0.856	0.175*	0.037	1.191
Less than high school	−0.105*	0.026	0.900	0.107	0.053	1.113
High school graduate	0.045	0.020	1.046	0.007	0.044	1.007
Some college	0.228*	0.018	1.256	0.140*	0.040	1.150
Part-time employed	−0.020	0.020	0.980	0.006	0.039	1.006
Unemployed	0.021	0.029	1.021	0.317*	0.048	1.373
Not in labor force	0.119*	0.018	1.126	0.043	0.037	1.044
Study year 2016	−0.105*	0.016	0.900	−0.138*	0.032	0.871
Study year 2017	−0.114*	0.016	0.892	−0.170*	0.032	0.844
Constant	−1.620	0.044	0.198	−5.183	0.116	0.006
Nagelkerke R^2	0.069			0.155		

Note: *$p \leq .001$ (two-tailed test).

Other variables are also associated with less reliance on prescribed opioids. Younger individuals ages 19–23 compared to those 65 years and older are less apt to use prescribed opioids (Table 2). Males are significantly less likely to use prescribed opioids compared to females (Table 2). Regarding race/ethnicity, non-Hispanic Asians and Hispanics demonstrate a lower aptitude to use prescribed opioids compared to non-Hispanic Whites, net the other controls (Table 2). Those never married are also less inclined to use prescribed opioids compared to married respondents (Table 2). Finally, those having less than a high school education have an attenuated likelihood to use prescribed opioids compared to college graduates (Table 2). For those in the 2016 survey, respondents had a 10% reduced log odds of using prescription opioids and in 2017 had a 10.8% reduced log odds of such use compared to 2015 subjects (Table 2).

Several other variables are also salient in predicting legitimate opioid pain reliever use in the equation. Those aged 50–64 are more likely to use prescribed opioids compared to those 65 years and older, net controls in the model (Table 2). Infrequent cannabis use (those with

less than 100 days of use during the previous year) is associated with increased prescription opioid use than non-cannabis users (Table 2). Non-Hispanic Blacks are more apt to use prescribed opioids compared to non-Hispanic Whites (Table 2). Those in poorer health, non-daily smokers, daily smokers, those with health insurance, divorced or separated individuals compared to married, those having some college compared to college graduates, and those not participating in the labor force are all associated with a higher proclivity to use opioid pain relievers (Table 2).

Opioid pain reliever misuse

The results reported in Table 2 fail to show a discernible negative relationship between the dummy coded variable measuring the presence of a MML in a state and the likelihood of opioid pain reliever misuse as reported by the survey respondents. However, while the effect of the MML is not substantively negative in the estimated misuse equation, a number of the other independent variables do have a discernible impact on the probability of opioid pain reliever misuse among respondents. As noted in Table 2, younger individuals across all age groups compared to those 65 and older are more likely to misuse opioids, but the magnitude of the effect is stronger for those in the categories under age 35. Cannabis users are also more inclined to misuse opioids (Table 2). The magnitude of this relationship increases along with greater reported frequency of cannabis use. People reporting less than excellent health, non-daily smokers, daily smokers, those divorced/separated and never married as compared to married, having some college compared to college graduate, and the unemployed are all more apt to misuse pain relievers (Table 2). Non-Hispanic Blacks and Asians compared to non-Hispanic Whites, however, are less likely to misuse opioids (Table 2). Respondents in both the 2016 (−12.9% reduced log odds) and 2017 (−15.6% reduced log odds) survey years showed a reduced likelihood of misusing opioids compared to those surveyed in 2015 (Table 2).

In sum, the results generated from the multivariate logistic regression equations show that MMLs are associated with a lower likelihood of opioid pain reliever use, but not misuse. Of note, because of methodological changes over time and coding schemes, the use variable could not be used as a control in the analysis examining misuse. As necessarily coded, the categories for later years are rendered completely and mutually exclusive. Introducing opioid use as a control would therefore serve as a constant in the models.

