ORIGINAL RESEARCH

Comparing Cannabis Use for Pain to Use for Other Reasons in Primary Care Patients

Morgan A. Ford, MS, Gwen T. Lapham, PhD, MPH, MSW, Theresa E. Matson, PhD, MPH, Casey Luce, MSPH, Malia M. Oliver, BA, and Ingrid A. Binswanger, MD, MPH, MS

Background: Medical cannabis is commonly used for chronic pain, but little is known about differences in characteristics, cannabis use patterns, and perceived helpfulness among primary care patients who use cannabis for pain versus nonpain reasons.

Methods: Among 1688 patients who completed a 2019 cannabis survey administered in a health system in Washington state, where recreational use is legal, participants who used cannabis for pain (n = 375) were compared with those who used cannabis for other reasons (n = 558) using survey and electronic health record data. We described group differences in participant characteristics, use patterns, and perceptions and applied adjusted multinomial logistic and modified Poisson regression.

Results: Participants who used cannabis for pain were significantly more likely to report using applied (50.7% vs 10.6%) and beverage cannabis products (19.2% vs 11.6%), more frequent use $(47.1\% \text{ vs } 33.1\% \text{ for use } \ge 2 \text{ times per day}$; 81.6% vs 69.7% for use 4 to 7 days per week), and smoking tobacco cigarettes (19.2% vs 12.2%) than those who used cannabis for other reasons. They were also significantly more likely to perceive cannabis as very/extremely helpful (80.5% vs 72.7%), and significantly less likely to use cannabis for nonmedical reasons (4.8% vs 58.8%) or report cannabis use disorder symptoms (51.7% vs 61.1%).

Discussion: Primary care patients who use cannabis for pain use it more frequently, often in applied and ingested forms, and have more co-use of tobacco, which may differentially impact safety and effectiveness. These findings suggest the need for different approaches to counseling in clinical care. (J Am Board Fam Med 2023;36:996–1007.)

Keywords: Cannabis, Chronic Pain, Medical Marijuana, Primary Health Care, Surveys and Questionnaires, Washington

Introduction

Chronic noncancer pain (CNCP) is a common reason for medical cannabis use in the United States. ^{1–7} While little is known about the perceived helpfulness of cannabis for patients who use it for pain, cannabis' widespread use suggests it is viewed as a helpful

primary or adjunctive treatment for some individuals. Although additional research is needed on the benefits of cannabis for pain, studies show a small but significant benefit of cannabis relative to placebo for CNCP. 8–10

Cannabis use is also associated with potential harms, which could be more marked in states with legal or medical cannabis, where various commercial

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From the Kaiser Permanente Colorado Institute for Health Research, Aurora, CO (MAF, IAB), Kaiser Permanente Washington Health Research Institute, Seattle, WA (GTL, TEM, CL, MMO), Department of Health Systems and Population Health, University of Washington, Seattle, WA (GTL), Colorado Permanente Medical Group, Aurora, CO (IAB), Division of General Internal Medicine, Department of Medicine, University of Colorado School of Medicine, Aurora, CO (IAB), Department of Health Systems Sciences, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA (IAB).

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Corresponding author: Morgan A. Ford, MS, Kaiser Permanente Colorado Institute for Health Research, 2550 S. Parker Rd., Suite 200, Aurora, CO 80014 (E-mail: morgan. ford@kp.org).

cannabis products are available and marketed with minimal standardization of preparations.¹¹ The harms of cannabis likely vary by product characteristics (eg, the ratio of THC [tetrahydrocannabinol] to CBD [cannabidiol]), mode of use (eg, ingestion vs application), and frequency of use. Depending on how patients use cannabis for pain, they may be more or less susceptible to adverse effects compared with patients who use cannabis for other reasons. For example, smoking cannabis may lead to respiratory complications, even in individuals who do not smoke tobacco, ^{12–16} and vaping cannabis can result in lung injury. 17,18 Little is known about the safety of applied and ingested forms of cannabis, which are commonly used for pain. 19 A dose-response relationship has been observed between cannabis consumption and the risk of psychosis and declines in psychosocial function, 15,20-23 and more frequent cannabis use may increase the risk of cannabis use disorder (CUD). 15,24 However, little research has explored cannabis use patterns and indicators of potentially problematic use in patients who use cannabis primarily for pain.

Roughly 8% to 24% of adults use cannabis at least once a month in states with medical and/or legal cannabis.²⁵ With widespread cannabis availability in legal contexts, it is critical to evaluate the safety and effectiveness of real-world cannabis use for pain. Patients with pain may be older, have more comorbidities and more complex medication regimens than patients who use cannabis for other reasons; these characteristics likely impact the absorption and metabolism, and, therefore, the safety and effectiveness of cannabis.

This primary-care based study was designed to identify and quantify differences in characteristics, cannabis use patterns (mode and frequency), CUD symptoms, and perceived helpfulness of cannabis for patients who use cannabis primarily for pain compared with patients who use cannabis for other reasons.

Methods

Study Setting

This study was conducted in Kaiser Permanente Washington (KPWA), a large health plan and care delivery system. Medical cannabis has been legal in Washington state since 1998 and nonmedical use since 2012.26 This study was funded by the National Drug Abuse Treatment Clinical Trials Network.

