HHS Public Access

Author manuscript

Gen Hosp Psychiatry. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

Gen Hosp Psychiatry. 2018 ; 50: 104–110. doi:10.1016/j.genhosppsych.2017.11.001.

Patterns and correlates of medical cannabis use for pain among patients prescribed long-term opioid therapy

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Abstract

Objective—Little is known about co-occurring long-term opioid therapy (LTOT) and medical cannabis use. We compared characteristics of patients prescribed LTOT who endorsed using medical cannabis for pain to patients who did not report cannabis use.

Method—Participants (n=371) prescribed LTOT completed self-report measures about pain, substance use, and mental health.

Results—Eighteen percent of participants endorsed using medical cannabis for pain. No significant differences were detected on pain-related variables, depression, or anxiety between those who endorsed medical cannabis use and those who did not. Medical cannabis users had higher scores of risk for prescription opioid misuse (median=17.0 vs. 11.5, $p<0.001$), rates of hazardous alcohol use (25% vs. 16%, $p<0.05$), and rates of nicotine use (42% vs. 26%, $p=0.01$). Multivariable analyses indicated that medical cannabis use was significantly associated with risk of prescription opioid misuse ($\beta=0.17$, $p=0.001$), but not hazardous alcohol use (aOR=1.96, 95% CI=0.96–4.00, $p=0.06$) or nicotine use (aOR=1.61, 95% CI=0.90–2.88, $p=0.11$).

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Conflicts of Interest: All other authors declare that they have no conflicts of interest.

Contributors: Drs. Morasco, Dobscha, Deyo, Yarborough, and Green collaborated in designing the research study. Drs. Nugent, Smith, and Morasco completed the statistical analyses and Drs. Nugent and Morasco wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conclusion—There are potential risks associated with co-occurring LTOT and medical cannabis for pain. Study findings highlight the need for further clinical evaluation in this population. Future research is needed to examine the longitudinal impact of medical cannabis use on pain-related and substance use outcomes.

Keywords

chronic pain; medical cannabis; long term-opioid therapy; prescription opioid misuse

INTRODUCTION

Approximately 30% of Americans may experience chronic pain [1], a figure that is estimated to increase as the population ages and acquires more chronic medical conditions [2]. Prescription opioid medications are commonly prescribed for chronic pain [3]; however, the benefits of long term opioid therapy (LTOT) remain unclear [4]. Furthermore, long-term opioid use is associated with adverse effects such as cardiovascular events, motor vehicle accidents, opioid use disorder, and overdose [5]. As a result, patients may seek alternative or adjunctive ways to treat their pain, including medical cannabis.

Currently, 28 U.S. states, Puerto Rico, and Washington D.C. have legalized medical cannabis, and eight states have legalized recreational cannabis [6]. While the evidence supporting the effectiveness of cannabis remains equivocal for most chronic pain conditions [7], recent studies suggest that among individuals who receive medical cannabis, 45–80% seek cannabis for pain management [8, 9]. Among patients prescribed opioid medications for the treatment of chronic pain, up to 39% report co-occurring use of cannabis [10, 11].

One prior study compared the clinical characteristics of patients with co-occurring prescription opioid therapy and medical cannabis to characteristics of those not using medical cannabis, and found that medical cannabis users had higher pain intensity, higher pain interference, and more symptoms of depression and anxiety than non-users [10]. Available evidence also suggests that among patients with chronic non-cancer pain, cannabis users are more likely to report recent non-cannabis substance use [9, 12] and are more likely to have a history of a substance use disorder (SUD) diagnosis [13, 9], and have higher rates of aberrant opioid related behaviors including more frequent refills [8, 9]. The most commonly documented SUD diagnosis is alcohol use disorder (AUD), which has an estimated lifetime prevalence of 55% in cannabis users compared to 26% in non-users [9]. The simultaneous use of alcohol and other substances with prescription opioids has been linked to serious adverse events including respiratory depression, risk of overdose, and unintentional death [14] suggesting that medical cannabis users, who also drink alcohol, may be at greater risk for the negative consequences associated with opioids.