Pain reliever use and misuse by year

Table 3 presents a summary table of three logistic regression equations predicting pain reliever use and misuse on MML state by years 2015 (Eq. 1), 2016 (Eq. 2), and 2017 (Eq. 3). Controls are the same as those used in Table 2 but were left out of the table for economy of space. The full results are available upon request. The .001 level of significance was used as criterion. As with all of the analyses, multicollinearity diagnostics indicated no problems. The percent transformations reported were calculated using the previously discussed formula.

Table 3
Logistic regression analysis predicting pain reliever use and misuse on MML state by year.

	Pain reliever use			Pain reliever misuse		
	B	S.E.	Exp(B)	B	S.E.	Exp(B)
Study year 2015 (N = 40,830)	−0.070	0.023	0.933	−0.044	0.046	0.957
Study year 2016 (N = 39,964)	−0.130*	0.024	0.878	−0.140	0.049	0.869
Study year 2017 (N = 39,970)	−0.106*	0.024	0.899	−0.089	0.050	0.915

Note: *$p \leq .001$ (two-tailed test). Control variables not shown but are available upon request.

The findings revealed that for 2016, there was a 12.2% reduction in the log odds of using prescribed opioids and a 10.1% reduction in 2017 for those in MML states compared to non-MML states (Table 3). No impact from the MML laws were observed on the prescribed use of pain relievers in 2015 and misuse of opioid drugs by survey respondents in 2015, 2016, and 2017 (Table 3).

Supplemental analysis

A longitudinal panel analysis of persons 18 years of age and older in the 50 U.S. states and the District of Columbia (Washington, DC) from 2002 to 2017 was employed to help ensure that our initial findings remained robust across different specifications and for the other reasons discussed above. This analysis uses data acquired from the Interactive National Survey on Drug Use and Health State Estimates (https://pdas.samhsa.gov/saes/state). These data encompass 14 measurement periods calibrated into two-year intervals (2002–03, 2003–04, 2004–05, 2005–06, 2006–07, 2007–08, 2008–09, 2009–10, 2010–11, 2011–12, 2012–13, 2013–14, 2015–16, and 2016–17). State estimates for pain reliever data were not available for the 2014–15 interval.

Measures

The dependent variable is the proportion of adults reporting *non-medical use of pain relievers in the past year*. However, beginning in 2015, the survey question was revised to reflect the proportion of adults reporting *pain reliever misuse in the past year*. Even though there were changes in the question wording, both variables capture the prevalence of pain reliever misuse among adults. Only opioid misuse is analyzed because no information is contained in the state data on prescription opioid use.

The independent variable of theoretical relevance in the longitudinal analysis is the year that medical cannabis legislation was implemented in a given state. This variable is coded 1 for the year that a state passed a MML and 0 otherwise. We also included a control variable reflecting the year that an MML state legalized recreational cannabis use. This variable is coded 1 for the year that a MML state passed a recreational cannabis law and 0 otherwise. Information on states with legal medical and recreational cannabis was obtained from ProCon.org (https://medicalmarijuana.procon.org/). Finally, we include a control variable reflecting the change in the survey question. This variable is coded 1 for the 2015–16 and 2016–17 time periods and 0 otherwise.

There are currently 33 legal MML states and DC and 11 legal recreational cannabis states and DC in the U.S. The first date noted in parentheses indicates the year the MML was passed, while the second date denotes the year recreational cannabis was enacted. An asterisk (*) denotes time periods outside the scope of our data and therefore are excluded from the analysis: Alaska (1998, 2014), Arizona (2010), Arkansas (2016), California (1996, 2016), Colorado (2000, 2012), Connecticut, (2012), Delaware (2011), Florida (2016), Hawaii (2000), Illinois (2013, 2019*), Louisiana (2016), Maine (1999, 2016), Maryland (2014), Massachusetts (2012, 2016), Michigan (2008, 2018*), Minnesota (2014), Missouri (2018*), Montana (2004), Nevada (2000, 2016), New Hampshire (2013), New Jersey (2010), New Mexico (2007), New York (2014), North Dakota (2016), Ohio (2016), Oklahoma (2018*), Oregon (1998, 2014), Pennsylvania (2016), Rhode Island (2006), Utah (2018*), Vermont (2004, 2018*), Washington (1998, 2012), Washington, DC (2010, 2014) and West Virginia (2017).

