Evidence Search Service
Medicinal Cannabis: recent evidence & information

This literature has been compiled following the recent government announcement (https://www.gov.uk/government/news/government-announces-that-medicinal-cannabis-is-legal), bringing together recent evidence and useful information on Medicinal Cannabis.


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1. **A quick guide to medical cannabis: infographic**

   With medical cannabis (CB) now likely to be legalised in UK, this infographic provides overview of what pharmacists need to know.

   [Available online via this link](#).

2. **Cannabinoids and clinical pharmacology- current issue and barriers to surmount.**
   British Journal of Clinical Pharmacology 2018 84 (11) Special Issue.

   [Available online via this link](#).

3. **Cannabis-based medicines for chronic neuropathic pain in adults.**
   Mücke Martin The Cochrane database of systematic reviews 2018;3:CD012182-.

   BACKGROUND This review is one of a series on drugs used to treat chronic neuropathic pain. Estimates of the population prevalence of chronic pain with neuropathic components range between 6% and 10%. Current pharmacological treatment options for neuropathic pain afford substantial benefit for only a few people, often with adverse effects that outweigh the benefits. There is a need to explore other treatment options, with different mechanisms of action for treatment of conditions with chronic neuropathic pain. Cannabis has been used for millennia to reduce pain. Herbal cannabis is currently strongly promoted by some patients and their advocates to treat any type of chronic pain. OBJECTIVES To assess the efficacy, tolerability, and safety of cannabis-based medicines (herbal, plant-derived, synthetic) compared to placebo or conventional drugs for conditions with chronic neuropathic pain in adults. SEARCH METHODS In November 2017 we searched CENTRAL, MEDLINE, Embase, and two trials registries for published and ongoing trials, and examined the reference lists of reviewed articles. SELECTION CRITERIA We selected randomised, double-blind controlled trials of medical cannabis, plant-derived and synthetic cannabis-based medicines against placebo or any other active treatment of conditions with chronic neuropathic pain in adults, with a treatment duration of at least two weeks and at least 10 participants per treatment arm. DATA COLLECTION AND ANALYSIS Three review authors independently extracted data of study characteristics and outcomes of efficacy, tolerability and safety, examined issues of study quality, and assessed risk of bias. We resolved discrepancies by discussion. For efficacy, we calculated the number needed to treat for an additional beneficial outcome (NNTB) for pain relief of 30% and 50% or greater, patient's global impression to be much or very much improved, dropout rates due to lack of efficacy, and the standardised mean differences for pain intensity, sleep problems, health-related quality of life (HRQoL), and psychological distress. For tolerability, we calculated number needed to treat for an additional harmful outcome (NNTH) for withdrawal due to adverse events and specific adverse events, nervous system disorders and psychiatric disorders. For safety, we calculated NNTH for serious...
adverse events. Meta-analysis was undertaken using a random-effects model. We assessed the quality of evidence using GRADE and created a 'Summary of findings' table. MAIN RESULTS We included 16 studies with 1750 participants. The studies were 2 to 26 weeks long and compared an oromucosal spray with a plant-derived combination of tetrahydrocannabinol (THC) and cannabidiol (CBD) (10 studies), a synthetic cannabinoid mimicking THC (nabilone) (two studies), inhaled herbal cannabis (two studies) and plant-derived THC (dronabinol) (two studies) against placebo (15 studies) and an analgesic (dihydrocodeine) (one study). We used the Cochrane 'Risk of bias' tool to assess study quality. We defined studies with zero to two unclear or high risks of bias judgements to be high-quality studies, with three to five unclear or high risks of bias to be moderate-quality studies, and with six to eight unclear or high risks of bias to be low-quality studies. Study quality was low in two studies, moderate in 12 studies and high in two studies. Nine studies were at high risk of bias for study size. We rated the quality of the evidence according to GRADE as very low to moderate. Primary outcomes Cannabis-based medicines may increase the number of people achieving 50% or greater pain relief compared with placebo (21% versus 17%; risk difference (RD) 0.05 (95% confidence interval (CI) 0.00 to 0.09); NNTB 20 (95% CI 11 to 100); 1001 participants, eight studies, low-quality evidence). We rated the evidence for improvement in Patient Global Impression of Change (PGIC) with cannabis to be of very low quality (26% versus 21%; RD 0.09 (95% CI 0.01 to 0.17); NNTB 11 (95% CI 6 to 100); 1092 participants, six studies). More participants withdrew from the studies due to adverse events with cannabis-based medicines (10% of participants) than with placebo (5% of participants) (RD 0.04 (95% CI 0.02 to 0.07); NNT 25 (95% CI 16 to 50); 1848 participants, 13 studies, moderate-quality evidence). We did not have enough evidence to determine if cannabis-based medicines increase the frequency of serious adverse events compared with placebo (RD 0.01 (95% CI -0.01 to 0.03); 1876 participants, 13 studies, low-quality evidence). Secondary outcomes Cannabis-based medicines probably increase the number of people achieving pain relief of 30% or greater compared with placebo (39% versus 33%; RD 0.09 (95% CI 0.03 to 0.15); NNTB 11 (95% CI 7 to 33); 1586 participants, 10 studies, moderate quality evidence). Cannabis-based medicines may increase nervous system adverse events compared with placebo (61% versus 29%; RD 0.38 (95% CI 0.18 to 0.58); NNT 3 (95% CI 2 to 6); 1304 participants, nine studies, low-quality evidence). Psychiatric disorders occurred in 17% of participants using cannabis-based medicines and in 5% using placebo (RD 0.10 (95% CI 0.06 to 0.15); NNT 10 (95% CI 7 to 16); 1314 participants, nine studies, low-quality evidence). We found no information about long-term risks in the studies analysed. Subgroup analyses We are uncertain whether herbal cannabis reduces mean pain intensity (very low-quality evidence). Herbal cannabis and placebo did not differ in tolerability (very low-quality evidence). AUTHORS' CONCLUSIONS The potential benefits of cannabis-based medicine (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) in chronic neuropathic pain might be outweighed by their potential harms. The quality of evidence for pain relief outcomes reflects the exclusion of participants with a history of substance abuse and other significant comorbidities from the studies, together with their small sample sizes.

4. Ethical issues in medical cannabis use.

The increasing use of medical cannabis (MC) in the past decade raises several ethical considerations for the clinician. Regulatory issues stem from a gap between MC registration and certification in each country. Professional issues derive from the lack of sufficient knowledge of MC characteristics and the intersection between the physician, the patient and commercial interests. Finally, there are medical and psychological implications which are related to the use of MC regimens. We will discuss these issues in the light of the current era, in which policy has rapidly shifted toward legalization of cannabis, which influences the decisions of both clinicians and patients.

Available online at this link

5. Medical Cannabis for Neuropathic Pain.
Lee Gemayel Current pain and headache reports 2018;22(1):8-.
PURPOSE OF REVIEW Many cultures throughout history have used cannabis to treat a variety of painful ailments. Neuropathic pain is a complicated condition that is challenging to treat with our current medications. Recent scientific discovery has elucidated the intricate role of the endocannabinoid system in the pathophysiology of neuropathic pain. As societal perceptions change, and legislation on medical cannabis relaxes, there is growing interest in the use of medical cannabis for neuropathic pain.

