Chronic pain, cannabis legalisation, and cannabis use disorder among patients in the US Veterans Health Administration system, 2005 to 2019: a repeated, cross-sectional study

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Summary

Background Cannabis use disorder is associated with considerable comorbidity and impairment in functioning, and prevalence is increasing among adults with chronic pain. We aimed to assess the effect of introduction of medical cannabis laws (MCL) and recreational cannabis laws (RCL) on the increase in cannabis use disorder among patients in the US Veterans Health Administration (VHA).

Methods Data from patients with one or more primary care, emergency, or mental health visit to the VHA in 2005–19 were analysed using 15 repeated cross-sectional VHA electronic health record datasets (ie, one dataset per year). Patients in hospice or palliative care were excluded. Patients were stratified as having chronic pain or not using an American Pain Society taxonomy of painful medical conditions. We used staggered-adoption difference-in-difference analyses to estimate the role of MCL and RCL enactment in the increases in prevalence of diagnosed cannabis use disorder and associations with presence of chronic pain, accounting for the year that state laws were enacted. We did this by fitting a linear binomial regression model stratified by pain, with time-varying cannabis law status, fixed effects for state, categorical year, time-varying state-level sociodemographic covariates, and patient covariates (age group [18–34 years, 35–64 years, and 65–75 years], sex, and race and ethnicity).

Findings Between 2005 and 2019, 3 234 382–4 579 994 patients were included per year. Among patients without pain in 2005, 5·1% were female, mean age was 58·3 (SD 12·6) years, and 75·7%, 15·6%, and 3·6% were White, Black, and Hispanic or Latino, respectively. In 2019, 9·3% were female, mean age was 56·7 (SD 15·2) years, and 68·1%, 18·2%, and 6·5% were White, Black, and Hispanic or Latino, respectively. Among patients with pain in 2005, 7·1% were female, mean age was 57·2 (SD 11·4) years, and 74·0%, 17·8%, and 3·9% were White, Black, and Hispanic or Latino, respectively. In 2019, 12·4% were female, mean age was 57·2 (SD 13·8) years, and 65·3%, 21·9%, and 7·0% were White, Black, and Hispanic or Latino, respectively. Among patients with chronic pain, enacting MCL led to a 0·135% (95% CI 0·118–0·153) absolute increase in cannabis use disorder prevalence, with 8·4% of the total increase in MCL-enacting states attributable to MCL. Enacting RCL led to a 0·188% (0·160–0·217) absolute increase in cannabis use disorder prevalence, with 11·5% of the total increase in RCL-enacting states attributable to RCL. In patients without chronic pain, enacting MCL and RCL led to smaller absolute increases in cannabis use disorder prevalence (MCL: 0·037% [0·027–0·048], 5·7% attributable to MCL; RCL: 0·042% [0·023–0·060], 6·0% attributable to RCL). Overall, associations of MCL and RCL with cannabis use disorder were greater in patients with chronic pain than in patients without chronic pain.

Interpretation Increasing cannabis use disorder prevalence among patients with chronic pain following state legalisation is a public health concern, especially among older age groups. Given cannabis commercialisation and widespread public beliefs about its efficacy, clinical monitoring of cannabis use and discussion of the risk of cannabis use disorder among patients with chronic pain is warranted.

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Introduction

Cannabis use disorder is a substance use disorder defined by the same symptoms as other such disorders,[1,2] including problematic patterns of use, tolerance, withdrawal, craving, neglect of other activities, clinically significant distress or impairment, and associated psychosocial and health-related problems.[3,4] Although many individuals can use cannabis without harm,

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Research in context

Evidence before this study

PubMed was searched by DSH for publications on US time trends in cannabis legalisation, cannabis use disorders, and pain from database inception until March 15, 2023, without language restrictions. The following search terms were used: (medical cannabis laws) AND (pain) AND (cannabis use disorder); (recreational cannabis laws) AND (pain) AND (cannabis use disorder); (cannabis laws) AND (pain) AND (cannabis use disorder). Only three studies have examined the role of state medical cannabis laws (MCL) or recreational cannabis laws (RCL) in the increasing prevalence of cannabis use disorder in US adults, finding significant MCL and RCL effects but with modest effect sizes. Effects of MCL and RCL might vary across important subgroups of the population, including individuals with chronic pain. Only one study was found that had cannabis use disorder as an outcome, and this study used cross-sectional data from a single year, which cannot be used to determine trends over time. Therefore, evidence has been lacking on whether the role of state medical and recreational cannabis legalisation in the increasing US adult prevalence of cannabis use disorder differed by chronic pain status.

Added value of this study

To our knowledge, this is the first study to show the relationship between state MCL and RCL and the nationally increasing US rates of adult cannabis use disorder differed by whether individuals experience chronic pain or not. Using electronic medical record data from patients in the Veterans Health Administration that included extensive information on medical conditions associated with chronic pain, the study showed that the associations of MCL and RCL with the increasing prevalence of cannabis use disorder were stronger among individuals with chronic pain aged 35–64 years and 65–75 years, with particularly pronounced differences in patients aged 65–75 years.

Implications of all the available evidence

MCL and RCL are likely to influence the prevalence of cannabis use disorder through commercialisation that increases availability and portrays cannabis use as normal and safe, thereby decreasing perception of cannabis risk. When developing cannabis legislation, unintended consequences should be considered, including increased risk of cannabis use disorder in large vulnerable subgroups of the population such as patients with chronic pain.