Analytic method

The panel regression procedure in LIMDEP, version 11 was used to ascertain the impact of MMLs on pain reliever misuse among the states

(Econometric Software Inc., 2016). This type of analytic design is ideally suited for studying both the spatial and temporal patterns of opioid misuse among the population because it can analyze multiple units (states) across multiple time periods (years). We are thus able to account for medical cannabis legislation and other state-specific variables that may help explain variation in pain reliever misuse among adults that cannot be considered with a national time series. Another advantage is that the analysis of panel data does not require many temporal observations, which is typically needed in a time series analysis.

We employed a fixed effects model to estimate our equation because a Hausman test (Hausman, 1978), which assesses whether the fixed effects model and the random effects model produce statistically similar results, favored the fixed effect model.

Supplemental analysis results

The results generated for this analysis showed that the coefficients for the MML (.002, $p. > .05$) and recreational cannabis (.001, $p. > .05$) variables were not sizable. The dummy control variable reflecting the change in question wording was also insignificant ($-.001$, $p. > .05$). These findings suggest that adult opioid pain reliever misuse is not more pronounced in states that allow for the use of medical and recreational cannabis.

Discussion and conclusion

This research sought to ascertain whether MMLs might influence overall opioid analgesic use and misuse through displacement away from opioids toward cannabis for arguably better or comparable pain management. If this displacement is occurring, such laws could ultimately serve to alleviate the negative, downstream consequences associated with overreliance on opioids. The results generated by this study provide evidence that MMLs may be effective at reducing opioid reliance as survey respondents living in states with MMLs are much less apt to report using opioid analgesics than people living in states without such laws, net other factors. This is a compelling finding that complements research already discussed demonstrating subjects' preference for medical cannabis over opioids for managing medical conditions and side effects (Bruce, Brady, Foster & Shattell, 2017; Lau et al., 2015; Reiman et al., 2017). Reiman et al.'s (2017) work is illustrative for review in showing that patients report experiencing less side effects with cannabis compared to opioids for the management of their conditions. In addition, cannabis enabled patients to reduce their reliance on opioids with a significant proportion indicating that cannabis was equal to opioids for pain relief and preferring cannabis over opioids if it were an available alternative (Reiman et al., 2017, p. 162–164). Such subjective appraisals by patients are important in this context as the success of a treatment plan is in part determined by the patient's perceptions of treatment efficacy and tolerance of side effects. Such work also highlights a desire and willingness for patients, at least to some degree, to transition away from opioids to cannabis.

Despite patient preference, however, there are concerns that such displacement away from opioids may result in a *cannabis epidemic* (also referred to as marijuana epidemic; Häuser et al., 2018; Kroenke & Cheville, 2017); that is, a problematic and widespread overreliance on cannabis, and with it, attributable risks. Ostensibly, cannabis is the less problematic alternative to opioids but some lament that more research is clearly needed to validate that position so that greater harms are not created via unsound policy (Kalant, 2015; Kroenke & Cheville, 2017). Also, little is known about which patients are most likely to benefit or be harmed from cannabis therapy, and empirically based guidance required for clinical practice is lacking (e.g., Timko & Cucciare, 2018 -but see MacCallum & Russo, 2018 for dosage research and recommendations). The central concerns from a public health perspective, then, are whether cannabis is effective for pain control while minimizing harm relative to opioids and other medically based pain management (Bonnie, Kesselheim & Clark, 2017). As offered by Rhem and Fischer, "Cannabis policy is not formulated in a vacuum: it needs to fit into an overall coherent policy framework for psychoactive substance use, where the policy approaches should somehow – also in relative comparison - be proportional to potential harms caused" (2015, p. 543). The challenge is in determining what the risks of cannabis are relative to opioid analgesics and other treatment modalities toward making informed and effective policy that goes beyond anecdotal, political and emotive reasoning.

