



# Analyzing the Impact of Cannabinoids on the Treatment of Spinal Disorders

Rohan M. Shah<sup>1</sup> · Anjay Saklecha<sup>1</sup> · Alpesh A. Patel<sup>2</sup> · Srikanth N. Divi<sup>2</sup> 

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## Abstract

**Purpose of Review** Cannabis is among the most used illicit substances globally, with medical applications, increased legalization, and shifting social attitudes leading to increased use in recent years. Cannabinoids are a group of psychoactive substances found within the cannabis plant, with the most common being  $\Delta^9$ -tetrahydrocannabinol and cannabidiol. Due to the high prevalence of use, it is increasingly important to evaluate the effects of cannabis and cannabinoids on spine patients, in both operative and nonoperative settings.

**Recent Findings** Cannabis and cannabinoids may be effective in treating patients with chronic conditions such as back pain and spinal cord injuries. Longitudinal effects and implications on surgical outcomes and complications are poorly understood. High-quality, outcomes-focused research can inform approaches for clinicians to approach cannabis and cannabinoid use. Studies to elucidate the standardization of cannabis regimens can help develop guidelines for potential therapeutic applications. Cannabis and cannabinoids may be useful alternatives or additions for many spine patients, but future research is needed for recommendations to be determined.

**Summary** Our manuscript reviews the available literature regarding cannabis use and various spinal conditions, organizing our findings into the following narrative themes: (1) the management of chronic lower back pain, (2) perioperative outcomes, (3) cannabis use in general orthopaedic procedures, and (4) spinal cord injuries.

**Keywords** Cannabis · Cannabinoids · Spine · Spine outcomes

## Introduction

Cannabis is one of the most used illicit substances, with nearly 147 million people globally reporting use in 2016 [1, 2]. Cannabinoids are a homogenous group of closely related psychoactive substances found in the cannabis plant. The plant consists of more than 400 compounds, approximately 140 of which are noted to be cannabinoids, with  $\Delta^9$ -tetrahydrocannabinol ( $\Delta^9$ -THC) and cannabidiol (CBD) being most commonly described psychoactive compounds [3]. It is commonly

ingested via inhalation (smoking) or consuming food products containing cannabis extract (i.e., edibles) [4]. The potency of cannabis is determined by the concentration of  $\Delta^9$ -THC, since it is the primary active psychoactive cannabinoid [3]. As a result, the effectiveness of cannabis for relaxation or pain relief is directly related to the concentration of  $\Delta^9$ -THC in the product. However, recent research has suggested that while CBD is less potent than  $\Delta^9$ -THC, it too may have a clinically noticeable effect. Studies have shown that CBD has both a milder and more regulating effect than  $\Delta^9$ -THC on cannabinoid receptors and the endocannabinoid system, modulating against potential adverse effects [3]. When taken together,  $\Delta^9$ -THC and CBD may have a synergistic therapeutic effect.

While cannabinoids have long been used recreationally, there is a growing body of literature supporting its use medically for various disease states, including the relief of musculoskeletal or neuropathic pain, both common elements in spinal disorders [5, 6]. Early studies also supported cannabis as a therapeutic tool for chronic neurological conditions including

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✉ Srikanth N. Divi  
srikanth.divi@nm.org

<sup>1</sup> Northwestern University, Chicago, IL, USA

<sup>2</sup> Department of Orthopaedic Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

epilepsy, Parkinson's disease, Tourette's syndrome, and chronic pain syndrome [7]. However, the lack of standardization of method of ingestion, dosage, and other pharmacologic confounders is reflected in the lack of high-quality studies. In addition, the growing number of cannabinoid products ranging from ingestible to topical formulations further confounds treatment recommendations. Under the Controlled Substances Act, cannabis has been classified as a Schedule I drug since 1970, which places it in the same category as heroin, lysergic acid diethylamide (LSD), and other substances that have a "high potential for abuse" and "no currently accepted medical use in treatment in the United States." With increased recreational and medical use of cannabis, decriminalization and removal from its status as a Schedule I drug have been repeatedly proposed. Historically, there has been a higher prevalence of use in younger age groups (15–30 years), but with more states across the country legalizing recreational and medical cannabis, the demographics of users has shifted with increased use noted in older adults [8].

