



Orthopaedic surgery patients who use recreational marijuana have less pre-operative pain

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Abstract

Aims To determine the baseline clinical characteristics of recreational marijuana users undergoing outpatient orthopaedic surgery. We hypothesized that patients who report marijuana use would have worse pain, function, and general health status.

Patients and methods Nine-hundred and thirty-seven patients undergoing outpatient orthopaedic surgery were asked to fill out patient-reported outcome (PRO) tools. These PROs included the Patient-Reported Outcomes Measurement Information Systems (PROMIS) computer adaptive tests and legacy PROs unique to each patients' surgical site.

Results Forty patients (4.2%) reported marijuana use. Marijuana use was associated with younger age (33 vs. 43 years, $p < 0.001$), having a history of fewer operations (1.8 vs. 3.2, $p < 0.05$), single marital status (68 vs. 38%, $p < 0.01$), and having a history of smoking cigarettes (63 vs. 31%, $p < 0.0001$). Marijuana use was found to be significantly associated with greater Marx lower extremity activity rating scale scores (8.5 points vs. 6.1 points, $p < 0.05$) and decreased pain intensity in the operative site (3.7 points vs. 5.0 points, $p < 0.05$). Multivariable analysis found that marijuana use was an independent factor associated with less pain intensity in the operative site ($p < 0.05$).

Conclusion Our studies support other national studies that report increased marijuana use among younger patients and those who smoke cigarettes. The results do not support our hypothesis, as marijuana use was associated with less pain and better lower extremity activity rating scale scores when compared to non-users. Further research is warranted to analyze the effects of marijuana use on orthopaedic surgery patients.

Study design Cross-sectional study.

Keywords Marijuana · Orthopaedic surgery · Clinical characteristics · Substance use

Introduction

Marijuana is one of the most widely used drugs in the USA, and its usage has increased over recent years [1, 2]. Currently, nine states and the District of Columbia allow recreational marijuana use, 22 states allow the prescription of medical marijuana, and 16 states allow the use of cannabidiol (Fig. 1) [3]. According to the 2015 National Survey on Drug Use and

Health (NSDUH), the prevalence of current marijuana use in children 12 to 17 years of age was 7.0% (1.8 million), and in adults 18 years of age and older was 8.3% (20.5 million) [1].

The *Cannabis sativa* (marijuana) plant contains multiple bioactive components, termed cannabinoids (CB). In the past decade alone, multiple studies have investigated the therapeutic potential of the non-psychoactive compound cannabidiol (CBD) for its potential to manage pain, nausea, vomiting, and spasms [4–7]. The most substantial research regarding marijuana use has pertained to the treatment of chronic and neuropathic pain, where the data suggests that marijuana has both beneficial [8–10] and detrimental effects [11]. The peri-operative management of recreational marijuana users is particularly important given that ingestion of marijuana by inhalation has physiologic effects similar to that of tobacco inhalation [12, 13]. The interaction between anaesthetic agents and marijuana, specifically the cross-tolerance

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Fig. 1 Marijuana legality in the USA



in chronic users has been postulated [14]. Published case reports of uvular oedema and post-operative airway obstruction in patients reporting marijuana use prior to surgery [15, 16] underscores the importance of eliciting a thorough history of substance use in the pre-operative period.

Given the growing interest in marijuana and its derivatives as a medical treatment [4–7] and the increased recreational use of marijuana, it is important to understand the demographic profile of marijuana users. However, there is very little information regarding marijuana users in the context of surgery, especially in orthopaedic surgery. The most recent study regarding the usefulness of medical marijuana in the orthopaedic population looked at patients' beliefs regarding the usefulness of medical marijuana [17]. However, this study only included orthopaedic trauma patients, who could have different demographics and substance-use habits compared to elective orthopaedic surgery patients. In order to understand the effects of marijuana use, it is important to first understand the health profile associated with marijuana consumption. The purpose of this study was to determine the demographics and baseline patient-reported outcomes (PROs) of recreational marijuana users undergoing elective orthopaedic surgery. We hypothesized that patients who reported marijuana use would have worse pain, function, and overall health status than non-users.

Patients and methods

A prospective orthopaedic database was used to evaluate patients pre-operatively from June 2015 to June 2017 at a single institution [18]. All patients undergoing orthopaedic surgery at our institution was eligible for enrollment into an institutional review board-approved, web-based registry. All study data was collected using the Research Electronic Data Capture (REDCap™) data collection system. Inclusion criteria were as follows: (1) patient undergoing orthopaedic surgery, (2) age more than 12 years, and (3) English speaking. We decided to include patients 12 years and older given that the rate of

marijuana use in children aged 12 to 17 years old (7.0%) is similar to the rate of use in adults aged 18 and over (8.3%) [1]. Similar to the National Survey on Drug Use and Health, we sub-grouped our patients into the age groups: ≥ 26 , 18–26, and 12–18 years. Nine-hundred and thirty-seven patients were available. Demographic data was self-reported by each respondent, and each patient's medical record was reviewed for relevant medical history, including their American Society of Anesthesiologists (ASA) score, smoking status, alcohol use, and current medications.