Understanding the risk profile of cannabis alone and relative to other psychoactive substances is essential to develop policy that informs the present concern of whether cannabis replacement therapy would represent a more or less safe and effective alternative or adjunct to opioids. Taken alone, cannabis is associated with dependency, lung injury, altered brain development (largely impacting those starting use in adolescence), mental illness, and increased motor vehicle accidents, among other potential problems (see Rhem & Fischer, 2015; Volkow, Baler, Compton & Weiss, 2014). Concerning comparative risk assessments, emerging research has sought to evaluate the relative risk of a number of psychoactive substances, including cannabis and opioids. Such risk assessment has commonly relied upon expert panel rankings of acute and chronic toxicity, tendencies for problematic use, and social harms (Lachenmeier & Rehm, 2015). It should be noted that such approaches have not been without criticism, among them being that they are based on subjective judgments. Irrespective, findings from these approaches consistently indicate that the relative risk of cannabis compared to a number of psychoactive substances, including opioids, is low to intermediate across a number of personal and social domains (e.g., Nutt, King & Phillips, 2010; van Amsterdam, Opperhuizen, Koeter & van den Brink, 2010; see also Lachenmeier & Rehm, 2015). These assessments also correspond well with early work seeking to produce a therapeutic index based on the toxicology of psychoactive substances, which found cannabis to have a very large safety margin compared to other substances (Gable, 1993, see also Gable, 2004). Hence, even amid research demonstrating that cannabis use has been associated with a number of risks, "it is important to recognize that cannabis in almost all comparative reviews is concluded to cause less individual and social harm than the legal substances of alcohol and tobacco, as well as many illegal substances (e.g., cocaine, amphetamines, or opioids;…" (Rehm & Fischer, 2015, p. 543).

Cannabis is used by a large segment of the population being third behind alcohol and tobacco in prevalence (Substance Abuse & Mental Health Services Administration, 2014). Given the findings of the current study, and as additional states enact MMLs, further displacement by patients away from opioids may result because legislation liberating the use of medical cannabis lessens the perceived riskiness of its use (Khatapoush & Hallfors, 2004; Schuermeyera et al., 2014; Wall et al., 2011). Owning to cannabis' widespread acceptance and usage, there is already a reasonable amount of social knowledge concerning its side effects and pitfalls. While experienced users may readily try medicinal cannabis as an alternative to opioids, there likely is some hesitancy among others lacking exposure to cannabis. For these inexperienced patients who may be dissatisfied with opioids, the legislative efforts may be enough to diminish concerns and persuade patients to try cannabis who might otherwise avoid it. Thus, the MML legislation independently can add to displacement among the inexperienced, while others may choose cannabis over opioids for pain based on prior knowledge. Both avenues would increase the numbers of medicinal cannabis users and perhaps lend to this feared cannabis epidemic. Conversely, it is unknown whether patients with complex pain management needs will revert to opioids overtime if they find medicinal cannabis inadequate to control pain or it loses its perceived effectiveness, which are similar complaints about other analgesics. Further research into this area should lend needed insight required to unpack the nuances of using cannabis as a line of therapy for pain management.

The findings generated in this study also demonstrate that MMLs do

not impact the misuse of opioids to any substantial degree. The results indicate that survey respondents living in MML states are no less likely to misuse opioids than people living in non-MML states. This finding is consistent with previous research, which found that MMLs have no discernable influence over misuse of psychoactive substances including opioids (Wen et al., 2015). The findings reported here offer some solace that the implementation of MMLs are not contributing to the problematic use of diffuse illegal substances, beyond perhaps recreational cannabis (Wen et al., 2015). It is possible that people who would misuse these substances are already doing so in spite of legislation liberating the use of cannabis for medicinal purposes. Such a rationale is in concert with the findings of this study.

