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Rescheduling Cannabis—Medicine or Politics?

Bertha K. Madras, PhD; Paul J. Larkin, JD

IMPORTANCE In 2023, the US Department of Health and Human Services (HHS) issued a letter to the administrator of the Drug Enforcement Administration (DEA) recommending rescheduling of cannabis (marijuana) from Schedule I to Schedule III under the Controlled Substances Act (CSA). This recommendation marked a significant departure from previous, consistent, and long-standing federal decisions on cannabis scheduling.

OBJECTIVE To critique the arguments made by HHS for recommending marijuana rescheduling.

EVIDENCE The HHS secretary (advisor) and US attorney general (decision maker) must consider 8 factors and a 5-part test when deciding whether to reschedule a controlled substance. CSA classification criteria include whether a drug has currently accepted medical use, whether it has abuse potential, and whether use is safe under medical supervision. HHS undermined these established legal scheduling criteria by introducing new, untested criteria.

FINDINGS HHS failed to adequately address the adverse effects of cannabis use, including the high prevalence of cannabis use disorder among users, risks associated with youth consumption, growing evidence linking cannabis to psychosis, and other significant concerns. HHS asserted that cannabis is widely accepted as a legitimate form of medicine, despite the reality that only a small fraction of patient-care physicians recommend it for symptom relief, in practices that often diverge from the norms of medical practice. Finally, the US Food and Drug Administration has not approved cannabis as a medicine, as evidence is deficient in several key areas, including data from high-quality clinical trials, standardized cannabis formulations, established purity, defined routes of administration, dosing guidelines, and specific frequencies of use.

CONCLUSIONS AND RELEVANCE The HHS rationale for reclassifying cannabis in myriad forms (edibles, smokables, drinkables, vaping products, suppositories) and potencies relies on a questionable selection of comparator drugs, downplays distinctive adverse events among cannabis users, and claims, unconvincingly, that cannabis has wide acceptance in medical practice supported by scientific evidence.

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Author Affiliations: McLean Hospital, Belmont, Massachusetts (Madras); Harvard Medical School, Boston, Massachusetts (Madras); The Heritage Foundation, Washington, DC (Larkin).

Corresponding Author: Bertha K. Madras, PhD, Department of Psychiatry, Harvard Medical School, McLean Hospital, Mailman Research Center, 115 Mill St, Room 315, Belmont, MA 02478 (bmadras@mgb.org; bertha_madras@hms.harvard.edu).

On October 6, 2022, President Biden directed the secretary of the US Department of Health and Human Services (HHS) and the US attorney general to review how cannabis should be classified,[1] yet 6 months earlier (April 12, 2022), Peter Hyun, acting assistant attorney general, issued a letter reflecting the Biden administration's stance that cannabis had not been scientifically proven to be a safe and effective treatment for any disease or condition. That finding was not new; every earlier presidential administration had reached the same conclusion since the 1970 passage of the Controlled Substances Act (CSA), which defines the law governing the scheduling and rescheduling of psychoactive substances. By August 29, 2023, Admiral Rachel L. Levine, HHS assistant secretary for Health, wrote to the administrator of the Drug Enforcement Administration (DEA) recommending rescheduling cannabis from Schedule I into Schedule III.[2] The rationale for rescheduling cannabis remains unconvincing.

Our ancestors identified numerous phytopharmaceuticals long before the existence of the US Food and Drug Administration (FDA). Ancient texts and physical evidence suggest that cannabis was used for therapeutic applications in antiquity, interspersed with phases of prohibition.[3,4] In the 19th century, the US and British pharmacopoeias listed cannabis because of its then-perceived analgesic and sedative benefits. By the 20th century, cannabis was removed, without contest, from both the British (1932) and US (1942) pharmacopeias because it had not gained widespread use as a remedy. Its slow onset and inconsistent potency rendered it less effective than opium and morphine for pain management during the Civil War. The development of more effective pharmaceuticals, such as aspirin, coupled with rising concerns over abuse potential further disfavored cannabis.

Cannabis prohibition in the United States arose incrementally, first by states, followed by passage of the federal Marihuana Tax Act in 1937 and the CSA, which created the current regulatory frame-

work for psychoactive drugs.[5] The CSA places psychoactive drugs with abuse potential into 1 of 5 schedules in descending order of abuse liability. Along with heroin, hallucinogens, and others, cannabis was placed into Schedule I, a classification that applies to drugs that have no legitimate medical use, have a high potential for abuse, and lack safe use even under medical supervision. Being contraband, Schedule I drugs are outside the scope of legitimate medical practice and cannot be prescribed for any use. Schedule III drugs have a moderate to low potential for physical and psychological dependence and a currently accepted medical use in the United States. The attorney general (or his designee, the DEA administrator), after consultation with the HHS secretary, may reclassify cannabis if a compelling case is made for its legitimate therapeutic use.