Overall, there is a paucity of research about patients with chronic pain who are prescribed LTOT and use medical cannabis for adjunctive pain treatment. In addition, there are limited data on the association between cannabis and the use of other substances among patients prescribed LTOT. Yet, these relationships are important to understand given the documented risks that are associated with non-cannabis substance use, alcohol, and prescription opioids. The present study expands the current literature by describing the pain, substance use, and

mental health related characteristics and adverse events among patients diagnosed with musculoskeletal pain who are prescribed LTOT and are also using medical cannabis. Based on the current literature, we hypothesized that individuals who endorsed medical cannabis use would have higher pain intensity and interference, and more symptoms of anxiety and depression. Furthermore, we hypothesized that endorsement of medical cannabis use would be positively associated with the presence of current hazardous alcohol use, nicotine use, and increased risk of prescription opioid misuse while controlling for demographic and clinical factors.

METHODS

2.1 Settings

The present manuscript focuses on baseline data from an ongoing, multisite prospective cohort study of patients prescribed LTOT; a more detailed description of the research methods has been previously described [15]. Study settings included Kaiser Permanente Northwest (KPNW) and VA Portland Health Care System (VAPORHCS). Both facilities maintain a full range of medical, mental health and addiction treatment, and provide patient care services in Oregon and SW Washington. At the time data were collected, medical cannabis was legal in Oregon, and recreational and medical cannabis was legal in Washington.

2.2 Participants

Participants were eligible for inclusion if they had a musculoskeletal pain diagnosis documented in their medical records. Participants must also have been receiving a stable dose of prescription opioid therapy for at least 90 consecutive days. Prior studies have defined 90+ days of consecutive opioid use as being indicative of LTOT [16]. Participants were excluded if they endorsed pending litigation or disability claim related to a pain condition (n = 37), received a cancer diagnosis in the last 12 months (n = 10), were enrolled in an opioid substitution program in the last 12 months (n = 1), were in the process of leaving the integrated health care system (n = 26) or whose only opioid prescriptions were for tramadol or buprenorphine (n = 11). Participants who had a current opioid dose greater than 120 mg morphine equivalent (n = 8) were also excluded because our overall study [15] is focused on examining outcomes from prescription opioid dose escalation; one of the sites included in this study had an institutional policy limiting opioid doses above a certain threshold, which would have led to potential site specific differences related to allowable opioid dose. Of the 517 participants who enrolled and completed study measures, 146 were excluded from the primary analyses because they denied use of medical cannabis, yet had a score of one or greater on the Drug Abuse Screening Test- 10 (DAST-10), indicating a potential problem with illicit substance use (DAST-10 measure described more below). We excluded these individuals from the analyses because it was unclear whether they were endorsing a potential problem with use of recreational cannabis or with use of another substance, which would complicate interpretation of analyses. These 146 individuals were included in sensitivity analyses (described more below) to ensure that their exclusion did not significantly alter study findings.

2.3 Study Procedures

Using administrative databases at both clinical sites, we identified potential study participants on the basis of their past-year ICD-9-CM musculoskeletal pain diagnoses and current prescription opioid use. A personalized invitation letter that provided study details, contact information, and a prepaid postcard to indicate interest in participating or to decline further contact was sent to each potential participant. Follow-up phone calls were conducted by study staff who provided additional details, answered questions, and conducted a brief screening. Individuals who met preliminary inclusion/exclusion criteria and indicated interest in participating were scheduled for their baseline assessment.

All study procedures were reviewed, approved, and monitored by the Institutional Review Boards of the involved institutions. All participants signed informed consent to participate. Participants were compensated with a store $50 gift card for participating.

2.4 Measures

Self-report measures—Basic demographic characteristics that were assessed included age, gender, race, marital status, employment, and socioeconomic status.

