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Khak M. The Evidence for Medical Cannabis in Chronic Musculoskeletal Pain Management. *SurgiColl*. 2025;3(4). doi:10.58616/001c.138573

Current Concepts

The Evidence for Medical Cannabis in Chronic Musculoskeletal Pain Management

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Keywords: Medical cannabis, Chronic musculoskeletal pain, Cannabinoids, Pain management, Orthopedic practice

https://doi.org/10.58616/001c.138573

SurgiColl

Vol. 3, Issue 4, 2025

Chronic musculoskeletal pain (CMP) is a pervasive condition that can impair daily functioning and quality of life. Traditional pharmaceutical therapies, including non-steroidal anti-inflammatory drugs, gabapentinoids, and opioids, often yield suboptimal results and carry notable risks, such as adverse side effects and dependence. Increasing interest has turned toward medical cannabis, particularly combined formulations of cannabidiol (CBD) and tetrahydrocannabinol (THC), as a potential alternative or complement to current pain management strategies. Evidence suggests that cannabinoids interact with the endocannabinoid system to modulate nociception and inflammation, offering meaningful pain relief and possibly reducing opioid requirements. However, heterogeneity in study designs, product formulations, and regulatory frameworks presents challenges in drawing definitive conclusions. Additionally, while most adverse effects, such as fatigue, dizziness, and mild cognitive changes, are generally reported as tolerable, concerns remain about long-term safety and standardization of dosing. Taken together, the existing literature points to a promising role for medical cannabis in CMP management, underscoring the need for further high-quality research to establish best practices, clarify patient selection, and guide clinicians in safe and effective cannabinoid therapy.

INTRODUCTION

Chronic musculoskeletal pain (CMP) is persistent pain in muscles, bones, or joints lasting over three months, significantly affecting quality of life and daily functioning.[1] It commonly stems from conditions such as osteoarthritis, inflammatory rheumatic diseases, or fibromyalgia, though the cause is often unclear, complicating diagnosis and management. CMP impairs physical activity and work performance, contributing substantially to global disease burden.[2,3] Approximately 50% of adults in the United States are affected by musculoskeletal disorders.[4] In Canada, The Arthritis Society reports that around 17% of the adult population suffers from musculoskeletal diseases, with nearly half over age 65.[5] CMP is often comorbid with a range of health issues, including sleep disturbances, depression, anxiety, fatigue, and a reduction in overall quality of life. Furthermore, CMP can significantly impair an individual's ability to engage in work or social activities and imposes a major economic burden of $304 billion annually in the United States (U.S.) due to healthcare costs and lost productivity.[4]

The optimal treatment options for CMP remain limited and often suboptimal. Common treatments include non-steroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, and antidepressants, which have shown effectiveness in managing fibromyalgia osteoarthritis, low back pain, and, to an extent, fibromyalgia. However, these treatments are frequently associated with significant adverse effects, which prevent many patients from reaching the recommended doses; only about one-third of patients experience at least 50% pain relief.[6,7]

Emerging evidence suggests that cannabis-based medications, particularly cannabidiol (CBD), may offer a promising alternative for managing CMP. Studies indicate that CBD can reduce chronic pain by 42% to 66%, providing relief without the high dependency risks associated with conventional medications like opioids.[8,9] Unlike opioids, CBD generally has a more favorable side-effect profile and minimal abuse potential.[10] However, discrepancies exist in

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the literature, with some reports also highlighting adverse effects of CBD, such as nausea, dizziness, and fatigue. Recent findings indicate that while adverse effects of medical cannabis are relatively uncommon, the most frequently reported symptom upon discontinuation is a worsening of the original condition for which it was used, with sleep disturbances also frequently reported.[11]

This scoping review aims to synthesize current evidence on medical cannabis for CMP, providing insights for clinicians, policymakers, and patients. Given the increasing interest in cannabis-based therapies and limited orthopedic-specific guidance, this review seeks to support evidence-based decision-making and identify priorities for future research.

