Preventive Medicine 125 (2019) 62–68

Contents lists available at ScienceDirect

Preventive Medicine

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

Association between cannabis laws and opioid prescriptions among privately insured adults in the US

Mukaila A. Raji[a,b,*], N. Ogechi Abara[a], Habeeb Salameh[c], Jordan R. Westra[d], Yong-Fang Kuo[b,d]

[a] Department of Internal Medicine, Division of Geriatrics, University of Texas Medical Branch, Galveston, TX 77555-0177, United States of America
[b] Sealy Center on Aging, University of Texas Medical Branch, Galveston, TX 77555-0177, United States of America
[c] Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Texas Medical Branch, Galveston, TX, United States of America
[d] Office of Biostatistics, Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, TX 77555-1148, United States of America

ARTICLE INFO

Keywords:
Medical cannabis
Marijuana
Opioid
Prescription
Commercial insurance
Cross-sectional
Cannabis

ABSTRACT

We examine the association between opioid prescription patterns in privately insured adults and changes in state cannabis laws among five age groups (18–25, 26–35 36–45, 46–55 and 56–64 years). Using the 2016 Clinformatics Data Mart, a nationwide commercial health insurance database, we performed a cross-sectional analysis of two types of opioid prescribing (> 30-day and > 90-day prescriptions) among all adults aged 18–64 based on the stringency of cannabis laws. We found a significant interaction between age and cannabis law on opioid prescriptions. Age-stratified multilevel multivariable analyses showed lower opioid prescription rates in the four younger age groups only in states with medical cannabis laws, when considering both > 30 day and > 90 day opioid use [> 30 day adjusted odds ratio (aOR) = 0.56, in 18–25, aOR = 0.67 in 26–35, aOR = 0.67 in 36–45, and aOR = 0.76 in 46–54 years; > 90 day aOR = 0.56, in 18–25, aOR = 0.68 in 26–35, aOR = 0.69 in 36–45, and aOR = 0.77 in 46–54 years, P < 0.0001 for all]. This association was not significant in the oldest age group of 55–64 years. There was no significant association between opioid prescriptions and other categories of cannabis laws (recreational use and decriminalization) in any of the age groups studied.

1. Introduction

The opioid crisis is a growing public health concern, with 29, 406 synthetic opioid overdose deaths in the United States in 2017 (National Institute on Drug Abuse, n.d.). Primarily considered to be “pain killers”, prescriptions for opioids have nearly tripled over the past quarter century (Blum et al., 2017). American adults on long-term prescription opioid are at high risk of dependence, addiction and opioid-associated deaths, especially among individuals who obtain opioids from illicit sources (Seth et al., 2018). As more states enact laws legalizing recreational or/and medical use of cannabis, there is growing interest in cannabis as a potential neuroactive agent to mitigate harmful effects associated with synthetic opioid use (Hill and Saxon, 2018; Wilkinson et al., 2016).

Since pain came to the fore as the 5th vital sign nearly twenty years ago (Finn, 2018; Jones et al., 2018), the medical community has been interested in a panacea to ease long suffering. Initially, opioids were seen as a cure and their use became widespread over time, with little attention paid to possible side effects or the risk of addiction. Now, with research highlighting both definite and possible harms of this medication, the desire to de-escalate the use of opioids has given rise to a search for non-opioid analgesic alternatives.

One such alternative is cannabis. For centuries, civilizations have used its unique properties as a cure for myriad ailments. The major psychoactive component of cannabis, 9-tetrahydrocannanol (THC), when consumed has various effects on the body, one of which is antinociception (Manzanares et al., 2006). While legal access is highly regulated in many countries, studies examining medical cannabis use have noted possible public health benefits where medical cannabis use is allowed (Lucas and Walsh, 2017).

In their 2015 paper, Powell and colleagues reviewed and found a potential unintended benefit associated with the legalization of cannabis: states with legal access to dispensaries experienced a decrease in opioid-related overdose deaths (Powell et al., 2018). Findings in this study have limited reach as they are reflective of non-medical use of cannabis rather than substitution with cannabis in cases of chronic pain. In 2018, Wen and colleagues reported that implementation of medical cannabis laws was associated with lower rates of opioid

* Corresponding author at: Division of Geriatrics, Department of Internal Medicine and Sealy Center on Aging, University of Texas Medical Branch, 301 University Blvd, Galveston, TX 77555-0177, United States of America.
E-mail address: muraji@utmb.edu (M.A. Raji).

https://doi.org/10.1016/j.ypmed.2019.05.012
Received 28 November 2018; Received in revised form 23 April 2019; Accepted 20 May 2019
Available online 21 May 2019

prescription in the Medicaid-insured population (Wen and Hockenberry, 2018). Because age differences exist within the sphere of cannabis use (Lloyd and Striley, 2018; Azofeifa et al., 2016), the association of medical cannabis with decreased opioid use in prior studies (which did not report age-specific data) may not be applicable to all age groups. A longitudinal study of older aged adults (age > 65 years) by Bradford and colleagues showed that opioid prescriptions in the Medicare population decreased in states where medical cannabis laws were implemented (Bradford et al., 2018). A number of challenges still remain in studying the association of cannabis laws and opioid prescribing, especially the current classification of cannabis.