Use of medical cannabis for treatment of pain was assessed using two single-item Likert scale questions which inquired about the frequency of medical cannabis use for pain in the past month, and participants' perception of the extent to which cannabis was helpful in providing pain reduction (where 1 = not helpful and 5 = very helpful). We defined the endorsement of medical cannabis use for pain as "medical cannabis use," and refer to it as such throughout the present manuscript. Participants were also asked if they possessed a current state-issued medical cannabis card.

The Chronic Pain Grade (CPG) questionnaire is a well-validated measure that was used to assess pain intensity and pain-related function [17, 18]. Pain intensity is calculated by the mean intensity ratings for reported current, worst, and average pain within the past three months. Pain-related disability is the mean rating for responses to questions about difficulty performing daily, social, or work related tasks. Scores on these two subscales range from 0–100, where higher scores reflect higher pain intensity/disability.

Quality of life was measured with the Short-Form Health Survey, Version 2, a 12-item, well-validated self-report measure that provides subscale scores on physical and mental health functioning; higher scores are associated with better functioning [SF-12v2; 19]. The Patient Health Questionnaire (PHQ) was used to assess depressive symptoms [20]. The PHQ is a brief, reliable, and psychometrically valid measure used to screen for depressive symptoms [20, 21]. In this study, we administered the PHQ-8, which excludes a question assessing current suicidal ideation [22]. Anxiety symptoms were assessed using the Generalized Anxiety Disorder-7 Scale (GAD-7), a brief self-report measure designed to assess the severity of anxiety symptoms that has been validated as a robust predictor of the different anxiety disorders [23, 24]

With regard to substance use, the 3-item Alcohol Use Disorder Identification Test [AUDIT-C; 25]; was used to screen for the presence of current hazardous alcohol use. In this study,

the presence of current hazardous alcohol use was indicated by scores of ≥ 4 for men and ≥ 3 for women [26, 27]. The Drug Abuse Screening Test-10 [DAST-10; 28] is a 10-item measure used to assess abuse of illicit substances. A potential active SUD was defined as a DAST-10 score ≥ 2 [29]. Nicotine dependence was assessed using a single item from the Fagerstrom Test of Nicotine Dependence [30] which asks: "How soon after waking do you first use nicotine?" (Less than 30 min. / 30 min. or more); endorsement of nicotine use less than 30 minutes upon waking is associated with greater nicotine dependence [31]. The Pain Medication Questionnaire (PMQ) is a self-report measure designed to assess beliefs and behaviors related to the risk of misuse of prescription opioid medications [32]. Studies of the PMQ have demonstrated that it has strong psychometric properties [32, 33]. We administered a 23-item version; higher PMQ scores reflect greater risk for misuse of prescription opioids. Pain medication treatment side effects were measured by the side effects subscale of the Pain Treatment Satisfaction Scale [PTSS; 35]. Scores on the PTSS range from 0–100, where a higher score means a patient is bothered by fewer medication-related side effects. Finally, we inquired about the occurrence of falls and opioid overdose.

EMR-derived variables—Prescription opioid status, including length of opioid prescription and dose, was extracted from the pharmacy data. Clinical diagnostic data on pain-related diagnoses were also extracted from the medical record. Participants were considered to have a diagnosis if it was given in one of the two clinical settings one or more times in the prior year. We measured overall medical comorbidity using the Selim index, a validated method for assessing medical comorbidity, using 31 chronic physical and six psychiatric diagnoses [36, 37]. Selim scores range from 0–37, with higher scores indicating greater medical comorbidity.

2.5 Data Analysis

Descriptive data were summarized for demographic variables, pain-related variables, and scores on self-report measures comparing subjects who endorsed using medical cannabis adjunctively to treat pain and those who did not. Bivariate analyses were conducted using t-tests when the data were normally distributed and the non-parametric Mann-Whitney U test when the data were non-normally distributed. Categorical variables were compared using Chi-square test when the expected value of each cell was five or higher, and Fisher's exact test when that assumption was violated. Unadjusted and adjusted logistic regression models were conducted to examine the association between medical cannabis use and 1) hazardous alcohol use and 2) nicotine use. Adjusted models included demographic (age, gender) and clinical (depression, pain intensity, opioid dose, and medical comorbidity index) covariates. Next, a linear regression model, adjusting for the same covariates, examined the relationship between medical cannabis use and the risk of prescription opioid misuse. The control variables were included in the regression models because they have been previously associated with the substance use [13, 10, 38, 39]. We also conducted sensitivity analyses for the bivariate comparisons and the logistic regression analysis. These sensitivity analyses included the 146 individuals, who were excluded from the primary analyses because they denied medical cannabis use yet had a score of one or greater on the DAST. We characterized this group as non-cannabis users. Inferential analyses used two-sided tests and