Study Sample

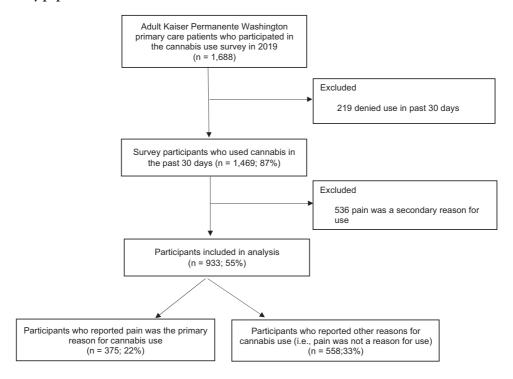
The sample included primary care patients who responded to a survey on cannabis use.²⁷ The original survey sample included 5000 patients selected from a representative cohort of KPWA patients aged ≥18 with primary care visits (January 28, 2019-September 12, 2019) and documentation of a routine cannabis screen (n = 108,950). Survey design, sampling, procedures, and sample characterization, including comparison of respondents to eligible primary care sample and nonrespondents, have been reported previously.²⁷ The validated single-item screen asks about the frequency of past-year cannabis use (ie, none, less than monthly, monthly, weekly, and daily).²⁸ Sample selection included patients who reported no past-year use, as well as random, stratified oversampling for Black, Indigenous, and other patients of color, and patients with weekly-to-daily cannabis use, to adequately account for the experiences of these subgroups who are often underrepresented in research.²⁷ Of the 5000 invited to complete the cannabis use survey, 1688 (34%) responded. (See Lapham et al., 2022²⁷ for comparison of eligible sample and survey responders.) Participants consented to use of data from their electronic health records (EHRs). Informed consent assured survey results were confidential and that study data were protected by a Certificate of Confidentiality from the National Institutes of Health. The KPWA Institutional Review Board approved the study, including waivers of consent to identify the eligible sample, documentation of informed consent for survey respondents, and HIPAA (Health Insurance Portability and Accountability Act) authorization.

This study included respondents who reported past 30-day cannabis use (n = 1469) (Figure 1). Among these, the primary analyses were conducted comparing participants who reported pain as the primary reason for use (n = 375) to those who did not report pain as a reason for use (n = 558). In secondary analyses, we compared participants who reported pain as a reason for cannabis use, but not the primary reason (n = 536). (See Appendix Table 1 for instrument.)

Data

Study data came from survey responses and EHRs. All research data were stored in limited access databases and deidentified before analysis.

Figure 1. Study population selection criteria.



Survey Measures

The cannabis survey was developed by an expert panel and pilot tested in a convenience sample of KPWA Health Research Institute colleagues. The survey included 2 to 75 items, depending on skip patterns, with de novo questions on reasons for cannabis use, mode and frequency of use, experience of CUD symptoms, and helpfulness of use. Participants could complete the survey online or by phone.

Participants reported whether cannabis use in the past 30 days was for medical, nonmedical, or both reasons for use (Question 1 in Appendix Table 1). Participants also reported whether they used cannabis to help manage any pain, which could include CNCP or other forms of pain; other symptoms or conditions (eg, seizures, nausea or vomiting); or none (Question 4 in Appendix 1). Those who reported more than 1 reason for cannabis use were asked to identify the reason they used it most often that is, their primary reason for use (Question 5 in Appendix 1). Participants who reported pain as their only or primary reason for cannabis use were included in the pain as primary reason for use subgroup (hereafter referred to as use for "pain"), whereas those who reported reason(s) for use other than pain (including 'none' or 'other') were included in the other reason(s) for use subgroup (hereafter referred to as use for "other reasons"). Participants who reported pain as a reason, but not the primary reason, for cannabis use were designated as pain as the secondary reason for use subgroup (hereafter referred to as use for "pain – secondary").

Participants were prompted to indicate modes of use and their most frequent mode of use in the past 30 days ('smoke it,' 'vaporize it,' 'dab it,' 'eat it,' 'drink it,' 'apply it to the skin' and 'other.'). Participants were additionally asked for the typical times per week and typical times per day they used cannabis in the past 30 days, as well as how helpful cannabis has been for the reasons they use it ('not at all helpful', 'slightly helpful,' 'somewhat helpful,' 'very helpful,' or 'extremely helpful'). In addition, participants were queried about symptoms of cannabis use disorder (CUD) in the past year, using questions from the Composite International Diagnostic Interview and based on Diagnostic and Statistical Manual of Mental Disorders, fifth Edition (DSM-5) CUD criteria.²⁹ Lastly, participants were asked about their tobacco and nicotine use, employment status, and education.³⁰

Electronic Health Record Measures

Clinical correlates of cannabis use, including CNCP diagnoses and substance use disorder

Table 1. Sociodemographic Characteristics of Survey Participants Who Used Cannabis for Pain and Who Used Cannabis for Other Reasons in the Past 30 Days

	Used cannabis for pain $(n = 375)$	Used cannabis for other reasons* $(n = 558)$	
Characteristic	n (%)	n (%)	P value
Age at cannabis screen			
18 to 29	43 (11.5)	177 (31.7)	< 0.001
30 to 49	116 (30.9)	204 (36.6)	
50+	216 (57.6)	177 (31.7)	
Gender			
Woman	197 (52.5)	249 (44.6)	0.018
Man	178 (47.5)	309 (55.4)	
Race			
American Indian/Alaska Native	16 (4.3)	7 (1.3)	0.057
Asian	13 (3.5)	34 (6.1)	
Black/African American	34 (9.1)	50 (9.0)	
Hawaiian/Other Pacific Islander	9 (2.4)	11 (2.0)	
White	271 (72.3)	399 (71.5)	
Other	17 (4.5)	29 (5.2)	
Unknown	15 (4.0)	28 (5.0)	
Ethnicity			
Hispanic/Latino	32 (8.5)	63 (11.3)	0.064
Not Hispanic/Latino	330 (88.0)	461 (82.6)	
Unknown	13 (3.5)	34 (6.1)	
Employment status [†]			
Full-time	175 (46.7)	355 (63.6)	< 0.001
Part-time	25 (6.7)	51 (9.1)	
School/vocational	4 (1.1)	25 (4.5)	
Retired	98 (26.1)	77 (13.8)	
Homemaker	9 (2.4)	12 (2.2)	
Unemployed	13 (3.5)	18 (3.2)	
Disabled	46 (12.3)	8 (1.4)	
Other	5 (1.3)	10 (1.8)	
Education [†]			
>4-year college degree	60 (16.1)	126 (22.7)	< 0.001
4-year college degree	57 (15.3)	158 (28.5)	
Some college	162 (43.4)	186 (33.5)	
High school/GED or less	94 (25.2)	85 (15.3)	

^{*}Other than pain, reasons for cannabis use assessed include muscle spasm, seizures, nausea or vomiting, sleep, stress, appetite, worry or anxiety, depression or sadness, focus or concentration, other symptoms, none.

diagnoses in the 2 years before the cannabis use survey completion date were identified from EHRs. CNCP diagnoses were defined as EHR documentation of 2 or more International Classification of Diseases-Tenth Revision (ICD-10) codes for similar pain types at least 30 days apart, or an ICD-10 diagnosis consistent with general CNCP. 31,32 Participant age, gender, race, and ethnicity were also derived from EHR data available on the cannabis use survey completion date.