Cannabis remains classified as a Schedule I substance under the Controlled Substances Act (National Conference of State Legislatures, n.d.), a schedule for all substances with "high potential for dependency and no accepted medical use". While some states may permit medical or recreational use of cannabis, distribution of cannabis represents a federal offense. States with laws for cannabis will usually differentiate recreational from medical use. Broadly, state cannabis use laws may allow for possession, medical use, and or recreational use. Other nuances concerning legal cannabis use exist within state-based legislation (National Conference of State Legislatures, n.d.; Wiese and Wilson-Poe, 2018). Within each category, there are varying degrees of liberalization. Regardless of the current classification of cannabis, states with medical cannabis laws had a 25% reduction in overall opioid overdose associated mortality in addition to a lower rate of opioid positive testing in fatally injured drivers aged 21–40 years (Kim et al., 2016).

This may suggest a public health benefit associated with medical cannabis laws but the association must be carefully examined across the different subpopulations to prevent unintended downsides of the any new cannabis legislation. For example, a number of studies have analyzed data from Medicaid and Medicare enrollees (Wen and Hockenberry, 2018; Bradford et al., 2018), prescription drug monitoring programs (Hallvik et al., 2018), with findings suggesting a relationship between cannabis laws and lower opioid use. However, to date, there is no study which exclusively explores whether the previously published cannabis law-opioid use associations are mirrored among commercially insured adults. Adults with private health insurance are typically employed, though the insurance may also cover immediate family members of the employees. Individuals who carry commercial insurance represent an important population which may exhibit different behaviors from Medicare and Medicaid subpopulations with regards to cannabis use. Interestingly, a recent report revealed that in a cohort of privately insured adults, the top 10% of opioid users represented 76% of all prescription opioid use (Sun and Jena, 2017). Examining patterns in this population may provide data with regards to cannabis use habits and opioid usage among employed populations and their adult family members covered by commercial insurance.

The purpose of this study is therefore twofold: to examine the demographic characteristics associated with prescription opioid use in the commercially insured population and investigate the relationship between cannabis law stringency and opioid prescription rates.

2. Methods

2.1. Source of data

We used data from Clinformatics Data Mart (CDM), a database of one of the nation's largest commercial health insurance providers that is mainly used for research (Optum Inc., n.d.). The CDM database contains approximately 13% Medicare enrollees and 87% commercial enrollees. Of all enrollees, 47% are primary subscribers while the rest are family members or dependents of the subscriber. The majority of enrollees have managed care plans including point of service (43.7%), health maintenance organization (31.4%), preferred provider organization (13%), and exclusive provider organization (8.9%). Compared with US population, CMD includes a higher proportion of enrollees from the South and a low proportion of enrollees in the Northeast. The database contains information regarding insurance eligibility, medical and pharmacy claims, and some demographic information including state of residence.

2.2. Study population

We created a retrospective cross-sectional cohort consisting of enrollees who were aged between 18 and 64 years old in 2016 and continuously enrolled in a commercial insurance plan in 2015–2016. We used 2015 as a look-back period to assess comorbidity. The University of Texas Medical Branch Institutional Review Board approved the study and waived any informed consent requirement as the research used de-identified data.

2.3. Study variables

The exposure of interest was the level of legalization of cannabis laws. Cannabis laws were assessed on January 1, 2016 and were separated into four categories: cannabis use illegal (level 1), cannabis use decriminalized (level 2), cannabis allowed for medical purposes, including states where cannabis is both decriminalized and allowed for medical purposes (level 3), and cannabis allowed for recreational purposes (level 4) (Marijuana Policy Project, n.d.).

It should be noted that decriminalization indicates that the possession of small, personal-consumption amounts is civil or local infraction, but not a state crime; this represents the lowest misdemeanor without possibility of jail time. Other covariates included in the analyses were: gender, age grouped by 10 (18–25, 26–35, 36–45, 46–55, 56–64), previous cancer diagnosis, and Elixhauser comorbidity score (Elixhauser et al., 1998) excluding cancer diagnoses at the patient level. At the state level, we included opioid-related regulations – physician exam, referral to specialist, and pain clinic regulations in 2016 (Center for Disease Control and Prevention, n.d.). Other state level characteristics which have been shown to have an effect on opioid use in published studies included level of education, median household income single income household, disability and insurance coverage from the 2011 to 2015 ACS 5-year estimates, and physician supply from the 2016–2017 Area Health Resource Files (Keyes et al., 2014; Goodwin et al., 2018; Zhou et al., 2018; *Area Health Resources Files (AHRF) 2016–2017,* n.d.).

2.4. Study outcomes

National Drug Code, product name, therapeutic class description, and US Drug Enforcement Administration class code from the Red Book Select database were used to identify opioid prescriptions. We counted total number of days for which each individual enrollee had an opioid prescription in 2016. We then determined whether they had > 30 days of opioid prescription during the year, and whether they had ≥90 days of opioid prescription during the year.

2.5. Statistical analysis

The proportion of enrollees with prescribed opioids categorized by each of two prescription durations, stratified by the four levels of cannabis law was calculated. We assessed the association between state cannabis laws and opioid prescription by unadjusted logistic regression, and then by multilevel analyses from a generalized linear mixed model (HGLM) with a binominal distribution and logit link for enrollees nested within states. The adjusted odds ratio from the HGLM adjusted for patient characteristics of age, sex, cancer diagnosis, comorbidity, and state opioid laws is described above. To achieve model parsimony, we removed state characteristics including education, income, single household, disability, insurance, and physician supply in the final

Table 1
Patient characteristics in 2016 stratified by cannabis law stringency.