While the results reported here are noteworthy, limitations and recommendations for improvements should be discussed. Measurement error was introduced into the equations as not all of the MMLs were enacted or implemented during the entire prior year, which was the time-frame of the dependent variables. During the 2015 study period, 24 of the current 29 states and Washington, DC had effective MMLs. Nevertheless, no MMLs were enacted in 2015, and only 3 MMLs became effective in 2014. Since 21 of the 24 states and Washington, DC had MMLs enacted between 1998 and 2013, the impact of measurement error is negligible. Additionally, some of the current study analyses are cross-sectional in nature and provide only a snap shot of the scrutinized relationships. However, survey year was controlled for and further analysis was conducted by year. As any significant association between the liberation of cannabis for medicinal purposes and the misuse of opioids may take some time to be revealed, further investigation of this relationship particular to prescribed opioid use would be aided by using a longitudinal approach. It also should be noted that there was limited variability in the opioid misuse variable. This lack of variability was present in other research (Wen et al., 2015) and was not surprising as survey questions related to illegal behaviour are commonly associated with biased responses, e.g., social desirability bias. This issue will likely persist in research using survey data to examine illicit drug use behaviours.

There will certainly remain a question as to whether the evidence presented in the supplemental panel analysis suffices to sufficiently buttress the claim that adult nonmedical opioid pain reliever use is not more marked in states that permit the use of medical cannabis because of the aggregate nature of the longitudinal data analyzed. A micro-level exploration could not be undertaken within the analytic panel framework because the data necessary for such an analysis were not readily available over an extended period. More detailed information on specific individuals over time will allow for a more precise appraisal as to whether MML laws influence pain reliever misuse among adults.

It is also worth noting that some have argued that using the enactment date of MML is insufficient as there are many factors influencing such laws implementation and patient usage of cannabis (Pacula, Boustead & Hunt, 2014). We did explore the availability of measures reflecting such insight, which concern the level of difficulty in obtaining medical cannabis, such as use of registries, variations in qualifying conditions, and or the sources and amount of cannabis available to patients, among other legislative variation, however such data were unavailable for the main and supplemental analysis. These variations between MMLs, including those noted by Pacula and colleagues, are assumed under the variable for MML in the aggregate. Notably, while MMLs vary across states, all states and jurisdictions used in the analysis allow for use of medical cannabis for pain as a primary or secondary condition, which is the focus of this study concerning patients and opioid use and misuse. If these variations in MMLs created such prohibitive difficulty for physicians and patients and the access of medicinal cannabis was insufficient, for example, we would not expect to find a significant impact from the medical cannabis legislation. However, there are significant results signaling the robustness of findings across all of our models, which mirror the findings from a range of samples examining patient preference that point toward replacement. This is important as it suggests that method effects are not operating, which would include the omission of important variables through model misspecification, and or the influence of these other factors are not strong enough to supplant displacement. The replication of findings across samples, methods, and levels of analysis, then, offer scholars and those interested some degree of confidence that replacement away from opioids is occurring owning to the availability of medicinal cannabis through MMLs even with the above noted concerns. However, future research examining Pacula et al. (2014) suppositions is warranted to determine which statutory indicators may influence access to medicinal cannabis in an effort to inform policy makers seeking to optimize legislation (e.g., Powell et al., 2018).

In conclusion, the present study found that in MML states some displacement is occurring away from opioids toward medicinal cannabis, but misuse of opioids is neither increasing nor decreasing owning to the policy. Such findings have far reaching implications if these associations hold up to scrutiny as further movement away from prescribed opioids is likely to influence the occurrence of opioid attributable risks. While cannabis has been argued by some to be addictive, it is not known to be associated with overdose related death or the morbidity that is seen with opioids. Since recent research has suggested that MMLs do influence the negative outcomes associated with opioid reliance, such as reducing premature death from overdose (Bachhuber et al., 2015), and there does not appear to be a concern that enacting MMLs increases opioid misuse directly, medicinal cannabis may be one avenue to combat the consequences of the opioid epidemic without amplifying, beyond perhaps recreational cannabis, further illicit drug use (Wen et al., 2015). The association between cannabis and opioid use, however, demands further empirical scrutiny to establish causal order amidst less restrictive environments toward cannabis.

