

In the Clinic®

Care of the Patient Using Cannabis

The past 2 decades have seen a revolution in legal access to cannabis, driven largely by activists and business interests. As a result, the population of cannabis users nationwide—especially daily users—has grown significantly. An estimated 4.5–7 million persons in the United States now meet criteria for cannabis use disorder annually. This article focuses on the effects of cannabis use, intoxication, and withdrawal while also reviewing the developmental pathways of cannabis use disorder as well as evidence-based pharmacologic and psychosocial treatments.

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Arthur Robin Williams, MD, MBE
Kevin P. Hill, MD, MHS
From New York State Psychiatric Institute, Columbia University, New York, New York (A.R.W.), and Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts (K.P.H.).

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Health Consequences of
Cannabis Use

Medical Benefits of Cannabis

Medicolegal Issues

Treatment of Cannabis
Use Disorder

Practice Improvement

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The past 20 years have witnessed an explosion nationwide in legal access to cannabis and cannabis-derived products for medical and recreational purposes (1). When referring to the whole plant (rather than cannabinoid-based derivatives), we use the term *cannabis* because *marijuana* was used in the past to refer to negative stereotypes attached to racial and ethnic groups, such as Mexican Americans and African Americans. For example, marijuana use was popular in Texas border towns in the early 1900s, and law enforcement officials in these towns ridiculed the plant as a drug of the Mexicans, whom they saw as immoral. Marijuana was similarly connected to African American jazz musicians, crime, and addicted young people in New Orleans at approximately the same time. For these reasons, we prefer *cannabis* as a scientific term that is free from negative associations.

As of September 2020, 11 states and the District of Columbia had passed laws allowing both medical and recreational use of cannabis. An additional 23 states (2) allow medical cannabis programs of varying design (3). Since 2013, 13 states (some of which also allow medical cannabis) have authorized the use of cannabidiol (CBD), primarily for patients with seizure disorders in research studies. Although CBD-based commercial products have flooded the market, including major retailers, in recent years,

they are prohibited by the U.S. Food and Drug Administration (FDA). With greater availability of legal cannabis, rates of use and heavy use (daily or near-daily use) have increased dramatically among adults (4). Clinicians should be aware that although state laws now often allow access to cannabis, federal law does not, creating a legal gray area that may be unpredictably enforced.

With expanded legal access to medical and recreational cannabis, there has been great concern that increased availability could lead to increases in adolescent use and feed a pipeline of addiction. To date, findings have been mixed on the effect of legalization on adolescents, likely because adolescents have historically had easier access to cannabis than adults. Paradoxically, studies have shown the greatest increases in cannabis use among adults, especially those older than 25 years (5). With expanded access, all age groups report higher rates of heavy use than in the past (4), and once-rare clinical presentations, such as cyclic vomiting syndrome, are becoming more common. One effect specifically from cannabis-derived products, such as gummy bears, chocolates, and other items that resemble candy, is the increasing rate of child poisonings (6). Greater surveillance is also needed for hazards from public intoxication, such as drugged driving (7).

Health Consequences of Cannabis Use

What are the direct and side effects of cannabis?

The effects of cannabis are caused by cannabinoid (for example, tetrahydrocannabinol [THC] or CBD) activity at the endogenous cannabinoid receptors CB1 and CB2, which are located

in the central nervous system and the periphery (**Table 1**). Acute intoxication from cannabis and cannabis-derived products, such as vape pens and edibles, is largely caused by the psychotropic cannabinoid THC. The "high" from THC can include relaxation

and anxiolysis, euphoria, altered perception and awareness of external stimuli, and increased appetite (8). Symptoms typically intensify over 1–2 hours of use, coinciding with peak plasma levels of THC (9). Undesirable side effects may include impaired coordination and motor skills, including driving; memory loss (anterograde) and learning difficulties; psychosis, including hallucinations and paranoia; extreme anxiety; and reddened, injected conjunctiva. However, frequent users tend to build a tolerance to many of these symptoms, such as cognitive disturbance. Although physical effects are typically minimal, some heavy users develop vulnerability to recurrent upper respiratory infections. Similarly, long-term users may experience additional psychiatric effects on cognition,

mood, and motivation that accrue over time.

Is acute cannabis intoxication possible?

Cannabis intoxication is marked by such effects as relaxation and anxiolysis (reduced anxiety), euphoria, altered time and sensory perception, hyperfocused awareness of external stimuli, and appetite stimulation (10) (**Table 2**). Although these effects are often desired by recreational users, they may be unpleasant for those who report discomfort or anxiety when using cannabis (**Table 3**). Given that the relative strength of THC in cannabis has increased dramatically in the past 2 decades (now upward of 12%–20%) (11–13), users are more likely to consume higher doses of THC, which can cause more dramatic effects during intoxication. The most frequently reported serious

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Table 1. Common Cannabinoid-Based Products and Routes of Administration*