RECENT FINDINGS We examined current basic scientific research and data from recent randomized controlled trials (RCTs) evaluating medical cannabis for the treatment of neuropathic pain. These studies involved patients with diverse etiologies of neuropathic pain and included medical cannabis with different THC concentrations and routes of administration. Multiple RCTs demonstrated efficacy of medical cannabis for treating neuropathic pain, with number needed to treat (NNT) values similar to current pharmacotherapies. Although limited by small sample sizes and short duration of study, the evidence appears to support the safety and efficacy of short-term, low-dose cannabis vaporization and oral mucosal delivery for the treatment of neuropathic pain. The results suggest medical cannabis may be as tolerable and effective as current neuropathic agents; however, more studies are needed to determine the long-term effects of medical cannabis use. Furthermore, continued research to optimize dosing, cannabinoid ratios, and alternate routes of administration may help to refine the therapeutic role of medical cannabis for neuropathic pain.

   Ananth Prasanna Pediatric blood & cancer 2018;65(2):--

   Medical marijuana (MM) has become increasingly legal at the state level and accessible to children with serious illness. Pediatric patients with cancer may be particularly receptive to MM, given purported benefits in managing cancer-related symptoms. In this review, we examine the evidence for MM as a supportive care agent in pediatric oncology. We describe the current legal status of MM, mechanism of action, common formulations, and potential benefits versus risks for pediatric oncology patients. We offer suggestions for how providers might approach MM requests. Throughout, we comment on avenues for future investigation on this growing trend in supportive care.

   Available online at this link

7. Medical use of cannabis
   House of Commons. Research Briefing. 2018;--

   This briefing provides a short overview of the control of cannabis in the UK, and information about the recently announced review on the medical use of cannabis. Commons Briefing papers CBP-8355

   Available online at this link

8. Medical use of cannabis and cannabinoids containing products - Regulations in Europe and North America.
   Abuhasira Ran European journal of internal medicine 2018;49:2-6

   In 1937, the United States of America criminalized the use of cannabis and as a result its use decreased rapidly. In recent decades, there is a growing interest in the wide range of medical uses of cannabis and its constituents; however, the laws and regulations are substantially different between countries. Laws differentiate between raw herbal cannabis, cannabis extracts, and cannabinoid-based medicines. Both the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA) do not approve the use of herbal cannabis or its extracts. The FDA approved several cannabinoid-based medicines, so did 23 European countries and Canada. However, only four of the reviewed countries have fully authorized the medical use of herbal cannabis - Canada, Germany, Israel and the Netherlands, together with more than 50% of the states in the United States. Most of the regulators allow the physicians to decide what specific indications they will prescribe cannabis for, but some regulators dictate only specific indications.
The aim of this article is to review the current (as of November 2017) regulations of medical cannabis use in Europe and North America.

**9. Practical considerations in medical cannabis administration and dosing.**

Cannabis has been employed medicinally throughout history, but its recent legal prohibition, biochemical complexity and variability, quality control issues, previous dearth of appropriately powered randomised controlled trials, and lack of pertinent education have conspired to leave clinicians in the dark as to how to advise patients pursuing such treatment. With the advent of pharmaceutical cannabis-based medicines (Sativex/nabiximols and Epidiolex), and liberalisation of access in certain nations, this ignorance of cannabis pharmacology and therapeutics has become untenable. In this article, the authors endeavour to present concise data on cannabis pharmacology related to tetrahydrocannabinol (THC), cannabidiol (CBD) et al., methods of administration (smoking, vaporisation, oral), and dosing recommendations. Adverse events of cannabis medicine pertain primarily to THC, whose total daily dose-equivalent should generally be limited to 30mg/day or less, preferably in conjunction with CBD, to avoid psychoactive sequelae and development of tolerance. CBD, in contrast to THC, is less potent, and may require much higher doses for its adjunctive benefits on pain, inflammation, and attenuation of THC-associated anxiety and tachycardia. Dose initiation should commence at modest levels, and titration of any cannabis preparation should be undertaken slowly over a period of as much as two weeks. Suggestions are offered on cannabis-drug interactions, patient monitoring, and standards of care, while special cases for cannabis therapeutics are addressed: epilepsy, cancer palliation and primary treatment, chronic pain, use in the elderly, Parkinson disease, paediatrics, with concomitant opioids, and in relation to driving and hazardous activities.

**10. The therapeutic effects of Cannabis and cannabinoids: An update from the National Academies of Sciences, Engineering and Medicine report.**

The National Academies of Sciences, Engineering and Medicine conducted a rapid turn-around comprehensive review of recent medical literature on The Health Effects of Cannabis and Cannabinoids. The 16-member committee adopted the key features of a systematic review process, conducting an extensive search of relevant databases and considered 10,000 recent abstracts to determine their relevance. Primacy was given to recently published systematic reviews and primary research that studied one of the committee’s 11 prioritized health endpoints-therapeutic effects; cancer incidence; cardiometabolic risk; respiratory disease; immune function; injury and death; prenatal, perinatal and postnatal outcomes; psychosocial outcomes; mental health; problem Cannabis use; and Cannabis use and abuse of other substances. The committee developed standard language to categorize the weight of evidence regarding whether Cannabis or cannabinoids use for therapeutic purposes are an effective or ineffective treatment for the prioritized health endpoints of interest. In the Therapeutics chapter reviewed here, the report concluded that there was conclusive or substantial evidence that Cannabis or cannabinoids are effective for the treatment of pain in adults; chemotherapy-induced nausea and vomiting and spasticity associated with multiple sclerosis. Moderate evidence was found for secondary sleep disturbances. The evidence supporting improvement in appetite, Tourette syndrome, anxiety, posttraumatic stress disorder, cancer, irritable bowel syndrome, epilepsy and a variety of neurodegenerative disorders was described as limited, insufficient or absent. A chapter of the NASEM report enumerated multiple barriers to conducting research on Cannabis in the US that may explain the paucity of positive therapeutic benefits in the published literature to date.

**11. A selective review of medical cannabis in cancer pain management.**
Blake Alexia Annals of palliative medicine 2017;6:S215-.
Insufficient management of cancer-associated chronic and neuropathic pain adversely affects patient quality of life. Patients who do not respond well to opioid analgesics, or have severe side effects from the use of traditional analgesics are in need of alternative therapeutic options. Anecdotal evidence suggests that medical cannabis has potential to effectively manage pain in this patient population. This review presents a selection of representative clinical studies, from small pilot studies conducted in 1975, to double-blind placebo-controlled trials conducted in 2014 that evaluated the efficacy of cannabinoid-based therapies containing tetrahydrocannabinol (THC) and cannabidiol (CBD) for reducing cancer-associated pain. A review of literature published on Medline between 1975 and 2017 identified five clinical studies that evaluated the effect of THC or CBD on controlling cancer pain, which have been reviewed and summarised. Five studies that evaluated THC oil capsules, THC:CBD oromucosal spray (nabiximols), or THC oromucosal sprays found some evidence of cancer pain reduction associated with these therapies. A variety of doses ranging from 2.7-43.2 mg/day THC and 0-40 mg/day CBD were administered. Higher doses of THC were correlated with increased pain relief in some studies. One study found that significant pain relief was achieved in doses as low as 2.7-10.8 mg THC in combination with 2.5-10.0 mg CBD, but there was conflicting evidence on whether higher doses provide superior pain relief. Some reported side effects include drowsiness, hypotension, mental clouding, and nausea and vomiting. There is evidence suggesting that medical cannabis reduces chronic or neuropathic pain in advanced cancer patients. However, the results of many studies lacked statistical power, in some cases due to limited number of study subjects. Therefore, there is a need for the conduct of further double-blind, placebo-controlled clinical trials with large sample sizes in order to establish the optimal dosage and efficacy of different cannabis-based therapies.