Analytic Approach

Descriptive statistics were used to characterize participants who used cannabis for pain and those who used cannabis for other reasons across demographic and clinical characteristics, mode-specific patterns of cannabis use, CUD symptoms, and perceived helpfulness of use. Between-group differences were estimated using c² tests of independence or Fisher's exact tests if cell sizes were <5 with an α level of

[†]Column sums for this variable may not total 375 for used cannabis for pain or 558 for used cannabis for other reasons due to missing responses (item-level non-response rate across participants $\leq 1\%$).

0.05. In participants who used cannabis for pain, we examined within-group patterns by mode of use and by perceived helpfulness.

Using multinomial logistic regression, we estimated the adjusted prevalence and relative risk ratio (RRR) of combined modes of cannabis use—inhale (smoke, vape, and dab), apply, ingest (eat and drink), or other—comparing participants who used cannabis for pain and those who used cannabis for other reasons. Using modified Poisson regression models,³³ we estimated the adjusted prevalence and relative risk (RR) of 2 measures of cannabis frequency—times per day and days per week-again comparing participants who used cannabis for pain and those who used cannabis for other reasons. Poisson, rather than logistic, regression models were used to estimate relative rates because outcomes were expected to be common.³⁴ Standard errors were calculated using a robust sandwich estimator to account for misspecification of the mean-variance relationship.³³ All models were adjusted for demographic characteristics (age, gender, race/ethnicity, employment status, education) and other cannabis outcomes.

In sensitivity analyses, we compared sociodemographic characteristics between participants who used cannabis for pain and participants who used cannabis for other reasons to excluded patients who used cannabis for pain – secondary. We also conducted descriptive analyses of CUD symptoms excluding participants who only used cannabis in applied forms.

Analyses were conducted using Stata, version 15.1 (StataCorp LLC, College Station, TX).

Results

Among 933 participants included in primary analyses, 375 reported using cannabis for pain and 558 reported using cannabis for other reasons in the past 30 days.

Sociodemographic and Clinical Characteristics

Compared with participants who used cannabis for other reasons, those who used cannabis for pain were more likely to be aged ≥ 50 , female, retired or have a disability, and have less than a bachelor's degree (Table 1). The prevalence of CNCP diagnoses among participants who used cannabis for pain was more than double that of participants who used cannabis for other reasons (54.9% [206/375] vs 21.9% [122/558]; P=.001) (Table 2). Participants who

used cannabis for pain had significantly higher prevalence of tobacco use disorder (16.0% vs 10.8%, P = .019) and were twice as likely to report that they smoke cigarettes every day (14.6% vs 7.2%, P = .001).

In sensitivity analysis, participants who used cannabis for pain – secondary (n=536) were more like participants who used cannabis for other (nonpain) reasons than those who used cannabis for pain in age, employment, and disability status (Appendix Table 2). However, they were more likely to be female and have less than a bachelor's degree, similar to participants who used cannabis for pain.

Cannabis Use Patterns

Participants who used cannabis for pain and those who used cannabis for other reasons endorsed an average of 4.1 (S.D. 2.4) and 2.5 (S.D. 1.8) reasons for use, respectively. Smoking was the most common mode of use for both groups (Table 2). Significantly more participants who used cannabis for pain reported applying cannabis (eg, lotion, ointment, patch, salve; 50.7% vs 10.6%; P<.001) and drinking cannabis (19.2% vs 11.6%; P = .001). Participants who used cannabis for pain were more likely to use it ≥ 3 times per day (47.5% vs 33.1%; P < .001) and >4 days per week (81.6% vs 69.7%; P < .001). These participants were also less likely to report their cannabis use was for nonmedical reasons only (4.8% vs 58.8%; *P* < .001). Across modes of use, most participants who used cannabis for pain used it for both medical and nonmedical reasons (Table 3).

Cannabis Use Disorder Symptoms and Diagnoses

Participants who used cannabis for pain were less likely than those who used cannabis for other reasons to report experiencing any DSM-5 CUD symptom in the past year (51.7% vs 61.1%; P=.005) (Table 4). These participants were also less likely to meet DSM-5 criteria for moderate or severe CUD (5.9% vs 21.0%; P<.001). These findings were robust in sensitivity analysis that excluded participants who apply cannabis only (Appendix Table 3).

Helpfulness of Cannabis Use

Perceived helpfulness of cannabis was high in both groups, with participants who used cannabis for pain being significantly more likely to report cannabis as very/extremely helpful compared with those

Table 2. Chronic Pain and Substance Use Disorder Diagnosis History; Current Cigarette Smoking Status and Vaping of Tobacco/Nicotine; and Mode, Frequency, and Helpfulness of Cannabis Use in Survey Participants Who Used Cannabis for Pain and Who Used Cannabis for Other Reasons in the Past 30 Days

