AMERICAN COLLEGE OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

Cannabis

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SUMMARY OF RECOMMENDATIONS

The Evidence-based Practice Chronic Pain Panel's recommendations on cannabis are based on critically-appraised higher-quality research evidence and on expert consensus observing First Principles when higher-quality evidence is unavailable or inconsistent (see Methodology). The reader is cautioned to utilize the more detailed indications, specific appropriate diagnoses, temporal sequencing, preceding testing or conservative treatment, and contraindications that are elaborated in more detail for each test or treatment in the body of this Guideline in using these recommendations in clinical practice or medical management. These recommendations are not simple "yes/no" criteria.

All ACOEM guidelines include analyses of numerous interventions, whether or not FDA-approved. For non-FDA-approved interventions, recommendations are based on the available evidence; however, this is not an endorsement of their use. In addition, many of the medications recommended are utilized off-label.

Recommendations are made under the following categories:

- Strongly Recommended, “A” level
- Moderately Recommended, “B” level
- Recommended, “C” level
- Insufficient - Recommended (consensus-based), “I” level
- Insufficient - No Recommendation (consensus-based), “I” level
- Insufficient - Not Recommended (consensus-based), “I” level
- Not Recommended, “C” level
- Moderately Not Recommended, “B” level
- Strongly Not Recommended, “A” level

Recommendation	Evidence
Cannabinoids for Chronic Pain	Not Recommended, Evidence (C)
Cannabinoids for Acute Pain	Not Recommended, Evidence (C)
Cannabinoids for Postoperative Pain	Moderately Not Recommended, Evidence (B)
Cannabinoid Use for Safety-Critical Workers	Not Recommended, Evidence (C)

SCOPE

The scope of this evidence-based guideline on cannabis is focused on the treatment of pain ensuing from disorders that have a reasonable probability of being work-related (e.g., spine pain, chronic radicular pain, osteoarthrosis). The scope for this guideline does not include Alzheimer disease, multiple sclerosis, amyotrophic lateral sclerosis, cancer, nausea/vomiting related to chemotherapy, cachexia, acquired immune deficiency syndrome, sleep disturbance, posttraumatic stress disorder, epilepsy, or terminal care. The scope of this evidence-based guideline for use among safety-critical workers is not limited to cannabinoid use for treatment of pain.

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

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

BASIC PRINCIPLES AND DEFINITIONS

Cannabidiol oil (CBD oil). CBD oil is derived from cannabis. The oil is extracted from the plant and is typically diluted with another oil (e.g., 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. CB2 receptors, which are throughout the body, are thought to affect pain and inflammation.

Cannabis. Cannabis is the genus name for marijuana plants, of which two species have psychoactive 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 (i.e., cannabis) refers to the dried leaves, flowers, stems, and seeds from two species of the cannabis plant (*C. sativa* and *C. indica*). Marijuana is used in various forms. It is smoked in hand-rolled cigarettes (i.e., 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, or tea. Derivatives include hash oil, honey oil, wax, budder, shatter, and dabs. Dabs may contain >80% THC,[2,3] which far exceeds current marijuana concentrations of ~15%.

Tetrahydrocannabinol (THC). Tetrahydrocannabinol (or delta-9-tetrahydrocannabinol) is considered to be the most psychoactively potent of the cannabinoids.

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

HISTORY

Cannabis use dates to at least ~12,000 years ago, with initial evidence from use in the Altai mountains (present-day Russia-Kazakhstan, Mongolia-China).[4] The use of topical applications to treat inflammation in Egypt was documented in Ebers papyrus and dates to ~1500 BC.[5] Cannabis use for treatment of medical disorders in China dates to 800 BC,[6,7] with cannabis identified in the grave of a presumptive shaman in China. Use of marijuana for religious purposes dates to at least ~3,000 years ago.[8] 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 U.S. Drug Enforcement Agency (DEA) due to its lack of accepted medicinal use, high misuse potential, risk of dependency, and lack of safety while under medical supervision.[8] Marijuana liberalization laws began in California in 1996 and have spread across the United States. As of May 2024, the DEA proposed reclassification to Schedule III.