Despite the widely appreciated positive effects of cannabis use, acute cannabis use has also been associated with negative effects on several components of physical and psychological health [9]. Chronic use may also have adverse effects on outcomes in patients undergoing surgery, with increased cardiopulmonary and anesthetic complications [10]. In addition, the concern for addiction has led to some providers recommending increased caution when suggesting medical cannabis use for use in pain management [11].

Currently, it is unclear whether patients with chronic pain secondary to spinal disorders can benefit from medical cannabis use in the nonoperative or perioperative setting. The intent of this review is to summarize the current research surrounding cannabis and cannabinoid use in select spinal disorders: chronic low back pain, spinal cord injury, and perioperative use. In addition, literature regarding cannabinoid use in the perioperative setting for general orthopaedic procedures will also be discussed.

## Management of Chronic Lower Back Pain

Therapies for chronic lower back pain (cLBP) can be divided into noninvasive and invasive methods. Noninvasive management includes pharmacological treatment with muscle relaxants, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, acetaminophen, and opioid analgesics [12]. Other noninvasive non-pharmacological treatments include physical therapy, exercise programs, and cognitive-behavioral therapies [13].

Several studies have assessed cannabis use in the treatment of cLBP, with the literature included in this review being outlined in Table 1. A study performed at the University of Minnesota analyzed the prevalence of cannabis use, among

other illicit substances, in patients with cLBP using data collected by the National Health and Nutrition Examination Survey (NHANES) between 2009 and 2010 [14]. Respondents with cLBP had greater odds of cannabis use than those without lower back pain (adjusted odds ratio (OR) [1.36; 95% CI: 1.06–1.74]). Yassin et al. conducted an observational cross-over study that included 31 patients with fibromyalgia and lower back pain [15]. Patients were treated using standard analgesic therapy (SAT) consisting of an opiate 2–3 times daily with 30 mg duloxetine daily for 3 months, after which they were able to utilize medical cannabis therapy (MCT) for at least 6 months. The opiate most commonly administered consisted of oxycodone 5 mg and naloxone 2.5 mg. MCT therapy was administered monthly with a 20-g dose, using a 1:4 ratio of  $\Delta^9$ -THC to CBD. Overall  $\Delta^9$ -THC levels were below 5%. Patient-reported outcomes (PROs) included Oswestry Disability Index (ODI), Revised Fibromyalgia Impact Questionnaire (FIQR), SF-12, Visual Analog Score (VAS), Patient Global Impression of Change (PGIC) Scale, and lumbar range of motion (ROM) using the Schober test. Outcomes were evaluated at screening, after 3 months of SAT (baseline), after 3 months of MCT, and at 6 months of MCT. Authors of the study found an advantage in using MCT, with significant improvements in PROs at both 3 and 6 months. After 3 months of standard therapies, minimal improvement to PROs was observed. When comparing 6 months of MCT treatment to baseline, a decrease in VAS ( $8.1 \pm 1.4$  to  $3.3 \pm 2.2$ ), increase in FIQR ( $45.3 \pm 10.2$  to  $80.5 \pm 12.2$ ), decrease in ODI ( $73.7 \pm 11.4$  to  $30.7 \pm 13.6$ ), and increase in ROM ( $3.5 \pm 1.8$  to  $5.3 \pm 1.5$ ) were observed. The same authors conducted a second study evaluating the effect of MCT on severity of chronic back pain, sciatica, and lumbar range of motion [16]. A cohort of 46 patients was observed for over a period of at least 12 months. Patients were included if they had received imaging documenting low back pain with irradiating symptoms of sciatica and had been managed with sufficient therapy. These factors were determined using patient history, a referral letter, and medical records. PROs included SF-12, VAS, ODI, the Brief Pain Inventory (BPI), and Saunders digital inclinometer to determine ROM. Use of opiates was evaluated at baseline and 12 months of MCT. Similar to the previous study, cannabis dosage was fixed at a monthly dose of 20 g, with an increase considered at 6 months. After 12 months of MCT, significant improvement was noted in all outcomes (SF12-MCS, SF12-PCS, VAS intensity, VAS frequency, BPI severity, BPI interference, and ROM). Notably, both studies were not randomized and had an open-label design, increasing the risk for bias.