33% of those who regularly use cannabis develop cannabis use disorder;[5] among US adults aged 18 years and older, the prevalence of cannabis use disorder is 5·9%, or 15 million adults.[6]

The legal status of cannabis varies across countries and time periods. In the UK, cannabis use is illegal, with stricter legal penalties under discussion.[7] By contrast, Canada legalised cannabis nationally for medical use in 2001 and recreational use in 2018, with legislation that emphasised public health concerns.[8] In the USA, legalisation has occurred on a state-by-state basis—since 1996, 39 US states have enacted medical cannabis laws (MCL), and since 2012, 21 states have enacted recreational cannabis laws (RCL). Much of the US legislation has been industry friendly rather than public health focused.[9]

Over the past two decades, the proportion of Americans favouring cannabis legalisation has increased to 68%, perceived risk of cannabis use has decreased,[10] and rates of US adult cannabis use[11,12] and cannabis use disorder have increased.[11–14] Adjusted for nationally increasing trends, MCL and RCL have been shown to play a part in the increasing prevalence of cannabis use.[15] However, a few similarly adjusted national studies examined MCL and RCL effects on trends in the prevalence of cannabis use disorder,[16,17] two using the same survey data from the US general population[16,17] and one using data from Veterans Health Administration (VHA) records.[18] These studies indicate that MCL and RCL had a role in the increasing prevalence of cannabis use disorder,[16,18,19] but that their effects were modest. The modest-sized effects could occur if MCL and RCL effects differ across subgroups, obscuring important differences when groups are combined. Specifically, studies have not investigated whether state MCL or RCL effects differ between individuals with and without chronic pain.

Chronic pain (ie, pain lasting ≥3 months[20]) is an increasing health problem in the USA.[21,22] Veterans have high rates of chronic pain.[22] Pain and cannabis use disorder are associated.[23] The prevalence of cannabis use disorder diagnoses has increased disproportionately among patients with chronic pain in the VHA system, particularly for older patients,[24] possibly due to an increasing use of cannabis to manage pain,[25] expanding the pool of individuals using cannabis who are vulnerable to cannabis use disorder. Most US adults, particularly in MCL and RCL states, believe that cannabis is effective for treating pain[26] despite inconclusive evidence,[27] and pain is the most common qualifying condition for medical cannabis.[28] Given that cannabis legalisation plays a part in increased cannabis use disorder prevalence, rates of chronic pain are high in patients in the VHA, pain is associated with cannabis use disorder, and beliefs that cannabis is useful for pain are more prevalent in MCL and RCL states, we hypothesised that MCL or RCL would play a greater part in the national increases in rates of cannabis use disorder in patients in the VHA with chronic pain than in patients without chronic pain. If so, the information would be important to convey to health-care policy makers tasked with formulating laws and regulations regarding cannabis use, and to clinicians treating patients with chronic pain in different jurisdictions.

Methods

Study design

The VHA is the largest integrated US health-care system. We leveraged VHA electronic health record data from 2005 to 2019 to investigate whether the role of MCL and RCL enactment in the increases in rates of cannabis use disorder diagnoses differed between patients with and without chronic pain. Because MCL and RCL have stronger effects in older adults[15,16,18] and disproportionate increases in cannabis use disorder are greatest in older patients with pain,[24] we also examined results by age group. Additionally, because the impact of MCL or RCL enactment could take time to emerge, we explored a 1-year time lag after enactment. Because enactment does not necessarily change cannabis availability, we also explored the dates that dispensaries were legally permitted.

This study examined changes in cannabis use disorder prevalence in sequential yearly VHA electronic health record data in the USA from 2005 to 2019. For this purpose, VHA data were configured to form repeated cross-sectional datasets. Data were obtained through the VHA corporate data warehouse, a data repository for care provided at VHA facilities or paid by the VHA. Veterans aged 18–75 years with one or more VHA primary care, emergency department, or mental health visit for any reason in a given calendar year were included, except those in hospice or palliative care or outside the 50 states plus Washington, DC. The institutional review boards at New York State Psychiatric Institute, VA Puget Sound, and VA New York Harbor Healthcare Systems approved the research. This included waivers or exemptions for the need to obtain informed consent for analyses of the electronic medical records, while implementing extensive procedures to protect the confidentiality of the patients.

Outcomes and exposures

The primary outcome was a clinician-assigned cannabis use disorder diagnosis at one or more outpatient or inpatient encounter within a calendar year, ICD-9-CM (2005–15: 305.2X, abuse; 304.3X, dependence), and ICD-10-CM (2016–19: F12.1X, abuse; F12.2X, dependence), excluding cannabis use disorder in remission and unspecified cannabis use codes.

As previously described,[24] patients were classified with chronic pain using an American Pain Society taxonomy and ICD-9-CM–ICD-10-CM crosswalk[29] to identify 11 clusters of chronic pain conditions:[30] back; neck; limb, extremity, or joint pain, and non-systemic non-inflammatory arthritic disorders; fibromyalgia; headache or migraine; orofacial, ear, or temporomandibular disorders; abdominal or bowel disorders; urogenital, pelvic, or menstrual disorders; neuropathy; systemic disorders; and other painful conditions. The ICD codes are available elsewhere.[31] We excluded cancer-related and acute pain (eg, fractures).[24] We required diagnoses for specific conditions from two or more outpatient visits or one or more inpatient hospitalisations within each study year. A binary variable was created indicating any chronic pain condition each year from 2005 to 2019.

Primary exposures were state cannabis laws, with state-year variables indicating state MCL or both MCL and RCL enactment. Patient state-of-residence was indicated by last health-care encounter for each year. States were categorised each year as no-cannabis law (No-CL), MCL-only, or MCL and RCL. For sensitivity analysis involving state legal dispensaries, which can occur subsequent to MCL or RCL enactment, we used RAND-USC OPTIC marijuana policy data[32] to create state-year variables indicating the years that legally protected dispensaries were operational.