IMPACT

Marijuana use continues to rapidly increase with the legalization of medical and recreational use (see Figures 1 and 2).[9] 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 Figure 2).[10] Medicinal use of marijuana ranges widely across the states, ranging from 0.01% of the California state population to 9.2% of the population of Oklahoma;[10] however, these data are likely confounded by the lack of nonmedicinal access in several states.

Use in the past year among U.S. young adults (19-30 years of age) increased by 48% from 2011 to 2021, whereas use in the past month increased from 17% to 29% (70.6% increase), and daily use increased from 5% to 11% (120% increase).[9] Marijuana vaping by young adults doubled in 4 years, from 6% in 2017 to 12% in 2021.[9] Usage rates for the U.S. 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.[11]

Historical use over the past 50 years shows two strong trends. Use was estimated to have peaked in 1978.[12] Among 12- to 25-year-olds, use was 27% in 1978, fell to ~8% in 1992, and has gradually increased since then. Marijuana rates of use are also inversely correlated to the acknowledged degree of hazard associated with its use (see Figure 3).[13]

However, and importantly, the marijuana being used today is far more potent as measured by THC.[14,15] The THC levels in marijuana have increased by ~380% over the past 30 years, from ~2% to ~15% today (see Figure 4).[2] Some products, such as dabs, now have THC concentrations of more than 80%.[16]

MECHANISMS OF ACTION

Endocannabinoids and cannabinoid receptors are found in numerous body organs, including the nervous system, internal organs, connective tissues, glands, and immune cells.[8] Disorders theorized to be involved in the endocannabinoid system include migraines, fibromyalgia, multiple sclerosis, Parkinson disease, schizophrenia, and depression.[17] 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.

THC 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.[8]

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 towards adverse respiratory effects (e.g., 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.[18] Ingestion results in a slower increase and longer duration of effects.[19,20]

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.[8]

ADVERSE EFFECTS

Adverse effects of marijuana/cannabis related to THC are common (see below). Assessments of these adverse effects may be confounded by a lack of standardized doses and the marked increase in potency over time. With increasing doses, risks may be understated in the published literature. In addition, there now may be unrecognized risks. These challenges may bias some publications.

Medical cannabis users may prefer products with a lower THC but higher cannabidiol ratio, which are associated with lower adverse effects.[21] However, evidence of efficacy for pain reduction is mostly among patients with multiple sclerosis and involves use of products with higher THC-CBD ratios.[22]

Adverse effects associated with marijuana use include the following:

- Motor vehicle crashes[23,24,25,26,27]
- Slips, trips, and falls[28,29,30,31]
- Worker injuries[32,33,34]
- Central nervous system effects:
    - Cognitive impairment[23,35,36]
    - Altered judgment[8]
    - Short-term memory impairment[8]
    - Impaired motor coordination[8]
    - Impaired attention[35]
    - Dizziness[22,37]
    - Sedation[22,35,37]
    - Vision changes[22]
    - Altered brain development[38]
    - Sleep disorders[23]
- Psychosocial effects:
    - Depressive disorders[22,23]
    - Anxiety disorders[22,23]
    - Mania[22,39]
    - Schizophrenia[40]
    - Paranoia[41]
    - Psychosis (5-fold increased risk)[23,26,41,42,43]
    - Psychiatric symptoms (7.5-fold increased risk for number and severity)[43]
    - Personality change[41]
    - Addiction/cannabis use disorder[44,45]

    - Premature cessation of education[38]
    - Relationship problems[46]
    - Reduced life satisfaction[38]

- Lower educational attainment[46]
- Lower career achievements[46]
- Unemployment[47]
- Aggression[41]
- Violence:
    - Partner[23]
    - Child[23]
- Crime[25]
- Respiratory effects[48]:
    - Bronchitis*
    - Dyspnea*
    - Chronic obstructive pulmonary disease*
    - Pneumonia
- Cardiovascular events[23,49]:
    - Increased systolic blood pressure[50]
    - Myocardial infarction (2.5-fold increased risk)[48,49,51,52,53]
    - Stroke[52]
    - Arrhythmias,[52] including ventricular[48]
    - Tachycardia[48]
    - Venous thromboembolism[52]
- Gastrointestinal disorders
    - Nausea[22,35,37]
    - Vomiting, including cannabinoid hyperemesis syndrome[35,37]
    - Diarrhea[22]
- Increased risk of developing pre-diabetes[54]
- Negative perioperative outcomes[55]
    - Perioperative myocardial infarction
    - Abnormal airway resistance
- Carcinogen production, increased cancer risks,[56,57] 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 cancer[58]
    - Increased tar and polyaromatic hydrocarbons compared with cigarette smoke[57,59,60,61,62,63,64,65]