All enrolled patients were pre-operatively administered six of the National Institute of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS) computer adaptive testing questionnaires (physical function, pain interference, fatigue, social satisfaction, anxiety, and depression; v1.2). Depending on the operative site, patients were then administered a joint-specific legacy PRO tool. These included the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, American Shoulder and Elbow Surgeons (ASES) Shoulder Assessment Form, and the Brief Michigan Hand Questionnaire (BHMQ). No joint-specific questionnaire was administered for patients undergoing foot, ankle, or hip surgery. Two Numeric Pain Scales (NPS) were completed to assess pain level in the surgical site and pain level in the body overall. Preoperative expectations were evaluated with the Musculoskeletal Outcomes Data Evaluation and Management System (MODEMS) expectations questionnaire. Patient activity levels were measured using the Tegner Activity Scale (TAS), the International Physical Activity Questionnaire (IPAQ), and Marx Activity Rating Scales (ARS) for upper and lower extremity.

Patients were stratified into two cohorts based on their answer to the question: "Have you used drugs other than those required for medical reasons?" Patients who reported using "marijuana," "weed," or "pot" were included in the marijuana-user study cohort. Patients who denied using recreational drugs, or reported using drugs other than marijuana, were included in the control cohort (marijuana non-users).

Statistical analysis

Descriptive statistics were used to summarize all study variables (means, medians, standard deviations, and frequency). Demographic and clinical data were compared using the Wilcoxon rank sum test for continuous variables and the Pearson chi-squared test or Fisher's exact test (when more than 20% of cells had frequencies < 5) for categorical variables. In order to determine which current procedural terminology (CPT) codes were significant independent predictors of marijuana use, one-way analysis of variance (ANOVA) tests were performed, wherein marijuana use was the factor and the CPT code performed was the response. Given our large sample size, and the inherent risk of multiple-test bias, we used the false discovery rate (FDR)-adjusted p value to determine significance ($p < 0.05$).

We used bootstrap forest partitioning to evaluate the contribution of all demographic and clinical variables as possible predictors of the response (marijuana use—YES). The ten highest-ranked predictors, marijuana use, and those factors identified through bivariate analysis to be significantly associated with marijuana use were then entered as independent variables in our multivariable model, with each respective PRO as a dependent variable. Our final list of predictors included marijuana use, age, number of surgeries, marital status, smoking status, BMI, overall expectations, gender, education level, alcohol consumption, pre-operative opioid use, history of depressions or anxiety, injury prior to surgery, operative joint, and primary procedure. We performed a backwards elimination stepwise technique using least squares multivariable linear regression that started with all of the predictors in the model. Our model was validated using a maximum validation RSquare method, where a stopping rule was imposed to avoid overfitting the model. The least contributory independent variable with the largest p value was removed, and the model was recalculated. This was repeated until only statistically significant ($p < 0.05$) variables remained. We used bootstrapped forest partitioning to determine which procedures (CPT codes) were possible predictors of lower extremity activity and pain intensity, respectively, among those patients who used marijuana pre-operatively. The ten highest ranked predictors for each measure were then analyzed using ANOVA tests to determine which were significantly associated with lower scores on each measure in marijuana users. Statistical software JMP Pro, version 13, software (JMP®, version 13. SAS Institute Inc., Cary, North Carolina) was used for all analyses.

Results

Our study population included a total of 937 patients, 4.2% ($n = 40$) of whom reported marijuana use. When compared to

non-users, patients who used marijuana were significantly younger (33.4 vs. 42.6 years, $p = 0.0007$) and had fewer total previous surgeries (1.83 vs. 3.18, $p = 0.015$) (see Table 1). When analyzed by age group, patients 18–26 years old had a significantly greater likelihood to be marijuana users ($p = 0.0009$) (Table 2). The majority of our patients were male ($n = 518$, 55%) and white ($n = 523$, 56%). We had 461 (49%) undergo knee surgery, 194 (21%) shoulder surgery, 166 (18%) hand or wrist surgery, 53 (6%) hip surgery, 41 (4%) elbow surgery, and 22 (2%) foot or ankle surgery (see Table 3). Significant, independent factors associated with marijuana use included marital status as single-never married (68 vs. 38%, $p = 0.0014$) and a history of smoking tobacco (63 vs. 31%, $p < 0.0001$).

Of the ten most performed procedures in the overall study population (see Table 4), the only procedure found to be significantly associated with marijuana use was “Arthroscopy, knee, surgical; abrasion arthroplasty (includes chondroplasty where necessary) or multiple drilling or microfracture” (CPT 29879, $p < 0.05$). After controlling for the operative site, marijuana use was a significant independent factor in only two of 17 collected PRO measures (see Table 5). None of the PROMIS CAT domains were found to be associated with marijuana use. Marijuana users were found to have a greater Marx ARS lower extremity score (8.49 points vs. 6.10 points, $p < 0.012$) and lower NPS scores in the operative site (3.73 points vs. 4.97 points, $p < 0.011$). Multivariate regression analysis found that marijuana use was an independent factor only for lower pain scores in the operative site ($p < 0.05$). On bivariate analysis, marijuana users who underwent anterior cruciate ligament reconstruction reported lower pre-operative knee pain (mean 1.00 ± 1.00 ; $p < 0.0385$). However, on multivariable analysis, no specific procedure was found to be an independent predictor of joint pain in those patients who used recreational marijuana. No significant association was found between activity level and procedure performed in recreational marijuana users on bivariate or multivariable analysis.