Age-group definitions followed previous studies and were categorised as 18–34 years, 35–64 years, and 65–75 years.[13,18,24] Patients aged 76 years or older were excluded because of their very low cannabis use disorder prevalence.[18] Control covariates included variables previously shown to be related to chronic pain[33] and to cannabis use disorder,[4] and were age, sex, and race and ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other or multiple, and unknown). Time-varying yearly state control covariates included those previously shown to be related to state rates of various health conditions; state and year rates from American Community Survey data; percentage male; non-Hispanic White; non-Hispanic Black; Hispanic; aged 18 years or older; unemployed; below the poverty threshold; and yearly median household income. 1-year estimates were used for 2005–08 and 5-year estimates were used for 2009–19, using R tidycensus.

Statistical analysis

We conducted the analyses in two stages. We began by describing overall time trends in yearly cannabis use disorder prevalence by pain status among patients living in states that had enacted MCL-only, MCL and RCL, or neither by the end of the study period, 2019. The purpose was to provide a general summary of the magnitude of differences and trend patterns across these three groups of states regardless of when laws were enacted during the period, while adjusting for background differences in demographics. To do this, we grouped diagnosed cannabis use disorder prevalence across 2005–19 by chronic pain and by state cannabis law (CL) status at the end of the study period (2019) into No-CL; MCL-only; and MCL and RCL. Adjusted yearly prevalence estimates were obtained from a linear binomial regression model interacting state law status in 2019 by year, controlling for age, sex, race, ethnicity, and time-varying state covariates. Additional models were run stratified by both chronic pain and age group.

The second stage of analysis took into account the specific timing of the year that MCL or RCL laws were enacted, testing whether cannabis use disorder

	2005 (N=3 234 382)		2019 (N=4 579 994)	
	Patients without pain (n=1 952 361)	Patients with pain (n=1 282 021)	Patients without pain (n=2 086 807)	Patients with pain (n=2 493 187)
Age (continuous)	58·33 (12·59)	57·23 (11·39)	56·67 (15·17)	57·19 (13·78)
Age (categorical)				
<35 years	122 708 (6·3%)	60 101 (4·7%)	261 075 (12·5%)	221 418 (8·9%)
35–64 years	1 125 137 (57·6%)	868 355 (67·7%)	939 778 (45·0%)	1 295 657 (52·0%)
65–75 years	704 516 (36·1%)	353 565 (27·6%)	885 954 (42·5%)	976 112 (39·2%)
Sex				
Female	100 228 (5·1%)	90 918 (7·1%)	194 585 (9·3%)	309 659 (12·4%)
Male	1 852 133 (94·9%)	1 191 103 (92·9%)	1 892 222 (90·7%)	2 183 528 (87·6%)
Race or ethnicity				
White	1 477 147 (75·7%)	948 825 (74·0%)	1 420 467 (68·1%)	1 629 004 (65·3%)
Black	305 221 (15·6%)	228 588 (17·8%)	379 810 (18·2%)	546 973 (21·9%)
Hispanic or Latino	70 609 (3·6%)	49 960 (3·9%)	136 680 (6·5%)	174 481 (7·0%)
Asian	11 542 (0·6%)	5 682 (0·4%)	26 669 (1·3%)	28 587 (1·1%)
American Indian or Alaska Native	10 190 (0·5%)	8 062 (0·6%)	14 597 (0·7%)	19 932 (0·8%)
Pacific Islander or Native Hawaiian	13 323 (0·7%)	9 550 (0·7%)	14 052 (0·7%)	19 180 (0·8%)
Multiple race or ethnicity	12 175 (0·6%)	10 569 (0·8%)	17 595 (0·8%)	23 717 (1·0%)
Unknown	52 154 (2·7%)	20 785 (1·6%)	76 937 (3·7%)	51 313 (2·1%)

Data are n (%) or mean (SD).

Table 1: **Patient demographics in patients with and without chronic pain, 2005 and 2019**

	Patients with chronic pain			Patients without chronic pain		
	CUD prevalence*		Absolute change	CUD prevalence*		Absolute change
	2005	2019		2005	2019	
Full sample, age ≥18 years	1 282 021	2 493 187	..	1 952 361	2 086 807	..
No-CL (17 states)	1·76%	2·92%	1·17%	1·01%	1·53%	0·52%
MCL-only (22 states)	1·76%	3·37%	1·61%†	1·01%	1·66%	0·65%†
MCL and RCL (11 states and DC)	1·77%	3·41%	1·64%‡	1·03%	1·73%	0·70%‡
Age 18–34 years	60 101	221 418	..	122 708	261 075	..
No-CL (17 states by 2019)	1·96%	5·61%	3·64%	1·24%	3·53%	2·29%
MCL-only (23 states by 2019)§	2·21%	6·10%	3·89%†	1·56%	3·65%	2·09%†
MCL and RCL (ten states and DC by 2019)§	2·53%	6·65%	4·12%‡	1·59%	4·02%	2·43%‡
Age 35–64 years	868 355	1 295 657	..	1 125 137	939 778	..
No-CL (17 states by 2019)	1·57%	3·49%	1·92%	1·00%	1·89%	0·89%
MCL-only (23 states by 2019)§	1·69%	4·26%	2·57%†	1·22%	2·16%	0·94%†
MCL and RCL (ten states and DC by 2019)§	1·91%	4·36%	2·45%‡	1·37%	2·24%	0·87%‡
Age 65–75 years	353 565	976 112	..	704 516	885 954	..
No-CL (17 states by 2019)	0·48%	1·34%	0·86%	0·18%	0·56%	0·38%
MCL-only (23 states by 2019)§	0·52%	1·62%	1·10%†	0·21%	0·64%	0·42%†
MCL and RCL (ten states and DC by 2019)§	0·48%	1·63%	1·16%‡	0·21%	0·68%	0·47%‡