- Neonatal effects[46]:
    - Fetal growth restriction
    - Premature birth
    - Stillbirth
    - Brain development problems
    - Hyperactivity
    - Poor cognitive function
- Deaths from other causes not listed above, including:
    - Overdose
    - Cardiovascular mortality (~2-fold increased risk)[66,67]
    - Suicide[22,23,25,68,69]

**Risks reported associated with smoking marijuana*

CANNABIS USE DISORDER, DEPENDENCY, AND PROBLEMATIC USE

SAMHSA estimates the risk of addiction is approximately 10%, which increases to 17% when use starts before age 18 years.[46] An estimated 30% of marijuana users have one of the forms of cannabinoid use disorder.[70] 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.[71] Population-based surveys suggest increasing risks over time for frequent cannabis use and cannabis use disorder, with greater risks among individuals with pain compared to individuals without pain.[72]

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.[46,73,74]

An analysis of 527 medical cannabis users reported that all experienced withdrawal symptoms, with 214 (40.6%) having mild withdrawal symptoms, 180 (34.2%) having moderate withdrawal symptoms, and 133 (25.2%) having severe withdrawal symptoms. Over 24 months, the proportions trended towards 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.[46]

A systematic review with a meta-analysis estimated that of those using cannabis, 22% had cannabis use disorder, 13% were classified as cannabis "abuse," and 13% had cannabis dependency.[75] Risks have been suggested to be higher among those with chronic nonmalignant pain, mental health disorders, and substance use disorders.[72,76] Overall, problematic use has been estimated to be as high as 33%.[72,76]

The risks of developing problematic cannabis use have been found to be increased with the following[77]:

- 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)

The following have been shown to ***not*** be risks for the development of problematic cannabis use[77]:

- 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)

A study of U.S. veterans found higher rates of cannabis use and cannabis use disorder among those who were younger, male, unmarried, earning lower income, residing in a state with medical marijuana laws, and diagnosed with other psychiatric and substance use disorders.[78] Another study reported increasing prevalence rates of cannabis use disorder among veterans.[79]

Some evidence also supports that marijuana is a "gateway drug."[70,80] For example, a significant increase in the use of hallucinogens was reported after the increased use of marijuana, from 3% of respondents reporting use during the past year in 2011 to 8% in 2021 (a 167% increase) (see Figure 5).[9] Marijuana is also the most frequent drug accompanying alcohol in polysubstance use among emergency department patients.[81] A systematic review reported that the risk of marijuana overdose was 3.6-fold higher after legalization of cannabis[82] and doubled in Colorado after legalization of medical marijuana.[83] Emergency department visits after legalization increased by 89% in California[84] and 267% in Arizona.[85]

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 4.5% of all U.S. adults drive under the

influence of cannabis annually, with proportions increasing to as high as 63.8% among those with cannabis use disorder.[86] After the legalization of cannabis in Canada, a study of moderately injured drivers involved in a crash finding any detectable THC increased from 9.2% to 17.9%.[87] Another study found that marijuana-related traffic injuries increased by 94% after Canada's legalization in 2018.[88]

Many studies have reported that marijuana is a risk for motor vehicle fatalities,[89,90] although a few have not.[91,92] The proportion of U.S. crash deaths involving marijuana more than doubled between 2000 and 2018,[93] and the legalization of marijuana has been associated with increased risks of crashes and deaths.[94] Sedation is a commonly reported adverse effect.[32] Impairments have been shown by both on-road driving tests[95] and in numerous driving simulator studies.[96-100] Impairments have also been shown on psychomotor tests.[101] One study evaluated work fatalities in the course of heavy vehicle operations and found that one in six fatalities involved either stimulants or cannabis.[102]