Discussion

The aim of this study was to determine the demographics and baseline PRO of recreational marijuana users undergoing elective orthopaedic surgery. This is the first study to report on marijuana use in an elective orthopaedic surgery population and also has the largest cohort ($n = 937$) of orthopaedic surgery patients in the literature. We hypothesized that marijuana users in our study population would have worse pain, function, and overall health. We found recreational marijuana users in our orthopaedic population to be younger, have had fewer prior surgeries, and more likely to be smokers when compared to non-users. In contrast to our hypothesis,

Table 1 Comparison of continuous patient demographic variables in marijuana users vs non-users in patients undergoing orthopedic surgery

	Overall cohort 937	Marijuana users 40 Mean (\pm SD)	Marijuana non-users 897 Mean (\pm SD)	<i>p</i> value ^a
Mean age in years	42.2 (\pm 16.6)	33.4 (\pm 13.4)	42.6 (\pm 16.6)	0.0007
Mean in BMI kg/m ²	29.7 (\pm 5.9)	28.3 (\pm 5.9)	29.7 (\pm 6.0)	0.235
Number of comorbidities	1.03 (\pm 1.23)	0.88 (\pm 1.3)	1.03 (\pm 1.26)	0.282
MODEMS—expectations overall	4.39 (\pm 0.72)	4.50 (\pm 0.57)	4.39 (\pm 0.73)	0.375
1. Relief from symptoms	4.43 (\pm 0.79)	4.55 (\pm 0.71)	4.42 (\pm 0.80)	0.243
2. Activities	4.42 (\pm 0.86)	4.63 (\pm 0.59)	4.41 (\pm 0.87)	0.176
3. Sleep	4.34 (\pm 0.95)	4.44 (\pm 0.87)	4.34 (\pm 0.96)	0.490
4. Usual work	4.41 (\pm 0.95)	4.58 (\pm 0.81)	4.41 (\pm 0.96)	0.145
5. Exercise	4.44 (\pm 0.87)	4.57 (\pm 0.77)	4.44 (\pm 0.87)	0.273
6. Disability	4.29 (\pm 0.93)	4.23 (\pm 1.02)	4.30 (\pm 0.93)	0.873
Number of surgeries (ANY)	3.12 (\pm 3.64)	1.83 (\pm 1.88)	3.18 (\pm 3.69)	0.015
Number of orthopedic surgeries	1.50 (\pm 2.19)	0.90 (\pm 1.01)	1.53 (\pm 2.22)	0.267
Number of surgeries on operative joint	0.40 (\pm 0.86)	0.35 (\pm 0.48)	0.40 (\pm 0.87)	0.388

MODEMS Musculoskeletal Outcomes Data Evaluation and Management System, SD standard deviation, NR not reported, BMI body mass index

^a Means of continuous variables were compared through a Wilcoxon rank sum test

recreational marijuana users had significantly lower pain scores in the operative site and greater lower extremity activity rating scores than non-users. Furthermore, multivariable analysis found recreational marijuana use to be a significant independent factor of lower pain scores in the operative site.

Currently, the role of marijuana in US society is dynamic. Although the use, sale, and possession of marijuana is illegal under federal law, its status varies under state law [17, 19]. It is regarded as a recreational substance, used in multiple forms, and as a pharmacologic agent for the treatment of multiple chronic pathologies. Marijuana is the most commonly used controlled drug in the USA, and according to the most recent NSDUH data collected by the Substance Abuse and Mental Health Services Administration in 2015, an estimated 8.3% (22.2 million) of Americans aged 12 or older were current users of marijuana, which is greater than that reported in previous years. We found the rate of marijuana use in our

orthopaedic outpatient population to be approximately half (4%) of that found in national surveys. According to an advocacy group, as of March 2016, 1.25 million patients are registered to use marijuana in 21 states with legal medical marijuana, accounting for approximately 8.1 patients per 1000 state residents [20]. This represents a slight increase from 7.7 patients per 1000 state residents in 2014. In a recent study of 500 orthopaedic trauma patients, 60% (302) of them reported having used marijuana at least once previously, and 21% (107) reported that they used marijuana in the past year [17].

Cigarette smoking remains the leading preventable cause of disease and premature mortality in the USA [20]. We found marijuana use to be significantly associated with a history of cigarette smoking. Approximately 32.5% of marijuana users reported being current smokers, and 30% reported being former smokers. Our findings follow the trends found in other large national studies, which report an increased prevalence of marijuana use among cigarette smokers [21–23] and cigarette smoking to be associated with an increased odd of marijuana dependence [24]. Moreover, marijuana use has been associated with the persistence of smoking [25, 26] and relapse to smoking among former smokers [27]. A recent study found increased daily cannabis use among current, former, and non-smokers over the past decade, with particularly rapid increases among youth and female cigarette smokers [28]. Marijuana use is typically ingested by inhalation, with similar symptoms of coughing, increased sputum production, and wheezing associated with tobacco smoking [29]. Furthermore, the practice of deep inhalation and breath-holding common in marijuana smokers can result in increased concentrations of pulmonary toxins, such as carboxyhaemoglobin, up to five times that of

Table 2 Use of recreational marijuana by age-group

	Marijuana use (<i>n</i> , %)			<i>p</i> value	
	Yes	No	Total		
Age Groups	\geq 26	22 (3.1%)	688 (96.9%)	710	0.0009 ^a
	18–26 ^b	17 (9.3%)	166 (90.7%)	183	
	12–18	1 (2.3%)	43 (97.7%)	44	
	Total	40 (4.3%)	897 (95.7%)	937	

^a Pearson chi-square test

^b Most likely to be recreational marijuana user (analysis of means for proportions)

Table 3 Comparison of categorical patient demographic variables in marijuana users vs non-users in patients undergoing orthopedic surgery