While some may argue that administrative challenges posed by the CSA and FDA hindered progress in demonstrating the therapeutic benefits of cannabis, it did not prevent cannabis or cannabinoid research. Two distinct phytocannabinoids, Δ9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD) resided in Schedule I until they were approved by the FDA after undergoing the rigorous FDA process. Δ9-THC was then classified as a Schedule III substance, whereas CBD, lacking psychoactive effects and abuse potential, was not scheduled. Both examples, along with clinical trials exploring the therapeutic potential of smoked, vaped, and edible cannabis for various health conditions, as well as studies of the Schedule I drugs psilocybin or 3,4-methylenedioxymethamphetamine (MDMA, or ecstasy), demonstrate the feasibility of conducting rigorous research on such drugs. Rescheduling cannabis may not significantly accelerate industry-sponsored clinical trials, given intellectual property constraints and strong market competition from state-regulated dispensaries.

Members of Congress have introduced numerous bills to deschedule or reschedule the drug, yet Congress has passed none.[6] Cannabis reform advocates have repeatedly urged US attorneys general to either deschedule cannabis altogether or to lower its classification downwards,[7] but every effort has failed. By contrast, advocates have successfully persuaded many states to revise their penal codes and allow physicians to "recommend" cannabis use for their patients despite contrary federal law.[8]

Eight-Factor Analysis and the 5-Part Test

When considering a rescheduling proposal, the CSA requires the HHS secretary and the attorney general to consider 8 factors (**Box 1**).[9] This assessment and use of a related 5-part test (**Box 2**)[10] govern any rescheduling judgment. Core criteria include assessing whether a drug has a currently accepted medical use, whether the drug has a high potential for abuse, and whether its use is considered safe under medical supervision. Since 1992, the DEA has determined that a drug has a currently accepted medical use only if the FDA has approved the drug for marketing in interstate commerce or if the drug meets the 5-part test that tracks with core standards developed under the Federal Food, Drug, and Cosmetic Act (FDCA) (Box 2). These core standards reflect a long-standing consensus among medical and scientific experts on the evidentiary threshold that must be met for inclusion in Schedules II through V, especially effectiveness and safety. No unapproved drug can be used for treatment regardless of what the states might decide.[11] In 2024, the FDA applied its rigorous standards by rejecting an application to approve MDMA for the treatment of posttraumatic stress disorder, citing significant design flaws in the clinical study.

Box 1. Eight Factors the HHS Secretary and the Attorney General Must Consider for Scheduling a Substance[9]

- The drug's actual or relative potential for abuse
- Scientific evidence of its pharmacological effect, if known
- The state of current scientific knowledge regarding the drug or other substance
- Its history and current pattern of abuse
- The scope, duration, and significance of abuse
- What, if any, risk there is to the public health
- Its psychic or physiological dependence liability
- Whether the substance is an immediate precursor of a substance already controlled

Abbreviations: HHS, US Department of Health and Human Services.

Box 2. Five-Part Test for Designating a Drug as a Medicine[10]

- The drug's chemistry must be known and reproducible.
- There must be adequate safety studies.
- There must be adequate and well-controlled studies proving efficacy.
- The drug must be accepted by qualified experts.
- The scientific evidence must be widely available.

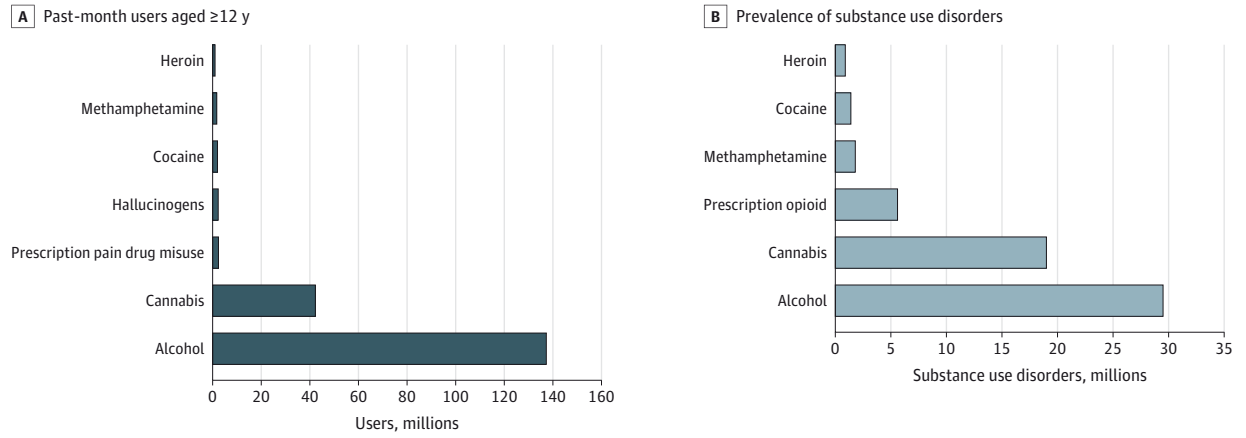
The FDA acted contrary to the provisions of the CSA and FDCA when making its 2023 recommendation in favor of rescheduling cannabis. They based reclassification of cannabis as a Schedule III substance on 3 key assertions that warrant careful examination.