HISTORICAL EVOLUTION OF CANNABIS IN MEDICINE

Cannabis, a genus in the Cannabaceae family, has long been recognized for its medicinal properties. Its use dates back to 2700 BC in China, with ancient societies in India and the Middle East also documenting therapeutic applications. The earliest recorded usage in Western cultures dates back to 1839 when a study first investigated its pain-relieving properties.[12] However, the early 20th century marked a turning point in the perception and use of cannabis in medical practice. Shifting social attitudes and the eventual criminalization of cannabis led to a significant decline in its medicinal application despite its historical prominence. Although some practitioners continued to advocate for its benefits, widespread regulatory restrictions stifled research and limited its use in clinical settings for several decades. In more recent decades after the 1960s, modern research has expanded our understanding of cannabis by identifying more than 100 cannabinoids, the chemically active compounds found primarily in the flowers and leaves of the plant.[13]

MECHANISMS OF ACTION OF CANNABIS

Scientific interest in cannabis for pain management accelerated with the discovery of the endocannabinoid system (ECS), comprising CB1 and CB2 receptors and endogenous ligands that regulate nociception, inflammation, and homeostasis.[14] Cannabinoids interact with these receptors to reduce inflammation, modulate pain signaling, and even lower opioid requirements—by up to 96% for codeine and 75% for methadone in some studies.[15,16] Cannabinoids also demonstrate considerable anti-inflammatory effects by reducing key mediators such as tumor necrosis factor-alpha (TNF-α), reactive oxygen species (ROS), and lipoxygenases. Additionally, cannabinoids may enhance tissue perfusion and oxygen delivery through vasodilatory and nitric oxide-related mechanisms.[17] These modulations can help interrupt the inflammatory cascade, potentially relieving pain and improving tissue perfusion.

Despite cannabis's long history of medical use, standardizing its therapeutic effects remains challenging. Different strains (commonly referred to as Cannabis sativa or Cannabis indica) and various consumption methods lead to diverse cannabinoid profiles, making it difficult to predict individual responses and optimal dosing.[18] Furthermore, plant-derived products contain a complex mixture of over 500 biologically active compounds, including minor cannabinoids such as cannabigerol, cannabinol, and tetrahydrocannabinolic acid (THCA) and non-cannabinoid components such as terpenes and flavonoids.[19] These compounds may work synergistically, a phenomenon sometimes referred to as the "entourage effect",[20] potentially enhancing beneficial effects and mitigating side effects when used together. Methods of preparation and heat application (e.g., decarboxylation during smoking, vaping, or cooking) also convert inactive acidic forms of cannabinoids into their active counterparts, further altering the overall physiological impact.

Among the primary compounds, tetrahydrocannabinol (THC) is known for its psychoactive properties, contributing to the "high" associated with cannabis, yet it also exhibits potential analgesic and anti-inflammatory effects in preclinical models.[21] In contrast, cannabidiol (CBD) is non-intoxicating with antipsychotic and anti-inflammatory properties.[22-24] When used together, THC and CBD can modulate each other's effects, suggesting that a combined formulation of THC and CBD may enhance therapeutic outcomes while reducing unwanted side effects.

Evidence indicates that using both THC and CBD together may yield superior pain relief compared to isolated extracts of either compound,[19,25,26] supporting the notion that whole-plant preparations may more effectively harness the full therapeutic potential of cannabis in managing chronic musculoskeletal pain.[20]

CURRENT EVIDENCE AND RESEARCH

Beyond naturally derived cannabinoids, several synthetic products, such as nabiximols (Sativex®), nabilone (Cesamet®), and dronabinol (Marinol®)—are approved in various countries for conditions like multiple sclerosis-related spasticity, chemotherapy-induced nausea, and HIV-associated weight loss.[27] More recently, the food and drug administration (FDA) approved a CBD-based medication (Epidiolex®) for severe forms of epilepsy.[28] Although clinical evidence for cannabinoids in chronic pain has grown rapidly, definitive guidelines are still hindered by variations in product composition, patient response, and dosing.