12. **Cannabinoids in treatment-resistant epilepsy: A review.**

Treatment-resistant epilepsy (TRE) affects 30% of epilepsy patients and is associated with severe morbidity and increased mortality. Cannabis-based therapies have been used to treat epilepsy for millennia, but only in the last few years have we begun to collect data from adequately powered placebo-controlled, randomized trials (RCTs) with cannabidiol (CBD), a cannabis derivative. Previously, information was limited to case reports, small series, and surveys reporting on the use of CBD and diverse medical marijuana (MMJ) preparations containing: tetrahydrocannabinol (THC), CBD, and many other cannabinoids in differing combinations. These RCTs have studied the safety and explored the potential efficacy of CBD use in children with Dravet Syndrome (DS) and Lennox-Gastaut Syndrome (LGS). The role of the placebo response is of paramount importance in studying medical cannabis products given the intense social and traditional media attention, as well as the strong beliefs held by many parents and patients that a natural product is safer and more effective than FDA-approved pharmaceutical agents. We lack valid data on the safety, efficacy, and dosing of artisanal preparations available from dispensaries in the 25 states and District of Columbia with MMJ programs and online sources of CBD and other cannabinoids. On the other hand, open-label studies with 100mg/ml CBD (Epidiolex®, GW Pharmaceuticals) have provided additional evidence of its efficacy along with an adequate safety profile (including certain drug interactions) in children and young adults with a spectrum of TREs. Further, Phase 3 RCTs with Epidiolex support efficacy and adequate safety profiles for children with DS and LGS at doses of 10- and 20-mg/kg/day. This article is part of a Special Issue titled "Cannabinoids and Epilepsy".

[Available online at this link](https://doi.org/10.1016/j.eplepsy.2017.04.006)

13. **Cannabis Epidemiology: A Selective Review.**

BACKGROUND Globally, the most widely used set of compounds among the internationally regulated drugs is cannabis. OBJECTIVE To review evidence from epidemiological research on cannabis, organized in relation to this field’s five main rubrics: quantity, location, causes, mechanisms, and prevention/ control. METHOD The review covers a selection of evidence from standardized population surveys, official statistics, and governmental reports, as well as published articles and books identified via MEDLINE, Web of Science, and Google Scholar as of July 2016.RESULTSIn relation to quantity, an estimated 3% to 5% of the world population is thought to
have tried a cannabis product, with at least one fairly recent use, mainly extra-medical and outside boundaries of prescribed use. Among cannabis users in the United States, roughly one in 7-8 has engaged in medical marijuana use. In relation to location, prevalence proportions reveal important variations across countries and between subgroups within countries. Regarding causes and mechanisms of starting to use cannabis, there is no compelling integrative and replicable conceptual model or theoretical formulation. Most studies of mechanisms have focused upon a 'gateway sequence' and person-to-person diffusion, with some recent work on disability-adjusted life years. A brief review of cannabis use consequences, as well as prevention and control strategies is also provided. CONCLUSION At present, we know much about the frequency and occurrence of cannabis use, with too little replicable definitive evidence with respect to the other main rubrics. Given a changing regulatory environment for cannabis products, new institutions such as an independent International Cannabis Products Safety Commission may be required to produce evidence required to weigh benefits versus costs. It is not clear that government sponsored research will be sufficient to meet consumer demand for balanced points of view and truly definitive evidence.

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14. Cannabis: A Treasure Trove or Pandora's Box?
Solymosi Katalin Mini reviews in medicinal chemistry 2017;17(13):1223-1291.

BACKGROUND & OBJECTIVE Cannabis is one of the earliest cultivated plants. Cannabis of industrial utility and culinary value is generally termed as hemp. Conversely, cannabis that is bred for medical, spiritual and recreational purposes is called marijuana. The female marijuana plant produces a significant quantity of bio- and psychoactive phytocannabinoids, which regained the spotlight with the discovery of the endocannabinoid system of the animals in the early 90's. Nevertheless, marijuana is surrounded by controversies, debates and misconceptions related to its taxonomic classification, forensic identification, medical potential, legalization and its long-term health consequences. METHOD In the first part, we provide an in-depth review of the botany and taxonomy of Cannabis. We then overview the biosynthesis of phytocannabinoids within the glandular trichomes with emphasis on the role of peculiar plastids in the production of the secreted material. We also compile the analytical methods used to determine the phytocannabinoid composition of glandular trichomes. In the second part, we revisit the psychobiology and molecular medicine of marijuana. RESULTS & CONCLUSION We summarize our current knowledge on the recreational use of cannabis with respect to the modes of consumption, short-term effects, chronic health consequences and cannabis use disorder. Next, we overview the molecular targets of a dozen major and minor bioactive cannabinoids in the body. This helps us introduce the endocannabinoid system in an unprecedented detail: its up-to-date molecular biology, pharmacology, physiology and medical significance, and beyond. In conclusion, we offer an unbiased survey about cannabis to help better weigh its medical value versus the associated risks.

15. Medical Cannabinoids in Children and Adolescents: A Systematic Review.
Wong Shane Shucheng Pediatrics 2017;140(5):--.

CONTEXT Legalization of medical marijuana in many states has led to a widening gap between the accessibility and the evidence for cannabinoids as a medical treatment. OBJECTIVE To systematically review published reports to identify the evidence base of cannabinoids as a medical treatment in children and adolescents. DATA SOURCES Based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a search of PubMed, Medline, and the Cumulative Index to Nursing and Allied Health Literature databases was conducted in May 2017. STUDY SELECTION Searching identified 2743 citations, and 103 full texts were reviewed. DATA EXTRACTION Searching identified 21 articles that met inclusion criteria, including 22 studies with a total sample of 795 participants. Five randomized controlled trials, 5 retrospective chart reviews, 5 case reports, 4 open-label trials, 2 parent surveys, and 1 case series were identified. RESULTS Evidence for benefit was strongest for chemotherapy-induced nausea and vomiting, with increasing evidence of benefit for epilepsy. At this time, there is insufficient evidence to support use for spasticity, neuropathic pain, posttraumatic stress disorder, and Tourette syndrome. LIMITATIONS The methodological quality of studies varied, with the majority of studies lacking control groups, limited by small sample size, and not designed to test for the statistical significance
of outcome measures. Studies were heterogeneous in the cannabinoid composition and dosage and lacked long-term follow-up to identify potential adverse effects. CONCLUSIONS Additional research is needed to evaluate the potential role of medical cannabinoids in children and adolescents, especially given increasing accessibility from state legalization and potential psychiatric and neurocognitive adverse effects identified from studies of recreational cannabis use.