	Cannabis not legal for any use N = 1,912,375		Cannabis decriminalized N = 377,273		Cannabis for medical purposes N = 1,770,081		Cannabis fully legal N = 265,359		Total n = 4,325,088	
	N	%	N	%	N	%	N	%	N	%
Sex										
Female	943,764	49.35	189,967	50.35	884,899	49.99	131,540	49.57	2,150,170	49.71
Male	968,611	50.65	187,306	49.65	885,182	50.01	133,819	50.43	2,174,918	50.29
Age group										
≤25	273,314	14.29	50,459	13.37	253,412	14.32	34,035	12.83	611,220	14.13
26–35	340,246	17.79	63,916	16.94	318,979	18.02	48,962	18.45	772,103	17.85
36–45	426,801	22.32	81,476	21.60	392,433	22.17	60,491	22.80	961,198	22.22
46–55	491,726	25.71	98,498	26.11	455,766	25.75	66,239	24.96	1,112,229	25.72
56–64	380,288	19.74	82,927	21.98	349,491	19.74	55,632	20.96	868,388	20.08
US census region										
Midwest	366,829	19.18	206,721	54.79	615,331	34.76	0	0.00	1,188,881	27.49
Northeast	0	0.00	0	0.00	428,493	24.21	0	0.00	428,493	9.91
South	1,481,688	77.48	170,552	45.21	124,112	7.01	4074	1.54	1,780,426	41.17
West	63,858	3.34	0	0.00	602,145	34.02	261,285	98.46	927,288	21.44
Cancer diagnosis 2015	42,974	2.25	9051	2.40	40,346	2.28	5834	2.20	98,205	2.27
Elixhauser comorbidity[a]										
0	1,082,335	56.60	207,446	54.99	1,069,172	60.40	160,071	60.32	2,519,024	58.24
1	391,874	20.49	79,978	21.20	352,324	19.90	54,465	20.53	878,641	20.31
2	205,387	10.74	42,118	11.16	172,460	9.74	25,142	9.47	445,107	10.29
3+	232,779	12.17	47,731	12.65	176,125	9.95	25,681	9.68	482,316	11.15

[a] Excludes cancer diagnoses.

HGLM model. We further tested the interaction between state cannabis law and age group in HGLM model and conducted a stratified model by age group. All analyses were preformed using SAS version 9.4 (SAS Inc., Cary, NC).

3. Results

Our study population consisted of > 4.3 million individuals and grouped individual opioid prescriptions based on state cannabis legislation. Most enrollees resided in states where cannabis was not legal for any use (n = 1,912,375) (Table 1). There were 1, 770, 081 enrollees from states where medical cannabis is allowed, 377,273 enrollees from states where cannabis is decriminalized, and 265, 359 from states where cannabis was fully legal.

States where medical cannabis is allowed were from all US Census Regions (Midwest, Northeast, South and West). In this category, most were from the Midwest, followed by the West region, then the Northeast and finally the South. All subjects from the Northeast region were from states that allowed cannabis for medical purposes in the year of interest. Overall, most enrollees had an Elixhauser comorbidity score of 0. Among states where cannabis is legal (for medical purposes or recreational use), < 10% of enrollees held the highest comorbidity score of > 3, as compared to 12.17% in states where cannabis use is not permitted and 12.65% where cannabis is decriminalized.

In 2016, there were 5 states which fully legalized cannabis, 21 states which allowed medical use of cannabis, and 21 states which did not allow any use of cannabis (Table 2). There were 4 states where cannabis was decriminalized. Among these four groups, the proportion of states that had pain clinic and pain treatment facilities was greatest in the group where cannabis is not allowed. In general, the states whose legislation did not allow any use of cannabis also appeared to have more restrictive laws regulating opioid prescriptions.

Comparing all four levels of cannabis law stringency, the greatest proportion (90.7%, standard deviation (SD) = 1.38) of high school graduates were found in those states where cannabis is fully legal (compared to 88.75% overall, SD = 2.92). Mean household income ranged from $48,414.25 (SD = $6004.41) in the states where medical cannabis is allowed to $63, 359.20 (SD = 6893.56) among states where cannabis is fully legal. Our review found that the greatest physician supply (as measured in physicians per 100,000 population) was in states where cannabis was decriminalized (352.88 per 100,000, SD = 157.76). The proportion of the population in states across all levels of cannabis law stringency was unchanged as was the proportion of single adult households and the proportion those who possessed health insurance.

Overall, the unadjusted odds ratios for opioid use show higher opioid prescription rates in level 2 states (cannabis use decriminalized), for both for > 30 days opioid prescription with uOR 1.12, 95% CI (1.1–1.14), and chronic opioid prescription > 90 days (uOR 1.1 (1.1–1.13). The lowest prescription rates of > 30 days and > 90 day opioid prescriptions were seen in level 3 states (medical use and includes states with decriminalization and those without) with rates of 3.8 for > 30 days opioid prescription and 2.6 for > 90 day opioid prescription, and uOR of 0.66, 95% CI (0.65–0.66) and 0.65, 95% CI (0.64–0.65) respectively. After adjusting for patient and state-level characteristics and opioid related regulations in the multivariate and multilevel models, there were statistically significant interactions between age groups and cannabis law for both outcomes ($p < 0.0001$) (Table 3).