In Ontario, more traffic fatalities tested positive for cannabis than for alcohol.[103] An analysis of the Fatality Analysis Reporting System from 1999-2010 found that the proportion of fatalities testing positive for cannabis approximately tripled (4.2-12.2%), whereas alcohol prevalence was stable.[104] One study reported that states with recreational marijuana laws experienced a 10% increase in motor vehicle fatalities.[105] Another study suggested less risk from those laws but increased risk from legalization of medicinal cannabis.[106] An ecological study estimated that a 15% increase in fatal motor vehicle collisions in the United States was associated with legalized recreational use.[107] Another study found an increased risk of fatal motor vehicle crashes after recreational but not medical cannabis legalization.[92]

After medical marijuana became widely available in Colorado in 2009 (registrants rose from <5,000 to ~125,000), the proportion of motor vehicle fatalities who were marijuana-positive increased 2.15-fold. A study estimated that fatal crashes increased an average of 10% in AL, CA, CO, MA, NV, OR, and WA based on recreational marijuana legalization.[105] 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.[108] THC-positivity tripled among motor vehicle fatalities in Hawaii after legalization of cannabis, while THC-positivity also doubled (from 11% to 20%) at the state's largest Level 1 trauma center.[89] Two studies found interactions between marijuana and alcohol in fatal crashes and two-vehicle crashes.[108] 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, 1.72 odds of non-fatal collision, and 1.65 odds of crash culpability.[109]

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."[110] Another study also reported driving after use of marijuana was common.[111] A randomized experimental study found regular users demonstrated driving impairments while also having false perceptions of safety accompanied by willingness to drive while impaired.[112]

ACCIDENTAL INJURY

An increased risk of accidents (55% increase) and injuries (85%) has been reported.[33,113] Injuries have been associated with cannabis among adolescents.[114,115] From 2009 to 2021, data from US poison centers show that intentional suspected suicidal cannabis exposures

more than doubled.[116] Ten of 459 (2.2%) workplace fatalities tested positive for cannabis, which was the only illicit drug found.[117]

WORK ABSENCES

Work absences are reportedly 78% greater among those using marijuana compared with those not using marijuana (7.1% vs. 4.0%).[113] There also is longitudinal evidence of a dose-response relationship with greater absences occurring among those with greater use.[118]

SCHIZOPHRENIA

Considerable evidence is building that schizophrenia is at least strongly associated with, and it may be caused by, marijuana/cannabis.[119,120,121] A 50-year population-based study in Denmark concluded that up to 30% of schizophrenia cases among men ages 21-30 years may have been preventable by averting cannabis use disorder.[121] A prior systematic review suggested the same, although it was based on 12 studies that mostly used weaker study designs.[40] 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.[122]

While associations with mental health issues are widely reported, one report of patients at a large pain center noted a lower prevalence of anxiety or depression among medical marijuana users when compared with opioid users.[123]

SAFE LEVEL

Some literature suggests reduced risks of adverse effects among those using lower doses.[22] However, there is no literature that shows a clearly defined "safe level" of use. One prospective case-control study found no increase in the risk of motor vehicle crashes with injuries for drivers with THC levels of 0-2 ng/mL and 2-5 ng/mL, but found a trend towards increased crash responsibility risk among those with THC levels of >5 ng/mL (OR=1.74, 95% CI 0.59-6.36).[124] 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.[125] 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.[126]

Duration of impairment is also unclear and likely related to both dose and route of administration.[19,125,127,128,129]

OPIOID SPARING

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.[130-137] Two studies provide somewhat contrasting evidence, with one showing greater opioid requirements among marijuana users after injury[138] and that high-frequency medical cannabis use is associated

with worse pain.[139,140] Quality of life has not been shown to be improved with cannabis use.[140]

A systematic review concluded that "[l]ow certainty evidence suggested little to no difference between cannabis and opioids for pain relief or sleep quality."[132] 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 to reductions with NSAIDs.[141]

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 (see evidence table). Also, the longest duration among quality studies is 3 months (Vela et al., 2022, Frank et al., 2008, Selvarajah et al., 2010). 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 or emotional awareness expression therapy), 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 (Zubcevic et al., 2023). A moderate-quality trial of CBD treatment (20-30 mg for 12 weeks) for hand osteoarthrosis and psoriatic arthritis found lack of efficacy (Vela et al., 2022). THC 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 (Berman et al., 2004).