Another study performed at a single-center cannabis medical practice in California gauged the ability for cannabis to decrease opioid use in cLBP patients [17]. A total of 180 patients with a primary complaint of lower back pain were identified, with 61 being active opioid users. Patients who

**Table 1** Literature investigating cannabis and chronic lower back pain

Author and year	Article type	Description of sample and size	Findings
Shmagel et al (2016) [14•]	Retrospective study	National Health and Nutrition Examination Survey (NHANES) Participants with pain between lower posterior margin of rib cage and horizontal gluteal fold for $\geq 3$ months $N = 700$	Respondents with cLBP were found to have significantly greater odds of cannabis use when compared with
Yassin et al. (2019) [15]	Cohort study	Patients with low-back pain related to fibromyalgia $N = 31$	Medical cannabis treatment was associated with improved PROs at both 3 and 6 months
Yassin et al. (2016) [16]	Prospective cohort study	Patients with low-back pain and sciatica $N = 46$	Patients treated with medical cannabis saw significant improvements in all PROs
Takakuwa et al. (2020) [17]	Cohort study	Patients with a primary complaint of lower back pain $N = 180$	Cannabis use provided an alternative to opioids in approximately half of participants, and was used in other chronic opioid users as a tool to reduce use
Eskander et al. (2020) [18]	Case report	Two patient case reports	Patients reported relief of chronic back pain when using CBD transdermal creams
Xantus et al (2021) [19]	Perspective article	N/A	CBD may have benefits in pain and fear reduction, which are important components in managing cLBP
Allan et al. (2018) [20•]	Practice Guidelines	N/A	CBD therapies are not currently recommended for use in managing cLBP, due to a lack of sufficient evidence regarding effectiveness and safety

used opioids to manage their back pain were recommended medical cannabis, and the outcomes measured included changes in morphine equivalents and the number of patients who stopped using opioids. Authors found that 50.8% of respondents stopped opioid use entirely. Of the remaining 29 patients, 9 (31%) reduced use, 3 (10%) remained at the same use, and 17 (59%) increased use. Participants who used greater doses of cannabis were more likely to stop opioid use. A total of 48% of patients subjectively felt that using cannabis was helpful in mitigating opioid intake; however, reporting this sentiment did not accurately predict cessation of opioid use.

The current body of literature for the efficacy of medical cannabis in the treatment of cLBP is sparse, but limited studies suggest that it may be an effective alternative to pain management than current pharmacologic therapies and may even present a useful method of decreasing opioid usage in challenging patients. PROs in these limited studies noted decreased cLBP and improved patient satisfaction with medical cannabis use compared to traditional treatments.

While most research has focused on using medical cannabis in pain relief, there is currently a large, growing market in products containing only CBD, the milder and less potent cannabinoid present in cannabis [21]. These products are sold in various formulations including topicals such as oils/tinctures/creams or lotions, edibles, or vaporizers. Currently, the Food and Drug Administration (FDA) does not regulate CBD products; therefore, the safety and efficacy of these products are not clearly established [22]. Two recent

case reports describe the use of topical CBD creams for the symptomatic relief of chronic and acute back pain [18]. Both reports noted patient-reported relief of back pain from CBD transdermal creams. The authors purport this may be secondary to the anti-inflammatory and antinociceptive effects of CBD. In addition, CBD may interact with multiple modalities of pain signaling and has potential benefits in fear and pain reduction, which are notable components of cLBP [19]. Outside of these case reports, CBD use in the setting of cLBP is not clearly established. Currently, there is insufficient evidence to provide any treatment recommendation [20•, 23–25]. Moving forward, high-quality research is necessary to better understand the potential benefits and harms of CBD therapies for back pain.

## Perioperative Outcomes and Cannabis Use

To date, the effects of cannabis use on perioperative outcomes in spine surgery have not been well studied. Currently, it is unclear to what extent cannabis use affects spine surgery outcomes. Tobacco use has a clear and proven negative effect on postoperative PROs, major complications, and fusion rates [26], but similar associations have yet to be elucidated with cannabis use. Theoretically, cannabis and cannabinoids may adversely affect spinal fusion given their ability to exert strong anti-inflammatory effects and immunosuppression [27]. In addition, the cardiovascular effects of cannabinoids are complex and may result in sympathetic-mediated vasoconstriction in

local vascular beds, possibly disrupting blood flow to the spinal column. Only recently, a few studies have explored the effects of cannabis use in elective spine surgeries, with relatively little high-quality data. The studies relating perioperative outcomes to cannabis use are referenced in Table 2.