	Overall cohort <i>N</i> (%)	Marijuana users <i>N</i> (%)	Marijuana non-users <i>N</i> (%)	<i>p</i> value*	
	937 (100)	40 (4)	897 (96)		
Sex					
Male	518 (55)	28 (70)	490 (55)	0.0557	
Female	419(45)	12 (30)	407 (45)		
Ethnicity					
Not Hispanic or Latino	858 (92)	35 (88)	823 (92)	0.347	
Hispanic or Latino	47 (5)	2 (5)	45 (5)		
NR	32 (3)	3 (8)	29 (3)		
Race					
Black	326 (35)	14 (35)	312 (35)	0.989	
White	523 (56)	22 (55)	501 (56)		
Other	88 (9)	4 (10)	84 (9)		
Education					
Some high school or below	75 (8)	4 (10)	71 (8)	0.576	
High school graduate or above	805 (86)	35 (88)	770 (86)		
NR	57 (6)	1 (3)	56 (6)		
Employment status					
Employed for wages	438 (47)	19 (48)	419 (47)	0.383	
Self-employed	66 (7)	2 (5)	64 (7)		
Out of work and looking for work	25 (3)	2 (5)	23 (3)		
Out of work but not currently looking for work	14 (1)	0 (0)	14 (2)		
Homemaker	16 (2)	1 (3)	15 (2)		
Student	135 (14)	8 (20)	127 (14)		
Military	4 (0)	0 (0)	4 (0)		
Retired	70 (7)	0 (0)	70 (8)		
Unable to work	98 (10)	7 (18)	91 (10)		
Other	16 (2)	1 (3)	15 (2)		
NR	55 (6)	0 (0)	55 (6)		
Income					
Less than \$10,000	83 (9)	7 (18)	76 (8)		0.444
\$10,000–\$19,999	38 (4)	3 (8)	35 (4)		
\$20,000–\$29,999	47 (5)	1 (3)	46 (5)		
\$30,000–\$39,999	55 (6)	1 (3)	54 (6)		
\$40,000–\$49,999	42 (4)	2 (5)	40 (4)		
\$50,000–\$59,999	36 (4)	1 (3)	35 (4)		
\$60,000–\$69,999	35 (4)	0 (0)	35 (4)		
More than \$70,000	272 (29)	11 (28)	261 (29)		
NR	329 (35)	14 (35)	315 (35)		
Marital status					
Single-never married	367 (39)	27 (68)	340 (38)	0.0014	
Married or domestic partnership	386 (41)	8 (20)	378 (42)		
Divorced, separated, or widowed	130 (14)	5 (13)	125 (14)		
NR	54 (6)	0 (0)	54 (6)		
Smoking status					
Daily	74 (8)	7 (18)	67 (7)	< 0.0001	
Less than daily	39 (4)	6 (15)	33 (4)		
Quit smoking	187 (20)	12 (30)	175 (20)		
Never smoked	583 (62)	14 (35)	569 (63)		

Table 3 (continued)

	Overall cohort <i>N</i> (%) 937 (100)	Marijuana users <i>N</i> (%) 40 (4)	Marijuana non-users <i>N</i> (%) 897 (96)	<i>p</i> value*
NR	54 (6)	0 (0)	53 (6)	
Alcohol consumption				
Never	280 (30)	8 (20)	272 (30)	0.162
Monthly or less	232 (25)	13 (33)	219 (24)	
2 to 4 times a month	162 (17)	11 (28)	151 (17)	
2 to 3 times a week	138 (15)	5 (13)	133 (15)	
4 or more times a week	62 (7)	3 (8)	59 (7)	
NR	63 (7)	3 (4)	63 (7)	
Preoperative narcotic use				
No	628 (67)	25 (63)	603 (67)	0.807
Yes	241 (26)	12 (30)	229 (26)	
NR	68 (7)	3 (8)	65 (7)	
ASA score				
1	315 (34)	18 (45)	297 (33)	0.365
2	572 (61)	22 (55)	550 (61)	
3	48 (5)	0 (0)	48 (5)	
4	2 (0)	0 (0)	2 (0)	
Depression or anxiety				
No	750 (80)	29 (73)	721 (80)	0.432
Yes	75 (8)	6 (15)	106 (12)	
NR	112 (12)	5 (13)	70 (8)	
Injury prior to surgery				
No	335 (36)	16 (40)	319 (36)	0.216
Yes	539 (58)	24 (60)	515 (57)	
NR	63 (7)	0 (0)	63 (7)	
Worker's compensation				
No	901 (97)	37 (93)	864 (96)	0.056
Yes	36 (4)	3 (8)	33 (4)	
Operative site				
Shoulder	194 (21)	3 (8)	191 (21)	0.388
Elbow	41 (4)	1 (3)	40 (4)	
Hand or wrist	166 (18)	9 (23)	157 (18)	
Hip	53 (6)	3 (8)	50 (6)	
Knee	461 (49)	23 (58)	438 (49)	
Foot or ankle	22 (2)	1 (3)	21 (2)	
Prior surgery on operative site				
No	670 (72)	25 (63)	645 (72)	0.418
Yes	253 (27)	14 (35)	239 (27)	
NR	14 (1)	1 (3)	13 (1)	

ASA American Society of Anesthesiologists, NR not reported

^aSignificance of categorical values were evaluated through the use of the Pearson chi-squared test

the typical tobacco smoker [12]. Given the effects of such toxins on intra-operative physiologic parameters and the post-operative implications of poor healing and increased morbidity seen in tobacco smokers, marijuana users may also benefit from similar peri-operative health optimization.