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16. Medical cannabis and mental health: A guided systematic review.
Walsh Zach Clinical psychology review 2017;51:15-29.

This review considers the potential influences of the use of cannabis for therapeutic purposes (CTP) on areas of interest to mental health professionals, with foci on adult psychopathology and assessment. We identified 31 articles relating to the use of CTP and mental health, and 29 review articles on cannabis use and mental health that did not focus on use for therapeutic purposes. Results reflect the prominence of mental health conditions among the reasons for CTP use, and the relative dearth of high-quality evidence related to CTP in this context, thereby highlighting the need for further research into the harms and benefits of medical cannabis relative to other therapeutic options. Preliminary evidence suggests that CTP may have potential for the treatment of PTSD, and as a substitute for problematic use of other substances. Extrapolation from reviews of non-therapeutic cannabis use suggests that the use of CTP may be problematic among individuals with psychotic disorders. The clinical implications of CTP use among individuals with mood disorders are unclear. With regard to assessment, evidence suggests that CTP use does not increase risk of harm to self or others. Acute cannabis intoxication and recent CTP use may result in reversible deficits with the potential to influence cognitive assessment, particularly on tests of short-term memory.

17. Medical marijuana: Challenges and risk issues for health care providers.

Laws on medical marijuana and recreational use of marijuana are sweeping the country and presenting real dilemmas for health care providers and facilities. However, due to disagreements between federal and state law, there are no easy answers. Additionally, the case law and statutory law on these issues is exceedingly sparse. It may take years for all of the issues to be ironed out, but health care facilities will need to act in the meantime on what may be little more than educated guesses. It may not be appropriate to simply prohibit the use of medical marijuana, but accommodating it also has risk. This article will address what is known about the subject and what is not known about the subject. Each provider and health care facility will need to devise their own approach to the subject based on principles that are presently known, while keeping an eye on the health and safety of all involved.

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18. Medical Marijuana: Just the Beginning of a Long, Strange Trip?

Medical marijuana continues to gain acceptance and become legalized in many states. Various species of the marijuana plant have been cultivated, and this plant can contain up to 100 active compounds known as cannabinoids. Two cannabinoids seem the most clinically relevant: Δ9-tetrahydrocannabinol (THC), which tends to produce the psychotropic effects commonly associated with marijuana, and cannabidiol (CBD), which may produce therapeutic effects without appreciable psychoactive properties. Smoking marijuana, or ingesting extracts from the whole plant orally (in baked goods, teas, and so forth), introduces variable amounts of THC, CBD, and other minor cannabinoids into the systemic circulation, where they ultimately reach the central and peripheral nervous systems. Alternatively, products containing THC, CBD, or a combination of both compounds, can be ingested as oral tablets or via sprays applied to the oral mucosal
membranes. These products may provide a more predictable method for delivering a known amount of specific cannabinoids into the body. Although there is still a need for randomized controlled trials, preliminary studies have suggested that medical marijuana and related cannabinoids may be beneficial in treating people with chronic pain, inflammation, spasticity, and other conditions seen commonly in physical therapist practice. Physical therapists, therefore, should be aware of the options that are available for patients considering medical marijuana and should be ready to provide information for these patients. Clinicians also should be aware that marijuana can produce untoward effects on cognition, coordination, balance, and cardiovascular and pulmonary function and should be vigilant for any problems that may arise if patients are using cannabinoids during physical rehabilitation.

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19. The Effects of Cannabis Among Adults With Chronic Pain and an Overview of General Harms: A Systematic Review.

Background Cannabis is increasingly available for the treatment of chronic pain, yet its efficacy remains uncertain. Purpose To review the benefits of plant-based cannabis preparations for treating chronic pain in adults and the harms of cannabis use in chronic pain and general adult populations. Data Sources MEDLINE, Cochrane Database of Systematic Reviews, and several other sources from database inception to March 2017. Study Selection Intervention trials and observational studies, published in English, involving adults using plant-based cannabis preparations that reported pain, quality of life, or adverse effect outcomes. Data Extraction Two investigators independently abstracted study characteristics and assessed study quality, and the investigator group graded the overall strength of evidence using standard criteria. Data Synthesis From 27 chronic pain trials, there is low-strength evidence that cannabis alleviates neuropathic pain but insufficient evidence in other pain populations. According to 11 systematic reviews and 32 primary studies, harms in general population studies include increased risk for motor vehicle accidents, psychotic symptoms, and short-term cognitive impairment. Although adverse pulmonary effects were not seen in younger populations, evidence on most other long-term physical harms, in heavy or long-term cannabis users, or in older populations is insufficient. Limitation Few methodologically rigorous trials; the cannabis formulations studied may not reflect commercially available products; and limited applicability to older, chronically ill populations and patients who use cannabis heavily. Conclusion Limited evidence suggests that cannabis may alleviate neuropathic pain in some patients, but insufficient evidence exists for other types of chronic pain. Among general populations, limited evidence suggests that cannabis is associated with an increased risk for adverse mental health effects. Primary Funding Source U.S. Department of Veterans Affairs. (PROSPERO: CRD42016033623).

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20. The Experiences of Medical Marijuana Patients: A Scoping Review of the Qualitative Literature.

Medical marijuana is now legal in more than half of the United States but remains federally prohibited and classified as a schedule 1 drug. The chemical compounds in marijuana are known neuroprotectants; however, their clinical efficacy and safety have not been proven. Many healthcare providers remain unaware of the therapeutic potential of marijuana and its adverse effects. The conflicting laws and lack of guidance from healthcare professionals can lead to confusion and frustration for patients seeking this medication. Multiple factors contribute to the unique and varied experiences of medical marijuana patients. Because more individuals with neurological disorders seek therapeutic marijuana, it is important for healthcare professionals to
understand their distinctive experiences. Qualitative research methodology is ideal to capture the thick descriptions of these experiences. This review examines the qualitative research exploring the experiences of medical marijuana patients and discusses common themes across all studies.

21. The impact of cannabis and cannabinoids for medical conditions on health-related quality of life: A systematic review and meta-analysis.

INTRODUCTION The use of cannabis or cannabinoids to treat medical conditions and/or alleviate symptoms is increasingly common. However, the impact of this use on patient reported outcomes, such as health-related quality of life (HRQoL), remains unclear.

METHODS We conducted a systematic review and meta-analysis, employing guidelines from Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We categorized studies based on design, targeted disease condition, and type of cannabis or cannabinoid used. We scored studies based on quality and risk of bias. After eliminating some studies because of poor quality or insufficient data, we conducted meta-analyses of remaining studies based on design.

RESULTS Twenty studies met our pre-defined selection criteria. Eleven studies were randomized controlled trials (RCTs; 2322 participants); the remaining studies were of cohort and cross-sectional design. Studies of cannabinoids were mostly RCTs of higher design quality than studies of cannabis, which utilized smaller self-selected samples in observational studies. Although we did not uncover a significant association between cannabis and cannabinoids for medical conditions and HRQoL, some patients who used them to treat pain, multiple sclerosis, and inflammatory bowel disorders have reported small improvements in HRQoL, whereas some HIV patients have reported reduced HRQoL.