A study using the National Inpatient Sample (NIS) from 2010 to 2014 investigated several orthopaedic procedures, including spinal fusion for associations between cannabis use and stroke, heart failure (HF), cardiac disease (CD), and in-hospital mortality [28••]. In spinal fusion patients, cannabis use was associated with increased odds of stroke (OR: 2.65;  $p < 0.0001$ ) and CD (OR: 1.39;  $p < 0.0001$ ).

Similarly, Chiu et al. retrospectively identified patients using NIS data from 2012 to 2015, focusing specifically on patients with cannabis use disorder who underwent elective spine surgeries [29]. Outcomes were peri- and postoperative complications, length of stay (LOS), costs, discharge disposition, and all-cause mortality. After baseline traits and tobacco use were controlled for, patients with cannabis use disorder had similar inpatient mortality but greater likelihood of thromboembolism (OR: 2.2;  $p = 0.005$ ), respiratory complications (OR: 2.0;  $p < 0.001$ ), neurologic complications (OR: 2.9;  $p = 0.007$ ), sepsis (OR: 1.5;  $p = 0.031$ ), and nonroutine discharge ( $p < 0.001$ ). Lengths of stay (7.1 vs. 5.2 days;  $p < 0.001$ ) were increased in cannabis-using patients, as were hospitalization costs (\$137,631.30 vs. \$116,112.60;  $p < 0.001$ ).

In another retrospective propensity-matched cohort study utilizing NIS data, Goel et al. studied patients undergoing one of 11 elective surgeries (including laminectomy and other unspecified spine surgery), finding no difference in the composite perioperative outcome for patients with cannabis use disorder [30]. The composite endpoint included stroke, postoperative in-hospital myocardial infarction, sepsis, respiratory failure, pulmonary embolism, deep vein thrombosis, acute kidney injury needing dialysis, and in-hospital mortality. Notably, patients with cannabis use disorder had greater odds of postoperative myocardial infarction (adjusted OR: 1.88 [95% CI 1.31 to 2.69],  $p < 0.001$ ). Authors concluded that perioperative cannabis may lead to a supply-demand mismatch in oxygen, and the increased cardiovascular oxygen demands surrounding surgery may underlie the higher risk of perioperative acute myocardial infarction, especially in patients with established coronary artery disease. However, one major drawback in extrapolating this study for spine patients is that it did not specifically analyze spine patients as a subgroup.

With regard to spinal fusion outcomes, there is a paucity of literature. Jakoi et al. identified 102 patients undergoing transforaminal lumbar interbody fusion and reported fusion outcomes and associations with cannabis use [31]. Outcomes of interest included ODI, postoperative complications, LOS, return to operating room, confirmed fusion, and revision surgery. The authors found that cannabis users had no

significant differences in return to the operating room, complications, or revision surgery. Postoperative ODI reduction was not limited by cannabis use and cannabis users had shorter LOS and similar 12-month fusion rates. A prospective, double-blind study is currently underway at the University of Colorado Spine Center, with an estimated completion date in June 2022 [32••]. The aim of this study is to investigate the efficacy of cannabis compared to oxycodone and placebo in the reduction of postoperative chronic back and neck pain, as measured by the pain Numeric Rating Scale (NRS) scores and pain threshold (kPa).

Though there is a lack of clinical data studying the effect of cannabinoid use on bone healing, in vitro and animal model studies have documented a role for the endocannabinoid system (ECS) in affecting bone metabolism and bone homeostasis [34]. Pre-clinical studies suggest that cannabidiol use improves bone healing, though  $\Delta^9$ -tetrahydrocannabinol ( $\Delta^9$ -THC) may inhibit bone repair [35]. Recent evidence has suggested that the ECS affects bone mass maintenance via the G protein-coupled receptors CB<sub>1</sub> and CB<sub>2</sub>. CB<sub>1</sub> receptor activity may have a protective role in the regulation of bone mass and osteoporosis via adipocyte and osteoblast differentiation, along with the modulation of various intracellular signaling proteins [36]. CB<sub>2</sub> receptors are similarly believed to regulate bone maintenance, with mice models deficient in CB<sub>2</sub> being observed to have significantly accelerated age-related trabecular bone loss and cortical expansion [37]. Mechanisms for the regulation of bone mass by CB<sub>2</sub> receptors include the stimulation of osteoblasts and stromal cells, and the inhibition of RANKL expression. Certain endogenous cannabinoids have been observed to activate the G protein-coupled receptor GPR55, which inhibits CB<sub>1</sub> and CB<sub>2</sub>; however, CBD antagonizes GPR55 [38]. In mouse models, GPR55 inactivation has resulted in phenotypes with increased bone mass and resorption. Though  $\Delta^9$ -THC is a CB<sub>1</sub> and CB<sub>2</sub> partial agonist, it is still likely to hinder bone repair, as it has a dual toxicity profile that instigates death in many cell types and prevents osteogenesis [39]. A recent cross-sectional study in the UK found that heavy cannabis use was associated with lower BMI, lower bone mineral density, higher bone turnover, and a greater likelihood of fracture [33]. The study concluded that heavy cannabis use may have a negative impact on bone health both directly and indirectly through an effect on BMI. To identify whether there is an effect of cannabis use on human bone health and in the setting of spine surgery and especially spine fusion, robust and well-designed clinical studies are necessary as the current findings are still largely unclear.