	Used cannabis for pain $(n = 375)$	Used cannabis for other reasons* $(n = 558)$	
	n (%)	n (%)	P value
Chronic pain diagnosis in past 2 years	206 (54.9)	122 (21.9)	< 0.001
Limb/joint	127 (33.9)	71 (12.7)	< 0.001
Back	93 (24.8)	47 (8.4)	< 0.001
Neck	45 (12.0)	30 (5.4)	< 0.001
Abdominal and bowel	38 (10.1)	17 (3.0)	< 0.001
Fracture/contusion/sprain	28 (7.5)	14 (2.5)	< 0.001
Neuropathy	18 (4.8)	4 (0.7)	<.001**
Muscle/chest	15 (4.0)	5 (0.9)	0.001
Headache	14 (3.7)	10 (1.8)	0.066
Other chronic pain diagnosis [†]	84 (22.4)	35 (6.3)	< 0.001
Any substance use disorder diagnosis in past 2 years	95 (25.3)	90 (16.1)	0.001
Tobacco use disorder	60 (16.0)	60 (10.8)	0.019
Alcohol use disorder	19 (5.1)	17 (3.0)	0.335
Cannabis use disorder	19 (5.1)	21 (3.8)	0.116
Opioid use disorder	10 (2.7)	6 (1.1)	0.066
Other drug use disorder [‡]	2 (0.5)	9 (1.6)	.215**
Current cigarette smoking status [§]	2 (0.3)	<i>y</i> (1.0)	.213
Every day	54 (14.6)	40 (7.2)	0.001
Some days	17 (4.6)	28 (5.0)	0.001
Not at all/never	300 (80.9)	488 (87.8)	
Current vaping of tobacco/nicotine§	200 (00.7)	100 (07.10)	
Every day	20 (5.3)	29 (5.2)	0.996
Some days	18 (4.8)	27 (4.9)	0.770
Not at all/never	337 (89.9)	500 (89.9)	
All modes of cannabis use endorsed	331 (07.7)	300 (07.7)	
Smoke	249 (66.4)	422 (75.6)	0.002
Apply	190 (50.7)	59 (10.6)	< 0.002
Eat	164 (43.7)	244 (43.7)	0.999
Vape	160 (42.7)	254 (45.5)	0.390
Drink	72 (19.2)	65 (11.6)	0.001
Dab	63 (16.8)	81 (14.5)	0.344
Other	26 (6.9)	13 (2.3)	0.001
Primary mode of cannabis use endorsed§	20 (0.7)	13 (2.3)	0.001
Smoke	164 (44.2)	284 (51.5)	< 0.001
Apply	55 (14.8)	3 (0.5)	\0.001
Eat	48 (12.9)	70 (12.7)	
Vape	57 (15.4)	139 (25.2)	
Drink	, ,	` '	
	18 (4.9)	14 (2.5)	
Dab	20 (5.4)	33 (6.0)	
Other	9 (2.4)	9 (1.6)	
Typical times per day of cannabis use, considering all modes of use [§]			
<1	7 (1.9)	14 (2.5)	< 0.001
1 to 2	188 (50.7)	355 (64.3)	
3 to 4	103 (27.8)	115 (20.8)	

Continued

Table 2. Continued

	Used cannabis for pain $(n = 375)$	Used cannabis for other reasons* $(n = 558)$		
	n (%)	n (%)	P value	
5 to 9	53 (14.3)	47 (8.5)		
10+	20 (5.4)	21 (3.8)		
Typical days per week of cannabis use, considering all modes of use§				
<1	17 (4.5)	45 (8.1)	< 0.001	
1 to 3	52 (13.9)	122 (21.1)		
4 to 7	305 (81.6)	384 (69.7)		
Medical use in the past 30 days ^{§,} ¶				
Both medical and non-medical	226 (60.4)	180 (32.5)	< 0.001	
Medical	130 (34.8)	48 (8.7)		
Non-medical	18 (4.8)	325 (58.8)		
Perceived helpfulness of cannabis use among those who provided a reason for use ^{§,#}				
Very/extremely	302 (80.5)	338 (72.7)	0.010**	
Slightly/somewhat	73 (19.5)	125 (26.9)		
Not at all	0 (0.0)	2 (0.4)		

^{*}Other than pain, reasons for cannabis use assessed include muscle spasm, seizures, nausea or vomiting, sleep, stress, appetite, worry or anxiety, depression or sadness, focus or concentration, other symptoms, none.

who used it for other reasons (80.5% vs 72.7%; P = .010) (Table 2). Among participants who used cannabis for pain, those who found cannabis very/extremely helpful were significantly more likely than those who found it slightly/somewhat helpful to endorse smoking as a mode of cannabis use and use it 4 to 7 days per week (Table 5).

Adjusted Analysis

In adjusted analyses comparing participants who use cannabis for pain to participants who use cannabis for other reasons, applying cannabis and ingesting (eating, drinking) cannabis were significantly more likely than inhaling (smoking, vaping, dabbing) cannabis (Appendix Table 4). RRRs were 109.5 (95% CI, 21.3 to 562.9; P < .001) for cannabis application and 2.0 (95% CI, 1.3–3.1; P = .003) for ingestion. After adjustment, participants who used

cannabis for pain had a higher risk of using cannabis more than twice per day and 4 to 7 days per week than those who use cannabis for other reasons. RRs were 1.4 (95% CI, 1.2-1.6; P < .001) for more than twice daily use and 1.1 (95% CI, 1.0 to 1.2; P = .025) for use 4 to 7 days per week.

Discussion

In this study of primary care patients who responded to a cannabis use survey and reported past 30-day cannabis use, participants who used cannabis for pain were older and more likely to be female, retired/have a disability, have a CNCP diagnosis, smoke tobacco cigarettes, and have a tobacco use disorder than participants who used cannabis for other reasons. Further, participants who used cannabis for pain were more likely to apply and ingest cannabis and use it frequently, and

[†]Includes acquired deformities (excluding back conditions), arthritic pain, bone infections, cancer-related pain, fibromyalgia, general pain, infectious diseases, orofacial/temporomandibular joint pain, post-operative pain, post-trauma pain, restless legs syndrome, spinal cord injury, systemic disorders, urogenital/pelvic pain, and other painful conditions.

[‡]Includes stimulant, hallucinogen, and other drug use disorders.

[§]Column sums for this variable may not total 375 for Used cannabis for pain or 558 for used cannabis for other reasons due to missing responses (item-level non-response rate across participants ≤1%).

Responses not mutually exclusive.

Response to question "When you used marijuana/cannabis during the past 30 days, was it: 1. For medical reasons, 2. For non-medical reasons, 3. For both medical and non-medical reasons."

^{*}Eighty-five participants in the used cannabis for other reasons group reported no reasons for cannabis use and therefore were not asked about the perceived helpfulness of cannabis.

^{**}P value obtained using Fisher's exact test.