CONCLUSION The relationship between HRQoL and the use of cannabis or cannabinoids for medical conditions is inconclusive. Some patient populations report improvements whereas others report reductions in HRQoL. In order to inform users, practitioners, and policymakers more clearly, future studies should adhere to stricter research quality guidelines and more clearly report patient outcomes.

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OBJECTIVE Marijuana has been approved for a number of psychiatric conditions in many states in the US including posttraumatic stress disorder (PTSD), agitation in Alzheimer's disease, and Tourette's disorder. In this systematic review, we examine the strength of evidence for the efficacy of marijuana and other cannabinoids for these psychiatric indications.

DATA SOURCES The literature (MEDLINE) was searched for studies published between January 1980 and March 2015 using search terms related to marijuana and other cannabinoids and the specific diagnosis.

STUDY SELECTION The best quality of evidence, namely placebo-controlled, randomized clinical trials (RCTs) and meta-analyses, was sought per PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. In the absence of RCTs, the next best available evidence (eg, observational studies, case reports) was reviewed. Of 170 publications that were screened, 40 were related to the topic, 29 were included in the qualitative synthesis, and 13 studies examined the efficacy of cannabinoids in humans.

DATA EXTRACTION The evidence was rated using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) method. RESULTS No RCTs have thus far examined the efficacy of marijuana for Tourette's disorder, PTSD, or Alzheimer's disease. Lower-quality studies examined the efficacy of marijuana, Δ²-tetrahydrocannabinol, and nabulione; the strength of evidence for the use of cannabinoids for these conditions is very low at the present time. The consequences of chronic cannabinoid exposure includes tolerance, dependence, and withdrawal. Early and persistent marijuana use has been associated with the emergence of psychosis. Marijuana impairs attention, memory, IQ, and driving ability.

CONCLUSIONS Given its rapidly changing legal status, there is an urgent need to conduct double-blind, randomized, placebo- or active-controlled studies on the efficacy and safety of marijuana or its constituent cannabinoids for psychiatric conditions.
Physicians and policy-makers should take into account the limited existing evidence and balance that with side effects before approving medical marijuana for psychiatric indications.

23. **Medical cannabis: considerations for the anesthesiologist and pain physician.**

PURPOSE New regulations are in place at the federal and provincial levels in Canada regarding the way medical cannabis is to be controlled. We present them together with guidance for the safe use of medical cannabis and recent clinical trials on cannabis and pain. SOURCE The new Canadian regulations on the use of medical cannabis, the provincial regulations, and the various cannabis products available from the Canadian Licensed Producers were reviewed from Health Canada, provincial licensing authorities, and the licensed producers website, respectively. Recent clinical trials on cannabis and pain were reviewed from the existing literature. PRINCIPAL FINDINGS Health Canada has approved a new regulation on medical marijuana/cannabis, the Marihuana for Medical Purposes Regulations: The production of medical cannabis by individuals is illegal. Health Canada, however, has licensed authorized producers across the country, limiting the production to specific licenses of certain cannabis products. There are currently 26 authorized licensed producers from seven Canadian provinces offering more than 200 strains of marijuana. We provide guidance for the safe use of medical cannabis. The recent literature indicates that currently available cannabinoids are modestly effective analgesics that provide a safe, reasonable therapeutic option for managing chronic non-cancer-related pain. CONCLUSION The science of medical cannabis and the need for education of healthcare professionals and patients require continued effort. Although cannabinoids work to decrease pain, there is still a need to confirm these beneficial effects clinically and to exploit them with acceptable benefit-to-risk ratios.

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24. **Plant-Derived and Endogenous Cannabinoids in Epilepsy.**

Cannabis is one of the oldest psychotropic drugs and its anticonvulsant properties have been known since the last century. The aim of this review was to analyze the efficacy of cannabis in the treatment of epilepsy in adults and children. In addition, a description of the involvement of the endocannabinoid system in epilepsy is given in order to provide a biochemical background to the effects of endogenous cannabinoids in our body. General tolerability and adverse events associated with cannabis treatment are also investigated. Several anecdotal reports and clinical trials suggest that in the human population cannabis has anticonvulsant properties and could be effective in treating partial epilepsies and generalized tonic-clonic seizures, still known as "grand mal." They are based, among other factors, on the observation that in individuals who smoke marijuana to treat epilepsy, cessation of cannabis use precipitates the re-emergence of convulsive seizures, whereas resuming consumption of this psychotropic drug controls epilepsy in a reproducible manner. In conclusion, there is some anecdotal evidence for the potential efficacy of cannabis in treating epilepsy. Though there has been an increased effort by patients with epilepsy, their caregivers, growers, and legislators to legalize various forms of cannabis, there is still concern about its efficacy, relative potency, availability of medication-grade preparations, dosing, and potential short- and long-term side effects, including those on prenatal and childhood development.

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25. **Cannabinoids for Medical Use: A Systematic Review and Meta-analysis.**

IMPORTANCE Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear. OBJECTIVE To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids. DATA SOURCES
Twenty-eight databases from inception to April 2015. STUDY SELECTION Randomized clinical trials of cannabinoids for the following indications: nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome. DATA EXTRACTION AND SYNTHESIS Study quality was assessed using the Cochrane risk of bias tool. All review stages were conducted independently by 2 reviewers. Where possible, data were pooled using random-effects meta-analysis. MAIN OUTCOMES AND MEASURES Patient-relevant/disease-specific outcomes, activities of daily living, quality of life, global impression of change, and AEs. RESULTS A total of 79 trials (6462 participants) were included; 4 were judged at low risk of bias. Most trials showed improvement in symptoms associated with cannabinoids but these associations did not reach statistical significance in all trials. Compared with placebo, cannabinoids were associated with a greater average number of patients showing a complete nausea and vomiting response (47% vs 20%; odds ratio [OR], 3.82 [95% CI, 1.55-9.42]; 3 trials), reduction in pain (37% vs 31%; OR, 1.41 [95% CI, 0.99-2.00]; 8 trials), a greater average reduction in numerical rating scale pain assessment (on a 0-10-point scale; weighted mean difference [WMD], -0.46 [95% CI, -0.80 to -0.11]; 6 trials), and average reduction in the Ashworth spasticity scale (WMD, -0.36 [95% CI, -0.69 to -0.05]; 7 trials). There was an increased risk of short-term AEs with cannabinoids, including serious AEs. Common AEs included dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination. CONCLUSIONS AND RELEVANCE There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term AEs.