CL=cannabis law. CUD=cannabis use disorder. DC=District of Columbia. MCL=medical cannabis law. RCL=recreational cannabis law. *Adjusted for categorical age, sex, race or ethnicity, all age, race or ethnicity, and sex interactions, state-level median income and percentages (male, Hispanic, non-Hispanic White, non-Hispanic Black, poverty, aged 18 years or older, unemployed). †Value used as denominator to determine percentage of overall increase attributable to MCL enactment based on difference-in-difference estimates of MCL effect (see table 3). ‡Value used as denominator to determine percentage of overall increase attributable to RCL enactment based on difference-in-difference estimates of RCL effect (see table 3). §During the period from 2005 to 2019, 22 states and DC made a change from no-CL to MCL-only; 11 states and DC made a change from MCL-only to MCL and RCL. Note, three of these states and DC made both changes between 2005 and 2019 (ie, from no-CL to MCL-only and then later to MCL and RCL). There were 20 states that by 2019 had made no law changes (three with MCL-only and 17 with no-CL).

Table 2: **Adjusted CUD prevalence in 2005 and 2019, by pain and enacted state law status as of 2019**

prevalence differences pre-MCL and RCL enactment and post-MCL and RCL enactment were greater than those expected given contemporaneous trends in states that did not enact the respective laws by that time. To do this, we used the staggered-adoption difference-in-difference (DiD) model. This model uses each state that enacts a law as its own control by comparing aggregated cannabis use disorder prevalence before and after MCL and RCL enactment while controlling for expected trends using data from all other states that did not enact the respective law in contemporaneous years. A time-varying indicator was constructed for each state-year indicating No-CL, MCL-only, or MCL and RCL for that year. DiD estimates and 95% CIs for results on MCL-only and MCL and RCL were obtained from a linear binomial regression model stratified by chronic pain, with fixed effects for state, categorical year, and time-varying state law status, controlling for age, sex, race, ethnicity, and time-varying state-level covariates. Since DiD estimation is typically performed as a difference in risk differences, we used the linear binomial model because it provides the absolute risk differences rather than relative measures of association.[34] Note that state was included as a fixed effect to account for all time-invariant differences between states. It was not possible to additionally control for state as a random effect; patients were clustered by design within state and year. Resulting DiD estimates include states moving from No-CL to MCL-only and from MCL-only to MCL and RCL among patients with and without pain. Differences in DiD results between patients with and without pain were determined by the CIs around the DiD estimates for both groups; non-overlapping CIs indicated that the DiD results for the two groups differed significantly. Additional DiD models were run stratified by both chronic pain and age group (18–34 years, 35–64 years, and 65–75 years), adjusting for within-group continuous age.

As noted previously, the ICD-9-CM to ICD-10-CM transition resulted in a slight downward shift in cannabis use disorder prevalence in 2015 across the VHA and all states.[13,18] DiD estimates took this into account by utilising states that had not yet passed MCL or RCL (which experienced the ICD transition at the same time) as contemporaneous controls.

Following previous procedures,[18] we illustrate the magnitude of the DiD estimates relative to the overall increases in cannabis use disorder prevalence (ie, the amount of change attributable to the laws) by dividing the DiD estimates by the absolute changes between 2005 and 2019 in the states with the respective laws by 2019. To explore whether law effects differed by earlier or later enactment, we produced state-specific DiD estimates using interaction terms between state and time-varying no-CL, MCL-only, and RCL status.

In sensitivity analyses, we explored two additional issues. First, we examined the potential influence on availability (ie, cannabis dispensaries), by replacing state and year no-CL, MCL-only, and RCL variables with the year dispensaries were first operational.[32] Second, because the impact of MCL-only or MCL and RCL could take time to emerge, we examined a time lag, replacing MCL-only or RCL state and year variables with 1-year post-enactment dates. The duration of this lag was chosen to maximise the number of RCL states that could be included, since many RCLs were enacted only in recent years.

Role of the funding source

The study sponsors had no role in the study design, analysis, interpretation of data, writing the paper, or the decision to submit for publication.

Results

In 15 repeated cross-sectional yearly datasets from the VHA (one for each year, 2005–19), the resulting numbers of patients included in the prevalence model ranged from 3 234 382 to 4 579 994 (see appendix p 2 for yearly numbers). Over the 15 years, of the 27 854 691 patients with chronic pain, the mean age (SD) was 56·74 (12·74) years, 25 097 693 (90·1%) were male, and 19 294 950 (69·3%) were white. Of the 31 791 112 patients without chronic pain over the 15 years, the mean age was 56·91 (14·02) years, 29 490 559 (92·8%) were male, and 22 875 493 (72·0%) were white (table 1).

See Online for appendix

Covariate-adjusted cannabis use disorder prevalence trends in the no-CL, MCL-only, and MCL and RCL states (defined by their 2019 status) are shown in table 2 and figure 1. Among patients with chronic pain, cannabis use disorder prevalence increased 1·17% (from 1·76% to 2·92%) in no-CL states, 1·61% (from 1·76% to 3·37%) in MCL states, and 1·64% (from

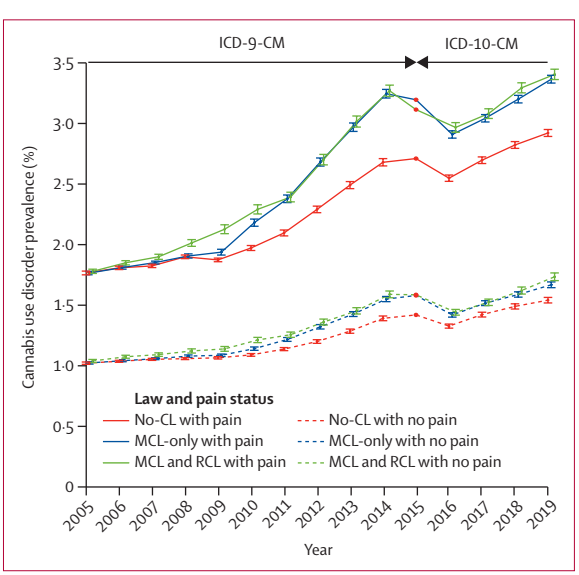

Figure 1: **Cannabis use disorder prevalence by state law status as of 2019, among patients with and without chronic pain**

No-CL=no cannabis law. MCL=medical cannabis law. RCL=recreational cannabis law.