Table 3. Cannabis Use Patterns Among Survey Participants Who Used Cannabis for Pain in the Past 30 Days, by Each Mode of Use*

		Mode(s) of use endorsed					
	Smoke (n = 249)	$Apply \\ (n = 190)$	Eat (n = 164)	Vape (n = 160)		Dab (n = 63)	Other (n = 26)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Medical use in the past 30 days [†]							
Both medical and non-medical	187 (75.1)	115 (60.5)	104 (63.8)	111 (69.4)	37 (52.1)	43 (68.3)	13 (50.0)
Medical	47 (18.9)	69 (36.3)	52 (31.9)	43 (26.9)	32 (45.1)	18 (28.6)	13 (50.0)
Non-medical	15 (6.0)	6 (3.2)	7 (4.3)	6 (3.8)	2 (2.8)	2 (3.2)	0 (0.0)
Typical times per day, specific to each mode of use [‡]							
<1	6 (2.4)	14 (7.4)	15 (9.1)	8 (5.0)	7 (9.7)	9 (14.3)	4 (15.4)
1 to 2	111 (44.9)	139 (73.2)	138 (84.1)	81 (50.6)	58 (80.6)	26 (41.3)	19 (73.1)
3 to 4	84 (34.0)	30 (15.8)	9 (5.5)	38 (23.8)	7 (9.7)	18 (28.6)	3 (11.5)
5 to 9	36 (14.6)	6 (3.2)	1 (0.6)	24 (15.0)	0 (0.0)	8 (12.7)	0 (0.0)
10+	10 (4.0)	1 (0.5)	1 (0.6)	9 (5.6)	0 (0.0)	2 (3.2)	0(0.0)
Typical days per week, specific to each mode of use [‡]							
<1	9 (3.6)	24 (12.6)	48 (29.3)	21 (13.2)	26 (36.1)	15 (24.2)	7 (26.9)
1 to 3	61 (24.6)	68 (35.8)	69 (42.1)	56 (35.2)	21 (29.2)	16 (25.8)	7 (26.9)
4 to 7	178 (71.8)	98 (51.6)	47 (28.7)	82 (51.6)	25 (34.7)	31 (50.0)	12 (46.2)

^{*}Participants could report more than one mode of use.

less likely to describe their cannabis use as 'nonmedical' and meet CUD criteria. Most participants in both groups perceived cannabis use as helpful, with a slightly greater proportion of those who used it for pain reporting it as very or extremely helpful.

To balance the harms and benefits of cannabis use for pain and guide patients, clinicians may find it helpful to assess patients' reasons for cannabis use; modes, frequency, and perceived helpfulness of use; and CUD symptoms. This approach is consistent with shared patient-clinician decision making guidance for other substances lacking clear evidence of benefits and risks. For example, although evidence on the effectiveness of opioid therapy for CNCP management continues to develop, the Centers for Disease Control and Prevention's "Clinical Practice Guideline for Prescribing Opioids for Pain" suggests clinicians evaluate the risks and benefits of opioid use with patients before initiating and throughout opioid therapy.35 A similar framework could be applied to cannabis use for pain. Clinicians should also carefully assess nicotine and tobacco use among patients who use cannabis for pain and provide nicotine and tobacco cessation counseling and medications as indicated.

Several of our findings are congruous with prior research. Prevalence studies show that CNCP is more common in females, older individuals, and those with chronic conditions, 36,37 consistent with the characteristics of participants who used cannabis primarily for pain in this study. Tobacco use disorder and nicotine use rates are high among people with CNCP, ^{37–40} concordant with our findings that a higher proportion of participants who used cannabis for pain had a diagnosis of tobacco use disorder. Finally, prior research involving adult primary care patients⁴¹ is consistent with our observations that most participants who used cannabis for pain or other reasons found it helpful. With regard to our finding that participants who used cannabis for pain used it more frequently and were more likely to report tobacco use, yet were less likely to report

[†]Response to question "When you used marijuana/cannabis during the past 30 days, was it: 1. For medical reasons, 2. For non-medical reasons, 3. For both medical and non-medical reasons."

[‡]Column sums for this variable may not equal the total for the mode of use due to missing responses.

Table 4. Past-Year Experience of Cannabis Use Disorder (CUD) Symptoms and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) CUD Category Among Survey Participants Who Used Cannabis for Pain and Who Used Cannabis for Other Reasons in the Past 30 Days

	Used cannabis for pain (n = 375)	Used cannabis for other reasons* (n = 558)	
	n (%)	n (%)	P value
Individual CUD Symptoms			
Tolerance	57 (15.5)	149 (26.8)	< 0.001
Withdrawal	45 (12.1)	118 (21.3)	< 0.001
Failed attempts to cut down	12 (3.2)	62 (11.2)	< 0.001
Craving	84 (22.5)	181 (32.8)	0.001
Uncontrolled escalation of use	97 (25.9)	219 (39.3)	< 0.001
Time spent	6 (1.6)	26 (4.7)	0.012
Continued use despite consequences	13 (3.5)	57 (10.3)	< 0.001
Interference with role obligations	5 (1.3)	48 (8.6)	< 0.001
Interpersonal problems	9 (2.4)	27 (4.8)	0.062
Hazardous situations	46 (12.4)	112 (20.1)	0.002
Gave up activities	6 (1.6)	45 (8.1)	< 0.001
Any CUD symptom	194 (51.7)	341 (61.1)	0.005
DSM-5 CUD Category			
No CUD (0 to 1 symptom)	278 (74.1)	317 (56.8)	< 0.001
Mild CUD (2 to 3 symptoms)	75 (20)	124 (22.2)	
Moderate CUD (4 to 5 symptoms)	19 (5.1)	63 (11.3)	
Severe CUD (6+ symptoms)	3 (0.8)	54 (9.7)	

^{*}Other than pain, reasons for cannabis use assessed include muscle spasm, seizures, nausea or vomiting, sleep, stress, appetite, worry or anxiety, depression or sadness, focus or concentration, other symptoms, none.

CUD symptoms, it is conceivable that pain requires more frequent dosing of cannabis, that people with pain may use other substances in addition to cannabis for pain, and that they are less likely to report or develop CUD symptoms due to use for pain.

