

Cannabis

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Objective: Cannabis use is expanding rapidly, and a guideline is needed to address workplace issues. **Methods:** The ACOEM Guidelines methodology was used to develop an evidence-based guideline. **Results:** There is some evidence suggesting potential efficacy of cannabis for treatment of spasticity associated with multiple sclerosis. There is no quality evidence of efficacy for treatment of common and typical work-related disorders such as back pain, chronic radiculopathy, neuropathic pain, and other acute or chronic pain disorders. Quality evidence supports lack of efficacy for postoperative pain. There are many adverse effects, including cancers, cardiovascular diseases, psychotic disorders, and safety risks. There is a rising concern that cannabis may cause schizophrenia. **Conclusions:** Cannabis is not recommended for treatment of typical potentially work-related conditions. Cannabis use for any purpose is not recommended for those in safety-sensitive positions. **Keywords:** cannabis, chronic pain, guidelines, workers in safety-sensitive positions

OVERVIEW

Objectives and Scope

The scope of this evidence-based guideline on cannabis is focused on the treatment of pain resulting from disorders that have a reasonable probability of being work related (eg, spine pain, chronic radicular pain, osteoarthritis). The scope of this guideline excludes Alzheimer's disease, multiple sclerosis, amyotrophic lateral sclerosis, cancer, nausea/vomiting related to chemotherapy,

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cachexia, acquired immune deficiency syndrome, sleep disturbance, posttraumatic stress disorder, epilepsy, and terminal care.

The health questions for acute, subacute, chronic, and postoperative pain treatment with cannabis, including marijuana/cannabidiol (CBD), addressed by this guideline are as follows:

- What evidence supports the use of cannabis for the treatment of acute, subacute, chronic, and postoperative nonmalignant pain?
- What evidence supports use of cannabis in workers performing safety-sensitive jobs?
- What is the dose-response relationship between tetrahydrocannabinol (THC) dose and fatalities, overdoses, and other adverse effects?
- What evidence addresses the balance of risk and benefits of cannabis use for chronic pain?
- Are cannabis products superior to other medications or other treatments for chronic pain relief and functional improvement?

Basic Principles and Definitions

CBD Oil

Cannabidiol oil is derived from cannabis. The oil is extracted from the plant and is typically diluted with another oil (eg, coconut or hemp seed oil). It purportedly causes pain relief without the mind-altering effects. The concentration of psychoactive compounds in CBD oil is sufficiently low that CBD is considered unlikely to cause either cognitive impairment or addiction.

Cannabinoids

Cannabinoids are chemical compounds contained in the cannabis (marijuana) plant that interact with cannabinoid receptors. Tetrahydrocannabinol is the most potent of the psychoactive compounds, but other cannabinoids may play roles in the overall psychoactive effects. Cannabinoid receptor type 1 (CB1) receptors are prominent in the central nervous system and are responsible for the psychoactive effects. Cannabinoid receptor type 2 receptors, which are throughout the body, are thought to affect pain and inflammation.

Cannabis

Cannabis is the genus name for marijuana plants, of which 2 species have psycho-

LEARNING OUTCOMES

After reading this article, readers will be able to:

- Identify the adverse effects associated with marijuana use
- Summarize the evidence base for use of cannabis for the treatment of acute, subacute, chronic, and postoperative nonmalignant pain
- Describe the evidence base for use of cannabis in workers performing safety-sensitive jobs

active properties (*C. indica* and *C. sativa*). Approximately 100 of the many hundreds of chemical compounds in the plant are classified as cannabinoids. Medical cannabis has been defined as the use of “the whole, unprocessed marijuana plant or its basic extracts to treat symptoms of illness and other conditions.”¹

Marijuana

Marijuana (ie, cannabis) refers to the dried leaves, flowers, stems, and seeds from 2 species of the cannabis plant (*C. sativa* and *C. indica*). Marijuana is used in various forms. It is smoked in hand-rolled cigarettes (ie, joints), pipes, water pipes, and blunts (an emptied cigar). Vaporizers deliver THC from marijuana. Edibles typically involve the use of concentrates in brownies, cookies, candy, gummies, or tea. Cannabinoid concentrates are also available in multiple forms collectively referred to as “dabs.” These include hash oil, honey oil, wax, budder, and shatter. Dabs may contain >80% THC,^{2,3} which far exceeds current marijuana concentrations of ~15%.

Tetrahydrocannabinol

Tetrahydrocannabinol (or delta-9-THC) is considered to be the most psychoactively potent of the cannabinoids. There also are synthetic cannabinoids (Spice, K2) that are not considered cannabis.⁴

See also Basic Principles and Definitions in the ACOEM Chronic Pain Guideline,⁵ as well as the Opioids Guideline,⁶ for additional relevant definitions.

Methods and Limitations

The Evidence-based Practice Chronic Pain Expert Panel and the Research Team, which formulated this guideline, have complete editorial independence from the ACOEM and Reed Group, LLC, the publisher of the ACOEM's guidelines, neither of which has influenced this guideline.

A document providing the in-depth methodology used to create this guideline, including evidence selection, scoring, incorporation of cost considerations,⁷⁻¹⁰ and formulation of recommendations, is available online.¹¹ Comprehensive literature searches were conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without publication date limits to ensure all relevant literature was gathered. Guidance was developed with sufficient detail to facilitate assessment of compliance⁹ and auditing/monitoring.¹⁰ In accordance with the Institute of Medicine's Trustworthy Guidelines, detailed records are kept, including responses to external peer reviewers.⁹

For cannabinoids for chronic pain, we found and reviewed 133 articles in PubMed, 54 in CINAHL, 4 in Cochrane Library, 16,900 in Google Scholar, and 0 from other sources. We considered for inclusion 32 from PubMed, 11 from CINAHL, 2 from Cochrane Library, 24 from Google Scholar, and 0 from other sources. Of the 56 articles considered for inclusion, 17 randomized trials and 25 systematic reviews met the inclusion criteria.