We found that marijuana users have lower pre-operative pain scores in the operative site and higher activity scores, and the multivariate analysis confirmed that marijuana use was a significant independent predictor of less pre-operative pain. The current evidence examining the role of marijuana as

Table 4 Most common procedures in overall cohort

CPT	Procedure	N
29881	Arthroscopy, knee, surgical; with meniscectomy (medial OR lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment (s), when performed	130
29888 ^b	Arthroscopically aided anterior cruciate ligament repair/augmentation or reconstruction	118
29876	Arthroscopy, knee, surgical; synovectomy, major, 2 or more compartments (e.g., medial or lateral)	104
29879^a	Arthroscopy, knee, surgical; abrasion arthroplasty (includes chondroplasty where necessary) or multiple drilling or microfracture	91
29882	Arthroscopy, knee, surgical; with meniscus repair (medial OR lateral)	76
29826	Arthroscopy, shoulder, surgical; decompression of subacromial space with partial acromioplasty, with coracoacromial ligament (i.e., arch) release, when performed (list separately in addition to code for primary procedure)	66
23430	Tenodesis of long tendon of biceps	47
27447	Arthroplasty, knee, condyle and plateau; medial AND lateral compartments with or without patella resurfacing (total knee arthroplasty)	41
29827	Arthroscopy, shoulder, surgical; with rotator cuff repair	40
23472	Arthroplasty, glenohumeral joint; total shoulder (glenoid and proximal humeral replacement (e.g., total shoulder))	33

^a Those CPT codes in bold were significantly associated with preoperative marijuana use ($p < 0.05$)

^b Recreational marijuana users who underwent anterior cruciate ligament reconstruction were associated with lower preoperative pain in their knee

an analgesic is unclear [8, 30–32]. High-level clinical studies evaluating marijuana therapy for pain demonstrate the complex effects of marijuana-related analgesia [32]. A recent systematic review and meta-analysis of 28 randomized controlled trials among 254 patients with chronic pain indicated that, compared to placebo, cannabinoids were associated with a greater reduction in pain (37 vs. 31%; OR 1.41, 95% CI 0.99 to 2.00) and greater average reduction in numeric pain ratings (-0.46 , 95% CI -0.80 to -0.11) [33]. Another systematic review of 18 randomized controlled trials studying the effectiveness of cannabis or cannabinoids for the treatment of non-cancer pain found a statistically significant improvement in pain intensity in their participants [9].

Chronic pain affects a wide range of outcomes that are typically assessed using self-reported measures, susceptible to recall biases, current mood, and pain intensity [34, 35]. The marked variation in pain intensity for a given painful stimulus can possibly be explained by symptoms of depression or anxiety, by stress and by catastrophic thinking or kinesiophobia [36]. The findings of studies that support the notion that marijuana can produce acute pain-inhibitory effects among individuals with chronic pain may explain the associations highlighted in our study. However, many of these trials were limited by small sample sizes and heterogeneity with respect to the route of cannabis administration [30, 31, 37]. It is important to highlight that given the mixed results of these studies, more research is needed to understand the efficacy, dose-response effects, routes of administration, and side effects of marijuana products commonly used in the USA.

Multimodal pain management for the control of severe post-operative pain includes options such as additional surgical procedures [38], non-steroidal anti-inflammatory drugs (NSAIDs) [39], narcotic analgesics, continuous epidural

anesthesia, patient-controlled analgesia (PCA) devices, nerve blocks, or local infiltration analgesia (LIA) [40–42]. The use of parenteral opioid drugs administered by means of PCA is generally the most commonly used method, but it is often associated with adverse reactions, including nausea and vomiting, respiratory compromise, altered mental status, constipation, and urinary retention. Recent studies have showed that patients receiving LIA had significantly lower pain levels post-operatively [42], less post-operative opioid use, and better early rehabilitation [40, 41].

In the present opioid epidemic affecting the USA, we must consider any and all methods of limiting prescription opioids. Studies have found that pre-operative opioid use is associated with worse post-operative outcomes, an increased incidence of in-hospital mortality, and increased rate of complications [43, 44]. Given the association of marijuana and pain identified in our study, a consideration should be given to its role in pain management. A recent study found that states with laws permitting medical marijuana had a 24.8% lower mean annual opioid overdose mortality rate (95% CI, -37.5 to -9.5% ; $p = .003$) compared with states without such laws [45]. In contrast to opioids, acute overdose with marijuana is very uncommon. The fatal dose of marijuana is between 15 and 70 g [46], which is much greater than the use by a heavy recreational user [47]. Marijuana is not without adverse effects. The cumulative probability estimate of transition to dependence was 8.9% for cannabis users [48]. Studies have demonstrated a dose-related impairment in reaction time, information processing, perceptual motor coordination, motor performance, attention, and tracking behavior [49], clearly establishing a link between marijuana intoxication and the risk of motor vehicle accidents [50]. Additional adverse effects on health and well-being associated with marijuana have been

Table 5 Analysis of PROMIS and other patient-reported outcome measures in preoperative marijuana users vs non-users in patients undergoing orthopaedic surgery