"Cannabis Has a Low Potential for Abuse Compared With Substances in Schedule I and II?"

In evaluating the actual or relative potential for cannabis abuse, HHS tapped various epidemiological databases of adverse outcomes from 2015 to 2021 involving cannabis or comparator drugs. It concluded that while some individuals consume cannabis in quantities that may pose a risk to their health, the safety of others, and the community, such cases appear to be relatively infrequent and less severe compared with the consequences (deaths, Poison Control Center reports) associated with alcohol (unscheduled), heroin (Schedule I), and cocaine (Schedule II). That conclusion is flawed for several reasons.

First, the report neglected to address emerging trends in cannabis use, the high prevalence of cannabis use disorder (CUD) among heavy or long-term users, or the proportion of individuals with CUD relative to those affected by the comparator substances, including alcohol (**Figure**).[12] As alcohol is explicitly excluded from the CSA, its selection as a comparator is peculiar; alcohol users still greatly outnumber cannabis users. In any event, accumulated data show alcohol morbidity and mortality are greater than cannabis. Recent data show an increasingly unfavorable outlook for cannabis use. Far more

Figure. Use of Alcohol and Other Drugs and Prevalence of Substance Use Disorders[12]



A, Past-month number of users of alcohol and other drugs. B, Prevalence of substance use disorders.

people drink alcohol (137.4 million in the past month) than the 42.3 million past-month consumers of cannabis (Figure, A), but high-frequency cannabis use is more common than high-frequency alcohol drinking: between 1992 and 2022, per capita rate of daily or near-daily cannabis use increased 15-fold.[13] Whereas the 1992 survey recorded 10 times as many daily or near-daily alcohol users as cannabis users (8.9 million vs 0.9 million), the 2022 survey for the first time recorded more daily and near-daily users of cannabis (17.7 million) than of alcohol (14.7 million). In 2022, past-month cannabis users were 7.4 times more likely to report daily use (28.2%) than alcohol consumers (3.8%).[13]

Frequent use is relevant because the prevalence of CUD, a clinical condition with considerable impairment and comorbidity, is especially high among those with a history of frequent, daily cannabis use.[14] Currently, the prevalence of CUD among adolescents and young adults (16.5%) is converging with alcohol use disorder (16.4%). Instances of severe and moderate CUD (44.9%) are numerically higher than alcohol use disorder (40.9%), and CUD prevalence far exceeds that of other illicit substance use disorders (Figure, B).[12] Importantly, the *DSM-5* criterion of "continued use despite physiological or psychological problems" was many times higher among those with CUD (31.9%) compared with disordered alcohol use (5.7%), prescription opioid use (7.3%), and cocaine use (9.7%). The percentage reporting tolerance and craving was also higher for CUD.[15] Nationally, representative data suggest that as many as 30% of those who use cannabis may develop CUD,[16] with minors developing CUD at twice the rate of adults.[17] The prevalence of CUD is similar whether used for medicinal or recreational purposes, increases with frequency of use,[18] and among medical cannabis users (past 6-12 months), reportedly ranges from 25% to 29%.[19] Equally discouraging are high numbers of new initiates of cannabis use, 3.7 million, 53% of whom started before 21 years old; corresponding values for alcohol (4.2 million), pain relief misusers (1.3 million), and hallucinogens (1.4 million); new users of other drugs in Schedule I or II were less than 1 million.[12]

Second, HHS ignored consequences more specifically associated with cannabis than comparator drugs. HHS contrasted cannabis with potentially lethal substances, such as opioids and psychostimulants, while overlooking the growing evidence linking cannabis use and CUD with severe, disabling, chronic, and sometimes fatal outcomes: suicidality,[20] psychosis,[21] schizophrenia,[22] bipolar disorder,[23] cognitive/memory impairment and reduced IQ,[24-27] violence,[28] childhood poisonings,[29] amotivational syndrome,[30] increased school absenteeism, dropouts; reduced likelihood of graduating high school, enrolling in university, and postsecondary degree attainment[31]; and others.[32-35] Assuming causality, one-fifth of cases of schizophrenia among young males might be prevented or delayed by averting CUD.[36] Cannabis can cause various adverse medical events, including increased emergency department visits,[37] cannabis hyperemesis syndrome (nausea, vomiting, abdominal pain),[38] respiratory problems, heart attacks, strokes,[32] and negative prenatal and postnatal effects on fetuses exposed in utero.[39] These risks, often attributed to nonmedical use, are included because HHS also assessed the risks of recreational drug use, as many people use cannabis for both medical and nonmedical purposes, cannabis products are similar across both uses, and CUD prevalence is comparable in both populations.