the alpha level was set at 0.05. Data analysis was conducted using SPSS version 22 and SAS version 9.4.

RESULTS

Among participants (n = 371), 18% (n = 67) endorsed using medical cannabis for pain within the last month. The majority of cannabis users (60%; n = 40) reported using cannabis for pain two or more times per week, and 66% (n = 44) of cannabis users rated medical cannabis as at least moderately helpful in reducing pain (Table 1). Among those who endorsed cannabis use, 31% (n = 21) possessed a current state-issued medical cannabis card.

An overview of demographic characteristics including comparisons between those who endorsed medical cannabis use and those who did not is provided in Table 2. Participants who endorsed medical cannabis use were more likely to be male (81% vs. 48%), have an annual income below $30,000 (46% vs. 25%), and less likely to be Caucasian (70% vs. 86%) (all *p*-values < 0.05). Age, education, and employment status were not significantly different between groups.

The most common pain-related diagnosis was arthritis (63%). There were no between group differences detected for pain diagnoses among those who endorsed medical cannabis and those who did not (Table 2). Furthermore, there were no significant group differences detected on pain intensity score (median = 66.7 vs. 63.3, $p = 0.46$) or pain-related disability score between users and non-users (median = 53.3 vs. 50.0, $p = 0.58$). There were no significant differences between groups on current prescription opioid dose (median = 30.0 vs. 30.0, $p = 0.45$). Finally, no group differences were detected on mental health (depression and anxiety) or quality of life variables based on endorsement of medical cannabis use (all *p*-values > 0.05; see Table 2).

Individuals who endorsed current medical cannabis use had significantly higher scores of risk for prescription opioid misuse (median = 17.0 vs. 11.5, $p < 0.0001$). Those who endorsed use of medical cannabis were more likely to meet criteria for current hazardous alcohol use (25% vs. 16%, $p = 0.024$) and were more likely to report using nicotine, compared with individuals who denied use of medical cannabis (42% vs. 26%, $p = 0.01$). Within the subset of participants who reported nicotine use, participants who also used medical cannabis smoked significantly more cigarettes per day (median number of cigarettes = 16.8 vs. 10.0, $p = 0.03$) and were more likely to smoke within 30 minutes of waking (61% vs. 39%, $p = 0.03$).

On a scale assessing medication-related side effects, those who endorsed medical cannabis reported less impairment from side effects than participants who denied use of medical cannabis (median score = 88.0 vs. 92.0, $p = 0.04$). Eighteen percent of participants who endorsed medical cannabis use reported having a fall within the past three months, compared with 29% of non-users, though this difference was not statistically significant ($p = 0.07$). There were no between group differences detected on the frequency of opioid overdoses in the past three months.

A linear regression model that examined the association between medical cannabis use and risk of prescription opioid misuse, and adjusted for age, gender, prescription opioid dose, medical comorbidity, symptoms of depression, and pain intensity, revealed that medical cannabis use was positively associated with risk of prescription opioid use ($\beta = 0.17$, $p = 0.001$) (Table 3). The overall model also explained a significant proportion of the variance (21%) in risk for prescription opioid misuse scores (adjusted $R^2 = 0.21$, $F(7, 363) = 14.59$, $p < 0.001$). Individual predictors that were also significantly associated with increased risk of prescription opioid misuse in the model included male gender ($\beta = 0.13$, $p = 0.009$), higher medical comorbidity ($\beta = 0.16$, $p = 0.003$), younger age ($\beta = -0.11$, p = 0.031), more symptoms of depression ($\beta = 0.22$, $p = <0.001$), and higher pain intensity ($\beta = 0.16$, $p = 0.002$).