For cannabinoids for acute pain, we found and reviewed 3 articles in PubMed, 3 in CINAHL, 0 in Cochrane Library, 11,000 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

For cannabinoids for postoperative pain, we found and reviewed 18 articles in PubMed, 5 in CINAHL, 0 in Cochrane Library, 2580 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 5 randomized trials and 0 systematic reviews met the inclusion criteria.

For cannabinoid use for safety-critical workers, we found and reviewed 0 articles in PubMed, 0 in CINAHL, 0 in Cochrane Library, 530 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 12 from Google Scholar, and 0 from other sources. Of the 12 articles considered for inclusion, 6 randomized trials and 4 systematic reviews met the inclusion criteria.

U.S. Marijuana Market: The Grass Is Getting Greener

Projected growth of U.S. recreational and medical marijuana sales (billion U.S. dollars)

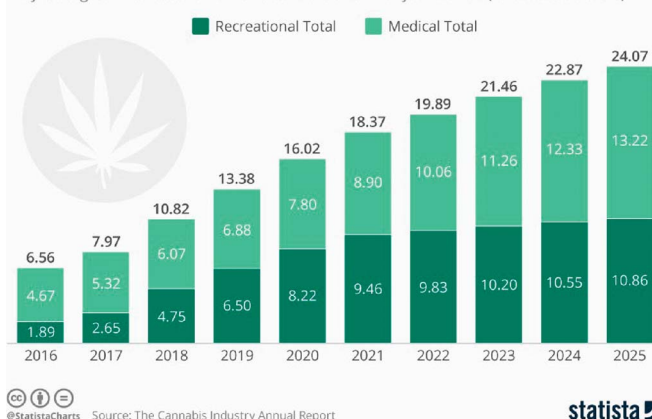


FIGURE 1. Estimated US recreational and medical marijuana market sales.¹⁸ Reprinted with permission from Statista.

History

Cannabis use dates back at least 12,000 years, with initial evidence from use in the Altai mountains (present-day Russia-Kazakhstan, Mongolia-China).¹² The use of topical applications to treat inflammation in Egypt was documented in Ebers papyrus and dates to ~1500 BC.¹³ Cannabis use for treatment of medical disorders in China dates to 800 BC,^{14,15} with cannabis identified in the grave of a presumptive shaman in China. Use of marijuana for religious purposes dates back at least 3000 years.¹⁶ Marijuana has also been used recreationally, which has been increasing in use since the liberalization of state laws in the United States.

Since 1973, marijuana has been classified as a schedule I controlled substance by the US Drug Enforcement Agency because of its lack of accepted medicinal use, high misuse potential, risk of dependency, and lack of safety while under medical supervision.¹⁶

Among the impacts of the schedule I classification are restrictions that have limited marijuana research in the United States, including clinical trials to thoroughly examine the medicinal effectiveness of cannabis.¹⁷ Marijuana liberalization laws began in California in 1996 and have spread across the United States. As of May 2024, the US Drug Enforcement Agency proposed reclassification to schedule III.

Impact

Marijuana use continues to rapidly increase with the legalization of medical and recreational use (see Fig. 1).^{19,20} As measured by sales, recreational use in the United States is estimated to modestly exceed medicinal use (2024 estimates of \$12.3B vs \$10.6B, respectively; see Fig. 1).¹⁸ Medicinal use of marijuana ranges widely across the states, from 0.01% of the California state population to 9.2% of the population of

Oklahoma¹⁸; however, these data are likely confounded by the lack of nonmedicinal access in several states.

Past-year use among US young adults (19 to 30 years of age) increased by 48% from 2011 to 2021, whereas past-month use increased from 17% to 29% (70.6% increase), and daily use increased from 5% to 11% (120% increase).¹⁹ Marijuana vaping by young adults doubled in 4 years, from 6% in 2017 to 12% in 2021.¹⁹ Usage rates for the US adult population are lower, but they have also increased sharply from 7% in 2013 to 17% in 2023 (243% increased usage), according to a 2024 Gallup survey; the rates decreased with age, with 26% of 18- to 34-year-olds, 18% of 35- to 54-year-olds, and 11% of >55-year-olds reporting use.²¹

Historical use over the past 50 years shows 2 strong trends. The first trend of increased use was estimated to have peaked in 1978.²² Among 12- to 25-year-olds, use was 27% in 1978 and fell to ~8% in 1992. Subsequently, the second trend is of strongly increasing rates of use since the 1990s and especially over the past 10 years. Marijuana rates are also inversely correlated to the acknowledged degree of hazard associated with its use (see Fig. 2).²³

However, and importantly, the marijuana being used today is far more potent as measured by THC.^{24,25} The THC levels in marijuana have increased by ~400% over the past 3 decades, from ~4% to ~16% (see Fig. 3).^{26,27} Some products, such as dabs, now have THC concentrations of more than 80%.²⁸

More than 350 synthetic cannabinoids have also been developed.²⁹⁻³¹ These include Spice, which is a full agonist that has high potency, and these compounds have many adverse effects.³²⁻³⁵

Cannabis use among workers is rising.³⁶ National survey data from 2021 to 2022 estimated 15.9% of workers reported