Recent studies have highlighted the potential role of medical cannabis in managing CMP **[Table 1]**. Notcutt et al.[29] conducted a 12-week randomized, double-blind crossover study evaluating THC, CBD, and a 1:1 combination. Results showed significant symptom relief—over 55% pain reduction—with THC-containing formulations being most effective, especially in fibromyalgia. Combining THC and CBD enhanced analgesic effects. Side effects were common but generally well-tolerated, and patients reported a preference for discreet sublingual spray formulations, as they could be administered without attracting unwanted attention. The study also stated that patients would recom-

mend CBD to a friend as a potential option for managing chronic pain.

Harris et al.[30] examined self-reported marijuana effects among 100 medical cannabis users with chronic osteoarthritis. Most had a history of cannabis use and perceived it as more effective than conventional therapies, with fewer severe side effects. However, interpretation was complicated by self-report bias, substance use comorbidities, and the presence of other drugs in urine assays. The authors emphasized the need for clinical oversight to ensure safety and accurate assessment of treatment effects. A systematic review by Furrer et al.[5] found that medical cannabis users—mostly aged 28 to 63—typically consumed cannabis via smoking, with daily intake ranging from 0.05 to 1 gram. Participants reported relief from both primary symptoms and secondary issues like psychological distress. Adverse effects were generally mild, though pulmonary risks related to smoking were noted.

Whiting et al.[31] reviewed 79 trials and found only four at low risk of bias, yielding moderate-quality evidence for cannabinoids in chronic pain. Though some studies showed pain reduction, the clinical relevance was limited, and long-term efficacy remains unclear. The review also found no consistent influence of cannabinoid type or delivery method on outcomes. In 2015, Lynch et al.[32] reviewed randomized clinical trials (RCTs) on cannabinoids for chronic non-cancer pain. Seven trials showed modest analgesic effects, improving sleep and muscle stiffness. Side effects, such as dizziness and fatigue, were typically well tolerated. In 2018, Stockings et al.[33] analyzed 47 RCTs and 57 observational studies (n=9,958) and found modest pain relief with cannabinoids. A 30% pain reduction was more common with cannabinoids (29%) than placebo (26%), but the number needed to treat (NNT) was 24. There was no significant difference for a 50% reduction in pain. Adverse events were more frequent (81% vs. 66%), with a low number needed to harm (NNH) of 6. Functional outcomes and sleep quality showed minimal or low-quality improvement. The findings suggest that while cannabinoids may offer modest pain relief, their high NNT and low NNH, along with limited effects on other outcomes, indicate that cannabinoids are unlikely to become a major treatment option for chronic non-cancer pain (CNCP).

Finally, Nugent et al.[34] highlighted potential risks of cannabis use, including impaired cognition, psychotic symptoms, and increased risk of motor vehicle accidents. While there was some evidence for neuropathic pain relief, benefits in other pain types were less clear. The review called for more rigorous studies to better define the therapeutic role of cannabis and its long-term safety.

CLINICAL APPLICATIONS

In recent years, the clinical application of medical cannabis for CMP has garnered significant attention as a potential alternative or complement to traditional therapies. Although variability in study design, dosing, and patient responses limits definitive conclusions, existing evidence suggests that cannabis-based products may improve pain control, functional outcomes, and quality of life. A range of formulations—including inhaled vapors, sublingual oils, and topical creams—allows individualized treatment approaches.

In clinical practice, THC and CBD are often combined to leverage their synergistic effects via the endocannabinoid system (CB1 and CB2 receptors). While CBD alone has shown limited analgesic benefit in some trials,[35-37] its combination with THC appears more effective.[35] Similarly, one study observed no notable difference in pain index between CBD and placebo and found that both had comparable side effects, such as sedation.[36] Studies have reported that THC/CBD formulations significantly alleviate pain, with CBD mitigating THC-associated psychotropic effects like anxiety and intoxication.[38]

Medical cannabis can be administered via multiple routes, including oral ingestion, sublingual drops, inhalation, transdermal gels, and nasal sprays.[39] In practice, the administration of cannabinoids is tailored to individual patient factors such as pain severity, comorbidities, and personal preferences. Clinicians have observed reduced pain severity and improved quality of life, although adverse effects—typically mild—can occur. However, standardized clinical trials are needed to better define optimal dosing regimens, formulations, and long-term safety profiles.