Currently, there is a dearth of literature examining the effects of cannabis in the spine perioperative setting. While cannabis may have a role in providing postoperative pain relief, other perioperative outcomes such as cardiopulmonary complications, wound healing, rates of spinal fusion, and need for revision surgery have not yet been elucidated.

**Table 2** Cannabis and perioperative outcomes literature

Author and year	Article type	Description of sample and size	Findings
Moon et al. (2019) [28••]	Retrospective study	National Inpatient Sample (NIS) Individuals who underwent one of five procedures: total hip (THA), total shoulder (TSA), and total knee (TKA) arthroplasties, traumatic femur fracture, and spinal fusion <i>N</i> = 9,561,963	In spinal fusion patients, cannabis use was associated with greater odds of stroke and cardiac disease
Chiu et al. (2021) [29]	Retrospective study	National Inpatient Sample Patients undergoing common elective spine surgeries <i>N</i> = 423,978	Patients with cannabis use disorder had greater odds of thromboembolism, sepsis, neurologic complications, respiratory complications, and nonroutine discharge. Cannabis users had longer postoperative stays and greater costs. Inpatient mortality was not affected by cannabis use
Goel et al. (2020) [30]	Retrospective study	National Inpatient Sample Patients for common elective surgeries <i>N</i> = 4,186,622	The composite perioperative outcome was not affected by the presence of cannabis use disorder. Patients with cannabis use disorder had a greater likelihood of postoperative myocardial infarction
Jakoi et al. (2020) [31]	Cohort study	Patients undergoing transforaminal lumbar interbody fusion <i>N</i> = 102	Cannabis users did not have significant differences in complications, return to operating room, postoperative ODI reduction, 12-month fusion rates, or likelihood of revision surgery. Cannabis use was associated with shorter LOS
Lindley et al. (2022) [32••]	Clinical trial	Prospective study currently being performed <i>N</i> = 100 (Target)	N/A
Sophocleous et al. (2017) [33]	Cross-sectional study	Individuals in the UK recruited from primary care Moderate ( <i>N</i> = 56) and heavy ( <i>N</i> = 144) cannabis smokers, with cigarette smokers as a control ( <i>N</i> = 114)	Heavy cannabis use was correlated with lower BMI, lower bone mineral density, higher bone turnover, and greater likelihood of having bone fracture

## Cannabis Use in General Orthopaedic Procedures

Outside of spine surgery, more research has been conducted on cannabis and its impact in general orthopaedic procedures. Studies included in our discussion of cannabis in general orthopaedics are summarized in Table 3. Over the past few decades, opioid prescriptions have been increasingly used by physicians in the USA for alleviating chronic pain, especially in those with musculoskeletal complaints [44]. Orthopaedic surgeons are among the top physician prescribers of opioids, and many orthopaedic patients are at risk for repercussions including opioid use disorder (OUD) from therapeutic or non-therapeutic use [45]. Because cannabis and cannabinoids may present an alternative to conventional therapies for pain management post-surgery, there is a relative abundance of literature for this modality in general orthopaedic procedures as compared to spine surgery. Analyzing this body of literature may provide insight into the perioperative use of cannabis in spine surgery.