Our findings highlight the need for effectiveness and safety studies of the risks, benefits, and helpfulness of ingested cannabis, given the prevalence of this mode of use for pain and lack of evidence on its safety. This is particularly important given the higher age, comorbidity prevalence, and frequency of use among patients who use cannabis for pain in our study. Further etiologic, epidemiologic, and intervention research on cannabis and tobacco and nicotine product use is also needed. Studies have noted a potential causative role of tobacco in the etiology of painful conditions³⁹ and possible analgesic effects of nicotine. 40 Improved understanding of the interactive effects of tobacco and cannabis use on health could advance the field. Although patients generally perceive cannabis as helpful, 41,42 research into perceived helpfulness by pain type and mode

and frequency of use could generate hypotheses for formal effectiveness studies, and identify areas for safety research.

This study has several limitations, including the inability to infer causation due to the cross-sectional design. For some comparisons, stratification by mode of use within the 933 participants compared in the primary analysis resulted in limited statistical power. Although cannabis potency may influence patterns and health effects of use, we could not reliably assess potency or the THC and CBD content of cannabis used with this survey design. Although patients were assured of confidentiality, some nonresponse could be attributed to patients not wanting to disclose aspects of their cannabis use on a survey. Depending on participant responses, the number of survey questions ranged from 2 to 75, with more questions potentially influencing completion rate. However, we observed limited item nonresponse. Although survey questions were developed through expert consensus and pretested, it is possible that interpretations of cannabis use

[†]P value obtained using Fisher's exact test.

Table 5. Past 30-Day Helpfulness of Cannabis among Survey Participants Who Used Cannabis for Pain, by Mode and Frequency of Use and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) Cannabis **Use Disorder (CUD) Category**

	Slightly/somewhat $(n = 73)$	Very/extremely $(n = 302)$	
Past 30-day helpfulness of cannabis	n (%)	n (%)	P value
Primary mode of use endorsed*			
Smoke	24 (33.3)	140 (46.8)	0.028^{\dagger}
Apply	17 (23.6)	38 (12.7)	
Eat	8 (11.1)	40 (13.4)	
Vape	10 (13.9)	47 (15.7)	
Drink	8 (11.1)	10 (3.3)	
Dab	4 (5.6)	16 (5.4)	
Other	1 (1.4)	8 (2.7)	
Typical times per day, considering all modes of use*			
<1	3 (4.2)	4 (1.3)	0.054^{\dagger}
1 to 2	44 (61.1)	144 (48.2)	
3 to 4	16 (22.2)	87 (29.1)	
5 to 9	5 (6.9)	48 (16.1)	
10+	4 (5.6)	16 (5.4)	
Typical days per week, considering all modes of use*			
<1	8 (11.0)	9 (3.0)	< 0.001
1 to 3	19 (26.0)	33 (11.0)	
4 to 7	46 (63.0)	259 (86.0)	
DSM-5 CUD Category			
No CUD (0 to 1 symptom)	61 (83.6)	217 (71.9)	0.052^{\dagger}
Mild CUD (2 to 3 symptoms)	12 (16.4)	63 (20.9)	
Moderate CUD (4 to 5 symptoms)	0 (0.0)	19 (6.3)	
Severe CUD (6+ symptoms)	0 (0.0)	3 (1.0)	

^{*}Column sums for this variable may not total 73 for slightly/somewhat or 302 for very/extremely due to missing responses.

for pain varied across participants with different behavioral and lifestyle characteristics. Although a 34% response rate is consistent with health survey research, 43,44 nonresponse may limit the external validity of our findings. Oversampling patients from minoritized racial and ethnic groups and with more frequent cannabis use allowed us to obtain perspectives from important subgroups, but may limit generalizability to primary care populations. Furthermore, this study was conducted in an integrated health system in a state with legal cannabis use; findings may not extrapolate to other health systems and settings.

In conclusion, in a state with legal cannabis use, primary care patients who used cannabis for pain used cannabis through different modes and more frequently than patients who used cannabis for other reasons. These use patterns and patient perceptions should inform clinician and patient discussions and

future effectiveness and safety studies about cannabis use for pain.

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Appendix.

Appendix Table 1. Cannabis Use Survey Items

TD C	1 1	11 1 6 1	c	/ 1 •			. 1	1 * . * . 1	. 20 1
Reasons for a	ind modes an	id helnfiilness	of mariillai	na/cannahis	use among surve	v narticina	ints who lise	1 if in the i	nast 301 davs
recusons for a	illa illoacs al	a neipiames	or marijua.	iiii cuiiiiiiiiiii	ase annong saire	y participa	iiico wiio asci	a it iii tiit	puse so duys

1. When you used marijuana/cannabis during the past 30 days, was it:	For medical reasons
· · · · · · · · · · · · · · · · · · ·	For non-medical reasons
	Both medical and non-medical reasons
2. During the past 30 days, how did you use marijuana/cannabis? (Select all that apply.)	Smoke it (for example, in a joint, bong, blunt, spliff or pipe)
	Vaporize it (for example, hash oil in an e- cigarette-like vaporizer, vape pen or anothe vaporizing device)
	Dab it (for example, using waxes or concentrates in a dab rig or other dabbing device)
	Eat it (for example, in brownies, cakes, cookies or candy)
	Drink it (for example, in a tincture, tea, cola, o alcohol)
	Apply it to skin (for example, lotion, ointment patch, or salve)
	Use it some other way (please list):
3. During the past 30 days, how did you use marijuana/cannabis most often?	AUTOFILL modes of use [smoke/vaporize/dab/eat/drink/apply/use it some other way] selected:
	□ ···
	□ □
	□ ····
	[LOGIC RULE: Allow one checked reason]
4. During the past 30 days, have you used marijuana/cannabis to help you	[yes/no] Pain
manage any of the following: (Select all that apply.)	[yes/no] Muscle spasm
	[yes/no] Seizures
	[yes/no] Nausea or vomiting
	[yes/no] Sleep
	[yes/no] Stress
	[yes/no] Appetite
	[yes/no] Worry or anxiety
	[yes/no] Depression or sadness
	[yes/no] Focus or concentration
	Other symptoms (please specify):
	None of the above
5. Please check the <u>reason</u> you used marijuana/cannabis <u>most often</u> during the <u>past 30 days</u> .	AUTOFILL reasons checked (in previous question):
	□
	□ □
	[LOGIC RULE: Allow one checked reason]
6. During the past 30 days, how helpful has marijuana/cannabis been for	Extremely helpful
[reason used most often during the past 30 days]?	Very helpful
	Somewhat helpful
	Slightly helpful
	Not at all helpful
	[LOGIC RULE: SKIP if no reason for use
	selected]