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 (Selvarajah et al., 2010). 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

(Wilsey et al., 2016). A small crossover trial found no differences in pain or quality of life but improved sleep with nabilone compared with amitriptyline over 2 weeks (Ware et al., 2010). A pragmatic RCT of immediate vs. delayed receipt of a medical marijuana card resulted in no differences in pain, although sleep was better in the early marijuana group (Gilman et al., 2022). Another crossover trial of oral nucosal spray with cannabinoids for treatment of chemotherapy-induced neuropathic pain found lack of efficacy (Lynch et al., 2014). A comparative trial of nabilone vs. dihydrocodeine for many types of chronic neuropathic pain found dihydrocodeine to be superior for both pain relief and having fewer adverse effects (Frank et al., 2008).

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 (Almog et al., 2020). A 4-hour experimental crossover trial for treatment of diabetic neuropathy found modest improvements in pain with THC compared with placebo (Wallace et al., 2015). A 3-hour experimental study of fibromyalgia suggested nonsignificant results with cannabis (van de Donk et al., 2019).

There are RCTs suggesting the potential efficacy of cannabinoid treatment for multiple sclerosis, particularly with spasticity (McDonagh et al., 2022, Notcutt et al., 2004). 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%) visceral pain, 50 (8.4%) fibromyalgia, and 26 (4.3%) diabetic neuropathy (McDonagh et al., 2022). Trials for treatment of fibromyalgia also conflict regarding efficacy (Chaves et al., 2020, Ware et al., 2015, van de Donk et al., 2019). Although out of scope for this guideline, multiple trials for treatment of cancer pain have shown lack of efficacy (Portenoy et al., 2012, Johnson et al., 2010, Fallon et al., 2017, Lichtman et al., 2018).

There is very weak evidence for the substitution of cannabinoids for opioids (Baron et al., 2018, Capano et al., 2020). However, there are concerns of an arising second follow-on epidemic. Other systematic reviews found similar major gaps in established knowledge (Lee et al., 2021, Petzke et al., 2022, McDonagh et al., 2022). One systematic review purportedly assessing efficacy for treatment of back pain concluded there was efficacy; however, the analysis relied on two small RCTs that both primarily studied patients with spinal cord injuries (Price et al., 2022).

There are no trials documenting improved objective functional outcomes, with more than 100 studies documenting many adverse effects, some of which are severe (see Adverse Events). 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). 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.

Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: cannabis and medical marijuana**;** chronic pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. 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, 11from 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.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

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 (Bebee et al., 2021). 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.

Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: cannabis and

medical marijuana**;** safety-sensitive work; chronic pain; acute pain relief, subacute pain relief, post-operative pain relief, and functional improvement controlled; clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. 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.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

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 four-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 (Beaulieu, 2006). A three-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 be 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 (Ostenfeld et al., 2011). A placebo-controlled trial of oral delta-9-tetrahydrocannabinol (5 mg) for the management of pain on postoperative day 2 after total abdominal hysterectomy found lack of efficacy (Buggy et al., 2003). 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 (Kalliomaki, 2013). One trial of cannabis for postoperative pain found increased rescue analgesia at lower cannabis doses; however, the trial was terminated due to adverse vasovagal events occurring among the higher-dose group (Holdcroft et al., 2006).

Systematic reviews and meta-analyses found no meaningful evidence of improvements in acute or postoperative management with cannabinoid usage (Stevens et al., 2017, Abdallah et al., 2020). One systematic review and meta-analysis reported efficacy but included trials with diverse primary outcomes, such as nausea and vomiting with pain (Gazendam et al., 2020). In a low-quality study of 155 cannabinoid users with 3,637 propensity-matched controls undergoing major orthopedic surgery, the cannabinoid users had worse pain and worse sleep postoperatively (Liu, 2019).

Cannabis is not invasive, 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.

Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: cannabis and medical marijuana**;** safety-sensitive work; chronic pain; acute pain relief, subacute pain relief, post-operative pain relief, and functional improvement controlled; clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 18 articles in PubMed, 5 in CINAHL, 0 in Cochrane Library, 2,580 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.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

CANNABINOID USE FOR SAFETY-CRITICAL WORKERS

Not Recommended

Acute or chronic cannabinoid use 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 (e.g., knives); work with injury risks (e.g., 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

See the section on Adverse Events for details on motor vehicle collision and injury risk. Epidemiological and driving simulator studies are largely consistent that there is significant risk of motor vehicle crashes associated with cannabinoids. 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 (Corbett MR, 2024) also noted the following:

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."