Age-stratified adjusted analysis showed lower rate of > 30 day opioid prescription in the four younger age groups (18–25, 26–35, and 36–45, 46–55 years groups) in states which allowed for medical cannabis use [aOR of 0.56, 95% CI (0.43–0.74) in 18–25 years; 0.67, 95% CI (0.5–0.88) in 26–35 years; 0.68, 95% CI (0.54–0.85) in 36–45 years; and 0.76, 95% CI (0.61–0.95) in 46–55 years ($p < 0.0001$)]. This pattern was similarly observed for > 90-day opioid use in those age groups. In the oldest age group aged 56–64 years, while there was a lower rate of both > 30 days and > 90 days opioid prescription in states with medical cannabis allowance, this was not statistically significant [> 30 day opioid use aOR 0.86 (0.66–1.12) and > 90 day opioid use aOR 0.88 (0.66–1.17)]. Similar results were not found for any age group with other legislation for cannabis use (decriminalized, illegal or fully legal). Overall, age-stratified adjusted analysis showed lowest rate of opioid prescription in states that allowed for medical cannabis use.

4. Discussion

Analysis of data among privately insured adults aged 18–64 years found that the overall prescription opioid use increased with age. This

Table 2
State characteristics (including state law regulating opioid prescription) stratified by stringency of cannabis laws.

	Cannabis not legal for any use (n = 21)		Cannabis decriminalized (n = 4)		Cannabis for medical purposes (n = 21)		Cannabis fully legal (n = 5)		Total (n = 51)	
	N	%	N	%	N	%	N	%	N	%
Practitioner education (N, %)	11	52.38	3	75	10	47.62	1	20	25	49.02
Physical examination and substance use disorder (N, %)	16	76.19	1	25	13	61.9	3	60	33	64.71
Referral or consultation with a specialist (N, %)	17	80.95	2	50	15	71.43	4	80	38	74.51
Prescription drug monitoring program (N, %)	15	71.43	2	50	16	76.19	3	60	36	70.59
Written consent/treatment plan (N, %)	18	85.71	2	50	16	76.19	4	80	40	78.43
Schedule II limitations (N, %)	21	100	4	100	21	100	4	80	50	98.04
Schedule III limitations (N, %)	8	38.1	2	50	13	61.9	3	60	26	50.98
Pain clinic and pain treatment facilities (N, %)	8	38.1	1	25	1	4.76	0	0	10	19.61

	Cannabis not legal for any use (n = 21)		Cannabis decriminalized (n = 4)		Cannabis for medical purposes (n = 21)		Cannabis fully legal (n = 5)		Total (n = 51)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Percent high school graduates (mean, SD)	88.08	2.98	89.19	2.93	87.5	3.22	90.7	1.38	88.75	2.92
Median household income (mean, SD)	$ 51,674.95	$ 6771.79	$ 61,005.62	$ 9753.70	$ 48,414.25	$6004.41	$ 63,359.20	$6893.56	$ 56,406.76	$ 9518.00
Physician supply per 100,000 population (mean, SD)	233.97	35.94	352.88	157.76	245.96	37.97	293.37	15.71	289.7	117.11
Percent single households (mean, SD)	16.36	2.62	16.85	2.4	17.65	4.19	15.84	1.92	16.61	2.57
Percent with disability (mean, SD)	13.76	2.45	12.6	1.75	13.95	2.08	12.44	1.81	13.17	2.13
Percent with health insurance (mean, SD)	89.89	3.02	92.95	2.69	89.53	1.92	91.5	3.67	91.28	3.17

was not unexpected, given the concomitant increase in the number of comorbidities and physician visits with increasing age. When results were examined within each individual age cohort, opioid prescription rate varied depending on the stringency of state cannabis laws. In particular, in states which implemented medical cannabis use laws (but not other categories of cannabis liberalization laws), lower rates of opioid prescription were seen in the younger age cohorts (18–25, 26–35, 36–45 and 46–54 years). It is possible that this finding from our cross-sectional study (which adjusted for opioid law at state level) is a reflection of not just the cannabis use law but also a reflection of the increasing number of the new legislation, federal laws and insurance policies which restrict opioid prescribing and expand oversight of prescription opioids. Given the growing concern regarding opioid use, several states have implemented programs which serve to closely monitor opioid prescriptions (Davis and Pierce, 2014; Kuehn, 2014). By mid-2012, many states had implemented prescription drug monitoring programs (PDMP) (Kuo et al., 2016). PDMPs are state-based electronic repositories which allow physicians to track controlled substance prescriptions (Centers for Disease Control and Prevention, n.d.). A 2016 study (Bao et al., 2016) found a 30% decrease in opioid prescriptions associated with PDMP implementation in a cohort of ambulatory clinics in 24 states from 2001 to 2010. Finally, a significant change in opioid prescription habits and patterns was likely affected by the 2014 Drug Enforcement Agency (Centers for Disease Control and Prevention, n.d.). This change up-schedules hydrocodone-containing products (the most prescribed opioids in the USA) thus imposing quantity limits, restricting refills and generally make it more onerous to prescribe opioids (United States Department of Justice, Drug Enforcement Administration, Diversion Control Division, 2014; United States Drug Department of Justice, Drug Enforcement Administration, n.d.).