Table 4 provides results of the unadjusted and adjusted logistic regression analyses that examined the association between medical cannabis use and 1) current hazardous alcohol use and 2) nicotine use. The adjusted models included the same covariates as the linear regression. In the adjusted model that examined the relationship between medical cannabis use and current hazardous alcohol use, results revealed that medical cannabis use was not associated with current hazardous alcohol use (aOR = 1.96, 95% CI = 0.96 – 4.00, $p = 0.06$). Female gender (aOR = 0.48, 95% CI = 0.25 - 0.92, $p = 0.026$), the presence of more medical comorbidities (aOR = 0.86, 95% CI = 0.75 - 0.99, $p = 0.04$), and higher current prescription opioid dose (aOR = 0.97, 95% CI = 0.96 - 0.90, $p<0.001$) were all associated with a decreased likelihood of current hazardous alcohol use (Table 4). In the adjusted model that examined nicotine use, medical cannabis use was not significantly associated with increased nicotine use (aOR = 1.61, 95% CI = 0.90 – 2.88, $p = 0.11$); age was the only significant covariate in that model (aOR = 0.96, 95% = 0.94 – 0.99, $p = 0.001$).

Sensitivity analyses for all the bivariate comparisons, the linear regression model, and the logistic regression models were conducted that included the 146 individuals who were originally removed from the primary analyses (because they had scores ≥1 on the DAST-10 and denied current use of medical cannabis for pain). All analyses were conducted including these 146 individuals as non-medical cannabis users. When these participants were included with the larger group who denied current use of medical cannabis for pain, the direction and significance of the bivariate, logistic, and linear regression analyses were not significantly different than the results obtained in the primary analyses.

DISCUSSION

Within this sample of patients prescribed LTOT for chronic pain, 18% endorsed past-month medical cannabis use for pain. We found that patients prescribed LTOT who endorsed the use of medical cannabis for pain were at greater risk for prescription opioid misuse (median = 17.0 vs. 11.5), were more likely to have current hazardous alcohol use (25% vs. 16%), and were more likely to use nicotine (42% vs. 26%). While the difference in rates of nicotine use and alcohol use did not remain after adjusting for relevant sociodemographic and clinical variables, the association between medical cannabis us and risk for prescription opioid remained. Our finding related to risk of prescription opioid misuse is consistent with other data suggesting an association between cannabis use and risky non-cannabis substance-

related behavior, including risk of aberrant opioid behaviors [9, 10, 43, 44]. One possible mechanism for this relationship is that the use of cannabis has been associated with impaired judgement and increased impulsivity [45, 46], which could place individuals at risk for misusing other substances and/or misusing opioids after using cannabis. This is concerning given that the simultaneous use of alcohol and illicit substances with prescription opioids has been linked to serious adverse events including respiratory depression, risk of overdose, and unintentional death [14, 5].

Contrary to our hypotheses, we did not identify between group differences on clinical variables such as prescription opioid dose, pain intensity scores, pain-related function, or depression/anxiety severity, based on use of medical cannabis. While this finding contrasts with some prior literature [10], there exist differences in the study methodology and study settings that may contribute to the discrepant findings. Notably, relative to prior research, there were differences in the legal status of cannabis in the study locations, recruitment methodology, inclusion criteria for use of prescription opioid medications, and methods of cannabis use measurement. The present findings may contribute to literature suggesting a lack of significant pain-related differences between groups. Prospective research is needed to elucidate longitudinal group differences on pain and psychosocial outcomes among those who use medical cannabis and those who do not among various chronic pain populations.