1·77% to 3·41%) in MCL and RCL states. Among patients without chronic pain, cannabis use disorder prevalence increased 0·52% (from 1·01% to 1·53%) in no-CL states, 0·65% (from 1·01% to 1·66%) in MCL-only states, and 0·70% (from 1·03% to 1·73%) in MCL and RCL states. Similar results were seen when results were assessed by age group, with the greatest increases seen in the youngest patients (table 2).

In patients with chronic pain by age group, prevalence of cannabis use disorders increased from 2005 to 2019 by 3·64% (no-CL), 3·89% (MCL-only), and 4·12% (MCL and RCL) in patients aged 18–34 years, 1·92% (no-CL), 2·57% (MCL-only), and 2·45% (MCL and RCL) in patients aged 35–64 years, and 0·86% (no-CL), 1·10% (MCL-only), and 1·16% (MCL and RCL) in patients aged 65–75 years.

The DiD estimate of the cannabis use disorder prevalence increase due to MCL enactment in patients with chronic pain was 0·135% (95% CI 0·118–0·153; table 3). Relative to the absolute change in states with MCL-only by 2019, 8·4% of this increase was attributable to MCL. The DiD estimate of the cannabis use disorder prevalence increase due to RCL enactment was 0·188% (0·160–0·217); relative to the absolute change in states with MCL and RCL by 2019, 11·5% of this increase was attributable to RCL.

By age group of patients with chronic pain (table 3), among those aged 18–34 years, neither MCL nor RCL played a significant part in the increases in cannabis use disorder prevalence. In patients aged 35–64 years, 7·9% of the cannabis use disorder prevalence increase was attributable to MCL and 5·8% was attributable to RCL; and in patients aged 65–75 years, 9·3% was attributable to MCL and 19·4% was attributable to RCL. Thus, in terms of the change attributable to CL, the laws (especially RCL) had greatest impact on older patients (aged 65–75 years), whose cannabis use disorder rates were lowest at the beginning of the study period, but increased more than 3-fold in MCL or RCL states.

The DiD estimate of the cannabis use disorder prevalence increase due to MCL enactment in patients without chronic pain was 0·037% (95% CI 0·027–0·048; table 3). Relative to the absolute change in states with MCL-only by 2019, 5·7% of this increase was attributable to MCL. The DiD estimate of the prevalence increase due to RCL enactment was 0·042% (0·023–0·060); relative to the absolute change in states with RCL by 2019, 6·0% of this increase was attributable to RCL. By age, DiD estimates for MCL and RCL were non-significant among patients aged 18–34 years. In patients aged 35–64 years, 8·1% of the increase in cannabis use disorder prevalence was attributable to MCL enactment, and for RCL, the result of –8·2% suggested that post-RCL enactment, patients aged 35–64 years without chronic pain had smaller increases in cannabis use disorder prevalence than other age groups. Among patients aged 65–75 years, 6·9% of the increase in cannabis use disorder prevalence

	Patients with chronic pain		Patients without chronic pain		p value§
	Model-based DiD law effect, % (95% CI)†	Percentage of absolute change attributable to law†	Model-based DiD law effect, % (95% CI)†	Percentage of absolute change attributable to law†	
Full sample, age ≥18 years					
No-CL to MCL-only‡	0·135% (0·118 to 0·153)	8·4%	0·037% (0·027 to 0·048)	5·7%	p<0·0001
MCL-only to RCL and MCL‡	0·188% (0·160 to 0·217)	11·5%	0·042% (0·023 to 0·060)	6·0%	p<0·0001
Age 18–34 years					
No-CL to MCL-only‡	0·133% (0·029 to 0·238)	3·4%	0·028% (–0·035 to 0·091)	1·4%	p=0·0138
MCL-only to RCL and MCL‡	–0·053% (–0·192 to 0·085)	–1·3%	0·033% (–0·052 to 0·118)	1·4%	p=0·1297
Age 35–64 years					
No-CL to MCL-only‡	0·203% (0·170 to 0·236)	7·9%	0·076% (0·053 to 0·100)	8·1%	p<0·0001
MCL-only to RCL and MCL‡	0·142% (0·093 to 0·192)	5·8%	–0·072% (–0·107 to –0·037)	–8·2%	p<0·0001
Age 65–75 years					
No-CL to MCL-only‡	0·102% (0·084 to 0·121)	9·3%	0·029% (0·017 to 0·041)	6·9%	p<0·0001
MCL-only to RCL and MCL‡	0·224% (0·191 to 0·258)	19·4%	0·075% (0·055 to 0·096)	16·1%	p<0·0001