Third, cannabis use confers risks on unwilling third parties because it impairs the ability to handle a motor vehicle safely,[40] with 1 study reporting that cannabis-involved fatal traffic collisions had increased from 9.0% of fatal crashes in 2000 to 21.5% in 2018.[41]

Fourth, from 2011 to 2021, states with legalized medical cannabis experienced an 42.7% increase in CUD and 88.6% increase in cannabis poisoning, compared with states without legalized medical cannabis.[42] State cannabis legalization has also led to diverse, potent products (high THC content), which are associated with more regular use, more CUD cases, and a higher risk of psychosis.[43]

In essence, HHS' reasoning is tantamount to saying that getting hit by a truck is relatively safe because it's less damaging than getting hit by a train. Specific risks (eg, cognitive impairment, psychotic disorders, cannabinoid hyperemesis syndrome, amotivational syndrome) associated with cannabis use and CUD compare unfavorably with alcohol and other drugs. Age at onset, frequency of cannabis use, THC content, and cumulative cannabis exposure can all contribute to these adverse outcomes in individuals with or without a preexisting medical condition or psychiatric disorder. The

American Academy of Pediatrics highlights that cannabis' negative effects on youth should be a salient criterion in rescheduling decisions.

In concluding that cannabis should be rescheduled, HHS proclaimed that the CSA is impermissibly narrow, yet HHS failed to provide a detailed explanation for disregarding existing criteria. Instead, the agency ignored established FDA practices and the DEA test to create 2 new standards without legal precedent or status, to address the recent political movement to medicalize cannabis: (1) there is widespread current experience with medical use of cannabis in the United States by licensed health care professionals according to state programs; (2) there is credible scientific support for at least 1 medical condition that meets the 5-part test (Box 2), another conclusion based on state-level programs.

"Cannabis Currently Has an Accepted Medical Use in Treatment in the United States?"

HHS relied on the fact that numerous states have allowed physicians to "recommend" marijuana to patients under state law without risk of criminal prosecution.[11] This rationale is legally flawed. Congress has not designated states as arbiters of a drug's safety, efficacy, or purity, and state cannabis programs were established through plebiscites or legislative votes, not clinical trials.

First, there is no medical consensus that cannabis is a legitimate medical treatment. Among the 777 143 patient-care physicians in the United States, approximately 2% recommend cannabis; among 29 500 clinicians; 53.5% of these hold a doctor of medicine (MD) or doctor of osteopathic medicine (DO) degree. Other clinicians include dentists, physician assistants, nurses, and other health care professionals.[44] The significant geographic variation in the number of authorizing clinicians per patient, ranging from 0.8 clinicians per 1000 patients in Oklahoma to 109 clinicians per 1000 patients in Mississippi, may reflect differing views of medicinal cannabis or creation of "weed mills" analogous to prescription opioid "pill mills."

Second, cannabis recommendations often lack details on dose, frequency, composition, route of administration, THC content, tapering, or product quality, unlike FDA-approved prescriptions.[45]

Third, cannabis dispensaries, rather than pharmacies, serve as the main retail source of cannabis. Typically, "budtenders" or managers are responsible for recommending specific cannabis products for particular medical symptoms. While state dispensary regulations can influence the products available to individuals, these regulations do not always align with staff recommendation.[46] According to 1 survey, respondents made recommendations based on factors such as feedback from other customers, the customer's previous experience with cannabis, and the staff member's personal experience.[47] Few provided guidance on cannabis use disorder, withdrawal, motor vehicle collision risk, or the potential for psychotic reactions.

Fourth, those who recommend cannabis as a medicine are often not primary care physicians; may not have a bona fide relationship with a patient; may not maintain regular medical records, follow up on patient health, or see patients more than once (depending on state regulations); and are less likely to check whether long-term use improves health or causes adverse events. In 2019, only 9 states and Washington, DC, required clinicians to register with a state program to certify patients, and only 9 jurisdictions required clinician training to certify patients.

Fifth, many states allow cannabis to be recommended for any medical condition without a physical examination or diagnostic tests to verify medical necessity or standardized terminology for documentation.[48]

Sixth, there is no standardized protocol for matching indications with dosage, dosing schedules, or guidelines for discontinuing use if symptoms improve or adverse effects occur.