In a prospective study, Chung et al.[40] examined the orthopedic conditions for which patients sought MC certification as an alternative pain management strategy. Low back pain was the most common indication (56%), followed by neck and extremity complaints. These patients reported lower quality-of-life scores than the general United States population, underscoring the burden of CMP and growing interest in non-opioid alternatives. Renslo et al.[41] assessed the impact of medical cannabis on opioid use in patients with osteoarthritis-related pain. Among 40 certified patients, daily opioid use dropped from 18 to 9.8 morphine milligram equivalents (MME) within six months, and 38% discontinued opioids entirely. Pain scores and physical health metrics also improved, suggesting cannabis may serve as an effective opioid-sparing therapy.

BENEFITS AND RISKS

Although CBD is known to have fewer adverse effects than THC, it can still cause issues like tiredness, diarrhea, appetite or weight changes,[42] drowsiness, nausea, vomiting, and dry mouth.[43] In rare cases, some individuals have also experienced hallucinations, panic attacks, and paranoia.[36, 44] While earlier studies have pointed to potential risks associated with recreational cannabis, often involving higher THC doses, inconsistent use patterns, and possible polysubstance use, a recent study focused on medical cannabis users with more controlled, therapeutic dosing regimens found that using medical cannabis regularly for a year did not significantly alter brain structure or cognitive abilities.[45]

In many studies, distinguishing between qualified and self-identified medical cannabis (MC) users can be challenging, particularly when a physician's endorsement and a confirmed diagnosis are unclear. This lack of distinction

Table 1. Summary of Key Studies on Medical Cannabis and Chronic Musculoskeletal Pain

Study	Study Type	Population / Sample Size	Key Findings
Notcutt et al.	Randomized, double-blind, placebo-controlled trial	CMP patients	THC & THC/CBD combo reduced pain (55.4%)
Harris et al.	Observational study	Cannabis users with OA	Users preferred cannabis over conventional treatments, with mixed side effects
Chung et al.	Prospective observational study	Orthopedic MC users	The most common indication is low back pain, high symptom burden
Renslo et al.	Cohort study	OA patients using MC	Significant opioid reduction and improved pain scores
Furrer et al.	Systematic review	Various studies; users aged 28–63	Daily users reported positive effects, minimal adverse events
Whiting et al.	Systematic review and meta-analysis	79 trials (only 4 with low risk of bias)	Moderate evidence for chronic pain, limited significance
Lynch et al.	Systematic review of RCTs	Randomized trials on CNCP	Safe and modest efficacy for CNCP
Stockings et al.	Systematic review and meta-analysis	47 RCTs and 57 observational studies	Modest pain reduction; high NNT, low NNH
Nugent et al.	Systematic review	Chronic pain patients	Limited efficacy; increased risks noted

Chronic non-cancer pain (CNCP); randomized clinical trial (RTC); number needed to treat (NNT); number needed to harm (NNH); Chronic musculoskeletal pain (CMP); cannabidiol (CBD) and tetrahydrocannabinol (THC)

makes it difficult to estimate the prevalence of self-medication, an important factor to consider. As self-medication with cannabis continues to rise, it is crucial to recognize that self-identified medical cannabis users may have different characteristics than those who use cannabis under the supervision of a healthcare provider. This growing trend highlights the importance for physicians to be aware of the possibility that some patients with CMP or other forms of chronic pain may be self-medicating with cannabis, which could impact treatment plans and overall care.[46]