	Marijuana users (\pm SD)	Non-marijuana users (\pm SD)	<i>p</i> value ^a
PROMIS—physical function	41.6 (\pm 8.63)	42.4 (\pm 8.77)	0.781
PROMIS—pain interference	59.5 (\pm 7.74)	60.9 (\pm 7.33)	0.247
PROMIS—fatigue	52.6 (\pm 10.12)	52.6 (\pm 10.56)	0.995
PROMIS—social satisfaction	43.1 (\pm 10.03)	42.1 (\pm 9.54)	0.335
PROMIS—anxiety	56.2 (\pm 8.96)	55.1 (\pm 9.11)	0.516
PROMIS—depression	50.3 (\pm 8.79)	49.2 (\pm 9.55)	0.431
IKDC	43.2 (\pm 17.91)	39.1 (\pm 18.09)	0.186
ASES—overall	48.8 (\pm 32.01)	43.3 (\pm 21.50)	0.841
ASES—function	40.0 (\pm 33.11)	37.6 (\pm 25.10)	0.939
MHQ	75.4 (\pm 3.42)	74.3 (\pm 10.82)	0.796
IPAQ—MET (<i>minutes/week</i>)	3648.7 (\pm 4166.8)	3426.6 (\pm 4072.6)	0.903
Tegner ARS (pre-injury problem)	6.92 (\pm 2.16)	6.44 (\pm 2.38)	0.373
Tegner ARS (current/pre-surgery)	2.63 (\pm 2.18)	2.43 (\pm 1.94)	0.484
Marx upper ARS	12.36 (\pm 6.07)	11.43 (\pm 5.71)	0.232
Marx lower ARS	8.49 (\pm 6.11)	6.10 (\pm 5.89)	0.012
Operative site pain	3.73 (\pm 3.17)	4.97 (\pm 2.84)	0.011
Body pain	1.65 (\pm 2.78)	1.63 (\pm 2.39)	0.559

PROMIS Patient Reported Outcome Measure Information Systems, IKDC International Knee Documentation Committee, ASES American Shoulder and Elbow Surgeons, MHQ Michigan Hand Questionnaire, IPAQ-MET International Physical Activity Questionnaire-Metabolic Equivalent, ARS Activity Rating Scale

^a All *p* values were determined through the use of a Wilcoxon rank sum test

reported, which include the exacerbation of psychiatric disorders, diminished long-term cognitive function, and possible cardiorespiratory pathology [51].

This study is limited by its design as a cross-sectional study. This prohibits the ability to define a causal relationship of the observed findings. Given that participation is voluntary, the study is limited by self-selection bias. It is also possible that marijuana use may have been underreported. Given the dynamic legal status of marijuana, patients may have been apprehensive to disclose their personal substance use habits. Another limitation is the method of assessing reported drug use. Patients were solely asked whether or not they used drugs other than those for medical reasons and which drugs they used. Neither the frequency of use nor quantity was included in our study. Therefore, stratification based on frequency and dosage of use could not be done. However, the large size ($n > 900$) and diversity of the study population are strengths that should limit these shortcomings.

Conclusion

Compared to non-users, pre-operative marijuana users were younger, more likely to be single, have had fewer prior operations, and more likely to be either current or former cigarette smokers. Furthermore, marijuana users had lower pain scores

in the operative site and had higher activity rating scores for the lower extremity. Marijuana use was corroborated to be an independent predictor of lower pain scores. The results inform orthopedic surgeons of the demographics and health profile of marijuana users in a large, diverse population undergoing orthopaedic surgery. Further research is necessary to determine the effects of marijuana use on this population.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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References

1. Substance Abuse Mental Health Services Administration (“SAMHSA”) (2007a) Results from the 2006 National Survey on drug use and health: National Findings (2010). SAMHSA, Rockville, MD
2. Cerda M, Wall M, Keyes KM, Galea S, Hasin D (2012) Medical marijuana laws in 50 states: investigating the relationship between