Our findings also indicated differences between groups in opioid treatment-related side effects. Those who endorsed medical cannabis use had lower general medication-related side effects, and a non-significant trend for fewer self-reported rates of falls. The causality of these relationships are unclear due to the cross-sectional nature of the data, so additional longitudinal data are needed to clarify whether cannabis may alleviate medication side effects such as dizziness, or if patients who are having fewer side effects from opioid therapy may be more likely to seek adjunctive medical cannabis.

In addition to safety considerations, prior research has documented that co-occurring substance use and chronic pain have been linked to worse pain-related outcomes [47]. Substance use can also be difficult to treat in chronic pain populations, as it can be triggered by pain and/or used as an avoidant coping mechanism for pain [48]. An additionally challenging factor is that cannabis appears to be perceived as generally helpful for pain management among patients who use it [10] and is receiving national attention as such [49], despite insufficient evidence supporting its efficacy for most chronic pain conditions, including musculoskeletal pain [7, 40]. These factors present a complicated landscape that clinicians treating chronic pain must navigate. Clinical practice recommendations for the care of patients using cannabis as pain therapy have recently been published, which may help guide clinicians to assess for safety concerns and aberrant cannabis related behaviors [41]. These medical cannabis clinical recommendations coupled with the recently published guidelines for prescribing opioids for chronic pain [5] offer a framework from which clinicians can engage in a discussion about the co-occurring use of medical cannabis and opioid therapy.

Taken as a whole, our findings highlight the importance of screening, assessing, and continually monitoring patients prescribed LTOT for substance use (with an emphasis on

medical cannabis, prescription opioid misuse, nicotine use, and alcohol), adverse events, and pain related function at all follow-up visits. Among those who screen positive for cannabis and alcohol, or aberrant opioid behaviors, provision of additional services including integrated SUD treatment and alternative pain management treatment options may be beneficial [50, 51]. In addition, smoking cessation and nicotine replacement therapy interventions may be beneficial to address tobacco use and the associated long term health harms [52].

4.1 Limitations

There are several limitations that should be taken into consideration when interpreting the results of this study. First, the cross-sectional nature of the design impedes the ability to draw causal conclusions about the relationships tested. Second, the way we measured medical cannabis use was based on self-report response to three cannabis use related questions and we did not gather details about cannabis dose, route of administration, or prior history of cannabis use. Among our sample, there was a high degree of variability in the frequency of cannabis use (monthly vs. 4 or more times per week), yet all “medical cannabis users” were grouped together for the purposes of the analyses. Also, due to the wording “medical marijuana” in our survey, we may have missed individuals who were using recreational cannabis for reasons other than pain, though our goal was to understand correlates of medical cannabis use not recreational cannabis use. A third limitation was that our sample was comprised of individuals who were prescribed a stable dose of LTOT and who agreed to participate in the study, so our findings may not generalize to other patients who are prescribed opioids for musculoskeletal pain. Finally, we did not assess for all potential covariates in the multivariate analyses, such as history of trauma or suicidal ideation, and future research may examine additional variables that could be associated with substance use and long-term prescription opioid use.

4.2 Conclusions

In sum, findings from this study suggest that among patients who are prescribed LTOT, medical cannabis is perceived as helpful for pain reduction among the 18% who use it. Medical cannabis use appears to be related to higher risk for prescription opioid misuse and may be related to nicotine use and risky alcohol use. We did not identify significant between group differences on clinical variables such as prescription opioid dose, pain intensity scores, pain-related function, or depression/anxiety severity, based on use of medical cannabis. Given the potential risks associated with LTOT and substance use, continual monitoring, and specialized integrated interventions may be beneficial to those seeking or using medical cannabis in addition to LTOT. In addition, future research needs to examine the longitudinal impact of medical cannabis use on pain-related *outcomes including opioid dose and use, as well as the occurrence of adverse events among patients prescribed LTOT simultaneously using medical cannabis.*

Acknowledgments

This study was supported in part by award 034083 from the National Institute on Drug Abuse. The work was supported with resources and the use of facilities at the VA Health Services Research and Development-funded Center to Improve Veteran Involvement in Care at the VA Portland Health Care System (CIN 13-404). The content

of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs or the National Institute on Drug Abuse.