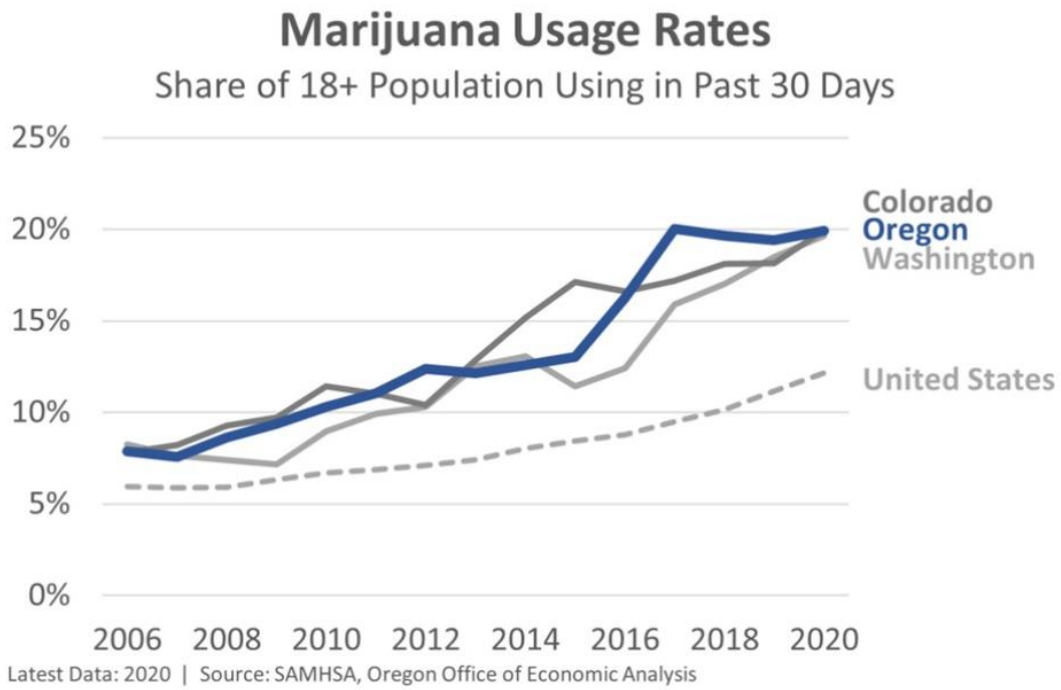
According to the 2024 National Safety Council-Alcohol, Drugs and Impairment Division position statement (Corbett MR, 2024): "Some scientific evidence exists to support that some persons can safely perform safety-sensitive duties 1 week after last cannabis use, [but] the bulk of scientific evidence reviewed 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."

Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: cannabis and medical marijuana**;** safety-sensitive work; chronic pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. 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.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

FIGURE 1. MARIJUANA USAGE RATES



Legalization of recreational use began in Washington in 2012, Colorado in 2014, and Oregon in 2015; the rate of increased use in those states has outstripped the increasing usage overall rate for the US.