Despite well-documented studies researching cannabinoid compounds for analgesic effects in animal models, their use in managing acute perioperative pain in humans has not been well studied [46, 47]. A double-blind, randomized placebo-controlled pilot study performed in Canada compared the

effects of two doses (1 mg and 2 mg) of nabilone, a synthetic oral form of cannabis typically used to treat nausea and vomiting, on relieving postoperative pain in patients undergoing gynecologic (46%), orthopaedic (44%), or other types of surgery (10%) [40]. Forty-one patients showed an increase in pain at rest with 2 mg nabilone compared to placebo and nabilone 1 mg. The study highlighted that though cannabinoids are effective in alleviating chronic pain, their role (specifically, nabilone) in acute postoperative pain remains uncertain. Hickernell et al. compared the effect of a standard pain regimen with the addition of dronabinol (another synthetic form of  $\Delta^9$ -THC) compared with a standard pain regimen alone in patients undergoing total joint arthroplasty (TJA). Eighty-one primary TJA patients who received 5 mg dronabinol twice daily in addition to the standard regimen were compared to a cohort of 162 TJA patients who received the standard regimen only [41]. Patients in the dronabinol group had a shorter average LOS ( $2.3 \pm 0.9$  days vs.  $3.0 \pm 1.2$  days,  $p = 0.02$ ) and also consumed fewer morphine equivalents (Mes) ( $252.5 \pm 131.5$  mg vs.  $313.3 \pm 185.4$  mg;  $p = 0.0088$ ), while still having similar PROs. Runner et al. studied CBD and  $\Delta^9$ -THC use following unilateral arthroplasty in a prospective cohort of 195 TKA/THA patients from a single institution [42]. Overall, 16.4% ( $n = 32$ ) reported inconsistent perioperative CBD/ $\Delta^9$ -THC use. When comparing CBD/ $\Delta^9$ -

**Table 3** Cannabis use in general orthopaedics procedures

Author and year	Article type	Description of sample and size	Findings
Beaulieu et al. (2006) [40]	Randomized, double-blind pilot study	Patients undergoing gynecologic, orthopaedic, and other surgeries <i>N</i> = 41	Cannabinoids are useful in managing chronic pain, but their application to acute postoperative pain is uncertain. Dosage may have an impact on effectiveness of cannabinoid therapies.
Hickernell et al. (2018) [41]	Randomized, double-blind study	Patients treated with total joint arthroplasty <i>N</i> = 243	Patients treated with dronabinol had shorter LOS and consumed fewer opioids, with similar PROs being reported.
Runner et al. (2020) [42]	Cohort study	Unilateral total knee and total hip arthroplasty patients <i>N</i> = 210	There were no differences in morphine milligram equivalents, narcotic pills taken, length of narcotic use, odds of needing a narcotic refill, average postoperative pain scores, or LOS between CBD/THC users and non-users.
Albelo et al. (2021) [43]	Retrospective study	Patients undergoing orthopaedic procedures <i>N</i> = 1103	Cannabis use was not found to be a predictor of any PRO after a multivariate analysis was performed.
Ishida et al. (2019) [44]	Cross-sectional study	United States adults <i>N</i> = 9,003	A total 20% of respondents discontinued opioid use in favor of cannabis. Pain management, fewer side effects, and withdrawal symptoms were commonly cited reasons.
Moon et al. (2019) [28••]	Retrospective study	National Inpatient Sample (NIS) Individuals who underwent one of five procedures: total hip (THA), total shoulder (TSA), and total knee (TKA) arthroplasties, traumatic femur fracture, and spinal fusion <i>N</i> = 9,561,963	Cannabis use was associated with decreased odds of mortality in THA, TSA, TKA, and traumatic femur fracture patients. In THA/TKA patients, cannabis users had greater odds of HF, CD, and stroke. In TSA patients, cannabis use decreased odds of stroke, with zero events. Traumatic femur fracture patients who used cannabis had lower odds of HF and CD.

THC users and non-users, the study found no significant differences in total morphine milligram equivalents taken, number of narcotic pills taken, length of use of narcotics, average postoperative pain scores, likelihood of requiring a narcotic refill, or LOS. Though the study was limited by a small sample size, it did not find an effect of CBD/ $\Delta^9$ -THC on narcotic use.