Declaration of Competing Interest

None

References

Abrams, D. I., Couey, P., Shade, S. B., Kelly, M. E., & Benowitz, N. L. (2011). Cannabinoid–opioid interaction in chronic pain. *Clinical Pharmacology & Therapeutics, 90*(6), 844–851.

Bachhuber, M. A., Saloner, B., Cunningham, C. O., & Barry, C. L. (2015). Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010. *JAMA Internal Medicine, 174*(10), 1668–1673.

Boehnke, K. F., Gangopadhyay, S., Clauw, D. J., & Haffajee, R. L. (2019). Qualifying conditions of medical cannabis license holders in the United States. *Health Affairs, 38*(2), 295–302.

Boehnke, K. F., Litinas, E., & Clauw, D. J. (2016). Medical cannabis associated with decreased opiate medication use in retrospective cross-sectional survey of chronic pain patients. *The Journal of Pain, 17*(6), 739–744.

Bonnie, R. J., Kesselheim, A. S., & Clark, D. J. (2017). Both urgency and balance needed in addressing opioid epidemic: A report from the National Academies of Sciences, engineering, and medicine. *JAMA, 318*(5), 423–424.

Bradford, A. C., & Bradford, W. D. (2016). Medical marijuana laws reduce prescription medication use in medicare part d. *Health Affairs, 35*(7), 1230–1236.

Bradford, A. C., & Bradford, W. D. (2017). Medical marijuana laws may be associated with a decline in the number of prescriptions for medicaid enrollees. *Health Affairs, 36*(5), 945–951.

Bruce, D., Brady, J. P., Foster, E., & Shattell, M. (2017). Preferences for medical marijuana over prescription medications among persons living with chronic conditions: Alternative, complementary, and tapering uses. *The Journal of Alternative and Complementary Medicine*. https://doi.org/10.1089/acm.2017.0184.

Burns, T. L., & Ineck, J. R. (2006). Cannabinoid analgesia as a potential new therapeutic option in the treatment of chronic pain. *Annals of Pharmacotherapy, 40*(2), 251–260.

Center for Behavioral Health Statistics and Quality. (2016a). *Key substance use and mental health indicators in the United States: Results from the 2015 National Survey on Drug Use and Health* (HHS Publication No. SMA 16-4984, NSDUH Series H-51). Retrieved from http://www.samhsa.gov/data/.

Center for Behavioral Health Statistics and Quality. (2016). *2015 National survey on drug use and health public use file codebook.* Rockville, MD: Substance Abuse and Mental Health Services Administration.

Center for Behavioral Health Statistics and Quality. (2016). *2015 national survey on drug use and health: Summary of the effects of the 2015 NSDUH questionnaire redesign: Implications for data users.* Rockville, MD: Substance Abuse and Mental Health Services Administration.