FIGURE 2. ESTIMATED US RECREATIONAL AND MEDICAL MARIJUANA MARKET SALES

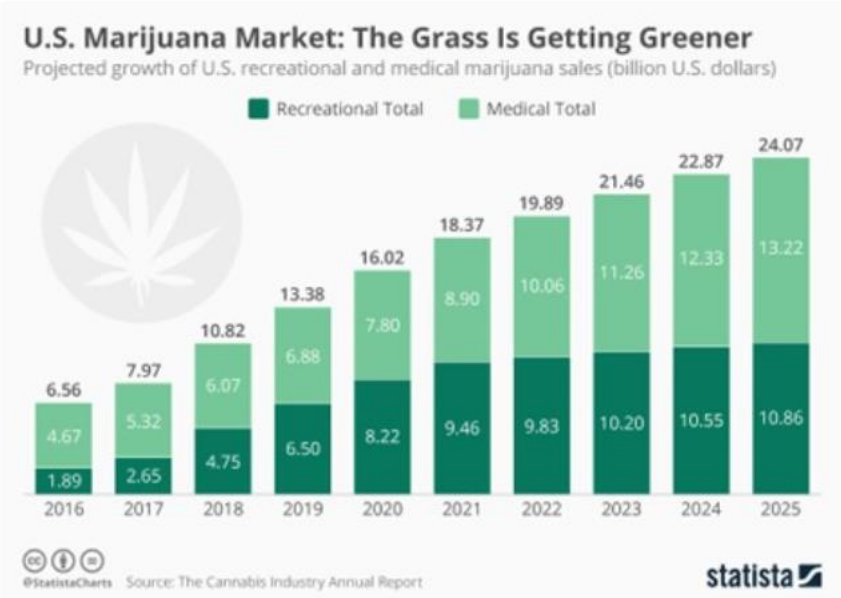


FIGURE 3. INVERSE RELATIONSHIP BETWEEN US TWELFTH GRADER'S MARIJUANA DAILY USE AND PERCEIVED RISK

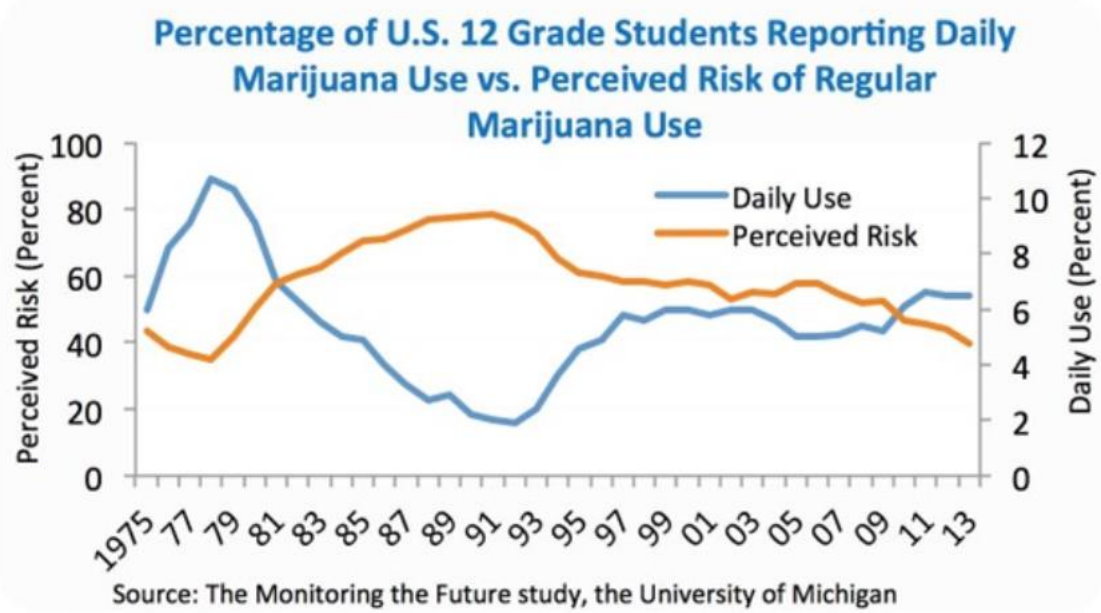