Seventh, physicians and budtenders are not required to inform patients of risks or adverse effects or to identify at-risk patients. Although Colorado, Washington, and Oregon explicitly prohibit health claims in advertising or labels, more than 90% of retailers there endorsed use for anxiety, insomnia, and/or pain; 54.3% endorsed use for pregnancy-related nausea even though fetal exposure to cannabis confers sufficient risk to warrant abstaining during pregnancy.[49]

Eighth, enrollment in medical cannabis programs grew from 2020 to 2022 but dropped in areas with nonmedical adult-use laws,[44,50] possibly because legal cover for nonmedical use was no longer necessary. Use for ailments without evidence or specific qualifying conditions increased during this period.

"There Is Credible Scientific Evidence Supporting Such Medical Use?"

That conclusion is dubious.

First, the evidence supporting generic "cannabis" as a treatment for medical conditions remains either low quality or nonexistent.[51,52] The FDA has not approved any cannabinoid-based, plant-derived product for the most common qualifying conditions, such as pain, anxiety, or posttraumatic stress disorder (PTSD).

The FDA has approved individual cannabinoids such as THC (within a specific dose range, 2.5-10 mg), nabilone, and CBD. HHS extrapolated from approval of these pure drugs that there is credible support for the medical use of whole-plant cannabis in treating nausea, vomiting, and anorexia. Yet cannabis contains more than a hundred cannabinoids and numerous other compounds and metals. The tested, safe-dose range of THC is not applicable to generic cannabis with strains and products containing much higher THC doses. Would the FDA extend digoxin's approval to foxglove for heart failure treatment? Never, because of its unpredictable dosage and high risk of toxicity. The adverse events arising from chronic use of potent smoked or vaped cannabis for pain remain uncertain.

Second, chronic pain, reported by 48.4% of qualifying patients in 2022, is the most frequent condition cited for use. HHS highlighted this indication as a key justification for rescheduling cannabis. In doing so, it cited the 2017 National Academies of Sciences, Engineering, and Medicine report, which found "substantial evidence supporting the effectiveness of cannabis in managing chronic pain in adults."[53] The report failed to account for critical variables that question a rating of "substantial evidence." Since then, 24 meta-analyses/reviews have examined cannabis for chronic pain but did not endorse it.

Third, a randomized clinical trial demonstrated that obtaining a medical cannabis card led to higher rates and severity of CUD without significantly improving pain, anxiety, or depressive symptoms, although participants did self-report some relief from insomnia.[54]

Fourth, the International Association for the Study of Pain (IASP) has explicitly stated: "There is not enough high-quality human clinical safety and efficacy evidence to allow IASP to endorse the general use of cannabis and cannabinoids for pain at this time." With no high-quality studies or meta-analyses, nor the endorsement of this key professional organization, the use of cannabis to treat "generic" chronic pain remains inconclusive.[55]

Fifth, various dispensary products (eg, concentrates, edibles, topicals, tinctures, oils, sublinguals, capsules, suppositories, vape cartridges) currently lack comprehensive high-quality scientific evidence to support recommendations for specific medical conditions or to caution on potential adverse effects. For these products, no standards have been established for dosage, product purity, shelf life, contaminants, THC-to-CBD ratios, routes of administration, usage frequency and duration, and criteria for discontinuation or tapering.

Sixth, the second and third most common patient-reported qualifying conditions in 2022 were anxiety and PTSD, even though no high-quality studies exist showing cannabis is effective in relieving anxiety or PTSD, or cancer-related deterioration of quality of life and mental health status.[56-58]

Seventh, state guidelines for treating medical conditions with cannabis vary widely. For example, South Dakota lists 6 qualifying conditions, Illinois lists 48, and some states accept "any medical condition." By late 2021, states had approved cannabis for 105 conditions, many without quality supportive research.[59] State approval can wrongly imply medical legitimacy and safety, while ignoring potential risks.

Rescheduling cannabis into Schedule III would not make cannabis legal, and it would remain subject to relevant criminal prohibitions of the CSA. Moving cannabis to Schedule III could grant the FDA greater authority to regulate medical claims and restrict access to dispensary cannabis. Thus far, the FDA has shown little inclination to intervene, even refraining from issuing warning letters or aggressively enforcing actions against state-legal marijuana businesses. There are no clear indications that rescheduling will lead to increased FDA oversight of cannabis-related claims or associated medical practice.

Conclusions

The criteria and evidence HHS used to recommend reclassifying cannabis to Schedule III are flawed. If the DEA agrees, it will contradict past federal health concerns and ignore emerging data on escalating use, disordered use, and negative health effects. This decision could undermine FDA authority and compromise the integrity of our drug approval process and pharmaceutical supply. The DEA should reject the HHS' conclusion.

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REFERENCES

1. Department of Health and Human Services. Letter from assistant secretary for health recommending rescheduling of marijuana. Accessed May 12, 2025. https://www.dea.gov/sites/default/files/2024-05/2016-17954-HHS.pdf

2. Schedules of controlled substances: rescheduling of marijuana. Proposed Rules; Department of Justice, Drug Enforcement Administration, 21 CRF Part 1308 [Docket No. DEA-1362; A.G. Order No. 5931-2024]. *Fed Regist*. 2024;89(99).