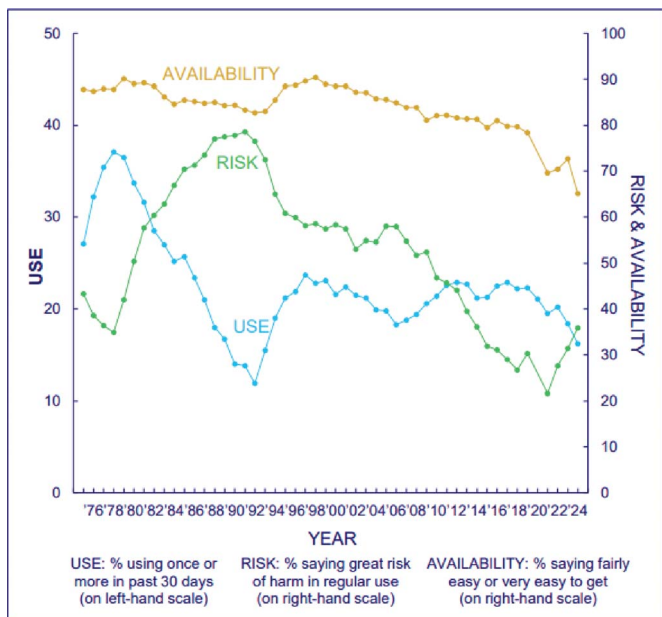


FIGURE 2. Inverse relationship between US 12th graders' regular marijuana use and perceived risk of harm.²³

past-month cannabis use.³⁷ One epidemiological study reported that of 362 medical cannabis-using patients, 34% self-reported using marijuana or being high on the job in the prior 6 months.³⁸ Cannabis use has been estimated to increase risk of workplace injury by 97%.³⁹

Mechanisms of Action

Endocannabinoids and cannabinoid receptors are found in numerous body organs, including the nervous system (central and peripheral), internal organs, connective tissues, glands, and immune cells.¹⁶ Disorders theorized to be involved in the endocannabinoid system include migraines, fibromyalgia, multiple sclerosis, Parkinson's disease, schizophrenia, and depression.⁴⁰ Cannabinoid receptor type 1 is most strongly expressed in the central nervous system, while also being present in adipocytes, hepatocytes, connective tissue, musculoskeletal tissue, and the gonads. Cannabinoid receptor type 2 is primarily expressed in the immune system.

Tetrahydrocannabinol activates the CB1 receptors. That activation is responsible for the impairing effects of cannabis/cannabinoids/THC. By contrast, CBD does not materially activate the CB1 receptors, with its uses including epilepsy, insomnia, pain, diabetes, cancer, and Huntington disease.¹⁶

Administration is commonly by smoking, inhalation, and ingestion. Smoking is believed to be the most hazardous due to the presence of numerous carcinogens and the propensity toward adverse respiratory effects (eg, chronic obstructive pulmonary disease). Inhalation and smoking both result in rapid increases of THC in the bloodstream,

with rapid reductions in THC over 4 hours.⁴¹ Ingestion results in a slower increase; however, the duration of effects is longer.^{42,43}

The medicinal use of cannabinoids is complicated by the numerous compounds that may be present (including psychoactive compounds), varying metabolic processes, and nonstandardized doses, which have resulted in varying effective doses among the many preparations/forms.¹⁶

ADVERSE EFFECTS

Adverse effects related to THC are common (see below). Assessments of adverse effects are confounded by a lack of standardization in product potency and dosing. Indeed, there has been marked increase in cannabis potency over time. With recently increasing doses, risks may be understated in the entirety of published literature. In addition, there now may be unrecognized risks. These challenges may introduce biases and errors into published results.

Medical cannabis users may prefer products with a lower THC but higher CBD ratio, which are associated with lower adverse effects.⁴⁴ However, evidence of cannabis-related analgesia exists mostly among patients with multiple sclerosis and involves use of products with higher THC-CBD ratios.⁴⁵

Adverse effects associated with marijuana use are detailed in Table 1.

Cannabis Use Disorder, Dependency, and Problematic Use

The Substance Abuse and Mental Health Services Administration estimates the risk of addiction is approximately 10%, which increases to 17% when use starts before the age of 18 years.⁷⁵ An estimated 22% to 30% of marijuana users have one of the forms of cannabis use disorder.^{102,103} According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, the conditions for a diagnosis of cannabis use disorder are met when a person meets at least 2 of 11 criteria within a 12-month period, including, among others, desire or unsuccessful efforts to cut down on use, ongoing use that causes failure to fulfill major obligations, ongoing use despite cannabis causing interpersonal problems, and withdrawal symptoms.¹⁰⁴ A population-based analysis of 55 million Medicare claims data showed the fastest rises in cannabis use disorder occurred in states with both legalized medical and recreational use.¹⁰⁵ Population-based surveys suggest increasing risks over time for frequent cannabis use and cannabis use disorder, with greater risks among individuals with pain compared with individuals without pain.¹⁰⁶

Safety-critical work concerns include motor vehicle crashes, slower reaction times, lane weaving, decreased coordination, reduced balance, cognitive issues, memory difficulties, and difficulty reacting to signals and sounds on the road.^{75,107,108}

An analysis of 527 medical cannabis users reported that all experienced withdrawal symptoms, with 214 (40.6%) having mild withdrawal symptoms, 180 (34.2%)

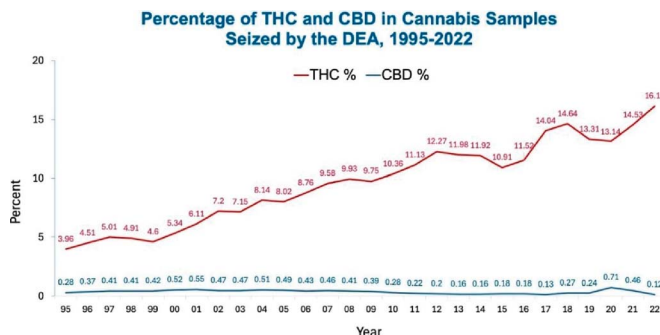


FIGURE 3. Percentage of THC in DEA seizures over time.²⁶ DEA, US Drug Enforcement Administration; THC, tetrahydrocannabinol.