While age-stratified analysis did show a lower rate of opioid prescription associated with states allowing for medical use of cannabis in the four younger age cohorts examined (18–25, 26–35, 36–45 and 46–55 years), this finding was not observed in the privately insured cohorts aged 56–64 years. This is in contrast to a 2018 cross-sectional study reviewing Medicaid enrollees, which found a 5.88% and 6.38% decline in opioid prescriptions overall, in states after implementation of medical and recreational cannabis use laws, respectively (Wen and Hockenberry, 2018). The Medicaid study, unlike our own, did not include patient-level data; rather, it looked at aggregate data, by year quarter and by state. Our own study did find a positive association between opioid prescriptions and implementation of medical cannabis laws, but not with states permitting use of recreational cannabis. This finding may be due to significant differences between commercially-insured population and the Medicaid population.

Our findings also differ from Bradford and colleagues' study (Bradford et al., 2018) which revealed, in a sample of Medicare enrollees, a 14.4% decrease in opioid use associated with increased number of medical cannabis dispensaries in place. Their study, a longitudinal analysis of daily doses of all opioids as a group, is different from our current age-stratified analysis of commercial insurance data.

Furthermore, the Bradford study looked at relationship between opioid prescription and medical cannabis laws alone and did not contain patient-level analysis (Bradford et al., 2018). While in our study the unadjusted odds ratio did reveal a significant reduction of opioid prescription in states with medical cannabis use laws, this effect became non-significant in the adjusted model within the oldest age cohort aged 55–64 years, which is closest in age to most Medicare enrollees. It should be noted that data in the previous study (Bradford et al., 2018) was prescriber-based without adjustment for patient-level data.

These findings suggest a difference between the privately insured versus Medicaid or Medicare insured populations, especially those who are older adults. Research has shown that Medicaid and Medicare beneficiaries generally have greater disability than those with commercial insurance, perhaps because a proportion of beneficiaries qualify for Medicare coverage based on a disability (Musumeci, n.d.). For this

Table 3
Opioid use stratified by level of cannabis law stringency.

	> 30 days opioid use	OR	aOR[a]	≥ 90 days opioid use	OR	aOR[a]
Overall						
Cannabis not legal for any use	5.6	REF	REF	4.0	REF	
Cannabis decriminalized	6.3	1.12 (1.1–1.14)	1.34 (0.9–1.97)	4.4	1.11 (1.1–1.13)	1.32 (0.85–2.04)
Cannabis for medical purposes	3.8	0.66 (0.65–0.66)	0.77 (0.61–0.97)	2.6	0.65 (0.64–0.65)	0.8 (0.62–1.04)
Cannabis fully legal	5.1	0.9 (0.89–0.92)	0.96 (0.67–1.38)	3.8	0.95 (0.93–0.97)	1.07 (0.71–1.61)
18–25						
Cannabis not legal for any use	0.6	REF	REF	0.3	REF	REF
Cannabis decriminalized	0.7	1.12 (1–1.26)	1.05 (0.68–1.62)	0.3	1.17 (0.98–1.4)	1.11 (0.74–1.68)
Cannabis for medical purposes	0.4	0.7 (0.64–0.75)	0.56 (0.43–0.74)	0.2	0.69 (0.61–0.78)	0.56 (0.43–0.74)
Cannabis fully legal	0.5	0.85 (0.73–1)	0.64 (0.4–1.02)	0.3	1.06 (0.85–1.31)	0.74 (0.46–1.19)
26–35						
Cannabis not legal for any use	1.9	REF		1.2	REF	REF
Cannabis decriminalized	2.1	1.07 (1.01–1.14)	1.19 (0.75–1.9)	1.2	1.03 (0.96–1.12)	1.17 (0.71–1.94)
Cannabis for medical purposes	1.3	0.67 (0.65–0.7)	0.67 (0.5–0.88)	0.8	0.67 (0.63–0.7)	0.68 (0.5–0.93)
Cannabis fully legal	1.6	0.83 (0.77–0.89)	0.81 (0.52–1.28)	1.0	0.85 (0.77–0.93)	0.86 (0.52–1.41)
36–45						
Cannabis not legal for any use	4.1	REF	REF	2.7	REF	REF
Cannabis decriminalized	4.5	1.1 (1.06–1.14)	1.19 (0.82–1.72)	3.0	1.09 (1.04–1.14)	1.18 (0.78–1.79)
Cannabis for medical purposes	2.6	0.63 (0.62–0.65)	0.68 (0.54–0.85)	1.7	0.63 (0.62–0.65)	0.69 (0.54–0.89)
Cannabis fully legal	3.4	0.82 (0.78–0.86)	0.95 (0.66–1.36)	2.3	0.85 (0.8–0.9)	0.96 (0.64–1.44)
46–55						
Cannabis not legal for any use	7.5	REF	REF	5.4	REF	REF
Cannabis decriminalized	8.3	1.12 (1.09–1.15)	1.3 (0.9–1.88)	6.0	1.12 (1.09–1.15)	1.31 (0.86–1.99)
Cannabis for medical purposes	5.0	0.64 (0.63–0.66)	0.76 (0.61–0.95)	3.5	0.63 (0.62–0.64)	0.77 (0.6–0.99)
Cannabis fully legal	6.7	0.88 (0.85–0.91)	0.97 (0.68–1.39)	4.9	0.91 (0.88–0.95)	1.04 (0.7–1.55)
56–64						
Cannabis not legal for any use	11.8	REF	REF	8.7	REF	REF
Cannabis decriminalized	12.2	1.03 (1.01–1.06)	1.38 (0.89–2.14)	8.9	1.02 (1–1.05)	1.37 (0.84–2.23)
Cannabis for medical purposes	8.2	0.66 (0.65–0.67)	0.86 (0.66–1.12)	5.9	0.65 (0.64–0.66)	0.88 (0.66–1.17)
Cannabis fully legal	11.1	0.93 (0.9–0.95)	1.11 (0.74–1.68)	8.5	0.98 (0.95–1.01)	1.15 (0.73–1.82)