PATIENT PERSPECTIVES ON CANNABINOID USE

Patient-reported experiences offer valuable insight into the real-world use of cannabinoids for chronic musculoskeletal pain (CMP). Many individuals report meaningful pain relief and improved quality of life, often viewing medical cannabis as a preferable alternative or complement to opioids. These perspectives are shaped by factors such as ease of use, prior exposure, and a perceived balance between benefits and side effects. Informal sources, such as online content or personal networks, commonly influence initial awareness and acceptance of CBD for pain management.[9,47] The discreet nature of some delivery forms, like sublingual THC-CBD sprays, further enhances patient satisfaction and willingness to recommend cannabis to others.[29]

Despite these positive views, some patients remain hesitant due to concerns about safety and adverse effects. Furrer et al.[5] noted a lack of detailed research on the motivations, expectations, and experiences of patients using medical cannabis for CMP and other chronic non-cancer pain. Their scoping review found that many users report improved quality of life, fewer side effects, and decreased reliance on opioids. However, much of this evidence is subjective and potentially biased, underscoring the need for more rigorous, patient-centered research.

Cannabis is often used not only for pain relief but also to address inflammation, sleep issues, and mood disturbances. Some patients rely on it exclusively, while others integrate it with conventional therapies. Familiarity with cannabis may influence how patients manage side effects such as dizziness, dry mouth, or cognitive fog—leading to better adherence. Still, evaluating cannabis's full impact on function and well-being is complex. THC's psychotropic effects may affect perceptions of health and blur the line between pharmacological and psychosocial influences. Importantly, anxiety and depersonalization, particularly in inexperienced users, can occur after THC use, especially in those with underlying mental health conditions.[30] In contrast, individuals with prior experience using cannabis rarely identify anxiety as a significant adverse effect, suggesting that prior exposure may mitigate such responses. This highlights the need for patient education, individualized dosing, and appropriate settings to optimize therapeutic outcomes while minimizing adverse effects.

LEGISLATIVE AND REGULATORY CONSIDERATIONS

The legal framework for cannabinoid uses in musculoskeletal pain management varies widely across regions due to historical, political, and scientific influences. While some countries and U.S. have embraced medical cannabis, others maintain restrictive policies that limit patient access. Even where medical cannabis is legal, challenges persist, including high costs, limited availability, restrictive prescribing rules, and lack of insurance coverage. Legal uncertainties

and concerns about dosing standardization and liability also deter many clinicians from recommending cannabis.

A major concern is the lack of consistent product quality. Many medical cannabis programs operate through dispensaries rather than pharmacies, leading to variability in potency, composition, and labeling. Patients may receive inconsistent dosages or encounter contaminants without regulatory oversight, complicating safety and efficacy. Nonetheless, regulations are evolving. Increased public acceptance and growing evidence are driving calls for science-based policymaking. Countries like Australia and the United Kingdom (UK) have revised cannabis policies to allow expanded medical use under strict guidelines. In 2018, the UK rescheduled cannabis-based products for prescription by specialists in treatment-resistant cases, including osteoarthritis.

In the U.S., cannabis remains federally classified as a Schedule I substance, but many states have implemented medical or recreational cannabis programs. FDA-approved cannabinoid medications such as Epidiolex, Marinol, and Cesamet exist, though none are explicitly approved for musculoskeletal pain. Canada legalized both medical and recreational cannabis in 2018, with Health Canada regulating production and distribution to ensure safety. Other countries, including Germany and Australia, allow limited medical cannabis access under strict regulatory conditions. Global differences in cannabis laws and oversight continue to affect patient access and research progress, underscoring the need for harmonized, evidence-informed policy development.[48]

INTERDISCIPLINARY COLLABORATION IN CANNABINOID-BASED PAIN MANAGEMENT

Managing chronic musculoskeletal pain (CMP) effectively requires a multidisciplinary approach, particularly when incorporating medical cannabis. Due to the complexity of CMP and the variable effects of cannabinoids, collaborative care among orthopedics, physical medicine and rehabilitation (PMR), pain management, rheumatology, psychiatry, and pharmacy enhance patient outcomes and safety.