DC=District of Columbia. DiD=difference-in-difference. MCL=medical cannabis law. No-CL=no cannabis law. RCL=recreational cannabis law. *Staggered-Adoption DiD regression model,[35] adjusted for categorical age, sex, race or ethnicity, all age, race or ethnicity, and sex interactions, state-level median income and percentages (male, Hispanic, non-Hispanic White, non-Hispanic Black, poverty, aged 18 years or older, unemployed). Model estimated effects represent absolute increase (positive values) or decrease (negative values) in cannabis use disorder prevalence due to law enactment. The DiD model compares the years after enactment (up to 2019 or until the next law change) in each state to the years before enactment (since 2005 or the previous law change) in the same state, and controls for contemporaneous trends in other states that have not yet passed the respective law.†22 states and DC made a change from no-CL to MCL-only during the period from 2005 to 2019; 11 states and DC made a change from MCL-only to RCL and MCL during the period. Note, three of these states and DC made both changes between 2005 and 2019 (ie, from no-CL to MCL-only and then later to RCL and MCL), hence contributing information to both effects. There were 20 states (three with MCL-only and 17 with no-CL in 2019) that made no law changes between 2005 and 2019; in the DiD model, they contribute to background secular trends. ‡DiD estimate divided by absolute change across period as shown in table 2. §Comparison of DiD effect between patients with chronic pain and without chronic pain based on non-overlapping CIs of the two DiD effects.

***Table 3*: MCL and RCL enactment and changes in cannabis use disorder prevalence in patients with and without pain using DiD* estimates across 2005–19**

was attributable to MCL enactment, and 16·1% was attributable to RCL.

In the overall sample of patients with and without chronic pain, a greater increase in cannabis use disorder prevalence attributable to MCL and RCL enactment occurred among patients with chronic pain than in patients without chronic pain (p<0·0001 for both MCL and RCL enactment; table 3). By age, DiD estimates for MCL and RCL did not differ between those with and without chronic pain in patients aged 18–34 years. However, non-overlapping CIs for the DiD estimates of MCL and RCL showed differences between patients with and without pain in patients aged 35–64 (p<0·0001 for both MCL and RCL enactment) and 65–75 years (p<0·0001 for both MCL and RCL enactment), with greater impact of MCL and RCL on patients with chronic pain (table 3).

Among patients with pain, 15 states that enacted MCL-only between 2005 and 2019 showed an increase in cannabis use disorder prevalence attributable to MCL, two a decrease, and five no change attributable to MCL; eight states that enacted RCL by 2019 showed an increase, one a decrease, and three no change attributable to RCL (figure 2A). Among patients without pain, 11 states that enacted MCL-only showed an increase in cannabis use disorder prevalence attributable to MCL enactment, eight a decrease, and three no change attributable to MCL; five states that enacted RCL showed an increase, two a decrease, and four had no change attributable to RCL (figure 2B). Thus, patients with pain had a greater number of state-specific increases attributable to MCL or RCL enactment than patients without pain. However, no state reached a 1% absolute increase in cannabis use disorder prevalence. We also saw no patterning of larger or smaller results in states enacting laws in earlier or later years.

Substituting legally permitted operational dispensary dates for law enactment dates (appendix pp 3–4), fewer states were analysed because four MCL-only and four MCL and RCL states had not authorised operational dispensaries by 2019. Using the dates dispensaries were legally permitted among patients with chronic pain, the DiD estimate was significant for MCL (0·040% [95% CI 0·021 to 0·059) although smaller than the corresponding result for MCL enactment. The DiD estimate for RCL (0·149% [0·115 to 0·182]) was similar to the estimate for the RCL enactment date. Among patients without chronic pain, the DiD estimate was small and negative in MCL-only states (–0·013 [–0·023 to 0·002]). Using 1-year lags in place of the dates for MCL and RCL enactment (appendix pp 5–6), DiD estimates in patients with and without chronic pain did not change substantially.