[a] Adjusted for sex, region, prior cancer diagnosis, Elixhauser comorbidity score, and state opioid laws (physical examination and substance use disorder, referral or consultation with a specialist, written consent/treatment plan, and pain clinic and pain treatment facilities).

reason, perhaps more Medicaid patients may have been prescribed opioids prior to implementation of laws compared to those with private insurance (i.e. lower rates of opioid use than Medicaid patients) (U.S. Department of Health and Human Services: Office of Inspector General, 2018). The already low opioid use rate in the privately insured population (especially those aged 56–64 years) may thus be associated with a floor effect, such that we are not able to observe any significant decrease in opioid prescription rate in the older privately insured patients when compared to those with public insurance, in response to cannabis-related laws.

The lack of significant decrease in opioid prescription in those aged 56–64 years in the face of increased leniency of cannabis use laws raises the question of whether these patients are more likely to use cannabis as an adjunct therapeutic agent for pain control. Baby Boomers, who are now in their mid- 50s and 60s, represent demographic cohort who experienced illicit drug use, including cannabis, as a societal norm, resulting from societal pressures and stresses in their youth (Lloyd and Striley, 2018). While younger adults appear to use cannabis with greater frequency than older adults (aged 50 and above) (Lloyd and Striley, 2018; Azofeifa et al., 2016), studies reveal that cannabis use among older adults may be increasing. In fact, a 2017 study noted past-year cannabis use among those 50 to 64 years old increased 10.1% annually, and increased 15.3% annually in those aged 65 and above (Salas-Wright et al., 2017). Our study does not address this directly.

The findings in our study underscore the need for investigators working on policy effects to pay attention to how concurrent prescription opioid regulating laws and regulations might affect association of any new policy change and opioid-related outcomes, especially given the rapid rise in cannabis-related laws in the USA and, more recently, in Canada. For example, Illinois, a state with restrictive laws permitting medical use of cannabis (Illinois General Assembly, n.d.), recently started a pilot program that expands medical cannabis access to any adult aged 21 years and older with a condition that might be treated with opioid medication (McCoppin, 2018). This essentially allows cannabis to be substituted for opioids.

Strengths of our study include the population focus on commercially insured enrollees, a large sample size and, unlike prior studies, an analysis of patient-level data. Our study was not designed to determine a causal relationship between opioid prescription rates and medical cannabis availability, so we cannot conclude that the findings indicate that declining opioid prescription is due to more permissive laws related to cannabis use.

There are some limitations to our findings. As our study is limited to a specified period, we cannot generalize the effect that cannabis laws may have had among other populations and at different time periods than those which we studied. In addition to this, data regarding opioid use and cannabis laws was obtained for a single year, 2016. Even during this year, state laws regarding cannabis may have been in flux—with some cities within states permitting cannabis use while state-based cannabis law changes were yet to be established. The dataset which was used contains a higher relative proportion of enrollees from the Southern states and a low proportion of enrollees from the Northeast. As a result, our findings may have been influenced by region-specific cultural behaviors or attitudes related to the use of cannabis or opioids. This could be an area of future study. Our study was restricted to measure opioids obtained by prescription; other sources of opioids may be particularly prevalent in this population. While we made an effort to identify > 90 day prescriptions, our methodology was unable to distinguish between appropriate short-term opioid use for pain management and abusive opioid prescriptions. Furthermore, given its cross-sectional nature, our study did not assess the patterns of opioid use following medical cannabis use to determine whether cannabis

substitution was actually associated with a decrease in opioid prescriptions in an individual. Lastly, prescription claims reflect what was dispensed, not whether the medication was in fact consumed.

5. Conclusion

Our study reviewed patterns of opioid and cannabis use in privately insured adults aged 18–64 years. It is well known that a number of efforts to decrease opioid prescriptions have emerged in recent years, including the 2016 CDC guidelines on opioids (Dowell et al., 2016). These changes have occurred in concurrence with many state- based and federal changes in legislation concerning cannabis use. The decline in opioid prescriptions may be occurring in specific populations independent of reduced strictness of cannabis use laws. Cannabis liberalization and decriminalization policies by themselves have positive and negative consequences in public health and legal arena (Hughes et al., 2018; National Academies of Sciences, Engineering, and Medicine, 2017; Hall and Lynskey, 2016); but if the goals of such policies include stemming opioid abuse and overdose, caution must be exercised by policy makers as current evidence of opioid users replacing opioids with cannabis is weak and prone to ecological fallacy (Finney et al., 2011; DiBenedetto et al., 2018). Furthermore, while our findings reveal an association between decreased opioid prescriptions and implementation of medical use cannabis laws, causation should not be implied. There are potential dangers related to careless substitution of cannabis for opioids. Cannabis use is associated with greater risk of developing schizophrenia and other psychoses, especially in adolescents who may normalize cannabis (National Academies of Sciences, Engineering, and Medicine, 2017). It is thought that cannabis also may represent a “reverse gateway”, leading to other addictive substance abuse (National Academies of Sciences, Engineering, and Medicine, 2017; Humphreys and Saitz, 2019).