3. Peters H, Nahas GG. A brief history of four millennia (BC 2000-AD 1974). In: *Marihuana and Medicine*. Nahas GG, Sutin KM, Harvey D, Agurell S, Pace N, Cancro R, eds. Humana Press Inc; 1999.

4. Zias J, Stark H, Sellgman J, et al. Early medical use of cannabis. *Nature*. 1993;363(6426):215. doi:10.1038/363215a0

5. Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. No. 91-513, 84 Stat. 1236.

6. Larkin PJ. Twenty-first century illicit drugs and their discontents: why the FDA could not approve raw cannabis as a "safe," "effective," and "uniform" drug. Heritage Foundation Special Report No. 275 (2023).

7. CaseMine. *Americans for Safe Access v Drug Enforcement Admin*. 706 F.3d 438 (DC Cir 2013). Accessed May 12, 2025. https://www.casemine.com/judgement/us/5914f591add7b0493498b09f

8. Federation of State Medical Boards. Medical marijuana: state by state overview. Accessed July 22, 2024. https://www.fsmb.org/siteassets/advocacy/key-issues/medical-marijuana-requirements-by-state.pdf

9. Authority and criteria for classification of substances, 21 USC §811 (2011). Accessed May 6, 2025. https://www.govinfo.gov/app/details/USCODE-2011-title21/USCODE-2011-title21-chap13-subchapI-partB-sec811

10. Marijuana scheduling petition; denial of petition; remand. *Fed Regist*. 1992;57(59):10499-10506.

11. Larkin PJ. States' rights and federal wrongs: the misguided attempt to label marijuana legalization efforts as a 'states' rights' issue. *Georgetown J Law Public Policy*. 2018;16(495):495-504. https://www.law.georgetown.edu/public-policy-journal/wp-content/uploads/sites/23/2018/10/16-2-States-Rights-Federal-Wrongs.pdf

12. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2022 National Survey on Drug Use and Health (HHS Publication No. PEP23-07-01-006, NSDUH Series H-58). Center for Behavioral Health Statistics and Quality (2023). Accessed October 14, 2024. https://www.samhsa.gov/data/report/2022-nsduh-annual-national-report

13. Caulkins JP. Changes in self-reported cannabis use in the United States from 1979 to 2022. *Addiction*. 2024;119(9):1648-1652. doi:10.1111/add.16519

14. Robinson T, Ali MU, Easterbrook B, et al. Identifying risk-thresholds for the association between frequency of cannabis use and development of cannabis use disorder: a systematic review and meta-analysis. *Drug Alcohol Depend*. 2022;238:109582. doi:10.1016/j.drugalcdep.2022.109582

15. Compton WM, Einstein EB, Han B. 12-Month prevalence estimates of substance use disorders using DSM-5 versus DSM-IV criteria among U.S.

nonelderly adults with substance use. *Am J Psychiatry*. 2024;181(11):1018-1021. doi:10.1176/appi.ajp.20231060

16. Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of marijuana use disorders in the United States between 2001-2002 and 2012-2013. *JAMA Psychiatry*. 2015;72(12):1235-1242. doi:10.1001/jamapsychiatry.2015.1858

17. Han B, Compton WM, Blanco C, Jones CM. Time since first cannabis use and 12-month prevalence of cannabis use disorder among youth and emerging adults in the United States. *Addiction*. 2019;114(4):698-707. doi:10.1111/add.14511

18. Leung J, Chan GCK, Hides L, Hall WD. What is the prevalence and risk of cannabis use disorders among people who use cannabis? a systematic review and meta-analysis. *Addict Behav*. 2020;109:106479. doi:10.1016/j.addbeh.2020.106479

19. Dawson D, Stjepanović D, Lorenzetti V, Cheung C, Hall W, Leung J. The prevalence of cannabis use disorders in people who use medicinal cannabis: a systematic review and meta-analysis. *Drug Alcohol Depend*. 2024;257:111263. doi:10.1016/j.drugalcdep.2024.111263

20. Hinckley JD, Mikulich-Gilbertson SK, He JP, et al. Cannabis use is associated with depression severity and suicidality in the National Comorbidity Survey-Adolescent Supplement. *JAACAP Open*. 2023;1(1):24-35. doi:10.1016/j.jaacop.2023.02.002

21. Hindley G, Beck K, Borgan F, et al. Psychiatric symptoms caused by cannabis constituents: a systematic review and meta-analysis. *Lancet Psychiatry*. 2020;7(4):344-353. doi:10.1016/S2215-0366(20)30074-2