Role of Funding Source: Funding for this study was provided in part by grant 034083 from the National Institute on Drug Abuse, which had no further role in study design; in the collection, analysis or interpretation of data; in the writing of the manuscript; or in the decision to submit for publication.

Drs. Yarborough and Green have received research grant support from Purdue Pharma LP, and the Industry PMR Consortium, a consortium of 10 companies working together to conduct FDA-required post-marketing studies that assess known risks related to extended-release, long-acting opioid analgesics.

Abbreviations

LTOT	Long term opioid therapy
AUD	Alcohol use disorder
QOL	Quality of life
IQR	Interquartile range
SUD	Substance use disorder
MED	Morphine equivalent dose

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Table 1

Medical cannabis use among cohort.

Among medical cannabis users (n = 67)	**N (%)**
Frequency of use	
Once per month	11 (16)
2–4 times per month	16 (24)
2–3 times per week	10 (15)
4 or more times per week	30 (45)
Pain reduction utility	
1 = Not Helpful	5 (8)
2	3 (5)
3	14 (21)
4	16 (24)
5 = Very Helpful	28 (42)
Possession of a state issued medical cannabis card	21 (31)

Table 2

A comparison of demographic, clinical, and substance use variables based on cannabis use.

Characteristic	**Overall Sample (N = 371)**	**Cannabis Use**		***p*-value**
		No 85% (304)	**Yes 18% (67)**	
Demographic				
Age in years, mean (*SD*)	60.0 (11.0)	60.5 (11.2)	57.7 (9.6)	0.062
	%(n)	%(n)	%(n)	
Male	54 (201)	48 (147)	81 (54)	<0.0001
Caucasian	83 (309)	86 (262)	70 (47)	0.003
Married	58 (214)	59 (179)	52 (35)	0.654
Income < 30,000	29 (106)	25 (75)	46 (31)	0.002
Completed some college	74 (276)	74 (225)	61 (41)	0.404
Employment				0.074
Retired	38 (142)	40 (122)	30 (20)	
Working	33 (124)	34 (104)	30 (20)	
Clinical				
Arthritis	63 (235)	65 (198)	55 (37)	0.128
Back	59 (218)	58 (175)	64 (43)	0.320
Neck/joint	54 (202)	55 (167)	35 (52)	0.688
Median pain intensity (IQR)	63.3 (53.3–73.3)	63.3 (53.3–73.3)	66.7 (56.7–73.3)	0.459
Median pain disability (IQR)	50.0 (30.0–70.0)	50.0 (30.0–70.0)	53.3 (36.7–73.3)	0.576
Median opioid dose (MED mg/day; IQR)	30.0 (15.0–45.0)	30.0 (15.0–45.0)	30.0 (15.0–46.7)	0.450
Median Depression (IQR)	8.0 (5.0–13.0)	8.0 (5.0–13.0)	9.0 (5.0–15.0)	0.282
Comorbidity Index (IQR)	4.0 (3.0–6.0)	4.0 (3.0–6.0)	4.0 (3.0–6.0)	0.930
Median Anxiety (IQR)	5.0 (2.0–10.0)	5.0 (2.0–10.0)	6.0 (2.0–12.0)	0.368
Median QOL: Physical (IQR)	32.3 (25.7–40.2)	33.8 (26.7–41.1)	30.3 (23.3–36.5)	0.052
Median QOL: Mental (IQR)	52.3 (43.3–57.5)	52.4 (43.8–58.1)	52.1 (40.3–56.8)	0.345
Substance Use				
Current nicotine use, %(n)	29 (108)	26 (80)	42 (28)	0.012
Median number of cigarettes (IQR) *	10.0 (7–20)	10.0 (6–15)	16.8 (9–20)	0.027
Nicotine use less than 30 min. after waking, %(n) *	45 (48)	39 (31)	61 (17)	0.025
Current hazardous alcohol use, %(n)	16 (58)	50 (16)	17 (25)	0.024
Median risk for prescription opioid misuse (IQR)	12.0 (7.0–18.0)	11.5 (7.0–17.5)	17.0 (12.0–21.0)	<0.0001
Adverse Events				
Median pain treatment side effects (IQR)	92.0 (78.0–97.0)	92.0 (80.0–97.0)	88.0 (77.0–95.0)	0.035