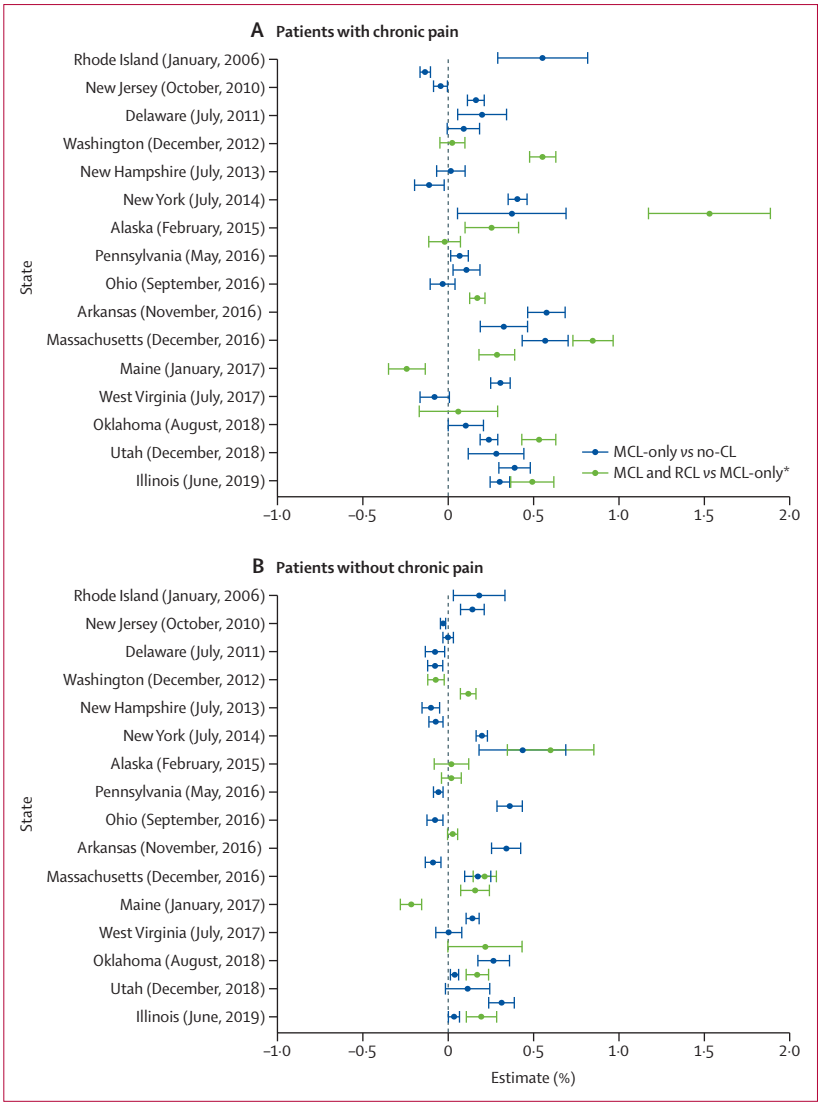

Figure 2: **Difference-in-difference estimates of change in cannabis use disorder prevalence, by change in state law status, in patients with chronic pain (A) and without chronic pain (B)**
MCL=medical cannabis law. No-CL=no cannabis law. RCL=recreational cannabis law. *Adjusted for categorical age, sex, race or ethnicity, all age, race or ethnicity, and sex interactions, state-level median income and percentages: (male, Hispanic, non-Hispanic White, non-Hispanic Black, poverty, aged 18 years or older, unemployed). In states that changed to MCL and RCL during the period, the MCL and RCL effect plotted is compared with No-CL for comparison with the MCL *vs* No-CL effect.

Discussion

To our knowledge, this is the first study to examine differences in the relationship of MCL and RCL to changes in cannabis use disorder prevalence by chronic pain status. The study also added to sparse information on an important group, older patients.

Using repeated cross-sectional yearly datasets from 2005 to 2019, we found that in VHA patients aged 35–64 years and 65–75 years, DiD estimates of the relationship of MCL and RCL to cannabis use disorder prevalence were significantly larger among patients with chronic pain than in patients without chronic pain. In a previous study that did not differentiate patients in the VHA by pain, MCL and RCL accounted for 4·7% and 9·8% of the increase in prevalence of cannabis use disorder between 2005 and 2019, respectively.[18] The

present study found that among patients with chronic pain, MCL and RCL enactment accounted for 8·4% and 11·5% of the increase in such prevalence, respectively. The relationship of RCL to cannabis use disorder prevalence was particularly pronounced among patients aged 65–75 years with chronic pain, in whom 19·4% of the increase in cannabis use disorder prevalence was attributable to RCL enactment, although these associations do not account for unmeasured time-varying confounders.

MCL and RCL are likely to influence the prevalence of cannabis use disorder by decreasing perception of cannabis risk[10,36] and by increasing access to more potent cannabis products. Commercialisation that increases access to cannabis once commercial markets are opened, and advertising and online information that portrays cannabis use as normal and safe, are also likely to be involved, leading to positive expectancies regarding cannabis use that have been demonstrated in the high rates of placebo response in randomised clinical trials.[37] In patients with chronic pain, the decline in prescribed opioids could also have contributed to our findings on MCL, RCL, and cannabis use disorder by leading to substitution of cannabis use that led to cannabis use disorder. The VHA offers evidence-based non-opioid pain treatment programmes,[38] including psychological therapies, physical rehabilitation, and complementary and integrative health interventions (eg, massage or acupuncture). However, positive media accounts of cannabis trials (regardless of their results[27]), positive online promotional efforts (eg, The Empowered Pain Patient[39]), and increasing beliefs that cannabis is a useful prevention and treatment agent[26] might increase patient interest in cannabis more than the evidence-based treatments offered by the VHA. That this could increase the risk for cannabis use disorder is supported by a trial showing that obtaining a medical cannabis card was associated with a rapid increase in risk for cannabis use disorder,[40] and also by a meta-analysis of randomised trials of cannabinoids for pain showing substantial placebo response.[27]

Our finding of the largest DiD estimates for RCL among patients with pain aged 65–75 years adds to evidence about important changes among older adults, among whom the prevalence of cannabis use is growing.[41] Many non-opioid pain medications are contraindicated among older individuals, limiting pain treatment options and potentially leading to cannabis use.[24] Pharmacokinetic parameters influenced by age might increase tetrahydrocannabinol (THC) bioavailability in older individuals, possibly increasing their risk for cannabis use disorder. In addition, older patients might be more concerned about the legality of cannabis than younger patients, and therefore more willing to use it only after it becomes legal. This could contribute to the impact of MCL and RCL among older patients. Taken together, these findings suggest that clinicians should monitor potential cannabis use among older patients with chronic pain, discussing the risks of cannabis use disorder and potential treatment alternatives.

Although we showed that MCL and RCL played a significant role in the increasing trends in cannabis use disorder prevalence in patients with chronic pain, a substantial proportion of the increases remains unexplained, leaving important questions unanswered. For example, among patients with chronic pain, are increases in cannabis use disorder prevalence also influenced by state-level opioid policies or other changing state characteristics? At an individual level, is the prevalence of cannabis use disorder growing faster among patients with chronic pain who also have specific psychiatric or other substance use disorders, or who were previously prescribed opioids but no longer have a prescription, or who now have a lower dose? In 2019, the two most common chronic pain clusters were back pain (22%) and a category for non-inflammatory arthritic pain (32%). Their rates are increasing, as is the use of cannabis in adults with these conditions.[24,42] Do one or both of these pain clusters account for most of the increases in cannabis use disorder prevalence, or for differences in the relationship of MCL and RCL to cannabis use disorder between those with and without chronic pain? Would the total number of painful conditions (a proxy for severity[24]) better account for the increases? These questions should be addressed in future research.