22. Hasan A, von Keller R, Friemel CM, et al. Cannabis use and psychosis: a review of reviews. *Eur Arch Psychiatry Clin Neurosci*. 2020;270(4):403-412. doi:10.1007/s00406-019-01068-z

23. Jefsen OH, Erlangsen A, Nordentoft M, Hjorthøj C. Cannabis use disorder and subsequent risk of psychotic and nonpsychotic unipolar depression and bipolar disorder. *JAMA Psychiatry*. 2023;80(8):803-810. doi:10.1001/jamapsychiatry.2023.1256

24. Dellazizzo L, Potvin S, Giguère S, Dumais A. Evidence on the acute and residual neurocognitive effects of cannabis use in adolescents and adults: a systematic meta-review of meta-analyses. *Addiction*. 2022;117(7):1857-1870. doi:10.1111/add.15764

25. Broyd SJ, van Hell HH, Beale C, Yücel M, Solowij N. Acute and chronic effects of cannabinoids on human cognition: a systematic review. *Biol Psychiatry*. 2016;79(7):557-567. doi:10.1016/j.biopsych.2015.12.002

26. Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A*. 2012;109(40):E2657-E2664. doi:10.1073/pnas.1206820109

27. Gowin JL, Ellingson JM, Karoly HC, et al. Brain function outcomes of recent and lifetime cannabis use. *JAMA Netw Open*. 2025;8(1):e2457069. doi:10.1001/jamanetworkopen.2024.57069

28. StepjanoviĆ D, Hall W, Leung J. Illicit drug use and violence. *Handb Clin Neurol*. 2023;197:121-145. doi:10.1016/B978-0-12-821375-9.00010-4

29. Hughes AR, Grusing S, Lin A, et al. Trends in intentional abuse and misuse ingestions in school-aged children and adolescents reported to US poison centers from 2000-2020. *Clin Toxicol (Phila)*. 2023;61(1):64-71. doi:10.1080/15563650.2022.2120818

30. Lac A, Luk JW. Testing the amotivational syndrome: marijuana use longitudinally predicts lower self-efficacy even after controlling for demographics, personality, and alcohol and cigarette use. *Prev Sci*. 2018;19(2):117-126. doi:10.1007/s11121-017-0811-3

31. Chan O, Daudi A, Ji D, et al. Cannabis use during adolescence and young adulthood and academic achievement: a systematic review and meta-analysis. *JAMA Pediatr*. 2024;178(12):1280-1289. doi:10.1001/jamapediatrics.2024.3674

32. Hoch E, Volkow ND, Friemel CM, Lorenzetti V, Freeman TP, Hall W. Cannabis, cannabinoids and health: a review of evidence on risks and medical benefits. *Eur Arch Psychiatry Clin Neurosci*. 2024;275(2):281-292. doi:10.1007/s00406-024-01880-2

33. Sorkhou M, Bedder RH, George TP. The behavioral sequelae of cannabis use in healthy people: a systematic review. *Front Psychiatry*. 2021;12:630247. doi:10.3389/fpsyt.2021.630247

34. Gobbi G, Atkin T, Zytynski T, et al. Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: a systematic review and meta-analysis. *JAMA Psychiatry*. 2019;76(4):426-434. doi:10.1001/jamapsychiatry.2018.4500

35. Sultan RS, Zhang AW, Olfson M, Kwizera MH, Levin FR. Nondisordered cannabis use among US adolescents. *JAMA Netw Open*. 2023;6(5):e2311294. doi:10.1001/jamanetworkopen.2023.11294

36. Hjorthøj C, Compton W, Starzer M, et al. Association between cannabis use disorder and schizophrenia stronger in young males than in females. *Psychol Med*. 2023;53(15):7322-7328. doi:10.1017/S0033291723000880

37. Myran DT, Gaudreault A, Pugliese M, Tanuseputro P, Saunders N. Cannabis-involvement in emergency department visits for self-harm following medical and non-medical cannabis legalization. *J Affect Disord*. 2024;351:853-862. doi:10.1016/j.jad.2024.01.264

38. McFee RB. Cannabinoid hyperemesis syndrome (CHS): an emerging gastrointestinal disorder and clinical challenge. *Dis Mon*. 2024;70(12):101832. doi:10.1016/j.disamonth.2024.101832

39. Baranger DAA, Paul SE, Colbert SMC, et al. Association of mental health burden with prenatal cannabis exposure from childhood to early adolescence: longitudinal findings from the Adolescent Brain Cognitive Development (ABCD) Study. *JAMA Pediatr*. 2022;176(12):1261-1265. doi:10.1001/jamapediatrics.2022.3191

40. Larkin PJ. Driving while stoned in Virginia. American Criminal Law Review Online (2022). Accessed May 7, 2025. https://www.law.georgetown.edu/american-criminal-law-review/wp-content/uploads/sites/15/2022/05/Larkin-Final.pdf

41. DuPont RL, Holmes EA, Talpins SK, Walsh JM. Marijuana-impaired driving: a path through the controversies. In: *Contemporary Health Issues on Marijuana*. Sabet KA, Winters KC, eds. Oxford University Press; 2018:183-218.