In the previously mentioned study by Moon et al. of patients identified in the NIS that underwent general orthopaedic procedures, cannabis use decreased odds of mortality [28••]. Cannabis use was associated with increased odds for HF (OR: 1.53;  $p$  = 0.018), CD (OR 1.31;  $p$  = 0.012), and stroke (OR: 2.62;  $p$  = 0.0068) in THA/TKA patients. For TSA patients, cannabis use decreased odds of stroke ( $p$  < 0.0001), indicated by zero events in this group. Cannabis-using patients with traumatic femur fractures had decreased odds of CD (OR: 0.58;  $p$  = 0.0003) and HF (OR: 0.44;  $p$  = 0.0076). A study performed by Albelo et al. retrospectively analyzed patients from the Maryland Orthopaedic Registry undergoing general orthopaedic surgery procedures (arthroscopy, arthroplasty, carpal tunnel release) from June 2015 to May 2018 [43]. The registry included preoperative demographic characteristics, surgical history, and social history (including self-reported cannabis use) as well as postoperative PROs. A total of 47 (4.3%) patients reported recreational cannabis use, with significantly worse 2-year outcomes for PROMIS Anxiety ( $p$  = 0.005), PROMIS Depression ( $p$  = 0.001), Surgical

Satisfaction Questionnaire-8 ( $p$  = 0.005), Numeric Satisfaction Scale ( $p$  = 0.041), and the question “met expectations.” In addition, active cannabis users also noted less improvement of pain at the operative site based on the Numeric Pain Scale ( $p$  = 0.024). However, on multivariate analysis, cannabis use was not found to be an independent predictor of any PRO.

The long-term effects of cannabis, including the possibility of addiction, are important to consider when weighing it as an alternative to conventional therapies. The similarity in the signaling pathways for opioids and cannabinoids has led to a concern that cannabis may also be an addictive substance [48]. Existing research regarding the addictive nature of cannabis suggests that the neurobiological changes in patients with cannabis use disorder parallel other addictions, though at a lesser degree in certain systems [49]. Controlled trials have also found that chronic pain patients who already use cannabis are inclined to take prescription opioids at higher doses [50]. Outside of the perioperative period, Ishida et al. conducted a survey with 9,003 US adult respondents investigating the potential substitution of cannabis for opioids, and found that 20% of respondents reported opioid discontinuation in favor of cannabis [44]. Pain management (36%), fewer side effects (32%), and withdrawal symptoms (26%) were the most common reasons for the substitution.

The current literature, though limited, suggests that cannabis may act as an adjunct therapy after orthopaedic procedures. Cannabis has been linked to pain reduction, increased patient activity, and decreased reliance on opioids. Patients also generally report fewer side effects from cannabis use than from opioids. However, research regarding long-term postoperative outcomes, including addiction, needs to be further studied. In addition, most studies assessed cannabis as an adjunct treatment. The impact of solely using cannabis for postoperative pain is not well understood. Randomized controlled trials and prospective studies comparing cannabis and opioids may provide greater insights on the potential use of cannabis postoperatively.

## Spinal Cord Injuries

SCI is a devastating condition resulting in significant functional deficits and chronic neuropathic pain. Individuals with SCI largely view cannabis as a safe therapeutic option, and commonly support cannabis legalization [51, 52]. However, medical cannabis is not commonly prescribed as a treatment option for SCI patients. A recent international survey found that nearly three-quarters of medical providers offered SCI patients narcotics, while only 13% offered medical cannabis [53].

Several studies have investigated the frequency of cannabis use in SCI patients. A cross-sectional study performed in Denmark utilized a survey sent to 1,101 SCI patients, with a total of 537 responses [54]. Investigators found that 36% of respondents had tried cannabis at some point and 9% were current, active users. Most current users began using prior to injury (79%), and 65% used cannabis partly for SCI-related consequences, with 59% indicating at least a good impact on spasticity and pain. Higher muscle stiffness was significantly associated with cannabis use, and an overlap between recreational and disability-associated use was noted. A study of individuals with chronic SCI with neurogenic bowel/bladder found that 22.5% reported therapeutic cannabis use at least monthly, with 70.4% of users citing pain management and 46.3% spasticity relief as reasons [55]. Interestingly, the authors found that cannabis utilization did not reduce opioid use, contrary to the literature mentioned previously with regard to cannabis use for cLBP. In a separate study, Clark et al. found that cannabis use was associated with an increased likelihood of pain medication abuse in SCI patients [56]. Notably, SCI patients may be at an increased risk for developing substance abuse disorders, including cannabis, compared to patients with other spinal disorders or chronic pain [57].