TABLE 1. Adverse Effects Associated With Cannabis Use

<ul style="list-style-type: none"> • Motor vehicle crashes^{46–50} and crashes involving injuries treated in emergency department visits⁵¹ • Slips, trips, and falls^{52–55} • Worker injuries^{39,56,57} • Central nervous system effects: <ul style="list-style-type: none"> • Cognitive impairment^{47,58,59} • Altered judgment¹⁶ • Short-term memory impairment¹⁶ • Impaired motor coordination¹⁶ • Impaired attention⁵⁸ • Dizziness^{45,60} • Sedation^{45,58,60} • Vision changes⁴⁵ • Altered brain development⁶¹ • Sleep disorders⁴⁷ • Psychosocial effects: <ul style="list-style-type: none"> • Depressive disorders^{45,47} • Anxiety disorders^{45,47,62,63} (31% increase in anxiety visits associated with cannabis involvement after cannabis legalization in Ontario)⁶³ • Mania^{45,64} • Schizophrenia⁶⁵ with the population-based estimated risk increasing 280% after cannabis legalization in Ontario;⁶⁶ cannabis use also had the highest population-based risk of transitioning to schizophrenia spectrum disorders among emergency department visits due to substance use, with a risk of an adjusted hazard ratio of 241.6 (95% CI, 225.5–258.9)⁶⁷ • Paranoia⁶⁸ • Psychosis (5-fold increased risk)^{47,48,68–72} • Psychiatric symptoms (7.5-fold increased risk for number and severity)⁷⁰ • Personality change⁶⁸ • Addiction/cannabis use disorder^{73,74} • Premature cessation of education⁶¹ • Relationship problems⁷⁵ • Reduced life satisfaction⁶¹ • Lower educational attainment⁷⁵ • Lower career achievements⁷⁵ • Unemployment⁷⁶ • Aggression⁶⁸ • Violence: <ul style="list-style-type: none"> • Partner⁴⁷ • Child⁴⁷ • Crime⁴⁶ • Self-harm⁷⁷ • Respiratory effects⁷⁸: <ul style="list-style-type: none"> • Bronchitis^a • Dyspnea^a • Chronic obstructive pulmonary disease^a • Pneumonia 	<ul style="list-style-type: none"> • Cardiovascular events^{47,79}: <ul style="list-style-type: none"> • Increased systolic blood pressure⁸⁰ • Myocardial infarction (2.5-fold increased risk)^{78,79,81–83} • Stroke⁸² • Arrhythmias,⁸² including ventricular⁷⁸ • Tachycardia⁷⁸ • Venous thromboembolism⁸² • Gastrointestinal disorders <ul style="list-style-type: none"> • Nausea^{45,58,60} • Vomiting, including cannabinoid hyperemesis syndrome^{58,60,84} • Diarrhea⁴⁵ • Increased risk of developing prediabetes⁸⁵ • Negative perioperative outcomes⁸⁶ <ul style="list-style-type: none"> • Perioperative myocardial infarction • Abnormal airway resistance • Carcinogen production, increased cancer risks,^{87,88} including 2.5-fold increased risk of oral cancer, 4.9-fold increased risk of oropharyngeal cancer, and 8.4-fold increased risk of laryngeal cancer⁸⁹ and 3.8-fold increased risk of lung cancer⁹⁰ <ul style="list-style-type: none"> • Increased tar and polyaromatic hydrocarbons compared with cigarette smoke^{87,91–97} • Neonatal effects⁷⁵: <ul style="list-style-type: none"> • Fetal growth restriction • Premature birth • Stillbirth • Brain development problems • Hyperactivity • Poor cognitive function • Deaths from other causes not listed above, including: <ul style="list-style-type: none"> • Overdose • Cardiovascular mortality (~2-fold increased risk)^{98,99} • Suicide^{45–47,100,101} • (5-year mortality among those with cannabis use disorders including from suicide [9.7-fold adjusted hazard ratio], trauma [4.55-fold adjusted hazard ratio], opioid poisoning [5.03-fold adjusted hazard ratio], other drug poisonings [4.56-fold adjusted hazard ratio], and lung cancer [3.81-fold adjusted hazard ratio])⁹⁰
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^aRisks reported associated with smoking marijuana.

having moderate withdrawal symptoms, and 133 (25.2%) having severe withdrawal symptoms. Over 24 months, the proportions trended toward moderate lessening of the experiencing of withdrawal symptoms: 236 (44.8%) with mild withdrawal symptoms, 199 (37.8%) with moderate withdrawal symptoms, and 92 (17.5%) with severe withdrawal symptoms. Younger age predicted greater severity and worsening of withdrawal symptoms over time.⁷⁵

A systematic review with a meta-analysis estimated that 48% of cannabis users had problematic use: 22% had cannabis use disorder, 13% had cannabis “abuse,” and 13% had cannabis dependency.¹⁰³ Risks have been suggested to be higher among those

with nonmalignant chronic pain, mental health disorders, and substance use disorders.^{106,109} Overall, problematic use has been estimated to be as high as 33%.^{106,109}

The risks of developing problematic cannabis use have been found to increase with many factors¹¹⁰ (see Table 2).