Orthopedic surgeons often manage patients with pain from degenerative conditions. While surgery addresses structural issues, conservative management—including physical therapy, NSAIDs, and injections—remains first-line. When standard treatments fail, collaboration with pain specialists may lead to considering cannabinoids within a multimodal pain strategy. Physical therapists, with their expertise in rehabilitation and functional recovery, play a key role in patient education. They help patients understand how cannabis can complement interventions like exercise and manual therapy, address misconceptions, and integrate cannabis into broader treatment plans. Pain specialists ensure cannabis is appropriately combined with pharmacologic or interventional treatments. Rheumatologists guide cannabinoid use in inflammatory conditions like rheumatoid arthritis and osteoarthritis. Pharmacists counsel patients on dosing, interactions, and adverse effects, especially those with complex medication regimens. Mental health professionals assess and manage the psychological impact of cannabis, including its effects on anxiety, depression, and potential for misuse. Nurses and nurse practitioners serve as frontline educators and symptom monitors, supporting safe and informed use.

This interdisciplinary collaboration ensures medical cannabis is used safely, effectively, and in context with each patient's broader health and functional goals.

CLINICAL GAPS AND FUTURE DIRECTIONS

Existing studies on medical cannabis (MC) for chronic pain are limited by variability in objectives, methodologies, and participant characteristics. Many involve small sample sizes (<100 participants), reducing generalizability. Reliance on self-reported data introduces recall and social desirability bias, while chart reviews may fail to capture patient experiences. Additionally, differing cannabis regulations across regions complicate comparisons and consistency in findings.

To strengthen evidence, future studies should focus on more homogeneous patient populations to minimize confounding from varying pain etiologies. Including individuals who discontinued medical cannabis would also provide insight into reasons for cessation—such as adverse effects or stigma. For instance, Zolotov et al.[49] found that 20% of medical cannabis users who stopped treatment reported higher rates of adverse effects compared to those who continued use.

WHEN AND HOW TO CONSIDER MEDICAL CANNABIS FOR CMP PATIENTS?

For orthopedic surgeons, medical cannabis may serve as a complementary therapy for patients with chronic musculoskeletal pain (CMP) who experience persistent symptoms despite standard treatments like physical therapy, NSAIDs, and injections. Particularly, THC-CBD formulations may offer meaningful pain relief and improvements in sleep, mood, and overall quality of life—especially for those intolerant to traditional analgesics or seeking to reduce opioid use.

However, prescribing medical cannabis requires an individualized assessment. Clinicians must evaluate comorbidities, risk of substance misuse, and potential drug interactions. Collaboration with pain specialists, rheumatologists, and mental health providers is essential to ensure cannabis use aligns with broader treatment goals. Educating patients on expected outcomes, dosing, and side effects helps reduce anxiety and supports informed shared decision-making.

CONCLUSION

his scoping review highlights the potential role of medical cannabis in managing musculoskeletal pain. Evidence suggests it may reduce pain, enhance well-being, and improve quality of life, particularly as an alternative or adjunct to

opioids. Adverse effects are typically mild, supporting its use as a safer long-term option. However, data on long-term efficacy, especially for CBD, remain limited. Given the risks of opioid dependence, cannabis offers a promising therapeutic alternative. Future research should focus on standardized dosing, long-term safety, and identifying which patients are most likely to benefit from cannabinoid-based therapies in chronic musculoskeletal pain management.

DECLARATION OF CONFLICT OF INTEREST

The author does NOT have any potential conflicts of interest for this manuscript.

DECLARATION OF FUNDING

This manuscript was produced and published through support from the Rothman Institute Foundation for Opioid Research & Education.

DECLARATION OF ETHICAL APPROVAL FOR STUDY

Not applicable for the review articles

DECLARATION OF INFORMED CONSENT

No information (names, initials, hospital identification numbers, or photographs) in the submitted manuscript that can be used to identify patients.

Submitted: March 05, 2025 EDT. Accepted: May 23, 2025 EDT.
Published: December 22, 2025 EDT.

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