Briefly mentioned previously, two commonly cited drivers of therapeutic cannabis use in individuals with SCI are pain management and spasticity relief [55, 58, 59]. In fact, the American Academy of Neurology has endorsed cannabinoid

**Table 4** Literature regarding cannabis and spinal cord injuries

Author and year	Article type	Description of sample and size	Findings
Dunn et al. (1974) [51]	Cross-sectional study	Individuals on a SCI ward who reported cannabis use N = 10	Respondents commonly endorsed the safety of cannabis
Stillman et al. (2019) [52]	Cross-sectional study	Patients across the USA with SCI N = 353	Participants largely supported the legalization of cannabis
Stillman et al. (2019) [53]	Cross-sectional study	International sample of clinicians caring for SCI patients N = 153	Prescribers rarely utilized medical cannabis when treating patients with SCI
Andresen et al. (2017) [54]	Cross-sectional study	Patients with SCI N = 1101	Approximately one-third of respondents (36%) reported trying cannabis, with 9% indicating current, active use. Over half of participants (65%) used cannabis partly for reasons related to SCI, and 59% found a positive impact on pain/spasticity
Drossel et al. (2020) [55]	Cross-sectional study	Individuals with chronic SCI and neurogenic bowel/bladder N = 244	Therapeutic cannabis use was reported by 22.5% of participants, with common reasons including pain and spasticity relief. Cannabis use did not reduce opioid use
Cardenas et al. (2006) [61]	Cross-sectional study	Adults with traumatic SCI and chronic pain N = 117	Conventional options for pain management such as NSAIDs and opioids are relatively ineffective in SCI patients. Cannabis was among the most common alternative therapies utilized
Bourke et al. (2019) [62]	Cross-sectional study	Well-informed marijuana users with SCI N = 8	Participants reported quick, effective pain reduction from cannabis use

use in the treatment of pain and spasticity in other neurological disorders such as multiple sclerosis but note that the safety profile has not been compared to other drugs [60]. Cannabis and cannabinoid treatments can be alternatives to traditional pain management such as opioids and NSAIDs, which are relatively ineffective for SCI patients [61]. A qualitative study in New Zealand interviewed eight adults with SCI about their experiences with using cannabis for pain management, with participants reporting quick and effective pain reduction [62]. Participants in this study were well-informed users and motivated to use cannabis when other pain management options were ineffective. Authors purported that one advantage of cannabis was that it allowed participants to engage in activities without feeling drowsy, an effect of opioid or neuromodulatory medications.

Table 4 organizes the included studies discussing the relationship between cannabis use and spinal cord injuries. Though the current literature indicates a potential for cannabis to be used as a therapeutic tool in individuals with SCI, its effect magnitude and clinical significance are still unclear. Further research is needed to understand optimal dosage, composition of compounds, and methods of ingestion for patients with SCI. Longitudinal, outcomes-focused studies need to be performed to understand the implications of cannabis use on individuals with SCI.

## Conclusion

Considering the increase in cannabis use and its shifting legality within the USA, it is important to understand its implications on spinal disorders. While it may present an effective modality of therapy for patients with chronic conditions such as back pain and spinal cord injuries, risks and long-term effects are not well understood. The myriad of other active cannabinoids other than  $\Delta^9$ -THC are potential therapeutic tools for managing symptoms of spinal disorders, yet evidence regarding safety and effectiveness is limited. In addition, the impact of cannabis in the perioperative setting in spine surgery with regard to outcomes and PROs is poorly understood. It is important to note that the current body of literature contains low-quality studies with small sample sizes, and therefore, there exists a significant gap in knowledge regarding the subject.

Outcomes-focused research can better inform guidelines for surgical providers to approach recommendations for patient use. Currently, there are many barriers to performing a well-designed study, including standardization of cannabis (form, route of ingestion, and dosage) and other medical and pharmacologic confounders. The mechanisms of action for cannabis and cannabinoids are still being studied, making it difficult to identify causative links between use and effects on clinical outcomes and complications. For many patients,

cannabis may present a viable alternative or adjunct to conventional pharmacologic therapies; however, at the present time, its therapeutic benefit in spinal disorders remains unclear.

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**Data Availability** N/A

**Code Availability** N/A

## Compliance with Ethical Standards

**Conflict of Interest** The authors do not have any relevant conflicts of interest, sources of financial support, corporate involvement, or patent holdings to disclose.

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- Of major importance

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