A study of US veterans found higher rates of cannabis use and cannabis use disorder among those who were younger, male, unmarried, earning a lower income, residing in a state with medical marijuana laws, and diagnosed with other psychiatric and substance use disorders.¹¹¹ Another study reported increasing prevalence rates of cannabis use disorder among veterans from 2005 to 2019.¹¹²

Some evidence also supports that marijuana is a “gateway drug.”²⁷ For example, a significant increase in the use of hallucinogens was reported after the increased use of marijuana, from 3% in the past year in 2011 to 8% in 2021 (a 167% increase) (see Fig. 4).¹⁹ Marijuana is also the most frequent drug accompanying alcohol in polysubstance use among emergency department patients.¹¹³

A systematic review reported that the risk of marijuana overdose was 3.6-fold higher after legalization of cannabis¹¹⁴ and doubled in Colorado after legalization of medical marijuana.¹¹⁵ Emergency department visits after legalization increased by 89% in California¹¹⁶ and 267% in Arizona.¹¹⁷

TABLE 2. Risk Factors for Developing Problematic Cannabis Use

Factors Found to Increase Risk	Factors not Found to Increase Risk
<ul style="list-style-type: none"> • Initiation at a younger age (substantial evidence) • Male sex (moderate evidence) • Frequency of use (substantial evidence) • Combined use of misused drugs (moderate evidence) • Male sex and cigarette smoker (substantial evidence) • Childhood anxiety (limited evidence) • Childhood depression (limited evidence) • Adulthood depression (moderate evidence) • Frequency of cannabis use, oppositional behaviors, younger age at first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse during adolescence (moderate evidence) • History of psychiatric treatment as a risk for persistence of problem use (moderate evidence) • Male sex and severity of problem use (substantial evidence) • Increased severity of posttraumatic stress disorder symptoms (moderate evidence) 	<ul style="list-style-type: none"> • Alcohol dependence alone (moderate evidence) • Nicotine dependence alone (moderate evidence) • Anxiety disorder (moderate evidence) • Bipolar disorder (moderate evidence) • Personality disorders (moderate evidence) • Adolescent attention-deficit hyperactivity disorder (moderate evidence)

Motor Vehicle Crashes

Assessment of motor vehicle crash risks attributable to cannabis is likely somewhat impaired by the lack of relatively uniform and systematic testing, in contrast with that for alcohol. Surveillance studies of drivers suggest that, annually, 4.5% of all US adults drive under the influence of cannabis, with proportions increasing to as high as 63.8% among those with cannabis use disorder.¹¹⁸ After the legalization of cannabis in Canada, a study of moderately injured drivers involved in a crash finding any detectable THC nearly doubled from 9.2% to 17.9%.¹¹⁹ Another study found that marijuana-related traffic injuries increased by 94% after Canada's legalization in 2018.⁵¹

Many studies have reported that marijuana is a risk for motor vehicle fatalities,¹²⁰⁻¹²⁷ although a few have not.^{128,129} The proportion of US crash deaths involving marijuana more than doubled between 2000 and 2018,¹²³ and the legalization of marijuana has been associated with increased risks of crashes and deaths.¹²² Sedation is a commonly reported adverse effect.⁵⁷ Marijuana-related impairment has been shown by both on-road driving tests,¹³⁰ in numerous driving simulator studies,¹³¹⁻¹³⁵ and on psychomotor tests.¹³⁶ One study evaluated work fatalities in the course of heavy vehicle operations and found that 1 in 6 fatalities involved either stimulants or cannabis.¹³⁷

In Ontario, more traffic fatalities tested positive for cannabis than for alcohol.¹²⁴ An analysis of the Fatality Analysis Reporting System found that the proportion of fatalities testing positive for cannabis approximately tripled between 1999 and 2010 (4.2% to 12.2%), whereas alcohol prevalence was stable.¹²⁵ One study reported that states with recreational marijuana laws experienced a

10% increase in motor vehicle fatalities.¹³⁸ Another study suggested less risk from those laws but increased risk from legalization of medicinal cannabis.¹²⁶ An ecological study estimated that a 15% increase in fatal motor vehicle collisions in the United States was associated with legalized recreational use.¹²⁷ Another study found an increased risk of fatal motor vehicle crashes after recreational but not medical cannabis legalization.¹²⁹

After medical marijuana became widely available in Colorado in 2009 (medical marijuana registrants rose from <5000 to ~125,000), and the proportion of motor vehicle fatalities among drivers that were marijuana-positive increased 2.15-fold.¹³⁹ A study estimated that fatal crashes increased an average of 10% in Alabama, California, Colorado, Massachusetts, Nevada, Oregon,

and Washington based on recreational marijuana legalization.¹³⁸ A case-control study reported marijuana was twice as likely to be involved in fatal crashes compared with controls (12.2% vs 5.9%), while also reporting an interaction with alcohol.¹⁴⁰ Tetrahydrocannabinol positivity tripled among motor vehicle fatalities in Hawaii after legalization of cannabis, whereas THC positivity also doubled (from 11% to 20%) at the state's largest level 1 trauma center.¹²¹ Two studies found interactions between marijuana and alcohol in fatal crashes and 2-vehicle crashes.¹⁴⁰ A systematic review found a 1.92 odds of motor vehicle collision from cannabis impairment compared with unimpaired drivers, a 2.10 odds of fatal collisions, a 1.72 odds of nonfatal collision, and a 1.65 odds of crash culpability.¹⁴¹