Typical marijuana/cannabis use among survey participants who used marijuana/cannabis in the past 30 days, by ways they used it

These next questions ask about your typical marijuana/cannabis use. You said that in the past 30 days, you used marijuana/cannabis in the following way(s):

[AUTOFILLED for questions if 'Smoke it', 'Vaporize it', 'Dab it', 'Eat it', 'Drink it', 'Apply it to skin', 'Use it some other way' endorsed]

7. How many days per week do you typically [smoke/vaporize/dab/eat/	Less than 1
drink/apply it/use marijuana/cannabis in another way]?	1
	2
	3
	4
	5
	6
	7
8. On a typical day that you [smoke/vaporize/dab/eat/drink/apply	Less than 1
marijuana/cannabis/use marijuana/cannabis in another way],	1 to 2
how many times per day do you [smoke/vaporize/dab/eat/drink/apply/use] it?	3 to 4
apply, asof its	5 to 9
	10 to 14
	15 to 19
	20 or more
[AUTOFILLED for questions if ≥ 2 modes of use selected]	
Now consider all the ways you use marijuana/cannabis	
9. How many days per week do you typically use any marijuana/cannabis?	Less than 1
	1
	2
	3
	4
	5
	6
	7
10. On a typical day that you use any marijuana/cannabis,	Less than 1
how many times per day do you use it?	1 to 2
	3 to 4
	5 to 9
	10 to 14
	15 to 19
	20 or more
Symptoms of cannabis use disorder in the past year	

11. In the past year, did you ever need larger amounts of marijuana/	Ye

cannabis to get an effect, or did you ever find that you could no longer get high on the amount you used to use?	No
12. Was there ever a time in the past year when you stopped, cut down, or went without using marijuana/cannabis and then experienced withdrawal symptoms?	Yes No
Withdrawal symptoms can include cravings for marijuana/cannabis, irritability, restlessness, anxiety, depression and other mood changes, sleeplessness, sweating, appetite loss, and headaches.	
13. Was there ever a time in the past year when you used marijuana/cannabis to keep from having withdrawal symptoms?	Yes
Withdrawal symptoms can include cravings for marijuana/cannabis, irritability, restlessness, anxiety, depression and other mood changes, sleeplessness, sweating, appetite loss, and headaches.	No
14. Were there times in the past year when you tried to stop or cut down on your use of marijuana/cannabis and found that you	Yes

were not able to do so?

No

Symptoms of cannabis use disorder in the past year, continued		
15. Was there ever a time in the past year when you often had such a strong desire to use marijua stop using or found it difficult to think of anything else?	na/cannabis that you couldn't	Yes No
16. Did you ever have times in the past year when you used marijuana/cannabis even though you used a lot more than you intended?	planned not to or when you	Yes No
17. Were there times in the past year when you used marijuana/cannabis more frequently or for intended?	nore days in a row than you	Yes No
18. In the past year, did you ever have several days or more when you spent so much time using of marijuana/cannabis use that you had little time for anything else?	or getting over the effects of	Yes No
19. In the past year, did you ever continue to use marijuana/cannabis when you knew you had a so problem that might have been caused by or made worse by using marijuana/cannabis?	erious physical or emotional	Yes No
20. Was there ever a time in the past year when your use of marijuana/cannabis frequently interfer responsibilities at school, on a job, or at home?	ered with your work or	Yes No
21. Was there ever a time in the past year when your use of marijuana/cannabis caused argument problems with your family, friends, neighbors, or co-workers?	s or other serious or repeated	Yes No
22. Did you continue to use marijuana/cannabis even though it caused problems with these people	le?	Yes
23. Were there times in the past year when you were often under the influence of marijuana/canr could have gotten hurt – for example when riding a bicycle, driving, operating a machine, or	nabis in situations where you anything else?	No Yes No
24. <u>In the past year</u> , were there times when you experienced strong desires or cravings to use mar	ijuana/cannabis?	Yes No
25. In the past year, was there ever a time when you gave up or greatly reduced important activitic cannabis use – for example, sports, work, or seeing friends and family?	es because of your marijuana/	Yes No
Tobacco/nicotine product use, employment, and education		
26. Have you ever smoked at least 100 cigarettes in your entire life?	Yes	
	No	
	Don't know	
If Yes: Do you now smoke cigarettes?	Every day	
	Some days	
	Not at all/never	
	Don't know	
27. Have you ever used an e-cigarette or other electronic vaping product for tobacco/nicotine,	Yes	
even just one time, in your entire life?	No	
	Don't know	
If Yes: Do you now use e-cigarettes or other electronic 'vaping' products for	Every day	
tobacco/nicotine?	Some days	
	Not at all/never	
	Don't know	
28. What best describes your current employment? Please check the best response.	Employed full time (includes self-employed)	s
	Employed part time (include self-employed)	
	In school or vocational train Retired	ing
	Home maker	
	Unemployed, laid-off or loo for work	king
	Disabled or unable to work the health reasons	for
	Other [SPECIFY:]	

Tobacco/nicotine product use, employment, and education, continued				
29. What is the highest grade or level of school that you completed?	8 th grade or less Some high school, but not a graduate High school graduate or GED Some college or 2-year degree 4-year college degree More than 4-year college degree			

Appendix Table 2. Sociodemographic Characteristics of Survey Participants Who Used Cannabis for Pain, for Pain - Secondary, and for Other Reasons in the Past 30 Days