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26. **Cannabinoids in the Treatment of Epilepsy.**

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27. **Cannabis for therapeutic purposes and public health and safety: a systematic and critical review.**

BACKGROUND The use of Cannabis for Therapeutic Purposes (CTP) has recently become legal in many places. These policy and legal modifications may be related to changes in cannabis perceptions, availability and use and in the way cannabis is grown and sold. This may in turn have effects on public health and safety. To better understand the potential effects of CTP legalization on public health and safety, the current paper synthesizes and critically discusses the relevant literature. METHOD Twenty-eight studies were identified by a comprehensive search strategy, and their characteristics and main findings were systematically reviewed according to the following content themes: CTP and illegal cannabis use; CTP and other public health issues; CTP, crime and neighbourhood disadvantage. RESULT The research field is currently limited by a lack of theoretical and methodological rigorous studies. The review shows that the most prevalent theme of investigation so far has been the relation between CTP and illegal cannabis use. In addition, the literature review shows that there is an absence of evidence to support many common concerns related to detrimental public health and safety effects of CTP legalization. CONCLUSION Although lack of evidence provides some reassurance that CTP legalization may not have posed a substantial threat to public health and safety, this conclusion needs to be examined in light of the limitations of studies conducted so far. Furthermore, as CTP policy continues to evolve, including incorporation of greater commercialization, it is possible that the full effects of CTP legalization have yet to take place. Ensuring study quality will allow future research to better investigate the
complex role that CTP plays in relation to society at large, and public health and safety in particular.

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Deshpande Amol Canadian family physician Medecin de famille canadien 2015;61(8):e372-.

OBJECTIVE To determine if medical marijuana provides pain relief for patients with chronic noncancer pain (CNCP) and to determine the therapeutic dose, adverse effects, and specific indications.

DATA SOURCES In April 2014, MEDLINE and EMBASE searches were conducted using the terms chronic noncancer pain, smoked marijuana or cannabinoids, placebo and pain relief, or side effects or adverse events.

STUDY SELECTION An article was selected for inclusion if it evaluated the effect of smoked or vaporized cannabinoids (nonsynthetic) for CNCP; it was designed as a controlled study involving a comparison group, either concurrently or historically; and it was published in English in a peer-review journal. Outcome data on pain, function, dose, and adverse effects were collected, if available. All articles that were only available in abstract form were excluded. Synthesis A total of 6 randomized controlled trials (N = 226 patients) were included in this review; 5 of them assessed the use of medical marijuana in neuropathic pain as an adjunct to other concomitant analgesics including opioids and anticonvulsants. The 5 trials were considered to be of high quality; however, all of them had challenges with masking. Data could not be pooled owing to heterogeneity in delta-9-tetrahydrocannabinol potency by dried weight, differing frequency and duration of treatment, and variability in assessing outcomes. All experimental sessions in the studies were of short duration (maximum of 5 days) and reported statistically significant pain relief with nonserious side effects.

CONCLUSION There is evidence for the use of low-dose medical marijuana in refractory neuropathic pain in conjunction with traditional analgesics. However, trials were limited by short duration, variability in dosing and strength of delta-9-tetrahydrocannabinol, and lack of functional outcomes. Although well tolerated in the short term, the long-term effects of psychoactive and neurocognitive effects of medical marijuana remain unknown. Generalizing the use of medical marijuana to all CNCP conditions does not appear to be supported by existing evidence. Clinicians should exercise caution when prescribing medical marijuana for patients, especially in those with nonneuropathic CNCP.

Detyniecki Kamil Current neurology and neuroscience reports 2015;15(10):65-.

Marijuana has been utilized as a medicinal plant to treat a variety of conditions for nearly five millennia. Over the past few years, there has been an unprecedented interest in using cannabis extracts to treat epilepsy, spurred on by a few refractory pediatric cases featured in the media that had an almost miraculous response to cannabidiol-enriched marijuana extracts. This review attempts to answer the most important questions a clinician may have regarding the use of marijuana in epilepsy. First, we review the preclinical and human evidences for the anticonvulsant properties of the different cannabinoids, mainly tetrahydrocannabinol (THC) and cannabidiol (CBD). Then, we explore the safety data from animal and human studies. Lastly, we attempt to reconcile the controversy regarding physicians' and patients' opinions about whether the available evidence is sufficient to recommend the use of marijuana to treat epilepsy.

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Jensen Bjorn Current pain and headache reports 2015;19(10):50-.

Cannabinoid compounds include phytocannabinoids, endocannabinoids, and synthetics. The two primary phytocannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), with CB1 receptors in the brain and peripheral tissue and CB2 receptors in the immune and hematopoietic systems. The route of delivery of cannabis is important as the bioavailability and metabolism are very different for smoking versus oral/sublingual routes. Gold standard clinical
trials are limited; however, some studies have thus far shown evidence to support the use of cannabinoids for some cancer, neuropathic, spasticity, acute pain, and chronic pain conditions.


IMPORTANCEAs of March 2015, 23 states and the District of Columbia had medical marijuana laws in place. Physicians should know both the scientific rationale and the practical implications for medical marijuana laws.OBJECTIVETO review the pharmacology, indications, and laws related to medical marijuana use.EVIDENCE REVIEWThe medical literature on medical marijuana was reviewed from 1948 to March 2015 via MEDLINE with an emphasis on 28 randomized clinical trials of cannabinoids as pharmacotherapy for indications other than those for which there are 2 US Food and Drug Administration-approved cannabinoids (dronabinol and nabilone), which include nausea and vomiting associated with chemotherapy and appetite stimulation in wasting illnesses.FINDINGSUse of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence. Six trials that included 325 patients examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on multiple sclerosis. Several of these trials had positive results, suggesting that marijuana or cannabinoids may be efficacious for these indications.CONCLUSIONS AND RELEVANCEMedical marijuana is used to treat a host of indications, a few of which have evidence to support treatment with marijuana and many that do not. Physicians should educate patients about medical marijuana to ensure that it is used appropriately and that patients will benefit from its use.

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Marijuana policy is rapidly evolving in the United States and elsewhere, with cannabis sales fully legalized and regulated in some jurisdictions and use of the drug for medicinal purposes permitted in many others. Amidst this political change, patients and families are increasingly asking whether cannabis and its derivatives may have therapeutic utility for a number of conditions, including developmental and behavioral disorders in children and adolescents. This review examines the epidemiology of cannabis use among children and adolescents, including those with developmental and behavioral diagnoses. It then outlines the increasingly well-recognized neurocognitive changes shown to occur in adolescents who use cannabis regularly, highlighting the unique susceptibility of the developing adolescent brain and describing the role of the endocannabinoid system in normal neurodevelopment. The review then discusses some of the proposed uses of cannabis in developmental and behavioral conditions, including attention-deficit hyperactivity disorder and autism spectrum disorder. Throughout, the review outlines gaps in current knowledge and highlights directions for future research, especially in light of a dearth of studies specifically examining neurocognitive and psychiatric outcomes among children and adolescents with developmental and behavioral concerns exposed to cannabis.

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33. Medical uses of marijuana (Cannabis sativa): fact or fallacy?