A survey of medical cannabis users found that 56.4% of 790 patients drove vehicles within 2 hours of use, 50.5% drove while "a little high," and 21.1% drove while "very high."¹⁴² Another study also reported driving after use of marijuana was common.¹⁴³ A randomized experimental study found regular cannabis users demonstrated driving impairments while also having false perceptions of safety accompanied by willingness to drive while impaired.¹⁴⁴

Accidental Injury

An increased risk of accidents (55% increase) and injuries (85% increase) has been reported.^{39,145} Injuries have been associated with cannabis among adolescents.^{146,147} From 2009 to 2021, data from US poison centers show that intentional suspected suicidal cannabis exposures more than doubled.¹⁴⁸ Ten of 459 (2.2%) workplace fatalities tested positive for cannabis, which was the only illicit drug found.¹⁴⁹

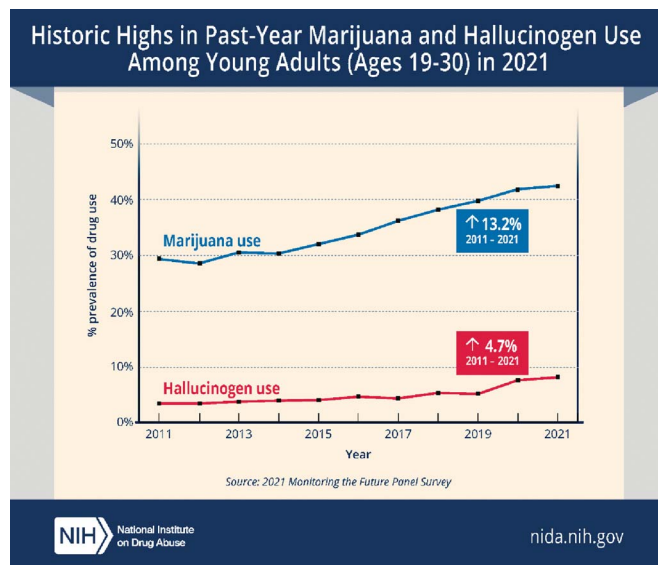


FIGURE 4. Past-year marijuana and hallucinogen use.¹⁹

Work Absences

Work absences are reportedly 78% greater among those using marijuana compared with those not using marijuana (7.1% vs 4.0%).¹⁴⁵ There also is longitudinal evidence of a dose-response relationship with greater absences occurring among those with greater use.¹⁵⁰

Schizophrenia

Population-based and longitudinal evidence is accumulating, suggesting that schizophrenia is at least strongly associated with, and may be caused by, cannabis.^{151–160} A 50-year population-based study in Denmark concluded that up to 30% of schizophrenia cases among men ages 21 to 30 years may have been preventable by averting cannabis use disorder.¹⁵³ A population-based study of Ontario's population of 13.6 million people found an approximate tripling of the population-attributable risk fraction of schizophrenia-related diagnoses after cannabis legalization (from 3.7% to 10.3%) and estimated the population-attributable fraction among males 19 to 24 years old was 18.9%.⁶⁶ A prior systematic review suggested the same, although it was based on 12 studies that mostly used weaker study designs.⁶⁵ The transition from substance-induced psychosis to schizophrenia has been estimated at 34% among cannabis users, which was higher than among those using hallucinogens, amphetamines, opioids, alcohol, or sedatives.¹⁶¹

While associations with mental health issues are widely reported, 1 report of patients at a large pain center noted reductions in the prevalence of anxiety or depression among medical marijuana users when compared with prescription opioid users.¹⁶²

Safe Level

Some literature suggests reduced risks of adverse effects among those using lower doses.⁴⁵ However, there is no quality literature that shows a clearly defined "safe level" of use, and this issue is confounded by a lack of standardized dosing and potency. One prospective case-control study found no increase in the risk of motor vehicle crashes with injuries for drivers with THC levels of 0 to 2 ng/mL and 2 to 5 ng/mL but found a potential trend toward increased crash responsibility risk among those with THC levels of >5 ng/mL (odds ratio = 1.74; 95% confidence interval, 0.59 to 6.36).¹⁶³ An experimental driving simulator study found approximately equivalent impairment between a moderate alcohol dose (0.5-g/kg body weight) and a low THC dose of 13 mg, while finding worse impairment with a high THC dose of 17 mg; impairments were not detectable at 24 hours.¹⁶⁴ Another driving simulator study found impairment with THC doses of 19 mg, while

neither found impairment with alcohol at 0.4 or 0.6 g/kg of body weight nor synergistic effects between THC and alcohol.¹⁶⁵

Duration of impairment is also unclear and likely related to both dose and route of administration.^{43,164,166–168}

Opioid Sparring

Some studies suggest that the use of marijuana is associated with a lower rate of opioid use, although there is agreement that the quality of evidence is low.^{169–176} Two studies provide somewhat contrasting evidence, with one showing greater opioid requirements among marijuana users after injury¹⁷⁷ and that high-frequency medical cannabis use is associated with worse pain.^{178,179} Quality of life has not been shown to be improved with cannabis use.¹⁷⁹

A systematic review concluded that "[l]ow certainty evidence suggested little to no difference between cannabis and opioids for pain relief or sleep quality."^{173,180,181} A separate review by the same research group found only a 0.69 pain rating reduction for opioids compared with placebo, which were also comparable with reductions with non-steroidal anti-inflammatory drugs (NSAIDs).¹⁸²

TREATMENT RECOMMENDATIONS

Cannabinoids for Chronic Pain

Not recommended: Cannabinoids are not recommended for the treatment of chronic pain.