	Used cannabis for pain $(n = 375)$	Used cannabis for pain– secondary ($n = 536$)	Used cannabis for other reasons* (n = 558)	
	n (%)	n (%)	n (%)	P value
Age at cannabis screen				
18 to 29	43 (11.5)	184 (34.3)	177 (31.7)	< 0.001
30 to 49	116 (30.9)	198 (36.9)	204 (36.6)	
50+	216 (57.6)	154 (28.7)	177 (31.7)	
Gender				
Woman	197 (52.5)	306 (57.1)	249 (44.6)	< 0.001
Man	178 (47.5)	230 (42.9)	309 (55.4)	
Race				
American Indian/Alaska Native	16 (4.3)	11 (2.1)	7 (1.3)	0.183
Asian	13 (3.5)	31 (5.8)	34 (6.1)	
Black/African American	34 (9.1)	61 (11.4)	50 (9.0)	
Native Hawaiian or Other Pacific Islander	9 (2.4)	9 (1.7)	11 (2.0)	
White	271 (72.3)	370 (69)	399 (71.5)	
Other	17 (4.5)	26 (4.9)	29 (5.2)	
Unknown	15 (4.0)	28 (5.2)	28 (5.0)	
Ethnicity				
Hispanic/Latino	32 (8.5)	57 (10.6)	63 (11.3)	0.234
Not Hispanic/Latino	330 (88.0)	452 (84.3)	461 (82.6)	
Unknown	13 (3.5)	27 (5.0)	34 (6.1)	
Employment status [†]				
Full time	175 (46.7)	335 (62.9)	355 (63.6)	< 0.001
Part time	25 (6.7)	49 (9.2)	51 (9.1)	
School/vocational	4 (1.1)	15 (2.8)	25 (4.5)	
Retired	98 (26.1)	74 (13.9)	77 (13.8)	
Homemaker	9 (2.4)	11 (2.1)	12 (2.2)	
Unemployed	13 (3.5)	23 (4.3)	18 (3.2)	
Disabled	46 (12.3)	15 (2.8)	8 (1.4)	
Other	5 (1.3)	11 (2.1)	10 (1.8)	
Education [†]				
>4-year college degree	60 (16.1)	68 (12.8)	126 (22.7)	< 0.001
4-year college degree	57 (15.3)	120 (22.6)	158 (28.5)	
Some college	162 (43.4)	238 (44.7)	186 (33.5)	
HS/GED or less	94 (25.2)	106 (19.9)	85 (15.3)	

^{*}Other than pain, reasons for cannabis use assessed include muscle spasm, seizures, nausea or vomiting, sleep, stress, appetite, worry or anxiety, depression or sadness, focus or concentration, other symptoms, none.

[†]Column sums for this variable may not total 375 for used cannabis for pain, 536 for used cannabis for pain - secondary, or 558 for used cannabis for other reasons due to missing responses.

Appendix Table 3. Sensitivity Analysis of Past-Year Experience of Cannabis Use Disorder (CUD) Symptoms and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) CUD Category Among Survey Participants Who Used Cannabis for Pain and Who Used Cannabis for Other Reasons in the Past 30 Days, Excluding Participants Who Apply Cannabis Only (n = 21)

	Used cannabis for pain $(n = 354)$	Used cannabis for other reasons* $(n = 558)$	P value
	n (%)	n (%)	
Individual CUD Symptoms			
Tolerance	57 (16.5)	149 (26.8)	< 0.001
Withdrawal	45 (12.8)	118 (21.3)	0.001
Failed attempts to cut down	12 (3.4)	62 (11.2)	< 0.001
Craving	84 (23.9)	181 (32.8)	0.004
Uncontrolled escalation of use	97 (27.5)	219 (39.3)	< 0.001
Time spent	6 (1.7)	26 (4.7)	0.018
Continued use despite consequences	13 (3.7)	57 (10.3)	< 0.001
Interference with role obligations	5 (1.4)	48 (8.6)	< 0.001
Interpersonal problems	9 (2.6)	27 (4.8)	0.086
Hazardous situations	46 (13.1)	112 (20.1)	< 0.001
Gave up activities	6 (1.7)	45 (8.1)	< 0.001
Any CUD symptom	194 (54.8)	341 (61.1)	0.059
DSM-5 CUD Category			
No CUD (0 to 1 symptom)	257 (72.6)	317 (56.8)	<0.001
Mild CUD (2 to 3 symptoms)	75 (21.2)	124 (22.2)	
Moderate CUD (4 to 5 symptoms)	19 (5.4)	63 (11.3)	
Severe CUD (6+ symptoms)	3 (0.8)	54 (9.7)	

^{*}Other than pain, reasons for cannabis use assessed include muscle spasm, seizures, nausea or vomiting, sleep, stress, appetite, worry or anxiety, depression or sadness, focus or concentration, other symptoms, none.

[†]P value obtained using Fisher's exact test.

Appendix Table 4. Adjusted Analysis*

	Used cannabis for pain		Used cannabis for other reasons		Comparison of pain groups		
Outcome 1: Most Com	non Mode of Use						
	Adjusted %	(95% CI)	Adjusted %	(95% CI)	RRR [†]	(95% CI)	P value
Inhale	63.9	(59.2 to 68.7)	82.7	(79.6 to 85.7)	REF		
Apply	15.6	(11.6 to 19.6)	0.3	(-0.1-0.8)	109.5	(21.3 to 562.9)	< 0.001
Ingest	18.2	(14.1 to 22.2)	15.3	(12.4 to 18.2)	2.0	(1.3-3.1)	0.003
Other	2.3	(0.7-3.9)	1.7	(0.6–2.9)	2.1	(0.7-6.4)	0.170
Outcome 2: Typical Tir	nes per Day						
	Adjusted %	(95% CI)	Adjusted %	(95% CI)	RR^{\ddagger}	(95% CI)	P value
>2 Times per day	46.4	(41.5 to 51.2)	33.4	(29.8 to 37.1)	1.4	(1.2–1.6)	<0.001
Outcome 3: Typical Day	ys per Week						
	Adjusted %	(95% CI)	Adjusted %	(95% CI)	RR [‡]	(95% CI)	P value
4 to 7 Days per week	77.8	(73.6 to 82)	71.4	(67.8 to 74.9)	1.1	(1.0 to 1.2)	0.025

^{*}Adjusted for age, gender, race/ethnicity, employment status, education, and other cannabis outcomes (i.e., most common mode of use is adjusted for typical times per day and typical days per week, typical times per day is adjusted for typical days per week and modes of use, and typical days per week is adjusted for typical times per day and modes of use).

[†]Relative risk ratio estimated using a multinomial logistic regression model.

[‡]Relative risk estimated using a modified Poisson regression model.

Abbreviation: CI, confidence interval.