Marijuana (Cannabis sativa) has been used throughout the world medically, recreationally and spiritually for thousands of years. In South Africa, from the mid-19th century to the 1920s, practitioners prescribed it for a multitude of conditions. In 1928 it was classified as a Schedule I substance, illegal, and without medical value. Ironically, with this prohibition, cannabis became the most widely used illicit recreational drug, not only in South Africa, but worldwide. Cannabis is generally regarded as enjoyable and relaxing without the addictive risks of opioids or stimulants. In alternative medicine circles it has never lost its appeal. To date 23 States in the USA have
legalised its medical use despite the federal ban. Unfortunately, little about cannabis is not without controversy. Its main active ingredient, δ-9-tetrahydrocannabinol (THC), was not isolated until 1964, and it was not until the 1990s that the far-reaching modulatory activities of the endocannabinoid system in the human body was studied. This system's elucidation raises the possibility of many promising pharmaceutical applications, even as restrictions show no sign of abating. Recreational use of cannabis continues to increase, despite growing evidence of its addictive potential, particularly in the young. Public approval drives medical cannabis legalisation efforts without the scientific data normally required to justify a new medication's introduction. This review explores these controversies and whether cannabis is a panacea, a scourge, or both.

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34. The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients Through a Written Document.

AIMPain practitioners would seem to have an obligation to understand and inform their patients on key issues of the evidence base on cannabinoid therapeutics. One way to fulfill this obligation might be to borrow from concepts developed in the prescription of opioids: the use of a written agreement to describe and minimize risks. Regrettably, the widespread adoption of opioids was undertaken while harmful effects were minimized; obviously, no one wants to repeat this misstep.OBJECTIVEThis article describes a method of educating patients in a manner analogous to other treatment agreements.BACKGROUNDSurveys have demonstrated that pain is the most common indication for medical use of cannabis. As more individuals gain access to this botanical product through state ballot initiatives and legislative mandate, the pain specialist is likely to be confronted by patients either seeking such treatment where permitted, or otherwise inquiring about its potential benefits and harms, and alternative pharmaceuticals containing cannabinoids.METHODSPubMed searches were conducted using the following keywords: cannabis guidelines, harmful effects of cannabis, medical marijuana, medicinal cannabis, opioid cannabis interaction, cannabis dependence and cannabis abuseRESULTS: The authors selected individual tenets a medicinal cannabis patient would be asked to review and acknowledge via signature.CONCLUSIONSUndoubtedly, the knowledge base concerning risks will be an iterative process as we learn more about the long-term use of medicinal cannabis. But we should start the process now so that patients may be instructed about our current conception of what the use of medicinal cannabis entails.

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35. What to make of cannabis and cognition in MS: In search of clarity amidst the haze.

Given data showing that cannabis (herbal drug from the Cannabis sativa plant) can impair cognition in healthy subjects, the possibility that it may also do so in people with multiple sclerosis (MS) should be cause for concern. Approximately 20% of people with MS inhale or ingest cannabis for a variety of symptoms, or as a lifestyle choice. In addition, pharmaceutically manufactured cannabis (in capsules or spray) is prescribed most often for pain and spasticity; however, there is a dearth of literature on the cognitive effects of cannabis. Furthermore, methodological limitations introduce a cautionary note when interpreting the data. The evidence, which must therefore be considered preliminary, suggests that smoked cannabis may further compromise information processing speed and memory, with magnetic resonance imaging (fMRI) demonstrating more inefficient patterns of cerebral activation during task performance. The findings related to pharmaceutically manufactured cannabis are equivocal. There is a pressing need for further research to inform clinical opinion, which at present reflects a combination of uncertainty and dogma.

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This systematic review aims to integrate the evidence on indications, efficacy, safety and pharmacokinetics of medical cannabinoids in older subjects. The literature search was conducted using PubMed, EMBASE, CINAHL and Cochrane Library. We selected controlled trials including solely older subjects (≥65 years) or reporting data on older subgroups. 105 (74%) papers, on controlled intervention trials, reported the inclusion of older subjects. Five studies reported data on older persons separately. These were randomized controlled trials, including in total 267 participants (mean age 47-78 years). Interventions were oral tetrahydrocannabinol (THC) (n=3) and oral THC combined with cannabidiol (n=2). The studies showed no efficacy on dyskinesia, breathlessness and chemotherapy induced nausea and vomiting. Two studies showed that THC might be useful in treatment of anorexia and behavioral symptoms in dementia. Adverse events were more common during cannabinoid treatment compared to the control treatment, and were most frequently sedation like symptoms. Although trials studying medical cannabinoids included older subjects, there is a lack of evidence of its use specifically in older patients. Adequately powered trials are needed to assess the efficacy and safety of cannabinoids in older subjects, as the potential symptomatic benefit is especially attractive in this age group.

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OBJECTIVETO determine the efficacy of medical marijuana in several neurologic conditions.METHODSWe performed a systematic review of medical marijuana (1948-Noveber 2013) to address treatment of symptoms of multiple sclerosis (MS), epilepsy, and movement disorders. We graded the studies according to the American Academy of Neurology classification scheme for therapeutic articles.RESULTSThirty-four studies met inclusion criteria; 8 were rated as Class I.CONCLUSIONSThe followin were studied in patients with MS: (1) Spasticity: oral cannabis extract (OCE) is effective, and nabiximols and tetrahydrocannabinol (THC) are probably effective, for reducing patient-centered measures; it is possible both OCE and THC are effective for reducing both patient-centered and objective measures at 1 year. (2) Central pain or painful spasms (including spasticity-related pain, excluding neuropathic pain): OCE is effective; THC and nabiximols are probably effective. (3) Urinary dysfunction: nabiximols is probably effective for reducing bladder voids/day; THC and OCE are probably ineffective for reducing bladder complaints. (4) Tremor: THC and OCE are probably ineffective; nabiximols is possibly ineffective. (5) Other neurologic conditions: OCE is probably ineffective for treating levodopa-induced dyskinesias in patients with Parkinson disease. Oral cannabinoids are of unknown efficacy in non-chorea-related symptoms of Huntington disease, Tourette syndrome, cervical dystonia, and epilepsy. The risks and benefits of medical marijuana should be weighed carefully. Risk of serious adverse psychopathologic effects was nearly 1%. Comparative effectiveness of medical marijuana vs other therapies is unknown for these indications.

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Cannabis, or marijuana, has been used for medicinal purposes for many years. Several types of cannabinoid medicines are available in the United States and Canada. Dronabinol (schedule III), nabilone (schedule II), and nabiximols (not U.S. Food and Drug Administration approved) are cannabis-derived pharmaceuticals. Medical cannabis or medical marijuana, a leafy plant cultivated for the production of its leaves and flowering tops, is a schedule I drug, but patients obtain it through cannabis dispensaries and statewide programs. The effect that cannabinoid compounds have on the cannabinoid receptors (CB1 and CB2) found in the brain can create varying pharmacologic responses based on formulation and patient characteristics. The cannabinoid Δ(9)
-tetrahydrocannabinol has been determined to have the primary psychoactive effects; the effects of several other key cannabinoid compounds have yet to be fully elucidated. Dronabinol and nabilone are indicated for the treatment of nausea and vomiting associated with cancer chemotherapy and of anorexia associated with weight loss in patients with acquired immune deficiency syndrome. However, pain and muscle spasms are the most common reasons that medical cannabis is being recommended. Studies of medical cannabis show significant improvement in various types of pain and muscle spasticity. Reported adverse effects are typically not serious, with the most common being dizziness. Safety concerns regarding cannabis include the increased risk of developing schizophrenia with adolescent use, impairments in memory and cognition, accidental pediatric ingestions, and lack of safety packaging for medical cannabis formulations. This article will describe the pharmacology of cannabis, effects of various dosage formulations, therapeutics benefits and risks of cannabis for pain and muscle spasm, and safety concerns of medical cannabis use.