Strength of evidence: Not recommended, Evidence (C)

Level of confidence: Low

Rationale

Randomized controlled trials (RCTs) have used varying products, routes of administration, potencies, and regimens for attempted treatment of chronic pain. Also, the longest duration among quality studies is 3 months.^{183–185} There are no quality long-term placebo-controlled trials documenting the efficacy of cannabinoids for the treatment of chronic pain conditions with or without reduced function that are likely to be work related. There also are no long-term randomized comparative trials for treating common work-related conditions that assessed the potential for superiority of cannabinoids to (1) NSAIDs, (2) functional restoration programs (especially the gold standard of combining aerobic/strengthening exercises with either cognitive behavioral therapy, emotional awareness, and expression therapy or empowered relief), and (3) other comparators of known efficacy.

The sole high-quality trial found lack of efficacy for variable-dose THC, CBD,

and THC-CBD combinations in comparison with placebo for 8 weeks of peripheral neuropathic pain treatment.¹⁸⁶ A moderate-quality trial of CBD treatment (20 to 30 mg for 12 weeks) for hand osteoarthritis and psoriatic arthritis found lack of efficacy.¹⁸³ Tetrahydrocannabinol was found to be ineffective for treatment of neuropathic pain from brachial plexus avulsions using 2 doses of THC and placebo in a randomized crossover trial of 2 weeks.¹⁸⁷

Sativex was found to be ineffective in comparison with placebo for 10 weeks of treatment for diabetic neuropathy; depression was found to be a significant confounder.¹⁸⁵ A variable-dose study of inhaled vaporized cannabis of 2.9%, 6.7%, and placebo for 8 hours of treatment for spinal cord injuries and diseases found evidence of modestly improved pain compared with placebo and stronger effects with the higher THC dose.¹⁸⁸ A small crossover trial found no differences in pain or quality of life but improved sleep with nabilone compared with amitriptyline over 2 weeks.¹⁸⁹ A pragmatic RCT of immediate versus delayed receipt of a medical marijuana card resulted in no differences in pain, although sleep was better in the early marijuana group.¹⁹⁰ Another crossover trial of oral mucosal spray with cannabinoids for treatment of chemotherapy-induced neuropathic pain found lack of efficacy.¹⁹¹ A comparative trial of nabilone versus dihydrocodeine for many types of chronic neuropathic pain found dihydrocodeine to be superior for both pain relief and having fewer adverse effects.¹⁸⁴

There are short term-experimental trials, which are included for completeness, although they are not able to be used for evidence-based treatment guidance. A moderate-quality trial of inhaled THC 0.5 mg, THC 1.0 mg, and placebo for treatment of various peripheral neuropathies found evidence of reduced pain for 150 minutes.¹⁹² A 4-hour experimental crossover trial for treatment of diabetic neuropathy found modest improvements in pain with THC compared with placebo.¹³⁶ A 3-hour experimental study of fibromyalgia suggested non-significant results with cannabis.¹⁹³

There are RCTs suggesting the potential efficacy of cannabinoid treatment for multiple sclerosis, particularly with spasticity.^{45,194} Of the trials using higher THC-to-CBD ratio products, which had greater evidence of efficacy for pain (while having more adverse effects), 598 patients in aggregate were included, 460 (76.9%) of whom had multiple sclerosis, 62 (10.4%) had visceral pain, 50 (8.4%) had fibromyalgia, and 26 (4.3%) had diabetic neuropathy.⁴⁵

Trials for treatment of fibromyalgia also conflict regarding efficacy.^{193,195,196} Although out of scope for this guideline, multiple trials for treatment of cancer pain have shown lack of efficacy.^{197–200}

There is very weak evidence for the substitution of cannabinoids for opioids in patients with various types of chronic pain.^{201,202} However, there are concerns of an arising second follow-on epidemic. Other systematic reviews found similar major gaps in established knowledge.^{45,203} One systematic review purportedly assessing efficacy for treatment of back pain concluded there was efficacy; however, the analysis relied on 2 small RCTs that both primarily studied patients with spinal cord injuries.²⁰⁴

There are no trials documenting improved objective functional outcomes, with more than 100 studies documenting many adverse effects, some of which are severe (see Table 1). As a principle of evidence-based medicine practice, where there is strong evidence that a treatment is effective, it should be necessarily prescribed ahead of those things with limited or no evidence of efficacy (see the ACOEM Initial Approaches to Treatment guideline).²⁰⁵ Cannabinoids have (1) no evidence of efficacy for the treatment of chronic pain conditions likely to be work-related with or without reduced function, (2) a lack of efficacy for other chronic pain conditions in their highest-quality trials, (3) numerous adverse effects, and (4) a lack of efficacy data for these indications, while many other medications and treatments have been shown to be effective for treatment of chronic pain. Thus, there is no clear rationale for the prescription of cannabinoids for disorders that are typically work related and cannabinoids are not recommended.

Cannabinoids for Acute Pain

Not recommended: Cannabinoids are not recommended for treatment of acute or subacute pain.

Strength of evidence: Not recommended, Evidence (C)

Level of confidence: Low

Rationale

There are few quality trials of cannabis use for disorders that are likely to be work related. One small placebo-controlled RCT of acute low back pain found a lack of efficacy for CBD 400 mg.²⁰⁶ Cannabis is not invasive, has significant adverse effects, is moderately costly, and has placebo-controlled evidence that suggests a lack of efficacy. Therefore, cannabis is not recommended for the treatment of acute and subacute pain.

Cannabinoids for Postoperative Pain

Not recommended: Cannabinoids are not recommended for the treatment of postoperative pain.