Characteristic	**Overall Sample (N = 371)**	**Cannabis Use**		***p*-value**
		No 85% (304)	**Yes 18% (67)**	
Fall in the past 3 months, %(n)	27 (99)	29 (87)	18 (12)	0.073
Median number of falls in past 3 months (IQR) *	2.0 (1.0–3.0)	2.0 (1.0–3.0)	1.5 (1.0–2.0)	0.062
Opioid overdose, %(n)	0.5 (2)	0.3 (1)	1.5 (1)	0.329

Note. Scores on the continuous variables were compared using the non-parametric Mann-Whitney *U* and are represented by median and interquartile range (IQR). Categorical variables are represented by n (%). MED = Morphine Equivalent Dose; QOL = Quality of Life.

*Median (IQR) for number of cigarettes and percent of individuals who endorsed nicotine use within 30 minutes of waking only calculated for those who endorsed smoking. Median (IQR) for number of falls only calculated for those who endorsed falling.

Table 3

Linear regression analysis examining the association between medical cannabis use and risk of prescription opioid misuse.

	R^2	Unadjusted B (SE)	Adjusted β*	95% CI	*p*-value
Risk of prescription opioid misuse	0.21				
Age		− 0.07 (0.03)	−0.11	− 0.14 – − 0.01	0.031
Gender		1.89 (0.72)	0.13	0.47 – 3.31	0.009
Medical comorbidity		0.44 (0.14)	0.16	0.15 – 0.72	0.003
Depression		0.30 (0.07)	0.22	0.16 – 0.43	<0.001
Prescription opioid dose		− 0.01 (0.01)	−0.05	− 0.04 – 0.01	0.332
Pain intensity		0.08 (0.27)	0.16	0.03 – 0.14	0.002
Cannabis use		3.21 (0.94)	0.17	1.36 – 5.05	0.001

Note: Adjusted models controlled for age, gender, depression, pain intensity, prescription opioid dose, and medical comorbidity score.

Table 4

Logistic regression analyses examining variables associated between medical cannabis use, current hazardous alcohol, and nicotine use.

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Hazardous alcohol use		
Age	0.98 (0.96 – 1.01)	1.00 (0.97 – 1.03)
Female gender	0.52 (0.29 – 0.94) *	0.48 (0.25 – 0.92) *
Medical comorbidity	0.85 (0.75 – 0.96) **	0.86 (0.75 – 0.99) *
Depression	0.97 (0.92 – 1.02)	1.00 (0.97 – 1.03)
Prescription opioid dose	0.97 (0.96 – 0.99) ***	0.97 (0.96 – 0.99) ***
Pain intensity	0.98 (0.96 – 1.00)	0.99 (0.96 – 1.01)
Cannabis use	2.18 (1.15 – 4.14) *	1.96 (0.69 – 4.00)
Nicotine use		
Age	0.93 (0.94 – 0.97) ***	0.96 (0.94 – 0.99) ***
Female gender	0.58 (0.39 – 0.85) **	0.64 (0.40 – 1.05)
Medical comorbidity	0.92 (0.86 – 0.99) *	0.96 (0.87 – 1.06)
Depression	1.04 (1.00 – 1.07) *	1.02 (0.98 – 1.07)
Prescription opioid dose	1.00 (0.99 – 1.01)	1.00 (0.99 – 1.01)
Pain intensity	1.10 (0.99 – 1.02)	1.00 (0.98 – 1.01)
Cannabis use	2.01 (1.16 – 3.48) *	1.61 (0.90 – 2.88)

Note: Adjusted models controlled for age, gender, depression, pain intensity, prescription opioid dose, and medical comorbidity score.

* $p<0.05$

** $p<0.01$

*** $p<0.001$