Chen, C. Y., Storr, C. L., & Anthony, J. C. (2009). Early-onset drug use and risk for drug dependence problems. *Addictive Behaviors, 34*(3), 319–322.
Chen, Q., Larochelle, M. R., Weaver, D. T., Lietz, A. P., Mueller, P. P., Mercaldo, S., …, & Pandharipande, P. V. (2019). Prevention of prescription opioid misuse and projected overdose deaths in the United States. *JAMA Network Open, 2*(2), e187621.
Corroon, J. M., Mischley, L. K., & Sexton, M. (2017). Cannabis as a substitute for prescription drugs - A cross-sectional study. *Journal of Pain Research, 10*, 989–998.
Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA, 315*(15), 1624–1645.
Econometric Software, Inc. (2016). *LIMDEP, version 11.* Plainview, NY: Econometric Software Inc.
Gable, R. S. (1993). Toward a comparative overview of dependence potential and acute toxicity of psychoactive substances used nonmedically. *American Journal of Drug and Alcohol Abuse, 19*, 263–281.
Gable, R. S. (2004). Comparison of acute lethal toxicity of commonly abused psychoactive substances. *Addiction, 99*, 686–696.
Hassunah, R., & McIntosh, J. (2016). Quality of life and cannabis use: Results from Canadian sample survey data. *Health, 8*, 1576–1588. http://dx.doi.org/10.4236/health.2016.814155.
Häuser, W., Finnerup, N. B., & Moore, R. A. (2018). Systematic reviews with meta-analysis on cannabis-based medicines for chronic pain: A methodological and political minefield. *Pain, 159*(10), 1906–1907.
Hausman, J. A. (1978). Specification tests in econometrics. *Econometrica : Journal of the Econometric Society, 46*, 1251–1271.
Hill, K. P. (2015). Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: A clinical review. *JAMA, 313*(24), 2474–2483.
IBM Corp. (2017). *IBM SPSS statistics for windows, version 25.0.* Armonk, NY: IBM Corp.
Institute of Medicine. (2011). *Relieving pain in America: A blueprint for transforming prevention, care, education and research.* Washington, DC: National Academies Press.
Johannes, C. B., Le, T. K., Zhou, X., Johnston, J. A., & Dworkin, R. H. (2010). The prevalence of chronic pain in United States adults: Results of an internet-based survey. *The Journal of Pain, 11*(11), 1230–1239.
Kalant, H. (2015). Cannabis control policy: No rational basis yet for legalization. *Clinical Pharmacology & Therapeutics, 97*(6), 538–540.
Khatapoush, S., & Hallfors, D. (2004). Sending the wrong message: Did medical marijuana legalization in California change attitudes about and use of marijuana. *Journal of Drug Issues, 34*, 751–770.
Kroenke, K., & Cheville, A. (2017). Management of chronic pain in the aftermath of the opioid backlash. *JAMA, 317*(23), 2365–2366.
Lachenmeier, D. W., & Rehm, J. (2015). Comparative risk assessment of alcohol, tobacco, cannabis and other illicit drugs using the margin of exposure approach. *Scientific Reports, 5*, 8126 (7 pages).
Lau, N., Sales, P., Averill, S., Murphy, F., Sato, S., & Murphy, S. (2015). A safer alternative: Cannabis substitution as harm reduction. *Drug and Alcohol Review, 34*(6), 654–659.
Lucas, P. (2012). Cannabis as an adjunct to or substitute for opioids in the treatment of chronic pain. *Journal of Psychoactive Drugs, 44*, 125–133.
Lucas, P., & Walsh, Z. (2017). Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. *International Journal of Drug Policy, 42*, 30–35.
MacCallum, C. A., & Russo, E. B. (2018). Practical considerations in medical cannabis administration and dosing. *European Journal of Internal Medicine, 49*, 12–19.
Mallow, P. J., Belk, K. W., Topmiller, M., & Strassels, S. A. (2018). Geographic variation in hospital costs, payments, and length of stay for opioid-related hospital visits in the USA. *Journal of Pain Research, 11*, 3079–3088.
Manchikanti, L., Helm, S., Fellows, B., Janata, J. W., Pampati, V., Grider, J. S., & Boswell, M. V. (2012). Opioid epidemic in the United States. *Pain Physician, 15* 2150-1149.
Martell, B. A., O'Connor, P. G., Kerns, R. D., Becker, W. C., Morales, K. H., Kosten, T. R., & Fiellin, D. A. (2007). Systematic review: Opioid treatment for chronic back pain: Prevalence, efficacy, and association with addiction. *Annals of Internal Medicine, 146*(2), 116–127.