In our analysis, opioid prescriptions did not see a statistically significant decline in states where recreational cannabis use is legal. This may be reflective of attitudes toward recreational drug use. Future studies are needed to investigate patterns of concurrent opioid and cannabis use. Clearly, this is an evolving area of public health interest. Future studies are also needed to examine the complex relationships between different categories of cannabis-related laws, degree of law enforcements, concurrent opioid-related regulations and patterns of opioid prescription rates. The findings from such studies and others will provide actionable data on the most effective state cannabis laws to guide state legislators and policy makers considering changes to current cannabis use laws.

Grant support

This work was supported by grants R01-DA039192 from the National Institute of Drug Abuse, P30-AG024832 from the National Institute on Aging, UL1-RR029876 from the National Center for Research Resources, National Institutes of Health.

Declaration of competing interest and verification statements

All authors declare no conflict of interest. All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2019.05.012.

References

Area Health Resources Files (AHRF) 2016–2017. US Department of Health and Human Services, Health Resources and Services Administration, Bureau of Health Workforce, Rockville, MD

Azofeifa, A., Mattson, M.E., Schauer, G., McAfee, T., Grant, A., Lyerla, R., 2016. National estimates of marijuana use and related indicators — National Survey on Drug Use and Health, United States, 2002–2014. MMWR Surveill. Summ. 65 (11), 1–28.

Bao, Y., Pan, Y., Taylor, A., Radakrishnan, S., Luo, F., Pincus, H.A., Schackman, B.R., 2016. Prescription drug monitoring programs are associated with sustained reductions in opioid prescribing by physicians. Health Aff. 35 (6), 1045–1051.

Blum, K., Gold, M.S., Jacobs, W., McCall, W.V., Febo, M., Baron, D., Dushaj, K., Demetrovics, Z., Badgaiyan, R.D., 2017. Neurogenetics of acute and chronic opiate/opioid abstinence: treating symptoms and the cause. Front. Biosci. 22 (1247–128).

Bradford, A.C., Bradford, W.D., Abraham, A., Adams, G.B., 2018. Association between US state medical cannabis laws and opioid prescribing in the Medicare Part D population. JAMA Intern. Med. 178 (5), 667–673.

Center for Disease Control and Prevention. State prescription drug laws. https://www.cdc.gov/drugoverdose/policy/laws.html. Updated March 23, 2016. Accessed January 8, 2018.

Centers for Disease Control and Prevention What states need to know about PDMPs. https://www.cdc.gov/drugoverdose/pdmp/states.html (Last updated October 3, 2017).

Davis, C.S., Pierce, M., Dasgupta, N., 2014. Evolution and convergence of state laws governing controlled substance prescription monitoring programs,1998–2011. Am. J. Public Health 104, 1389–1395.

DiBenedetto, D.J., Weed, V.F., Wawrzyniak, K.M., Finkelman, M., Paolini, J., Schatman, M.E., Herrera, D., Kulich, R.J., 2018. The association between cannabis use and aberrant behaviors during chronic opioid therapy for chronic pain. Pain Med. 19 (10), 1997–2008.

Dowell, D., Haegerich, T.M., Chou, R., 2016. CDC guideline for prescribing opioids for chronic pain-United States, 2016. JAMA 315 (15), 1624–1645.

Elixhauser, A., Steiner, C., Harris, D.R., Coffey, R.M., 1998. Comorbidity measures for use with administrative data. Med. Care 36, 8–27.

Finn, K., 2018. Why marijuana will not fix the opioid epidemic. J. Miss. State Med. Assoc. 155 (3), 191–193.

Finney, J.W., Humphreys, K., Kivlahan, D.R., Harris, A.H., 2011. Why health care process performance measures can have different relationships to outcomes for patients and hospitals: understanding the ecological fallacy. Am. J. Public Health 101 (9), 1635–1642.

Goodwin, J.S., Kuo, Y.-F., Brown, B., Juurlink, D., Raji, M., 2018. Association of chronic opioid use with presidential voting patterns in US counties in 2016. JAMA Netw. Open 1 (2), e180450.

Hall, W., Lynskey, M., 2016. Evaluating the public health impacts of legalizing recreational cannabis use in the United States. Addiction 111 (10), 1764–1773.

Hallvik, S.E., Geissert, P., Wakeland, W., Hildebran, C., Carson, J., O'Kane, N., Deyo, R.A., 2018. Opioid prescribing continuity and risky opioid prescriptions. Ann. Fam. Med. 16, 440–442.

Hill, K.P., Saxon, A.J., 2018. The role of cannabis legalization in the opioid crisis. JAMA Intern. Med. 78 (5), 679–680.

Hughes, B., Wiessing, L., Des Larlais, D., Griffiths, P., 2018. Could cannabis liberalisation lead to wider changes in drug policies and outcomes? Int. J. Drug Policy 51, 156–159.

Humphreys, K., Saitz, R., 2019. Should physicians recommend replacing opioids with cannabis? JAMA 321 (7), 639–640.

Illinois General Assembly Compassionate Use of Medical Cannabis Pilot Program Act, 410 ILCS 130. P.A. 98-122, eff. 1-1-14. http://www.ilga.gov/legislation/ilcs/ilcs3.asp?ActID=3503&ChapterID=35.