Study limitations are noted. First, patients in the VHA differ from the general population in that a large majority of them are White and male and many are in the older age group (65–75 years). As such, they are not representative of all veterans or of the US general adult population. Second, cannabis use disorder diagnoses were made by clinicians, who are most likely to diagnose severe disorders[43] and miss mild cases found using structured assessments.[4,11] Third, no subjective pain measure (ie, perceived pain intensity) was available, which future studies should employ. Fourth, cannabis laws are heterogeneous. We examined whether states permitted dispensaries, but other differences (eg, price and taxation) should be addressed in future studies. Fifth, the impact of state law changes might be delayed. We analysed 1-year lags to include as many RCL states as possible, but longer lags should be analysed when more recent data become available. Sixth, additional sources of cannabis availability (eg, black market dispensaries) need to be taken into consideration when assessing legal dispensaries as the determinant of cannabis availability. Seventh, a cannabis use measure was not available, so cannabis use disorder within those endorsing use and specific use patterns (eg, frequency) was not examined.

Additional limitations include the following: many time-varying state-level covariates and confounders were controlled, but others (eg, state opioid policies) should be addressed in future studies; the DiD method estimates law effects in states that enact them, but not spillover effects in adjacent states. If patients in no-CL states are

influenced by MCL or RCL laws in nearby states, findings will be biased towards the null. For example, patients in no-CL states living near an MCL-only or MCL and RCL state might border-cross to buy cannabis, elevating cannabis use disorder rates in no-CL states and mitigating MCL or RCL effects; interaction tests require large amounts of statistical power and are model-dependent. Although lack of statistical power was not an issue in our study, we note that our model was on the additive, not multiplicative scale, as the additive scale is often seen as the more relevant public health measure. Finally, no observational study is unequivocal about causality.

Cannabis does not have the same serious overdose and mortality risk as opioids. However, cannabis use disorder, a disorder with many associated problems,[3,44,45] occurs more often among cannabis users than commonly assumed.[5] The national increases in cannabis use disorder prevalence, including the disproportionate increase among those with chronic pain, underscore a growing need in the VHA and elsewhere to screen for cannabis use and offer evidence-based treatments for cannabis use disorder.

The multibillion-dollar US cannabis industry[46] requires new customers or greater use among existing customers to increase demand.[47] Websites of medical cannabis companies often make unconfirmed claims about product safety and efficacy, potentially leading to increasingly positive public beliefs about cannabis use.[48,49] Cannabis industry social responsibility programmes, ostensibly designed to mitigate harms, mirror tobacco industry programmes that actually serve to recruit customers, encourage consumption, expand markets, and legitimise products.[30] Such activities could change attitudes within and across US state boundaries, increasing cannabis use and cannabis use disorder, including among those with pain.[27]

In the USA, public health concerns regarding alcohol, tobacco, and prescription opioids have long competed with commercial interests. With cannabis increasingly legalised across US states, similar competing public health and commercial interests are emerging,[9] with state cannabis laws largely industry-friendly rather than protective of public health.[9] In this study, RCL was associated with the greatest increases in cannabis use disorder prevalence in the oldest patients with chronic pain, who had lower prevalence of the disorder at the beginning of the study period but greater relative increases by the end. To inform health and policy efforts, researchers should monitor harms related to increasing cannabis use disorder, particularly in those with chronic pain, and clearly communicate this knowledge to policy makers, clinicians, patients, and the public in the USA and in other countries. Educational messages regarding the risk for cannabis use disorder among those with pain who are using cannabis are warranted, both to the general public and to heath-care providers. Finally, clinicians should monitor patients with chronic pain who use cannabis for signs of cannabis use disorder, particularly patients in settings where cannabis use has been legalised—for example, in all of Canada and in the majority of US states.

Contributors

DSH contributed to the conceptualisation, methodology, software, validation, formal analysis, investigation, resources, data curation, writing of the original draft, writing–review and editing of the revised manuscript, visualisation, supervision, project administration, and funding acquisition. MMW contributed to the conceptualisation, methodology, validation, formal analysis, writing of the original draft, writing–review and editing of the revised manuscript, visualisation, and supervision. DMA contributed to the formal analysis, software, and visualisation. ZLM contributed to the methodology and writing–review and editing of the revised manuscript. CM contributed to the formal analysis, software, visualisation, and data curation. MO, KMK, JLG, and MC contributed to the conceptualisation, methodology, and writing–review and editing of the revised manuscript. CCM, SK, SSM, DSF, OL, and YM contributed to the methodology, and writing–review and editing of the revised manuscript. SS contributed to the writing–review and editing of the revised manuscript and project administration. AJS contributed to the conceptualisation, resources, writing–review and editing of the revised manuscript, supervision, and project administration. MMW, DMA, CM, and DSF had access to the raw data. MMW, DMA, and CM directly accessed and verified the data. DSH had final responsibility for the decision to submit for publication.

Declaration of interests

DSH receives support from Syneos Health for an unrelated project. JLG reports consulting fees from Hoffman-La Roche, a patent pending (use of glecaprevir and pibrentasvir for the treatment of post-traumatic stress disorder), and participation on a data safety monitoring board or advisory board for National Institute of Mental Health (using machine learning to optimise user engagement and clinical response to digital mental health interventions). SSM serves on the Board of Directors for the College on Problems of Drug Dependence. AJS has received consulting fees from Indivior, travel support from Alkermes, research support from MedicaSafe, and royalties from UpTo-Date. KMK has served as an expert witness in litigation. All other authors declare no competing interests.

Data sharing

The data were taken from VHA electronic medical records which must be kept behind the VHA firewall at all times, and only VHA-authorised users are permitted to access them.

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