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For 5 millennia, Cannabis sativa has been used throughout the world medically, recreationally, and spiritually. From the mid-19th century to the 1930s, American physicians prescribed it for a plethora of indications, until the federal government started imposing restrictions on its use, culminating in 1970 with the US Congress classifying it as a Schedule I substance, illegal, and without medical value. Simultaneous with this prohibition, marijuana became the United States' most widely used illicit recreational drug, a substance generally regarded as pleasurable and relaxing without the addictive dangers of opioids or stimulants. Meanwhile, cannabis never lost its cachet in alternative medicine circles, going mainstream in 1995 when California became the first of 16 states to date to legalize its medical use, despite the federal ban. Little about cannabis is straightforward. Its main active ingredient, δ-9-tetrahydrocannabinol, was not isolated until 1964, and not until the 1990s were the far-reaching modulatory activities of the endocannabinoid system in the human body appreciated. This system's elucidation raises the possibility of many promising pharmaceutical applications, even as draconian federal restrictions that hamstring research show no signs of softening. Recreational use continues unabated, despite growing evidence of marijuana's addictive potential, particularly in the young, and its propensity for inducing and exacerbating psychotic illness in the susceptible. Public approval drives medical marijuana legalization efforts without the scientific data normally required to justify a new medication's introduction. This article explores each of these controversies, with the intent of educating physicians to decide for themselves whether marijuana is panacea, scourge, or both. PubMed searches were conducted using the following keywords: medical marijuana, medical cannabis, endocannabinoid system, CB1 receptors, CB2 receptors, THC, cannabidiol, nabilone, dronabinol, nabiximols, rimonabant, marijuana legislation, marijuana abuse, marijuana dependence, and marijuana and schizophrenia. Bibliographies were hand searched for additional references relevant to clarifying the relationships between medical and recreational marijuana use and abuse.

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Neuropathic pain is a debilitating form of chronic pain resulting from nerve injury, disease states, or toxic insults. Neuropathic pain is often refractory to conventional pharmacotherapies, necessitating validation of novel analgesics. Cannabinoids, drugs that share the same target as Delta(9)-tetrahydrocannabinol (Delta(9)-THC), the psychoactive ingredient in cannabis, have the potential to address this unmet need. Here, we review studies evaluating cannabinoids for neuropathic pain management in the clinical and preclinical literature. Neuropathic pain associated with nerve injury, diabetes, chemotherapeutic treatment, human immunodeficiency virus, multiple sclerosis, and herpes zoster infection is considered. In animals, cannabinoids attenuate neuropathic nociception produced by traumatic nerve injury, disease, and toxic insults. Effects of mixed cannabinoid CB(1)/CB(2) agonists, CB(2) selective agonists, and modulators of the endocannabinoid system (i.e., inhibitors of transport or degradation) are compared. Effects of genetic disruption of cannabinoid receptors or enzymes controlling endocannabinoid degradation on neuropathic nociception are described. Specific forms of allodynia and hyperalgesia modulated by cannabinoids are also considered. In humans, effects of smoked marijuana, synthetic Delta(9)-THC analogs (e.g., Marinol, Cesamet) and medicinal cannabis preparations containing both Delta(9)-THC and cannabidiol (e.g., Sativex, Cannador) in neuropathic pain states are reviewed. Clinical studies largely affirm that neuropathic pain patients derive benefits from cannabinoid treatment. Subjective (i.e., rating scales) and objective (i.e., stimulus-evoked) measures of pain and quality of life are considered. Finally, limitations of cannabinoid pharmacotherapies are discussed together with directions for future research.


SETTINGCannabis preparations have been used as a remedy for thousands of years in traditional medicine. Clinical use of cannabinoid substances is restricted, due to legal and ethical reasons, as well as limited evidence showing benefits.OBJECTIVETo assess the efficacy and harms of cannabis preparations in the treatment of chronic pain.DESIGNSystematic review and meta-analysis of double-blind randomized controlled trials that compared any cannabis preparation to placebo among subjects with chronic pain. An electronic search was made in Medline/Pubmed, Embase, and The Cochrane Controlled Trials Register (TRIALS CENTRAL) of all literature published until February 2008, as well as specific web pages devoted to cannabis. Studies were cross-checked, selected, and assessed.RESULTSEighteen trials were included. The efficacy analysis (visual analog scales) displayed a difference in standardized means in favor of the cannabis arm of -0.61 (-0.84 to -0.37), with statistical homogeneity (I(2) = 0.0%; P = 0.50). For the analysis of harms, the following Odds Ratios (OR) and number needed to harm (NNH) were obtained: for events linked to alterations to perception, OR: 4.51 (3.05-6.66), NNH: 7 (6-9); for events affecting motor function, 3.93 (2.83-5.47), NNH: 5 (4-6); for events that altered cognitive function, 4.46 (2.37-8.37), NNH: 8 (6-12).CONCLUSIONSCurrently available evidence suggests that cannabis treatment is moderately efficacious for treatment of chronic pain, but beneficial effects may be partially (or completely) offset by potentially serious harms. More evidence from larger, well-designed trials is needed to clarify the true balance of benefits to harms.


BACKGROUNDThe therapeutic use of cannabis and cannabis-based medicines raises safety concerns for patients, clinicians, policy-makers, insurers, researchers and regulators. Although the
efficacy of cannabinoids is being increasingly demonstrated in randomized controlled trials, most safety information comes from studies of recreational use. METHODS We performed a systematic review of safety studies of medical cannabinoids published over the past 40 years to create an evidence base for cannabis-related adverse events and to facilitate future cannabis research initiatives. We critically evaluated the quality of published studies with a view to identifying ways to improve future studies. RESULTS A total of 321 articles were eligible for evaluation. After excluding those that focused on recreational cannabis use, we included 31 studies (23 randomized controlled trials and 8 observational studies) of medical cannabis use in our analysis. In the 23 randomized controlled trials, the median duration of cannabinoid exposure was 2 weeks (range 8 hours to 12 months). A total of 4779 adverse events were reported among participants assigned to the intervention. Most (4615 [96.6%]) were not serious. Of the 164 serious adverse events, the most common was relapse of multiple sclerosis (21 events [12.8%]), vomiting (16 events [9.8%]) and urinary tract infection (15 events [9.1%]). The rate of nonserious adverse events was higher among participants assigned to medical cannabinoids than among controls (rate ratio [RR] 1.86, 95% confidence interval [CI] 1.57-2.21); the rates of serious adverse events did not differ significantly between these 2 groups (RR 1.04, 95% CI 0.78-1.39). Dizziness was the most commonly reported nonserious adverse event (714 events [15.5%]) among people exposed to cannabinoids. INTERPRETATION Short-term use of existing medical cannabinoids appeared to increase the risk of nonserious adverse events. The risks associated with long-term use were poorly characterized in published clinical trials and observational studies. High-quality trials of long-term exposure are required to further characterize safety issues related to the use of medical cannabinoids.

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