National Institute on Drug Abuse. (2015). *The latest prescription trends for controlled prescription drugs.* National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
National Institute on Drug Abuse. (2019). *Overdose death rates.* National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Nuckols, T. K., Anderson, L., Popescu, I., Diamant, A. L., Doyle, B., & Di Capua, P. (2014). Opioid prescribing: A systematic review and critical appraisal of guidelines for chronic pain. *Annals of Internal Medicine, 160*(1), 38–47.
Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug harms in the UK: A multicriteria decision analysis. *The Lancet, 376*(9752), 1558–1565.
Pacula, R. L., Boustead, A. E., & Hunt, P. (2014). Words can be deceiving: A review of variation among legally effective medical marijuana laws in the United States. *Journal of Drug Policy Analysis, 7*(1), 1–19.
Piper, B. J., DeKeuster, R. M., Beals, M. L., Cobb, C. M., Burchman, C. A., Perkinson, L., et al. (2017). Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep. *Journal of Psychopharmacology, 31*(5), 569–575.
Powell, D., Pacula, R. L., & Jacobson, M. (2018). Do medical marijuana laws reduce addictions and deaths related to pain killers? *Journal of Health Economics, 58*, 29–42.
Rehm, J., & Fischer, B. (2015). Cannabis legalization with strict regulation, the overall superior policy option for public health. *Clinical Pharmacology & Therapeutics, 97*(6), 541–544.
Reiman, A., Welty, M., & Solomon, P. (2017). Cannabis as a substitute for opioid-based pain medication: Patient self-report. *Cannabis and Cannabinoid Research, 2*(1), 160–166.
Reuben, D. B., Alvanzo, A. A., Ashikaga, T., Bogat, G. A., Callahan, C. M., Ruffing, V., & Steffens, D. C. (2015). National institutes of health pathways to prevention workshop: The role of opioids in the treatment of chronic pain. *Annals of Internal Medicine, 162*(4), 295–300.
Schuermeyera, J., Salomonsen-Sautela, S., Price, R. K., Balanb, S., Thurstone, C., Mind, S., et al. (2014). Temporal trends in marijuana attitudes, availability and use in Colorado compared to non-medical marijuana states: 2003–2011. *Drug and Alcohol Dependence, 140*, 145–155.
Socias, M. E., Wood, E., Lake, S., Nolan, S., Fairbairn, N., Hayashi, K., et al. (2018). High-intensity cannabis use is associated with retention in opioid agonist treatment: A longitudinal analysis. *Addiction, 113*, 2250–2258.
Substance Abuse and Mental Health Services Administration. (2014). *Results from 2013 national survey on drug use and health.* Rockville, MD: Substance Abuse and Mental Health Services Administration.
Timko, C., & Cucciare, M. A. (2018). Commentary on Socias et al.(2018): Clinical research perspectives on cannabis use in opioid agonist treatment. *Addiction, 113*(12), 2259–2260.
van Amsterdam, J., Opperhuizen, A., Koeter, M., & van den Brink, W. (2010). Ranking the harm of alcohol, tobacco and illicit drugs for the individual and the population. *European Addiction Research, 16*(4), 202–207.
Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. (2014). Adverse health effects of marijuana use. *New England Journal of Medicine, 370*(23), 2219–2227.
Volkow, N. D., & McLellan, A. T. (2016). Opioid abuse in chronic pain—Misconceptions and mitigation strategies. *New England Journal of Medicine, 374*(13), 1253–1263.
Walker, J. M., & Huang, S. M. (2002). Cannabinoid analgesia. *Pharmacology & Therapeutics, 95*, 127–135.
Wall, M. M., Poh, E., Cerda´, M., Keyes, K. M., Galea, S., & Hasin, D. S. (2011). Adolescent marijuana use from 2002 to 2008: Higher in states with medical marijuana laws, cause still unclear. *Annals of Epidemiology, 21*, 714–716.
Wen, H., & Hockenberry, J. M. (2018). Association of medical and adult-use marijuana laws with opioid prescribing for Medicaid enrollees. *JAMA Internal Medicine, 178*(5), 673–679.
Wen, H., Hockenberry, J. M., & Cummings, J. R. (2015). The effect of medical marijuana laws on adolescent and adult use of marijuana, alcohol, and other substances. *Journal of Health Economics, 42*, 64–80.