- state legalization of medical marijuana and marijuana use, abuse and dependence. *Drug Alcohol Depend* 120(1–3):22–27. <https://doi.org/10.1016/j.drugalcdep.2011.06.011>
3. Gallup AM, Newport F (2010) The Gallup poll: public opinion 2009. Rowman & Littlefield Publishers,
 4. Phillips TJ, Cherry CL, Cox S, Marshall SJ, Rice AS (2010) Pharmacological treatment of painful HIV-associated sensory neuropathy: a systematic review and meta-analysis of randomised controlled trials. *PLoS One* 5(12):e14433. <https://doi.org/10.1371/journal.pone.0014433>
 5. Martin-Sanchez E, Furukawa TA, Taylor J, Martin JL (2009) Systematic review and meta-analysis of cannabis treatment for chronic pain. *Pain Med* 10(8):1353–1368. <https://doi.org/10.1111/j.1526-4637.2009.00703.x>
 6. Machado Rocha FC, Stefano SC, De Cassia HR, Rosa Oliveira LM, Da Silveira DX (2008) Therapeutic use of Cannabis sativa on chemotherapy-induced nausea and vomiting among cancer patients: systematic review and meta-analysis. *Eur J Cancer Care (Engl)* 17(5):431–443. <https://doi.org/10.1111/j.1365-2354.2008.00917.x>
 7. Flachenecker P (2013) A new multiple sclerosis spasticity treatment option: effect in everyday clinical practice and cost-effectiveness in Germany. *Expert Rev Neurother* 13(3 Suppl 1):15–19. <https://doi.org/10.1586/em.13.1>
 8. Jensen B, Chen J, Furnish T, Wallace M (2015) Medical marijuana and chronic pain: a review of basic science and clinical evidence. *Curr Pain Headache Rep* 19(10):50. <https://doi.org/10.1007/s11916-015-0524-x>
 9. Lynch ME, Campbell F (2011) Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. *Br J Clin Pharmacol* 72(5):735–744. <https://doi.org/10.1111/j.1365-2125.2011.03970.x>
 10. Robson P (2001) Therapeutic aspects of cannabis and cannabinoids. *Br J Psychiatry* 178:107–115
 11. Polen MR, Sidney S, Tekawa IS, Sadler M, Friedman GD (1993) Health care use by frequent marijuana smokers who do not smoke tobacco. *West J Med* 158(6):596–601
 12. Benson MK, Bentley AM (1995) Lung disease induced by drug addiction. *Thorax* 50(11):1125–1127
 13. Sridhar KS, Raub WA Jr, Weatherby NL, Metsch LR, Surratt HL, Inciardi JA, Duncan RC, Anwyl RS, McCoy CB (1994) Possible role of marijuana smoking as a carcinogen in the development of lung cancer at a young age. *J Psychoactive Drugs* 26(3):285–288. <https://doi.org/10.1080/02791072.1994.10472442>
 14. Flisberg P, Paech MJ, Shah T, Ledowski T, Kurowski I, Parsons R (2009) Induction dose of propofol in patients using cannabis. *Eur J Anaesthesiol* 26(3):192–195. <https://doi.org/10.1097/EJA.0b013e328319be59>
 15. Lawson TM, Rees A (1996) Stroke and transient ischaemic attacks in association with substance abuse in a young man. *Postgrad Med J* 72(853):692–693
 16. Mallat A, Roberson J, Brock-Utne JG (1996) Preoperative marijuana inhalation—an airway concern. *Can J Anaesth* 43(7):691–693. <https://doi.org/10.1007/BF03017953>
 17. Heng M, McTague MF, Lucas RC, Harris MB, Vrahas MS, Weaver MJ (2018) Patient perceptions of the use of medical marijuana in the treatment of pain after musculoskeletal trauma: a survey of patients at 2 trauma centers in Massachusetts. *J Orthop Trauma* 32(1):e25–e30. <https://doi.org/10.1097/BOT.0000000000001002>
 18. Henn RF 3rd, Dubina AG, Jauregui JJ, Smuda MP, Tracy JK (2017) The Maryland Orthopaedic Registry (MOR): design and baseline characteristics of a prospective registry. *J Clin Orthop Trauma* 8(4):301–307. <https://doi.org/10.1016/j.jcot.2017.04.003>
 19. Iannotti JP, Deutsch A, Green A, Rudicel S, Christensen J, Marraffino S, Rodeo S (2013) Time to failure after rotator cuff repair: a prospective imaging study. *J Bone Joint Surg Am* 95(11):965–971. <https://doi.org/10.2106/JBJS.L.00708>
 20. Bartl C, Kouloumentas P, Holzapfel K, Eichhorn S, Wortler K, Imhoff A, Salzmann GM (2012) Long-term outcome and structural integrity following open repair of massive rotator cuff tears. *Int J Shoulder Surg* 6(1):1–8. <https://doi.org/10.4103/0973-6042.94304>
 21. Agrawal A, Lynskey MT (2009) Tobacco and cannabis co-occurrence: does route of administration matter? *Drug Alcohol Depend* 99(1–3):240–247. <https://doi.org/10.1016/j.drugalcdep.2008.08.007>
 22. Weinberger AH, Funk AP, Goodwin RD (2016) A review of epidemiologic research on smoking behavior among persons with alcohol and illicit substance use disorders. *Prev Med* 92:148–159. <https://doi.org/10.1016/j.ypmed.2016.05.011>
 23. Schauer GL, Berg CJ, Kegler MC, Donovan DM, Windle M (2015) Assessing the overlap between tobacco and marijuana: trends in patterns of co-use of tobacco and marijuana in adults from 2003–2012. *Addict Behav* 49:26–32. <https://doi.org/10.1016/j.addbeh.2015.05.012>
 24. Hindocha C, Shaban ND, Freeman TP, Das RK, Gale G, Schafer G, Falconer CJ, Morgan CJ, Curran HV (2015) Associations between cigarette smoking and cannabis dependence: a longitudinal study of young cannabis users in the United Kingdom. *Drug Alcohol Depend* 148:165–171. <https://doi.org/10.1016/j.drugalcdep.2015.01.004>
 25. Ramo DE, Liu H, Prochaska JJ (2012) Tobacco and marijuana use among adolescents and young adults: a systematic review of their co-use. *Clin Psychol Rev* 32(2):105–121. <https://doi.org/10.1016/j.cpr.2011.12.002>
 26. Goodwin RD, Sheffer CE, Chartrand H, Bhaskaran J, Hart CL, Sareen J, Bolton J (2014) Drug use, abuse, and dependence and the persistence of nicotine dependence. *Nicotine Tob Res* 16(12):1606–1612. <https://doi.org/10.1093/ntr/ntu115>
 27. Prudius D, Weber P, Matejovska Kubsova H, Meluzinova H, Polcarova V, Bielakova K (2017) Pulmonary embolism in the hospitalized patients 65+ in relation to presence of diabetes in 2007–2015. *Adv Gerontol* 30(5):703–708
 28. Goodwin RD, Pacek LR, Copeland J, Moeller SJ, Dierker L, Weinberger A, Gbedemah M, Zvolensky MJ, Wall MM, Hasin DS (2018) Trends in daily cannabis use among cigarette smokers: United States, 2002–2014. *Am J Public Health* 108(1):137–142. <https://doi.org/10.2105/AJPH.2017.304050>
 29. Bryson EO, Frost EA (2011) The perioperative implications of tobacco, marijuana, and other inhaled toxins. *Int Anesthesiol Clin* 49(1):103–118. <https://doi.org/10.1097/AIA.0b013e3181dd4f53>
 30. Campbell FA, Tramer MR, Carroll D, Reynolds DJ, Moore RA, McQuay HJ (2001) Are cannabinoids an effective and safe treatment option in the management of pain? A qualitative systematic review. *BMJ* 323(7303):13–16
 31. Fitzcharles MA, Baerwald C, Ablin J, Hauser W (2016) Efficacy, tolerability and safety of cannabinoids in chronic pain associated with rheumatic diseases (fibromyalgia syndrome, back pain, osteoarthritis, rheumatoid arthritis): a systematic review of randomized controlled trials. *Schmerz* 30(1):47–61. <https://doi.org/10.1007/s00482-015-0084-3>
 32. Hill KP (2015) Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: a clinical review. *JAMA* 313(24):2474–2483. <https://doi.org/10.1001/jama.2015.6199>
 33. Whiting PF, Wolff RF, Deshpande S, Di Nisio M, Duffy S, Hernandez AV, Keurentjes JC, Lang S, Misso K, Ryder S, Schmidtkofer S, Westwood M, Kleijnen J (2015) Cannabinoids for medical use: a systematic review and meta-analysis. *Jama* 313(24):2456–2473. <https://doi.org/10.1001/jama.2015.6358>
 34. Jamison RN, Sbrocco T, Parris WC (1989) The influence of physical and psychosocial factors on accuracy of memory for pain in chronic pain patients. *Pain* 37(3):289–294