Strength of evidence: Moderately not recommended, Evidence (B)

Level of confidence: Moderate

Rationale

A 4-arm placebo-controlled trial compared thrice-daily nabilone (1 mg), nabilone (2 mg), ketoprofen (50 mg), and placebo for 24 hours as adjunctive treatment to patient-controlled analgesia for treatment of postoperative pain (from mostly gynecological or orthopedic surgeries). The study found that higher doses of nabilone were associated with paradoxically worse pain scores; in addition, there was a trend toward lower morphine consumption in the ketoprofen group.²⁰⁷ A 3-arm placebo-controlled comparative trial for treatment of pain from third molar extraction found that submaximal ibuprofen (400 mg after an initial 800-mg dose) was superior to both placebo and the cannabinoid receptor-2 agonist GW842166 (100 and 800 mg); there also was no benefit for the cannabinoid compared with placebo.²⁰⁸ A placebo-controlled trial of oral delta-9-THC (5 mg) for the management of pain on postoperative day 2 after total abdominal hysterectomy found lack of efficacy.²⁰⁹ A comparative trial of a cannabinoid agonist (AZD1940, 800 µg) or naproxen (500 mg) for treatment of lower third molar extraction found superiority for naproxen and a lack of efficacy for the cannabinoid.²¹⁰ One trial of cannabis for postoperative pain found increased rescue analgesia at lower cannabis doses; however, the trial was terminated because of adverse vasovagal events occurring among the higher-dose group.²¹¹

Systematic reviews and meta-analyses found no meaningful evidence of improvements in acute or postoperative management with cannabinoid use.^{212,213} One systematic review and meta-analysis reported efficacy but included trials with diverse primary outcomes, such as nausea and vomiting with pain.²¹⁴ In a low-quality study of 155 cannabinoid users with 3637 propensity-matched controls undergoing major orthopedic surgery, the cannabinoid users had worse pain and worse sleep postoperatively.²¹⁵

Cannabis has significant adverse effects and is moderately costly. It has consistent evidence suggesting both lack of efficacy in comparison with placebo and comparative inferiority to NSAIDs. Thus, cannabis is not recommended for the treatment of postoperative pain.

Cannabinoid Use for Safety-Critical Workers

Not recommended: Acute or chronic cannabinoid use, whether medicinal or recreational, is not recommended for individuals who perform safety-critical jobs. These jobs include the operation of motor vehicles, forklifts, overhead cranes, heavy equipment, or other modes of transportation; sharps work (eg, knives); work with injury

risks (eg, heights); and tasks involving high levels of cognitive function and judgment. There are other management strategies with less risk of impairment.

Strength of evidence: Not recommended, Evidence (C)

Level of confidence: Moderate

Rationale

Epidemiological and driving simulator studies are largely consistent that there is significant risk of motor vehicle crashes associated with cannabinoids. See also Table 1 on adverse events for details on motor vehicle collision and injury risk. Thus, the preclusion of safety-critical job functions while under treatment with either medical or recreational cannabinoids is recommended.

A 2024 National Safety Council Alcohol, Drugs and Impairment Division position statement also noted the following²¹⁶:

1. "Cannabis and related products can impair numerous aspects of human performance to include cognitive and psychomotor functions such as alertness, reaction time, estimating distance, decision-making, and memory."
2. "THC concentrations in biological fluids do not correlate with the degree of human performance impairment."
3. "There is no support from the literature for a (delta 9) THC threshold concentration in biological fluids to ensure that there is no performance impairment in safety-sensitive positions."
4. "Recent studies proposed various wait-times depending on the route of consumption.... However these proposals are not rigorous enough to ensure public safety, as almost all the studies reviewed involved single acute dosing and inhaled route of administration."
5. "Clear, robust scientific evidence from published studies is lacking to support persons working in safety-sensitive positions within 24 h after last use of cannabis and/or related products."

According to the 2024 National Safety Council Alcohol, Drugs and Impairment Division position statement²¹⁶: "Some scientific evidence exists to support that some persons can safely perform safety-sensitive duties 1 week after last cannabis use, [but] the bulk of scientific evidence reviewed would support most persons performing in a safety-sensitive position 1 month after last cannabis use." The statement concluded that a "large body of research indicates that the use of cannabis and related products is more likely than not incompatible with the performance of safety-sensitive functions" and that "cannabis and related product use is incompatible with those persons engaged in safety-sensitive tasks and positions."

CONCLUSION

Cannabis use is rapidly expanding across the United States, necessitating a guideline. Evidence regarding treatment efficacy is limited. There is some quality evidence suggesting the potential efficacy of cannabis for the treatment of spasticity associated with multiple sclerosis. There is no quality evidence of efficacy for treatment of common and typical work-related disorders such as back pain, chronic radiculopathy, neuropathic pain, and other acute or chronic pain disorders. Quality evidence supports a lack of efficacy for the treatment of postoperative pain. Adverse effects include increased risks of many cancers, pulmonary disorders, and cardiovascular diseases and are appearing to mirror many of the impacts of tobacco of 100 years ago. Cannabis is strongly associated with psychotic disorders. Based on prospective, population-based data, the reported strengths of association, and apparent dose-response relationships, there is growing concern that cannabis use may be causal for schizophrenia. Safety risks include motor vehicle crashes, falls, workplace injuries, and other injuries. Impairments are substantially longer lasting with edibles than with inhalation. Quality evidence was not identified to support the practice of allowing cannabis use the day prior to work, and it is thus not recommended. In conclusion, cannabis use is not recommended for the treatment of typical potentially work-related conditions, and its use for any purpose is not recommended for those required to perform safety-sensitive work.

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