Jones, M.R., Viswanath, O., Peck, S.J., Kaye, A.D., Gill, J.S., Simopoulos, T.T., 2018. A brief history of the opioid epidemic and strategies of pain medicine. Pain Ther. 7, 13–21.

Keyes, K.M., Cerdá, M., Brady, J.E., Havens, J.R., Galea, S., 2014. Understanding the rural-urban differences in nonmedical prescription opioid use and abuse in the United States. Am. J. Public Health 104 (2), e52–e59.

Kim, J.H., Santaella-Tenorio, J., Mauro, C., Wrobel, J., Cerda, M., Keyes, K.M., et al., 2016. State medical marijuana laws and the prevalence of opioids detected among fatally injured drivers. Am. J. Public Health 106 (11), 2032–2037.

Kuehn, B.M., 2014. CDC: major disparities in opioid prescribing among states: some states crack down on excess prescribing. JAMA 312, 684–686.

Kuo, Y.-F., Raji, M.A., Chen, N.-W., Hasan, H., Goodwin, J.S., 2016. Trends in opioid prescriptions among part D medicare recipients from 2007 to 2012. Am. J. Med. 129 (2) (221.e21-30).

Lloyd, S.L., Striley, C.W., 2018. Marijuana use among adults 50 years or older in the 21st century. Gerontol. Geriatr. Med. 108 (4), 1–4.

Lucas, P., Walsh, Z., 2017. Medical cannabis access, use, and substitution for prescription opioids and other substances: a survey of authorized medical cannabis patients. Int. J. Drug Pol. 42, 30–35.

Manzanares, J., Julian, M.D., Carrascosa, A., 2006. Role of the cannabinoid system in pain control and therapeutic implications for the management of acute and chronic pain episodes. Curr. Neuropharmacol. 4 (3), 239–257.

Marijuana Policy Project State Policy. MPPwww.mpp.org/states/, Accessed date: 21 March 2019.

McCoppin, R., 2018. 5 things to know about the expanded medical marijuana law in Illinois. In: Chicago Tribune, August 29. http://www.chicagotribune.com/news/ct-met-medical-marijuana-illinois-five-things-20180829-story.html, Accessed date: 17 October 2018.

Musumeci, M. The Affordable Care Act's Impact on Medicaid Eligibility, Enrollment, and Benefits for People With Disabilities. Kaiser Commission on Medicaid and the Uninsured. https://www.kff.org/health-reform/issue-brief/the-affordable-care-acts-impact-on-medicaid-eligibility-enrollment-and-benefits-for-people-with-disabilities/. (Updated April 8, 2014).

National Academies of Sciences, Engineering, and Medicine, 2017. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. The National Academies Press, Washington.

National Conference of State Legislatures State medical marijuana laws. http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx (Updated October 17, 2018).

National Institute on Drug Abuse Overdose death rates. Retrieved on October 1, 2018 from. https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates.

Optum Inc. Clinformatics Data Mart. https://www.optum.com/content/dam/optum/resources/productSheets/Clinformatics_for_Data_Mart.pdf (Updated October 2017).

Powell, D., Licceardo, R., Jacobson, M., 2018. Do medical marijuana laws reduce addictions and deaths related to pain killers ? J. Health Econ. 58, 29–42.

Salas-Wright, C.P., Vaughn, M.G., Cummings-Vaughn, L.A., Holzer, K.J., Nelson, E.J., AbiNader, M., Oh, S., 2017. Trends and correlates of marijuana use among late middle-aged and older adults in the United States, 2002–2014. Drug Alcohol Depend. 171, 97–106.

Seth, P., Rudd, R.A., Noonan, R.K., Haegerich, T.M., 2018. Quantifying the epidemic of prescription opioid overdose deaths. Am. J. Public Health 108 (4), 500–502.

Sun, E., Jena, A., 2017. Distribution of prescription opioid use among privately insured adults without cancer: United States, 2001 to 2013. Ann. Intern. Med. 167 (9), 684–686.

U.S. Department of Health & Human Services: Office of Inspector General, 2018. Opioids in Ohio Medicaid: review of extreme opioid use and prescribing. https://oig.hhs.gov/oei/reports/oei-05-18-00010.pdf.

United States Department of Justice, Drug Enforcement Administration, Diversion Control Division, 2014. Final rule: rescheduling of hydrocodone combination products from schedule III to schedule II. https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm (Updated August 15, 2014).

United States Drug Department of Justice, Drug Enforcement Administration DEA to publish final rule rescheduling hydrocodone combination products. https://www.dea.gov/press-releases/2014/08/21/dea-publish-final-rule-rescheduling-hydrocodone-combination-products (Updated August 24, 2018).

Wen, H., Hockenberry, J.M., 2018. Association of medical and adult-use marijuana laws with opioid prescribing for medicaid enrollees. JAMA Intern. Med. 178 (5), 673–679.

Wiese, B., Wilson-Poe, A.R., 2018. Emerging evidence for cannabis' role in opioid use disorder. Cannabis Cannabinoid Res. 3 (1), 179–189.

Wilkinson, S.T., Yarnell, S., Radhakrishnan, R., Ball Sam D'Souza, D.C., 2016. Marijuana legalization: impact on physicians and public health. Annual Rev. Med. 67, 453–466.

Zhou, C., Yu, N.N., Losby, J.L., 2018. The association between local economic conditions and opioid prescriptions among disabled medicare beneficiaries. Med. Care 56 (1), 62–68.