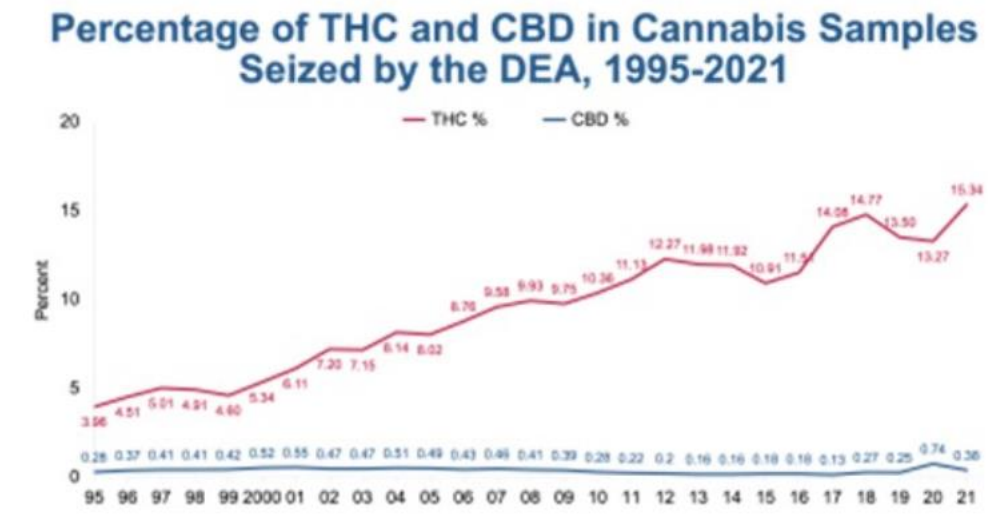
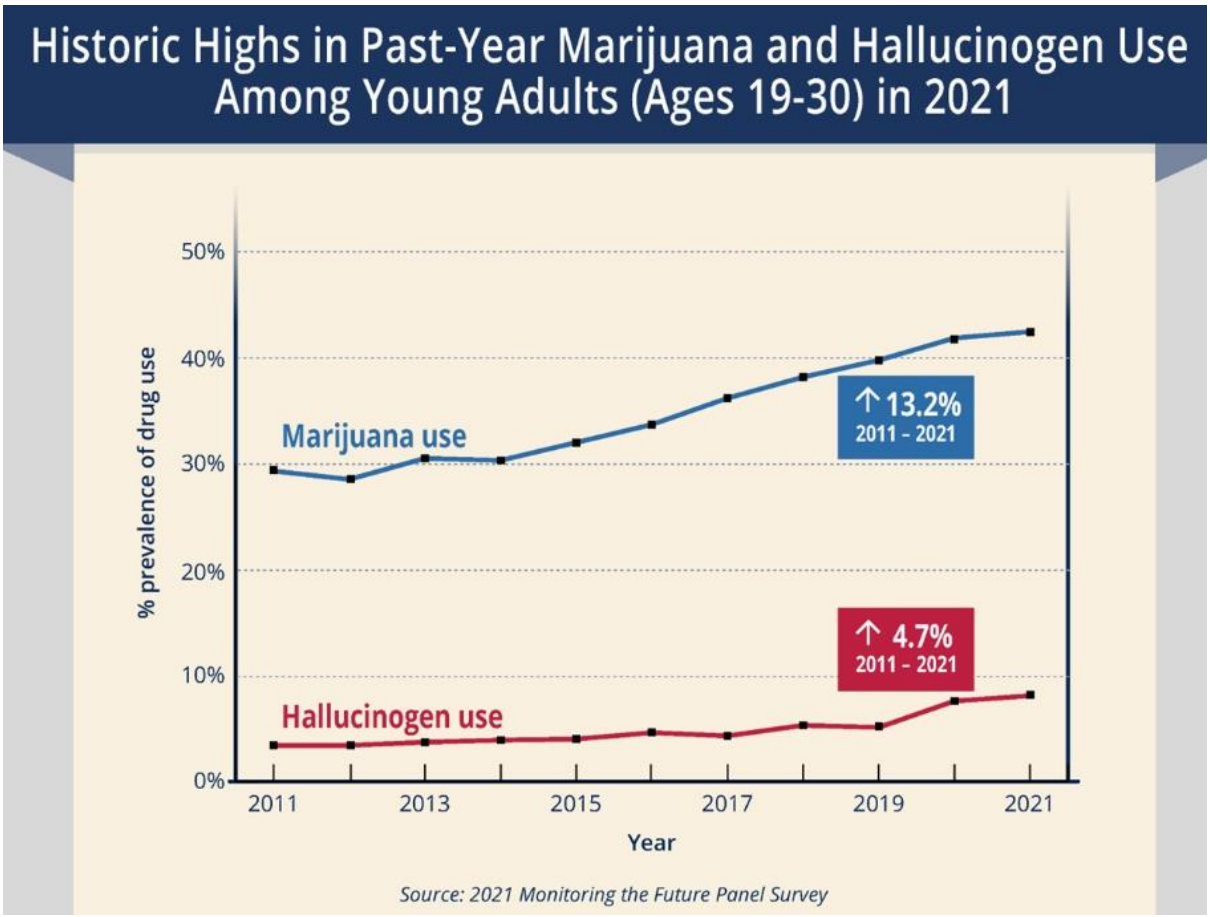


FIGURE 4. PERCENTAGE OF THC IN DEA SEIZURES OVER TIME



SOURCE: U Miss, Potency Monitoring Project

FIGURE 5. PAST-YEAR MARIJUANA AND HALLUCINOGEN USE



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