35. Eich E, Reeves JL, Jaeger B, Graff-Radford SB (1985) Memory for pain: relation between past and present pain intensity. *Pain* 23(4): 375–380
36. Bernstein DN, Sood A, Mellema JJ, Li Y, Ring D (2017) Lifetime prevalence of and factors associated with non-traumatic musculo-skeletal pains amongst surgeons and patients. *Int Orthop* 41(1):31–38. <https://doi.org/10.1007/s00264-016-3338-5>
37. Deshpande A, Mailis-Gagnon A, Zoheiry N, Lakha SF (2015) Efficacy and adverse effects of medical marijuana for chronic noncancer pain: systematic review of randomized controlled trials. *Can Fam Physician* 61(8):e372–e381
38. Pritchett JW (2018) Outcome of surgery for nerve injury following total hip arthroplasty. *Int Orthop* 42(2):289–295. <https://doi.org/10.1007/s00264-017-3724-7>
39. Andrei D, Popa I, Brad S, Iancu A, Oprea M, Vasilian C, Poenaru DV (2017) The variability of vertebral body volume and pain associated with osteoporotic vertebral fractures: conservative treatment versus percutaneous transpedicular vertebroplasty. *Int Orthop* 41(5):963–968. <https://doi.org/10.1007/s00264-017-3409-2>
40. Motififard M, Omidian A, Badiei S (2017) Pre-emptive injection of peri-articular-multimodal drug for post-operative pain management in total knee arthroplasty: a double-blind randomized clinical trial. *Int Orthop* 41(5):939–947. <https://doi.org/10.1007/s00264-016-3357-2>
41. Li D, Tan Z, Kang P, Shen B, Pei F (2017) Effects of multi-site infiltration analgesia on pain management and early rehabilitation compared with femoral nerve or adductor canal block for patients undergoing total knee arthroplasty: a prospective randomized controlled trial. *Int Orthop* 41(1):75–83. <https://doi.org/10.1007/s00264-016-3278-0>
42. Song MH, Kim BH, Ahn SJ, Yoo SH, Kang SW, Kim YJ, Kim DH (2016) Peri-articular injections of local anaesthesia can replace patient-controlled analgesia after total knee arthroplasty: a randomised controlled study. *Int Orthop* 40(2):295–299. <https://doi.org/10.1007/s00264-015-2940-2>
43. Menendez ME, Ring D, Bateman BT (2015) Preoperative opioid misuse is associated with increased morbidity and mortality after elective orthopaedic surgery. *Clin Orthop Relat Res* 473(7):2402–2412. <https://doi.org/10.1007/s11999-015-4173-5>
44. Rozell JC, Courtney PM, Dattilo JR, Wu CH, Lee GC (2017) Preoperative opiate use independently predicts narcotic consumption and complications after total joint arthroplasty. *J Arthroplast* 32(9):2658–2662. <https://doi.org/10.1016/j.arth.2017.04.002>
45. Bachhuber MA, Saloner B, Cunningham CO, Barry CL (2014) Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010. *JAMA Intern Med* 174(10):1668–1673. <https://doi.org/10.1001/jamainternmed.2014.4005>
46. Gable RS (2004) Comparison of acute lethal toxicity of commonly abused psychoactive substances. *Addiction* 99(6):686–696. <https://doi.org/10.1111/j.1360-0443.2004.00744.x>
47. Hall W, Degenhardt L (2009) Adverse health effects of non-medical cannabis use. *Lancet* 374(9698):1383–1391. [https://doi.org/10.1016/S0140-6736\(09\)61037-0](https://doi.org/10.1016/S0140-6736(09)61037-0)
48. Lopez-Quintero C, de los Perez CJ, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C (2011) Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend* 115(1–2):120–130. <https://doi.org/10.1016/j.drugalcdep.2010.11.004>
49. Ramaekers JG, Berghaus G, van Laar M, Drummer OH (2004) Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend* 73(2):109–119
50. Brady JE, Li G (2014) Trends in alcohol and other drugs detected in fatally injured drivers in the United States, 1999–2010. *Am J Epidemiol* 179(6):692–699. <https://doi.org/10.1093/aje/kwt327>
51. Volkow ND, Baler RD, Compton WM, Weiss SR (2014) Adverse health effects of marijuana use. *N Engl J Med* 370(23):2219–2227. <https://doi.org/10.1056/NEJMra1402309>