42. Jayawardhana J, Hou J, Freeman P, Talbert JC. Association of state cannabis legalization with cannabis use disorder and cannabis poisoning. *JAMA Psychiatry*. 2025;82(3):228-236. doi:10.1001/jamapsychiatry.2024.4145

43. Petrilli K, Ofori S, Hines L, Taylor G, Adams S, Freeman TP. Association of cannabis potency with mental ill health and addiction: a systematic review. *Lancet Psychiatry*. 2022;9(9):736-750. doi:10.1016/S2215-0366(22)00161-4

44. Boehnke KF, Sinclair R, Gordon F, et al. Trends in U.S. medical cannabis registrations, authorizing clinicians, and reasons for use from 2020 to 2022. *Ann Intern Med*. 2024;177(4):458-466. doi:10.7326/M23-2811

45. Humphreys K, Shover CL. Recreational cannabis legalization presents an opportunity to reduce the harms of the US medical cannabis industry. *World Psychiatry*. 2020;19(2):191-192. doi:10.1002/wps.20739

46. Slawek DE, Althouse AD, Feldman R, et al. Cannabis dispensary staff approaches to counseling on potential contraindications to cannabis use: insights from a national self-report survey. *BMC Prim Care*. 2023;24(1):145. doi:10.1186/s12875-023-02095-5

47. Merlin JS, Althouse A, Feldman R, et al. Analysis of state cannabis laws and dispensary staff recommendations to adults purchasing medical cannabis. *JAMA Netw Open*. 2021;4(9):e2124511. doi:10.1001/jamanetworkopen.2021.24511

48. Carrell DS, Cronkite DJ, Shea M, et al. Clinical documentation of patient-reported medical cannabis use in primary care: toward scalable extraction using natural language processing methods. *Subst Abus*. 2022;43(1):917-924. doi:10.1080/08897077.2021.1986767

49. Romm KF, Cavazos-Rehg PA, Williams R, et al. Cannabis retailer communication about cannabis products, health benefits, and risks: a mystery shopper study of licensed retailers in five U.S. cities. *J Stud Alcohol Drugs*. 2024;85(1):100-108. doi:10.15288/jsad.23-00034

50. Okey SA, Castro SA, Waddell JT, et al. Are recreational cannabis laws associated with declining medical cannabis program enrollment in the U.S.? an analysis of cardholder enrollment and demographic characteristics from 2013 to 2020. *Int J Drug Policy*. 2022;100:103531. doi:10.1016/j.drugpo.2021.103531

51. Madras BK. Update of cannabis and its medical use (2015). Commissioned by the Secretariat of the Expert Committee on Drug Dependence, Department of Essential Medicines and Health Products, World Health Organization, Geneva Switzerland. Accessed May 7, 2025. https://ncsbn.org/public-files/WHO_Cannabis_and_its_medical_use.pdf

52. Epistemonikos. Search results for medical marijuana. Accessed February 14, 2025. https://www.epistemonikos.org/en/search?q=medical+marijuana+

53. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. National Academies Press; 2017.

54. Gilman JM, Schuster RM, Potter KW, et al. Effect of medical marijuana card ownership on pain, insomnia, and affective disorder symptoms in adults: a randomized clinical trial. *JAMA Netw Open*. 2022;5(3):e222106. doi:10.1001/jamanetworkopen.2022.2106

55. Haroutounian S, Arendt-Nielsen L, Belton J, et al. International Association for the Study of Pain Presidential Task Force on Cannabis and Cannabinoid Analgesia: research agenda on the use of cannabinoids, cannabis, and cannabis-based medicines for pain management. *Pain*. 2021;162 (Suppl 1):S117-S124. doi:10.1097/j.pain.0000000000002266

56. Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. *Lancet Psychiatry*. 2019; 6(12):995-1010. doi:10.1016/S2215-0366(19)30401-8

57. Belgers V, Röttgering JG, Douw L, et al. Cannabinoids to improve health-related quality of life in patients with neurological or oncological disease: a meta-analysis. *Cannabis Cannabinoid Res*. 2023;8(1):41-55. doi:10.1089/can.2021.0187

58. Rehman Y, Saini A, Huang S, Sood E, Gill R, Yanikomeroglu S. Cannabis in the management of PTSD: a systematic review. *AIMS Neurosci*. 2021;8 (3):414-434. doi:10.3934/Neuroscience.2021022

59. Incze MA, Kelley AT, Singer PM. Heterogeneous state cannabis policies: potential implications for patients and health care professionals. *JAMA*. 2021; 326(23):2363-2364. doi:10.1001/jama.2021.21182