Product	Route of Administration	Notes on Potency
Whole-plant cannabis, “bud,” leaf, “weed”	Smoked in joints or pipes or rolled into blunts (with tobacco) Vaporized with pens or devices Orally ingested if cooked into foods or butters	THC potency has increased over the past 20 years from around 4% to 20% in cannabis seized by law enforcement. Dispensaries often sell whole-plant cannabis with >20% THC. Increased THC is bred into cannabis at the expense of CBD because both share precursors.
Cannabinoids (primarily THC and CBD)	Products manufactured with cannabinoids are often packaged as cartridges to be vaporized, sublingual tinctures, pills/capsules, and topical creams. There are 3 FDA-approved cannabinoid-based pharmaceuticals that are taken orally: dronabinol, nabilone, and Epidiolex (Greenwich Biosciences).	With additional layers of processing, cannabinoid-based products are myriad and can range in cannabinoid content, often expressed as a ratio, such as THC:CBD of 20:1. Because nabilone is more potent than dronabinol, it is a Schedule II controlled drug.
Concentrates, “wax,” “shatter,” “dab,” “butane honey oil”	Small amounts of highly potent THC concentrates can be smoked, sometimes by spreading on metal and then igniting with a blowtorch, thus releasing a plume of smoke, which is sniffed.	Extremely high potency (e.g., THC often >90%)
Edibles: brownies, candies, mints, muffins, beverages	Oral ingestion Note that because edibles resemble common foods, children and adults are at increased risk for accidental ingestion and possible poisoning.	Typically limited to ≤10 mg of THC per “serving,” edibles can have a T_{max} of a few hours, more easily leading to inadvertent overdose. In addition, ingestion of edibles with food increases C_{max} compared with ingestion while fasting.

CBD = cannabidiol; C_{max} = maximum serum concentration; FDA = U.S. Food and Drug Administration; THC = tetrahydrocannabinol; T_{max} = time to reach C_{max}
* From references 58 and 59.

Table 2. Treatment for Cannabis-Related Indications

Indication	Treatment
Intoxication or overdose from cannabis and cannabis-derived products	<p>Nonpharmacologic</p> <ul style="list-style-type: none"> • Supportive care with hydration, monitoring of vital signs • Place patient in quiet room with minimal stimuli • Reassurance <p>Pharmacologic</p> <ul style="list-style-type: none"> • Oral and/or intramuscular sedative-hypnotics (clonazepam, lorazepam, oxazepam) • Antipsychotics, typically second generation (risperidone, quetiapine) • Nonbenzodiazepine anxiolytics, such as hydroxyzine
Intoxication or overdose from synthetic cannabinoid products	<p>Mild cases may require only supportive care or typical management for cannabis intoxication per above</p> <p>Severe cases may require the following:</p> <ul style="list-style-type: none"> • Repeated administration of high-potency antipsychotics (i.e., haloperidol) • Sedating antipsychotics when agitation is dangerous (i.e., chlorpromazine or olanzapine) • Sedative-hypnotics (clonazepam, lorazepam, oxazepam) • Consider behavioral isolation precautions
Cannabis use disorder	<p>Treatment should start with a comprehensive assessment and obtaining of collateral information when feasible and may include the following clinical targets under long-term outpatient care:</p> <p>Anticraving pharmacology</p> <ul style="list-style-type: none"> • N-acetylcysteine, 1200 mg orally 3 times per day • Naltrexone, 50 mg orally per day (maximum total daily dose, 100 mg) • Bupropion, 150–300 mg orally per day • CB1 modulators, such as nabilone, 2 mg orally 2 times per day <p>Manage withdrawal, including acute (1–7 d) and protracted (1–3 mo) withdrawal</p> <ul style="list-style-type: none"> • Anxiety: hydroxyzine, gabapentin, buspirone • Insomnia: mirtazapine, quetiapine <p>Psychiatric comorbidity: May require coordinated care with a mental health specialist</p> <ul style="list-style-type: none"> • General anxiety disorder, social anxiety disorder, depressive disorders, posttraumatic stress disorder, attention deficit-hyperactivity disorder <p>Psychosocial and behavioral approaches often requiring specialist treatment settings</p> <ul style="list-style-type: none"> • Cognitive behavioral therapy and motivational interviewing • Voucher-based and contingency management incentives

psychiatric effects include anxiety (14) and transient psychosis (15, 16). For persons who develop psychosis, symptoms may persist for a week or longer (9). Agitation, irritability, and paranoia (16, 17); lack of responsiveness and

lethargy (18, 19); and hallucinations (19, 20) may also occur.

Using large amounts (≥ 20 mg THC equivalent) is more likely to lead to such effects, especially among persons with low or no

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Table 3. Signs and Symptoms of Complications From Cannabis Intoxication in Adults*

Type	Complications
Physiologic	<p>Mild: Pupil constriction, nystagmus, headache, tachypnea, tremor, urine retention, ataxia, sedation, lethargy</p> <p>Moderate: Conjunctival injection/redness, orthostatic hypotension, increased heart rate, palpitations, arrhythmia, decreased blood pressure, decreased coordination, increased appetite</p>
Psychiatric	<p>Mild: "Abnormal" behavior and/or appearance, inappropriate affect, depressed mood, hallucinations, bizarre behavior, dangerous behavior toward others</p> <p>Moderate: Impaired memory, expansive or euphoric mood, disorganized thought process, suicidal or dangerous behaviors toward self</p> <p>Severe: Delusions, impaired judgment</p>

* Adapted from references 9, 55, and 56.

tolerance. Inadvertent consumption of high-dose cannabis is more common among novice users consuming edible or oral formulations (such as candies, brownies, or beverages) that are often mislabeled or inconsistently packaged and have delayed and unpredictable onsets (21). Oral ingestion of cannabinoids in combination with food (compared with a fasting state), especially fatty foods, can greatly increase blood levels, but most clinicians and patients are unaware of this.

Can stopping cannabis use cause physical withdrawal?

The cardinal physical symptoms of cannabis withdrawal include insomnia, anorexia, anxiety, irritability, and restlessness (22) (**Table 4**). However, withdrawal is highly variable; some persons have significant symptoms, whereas others report minimal or no symptoms. This partly reflects the lipophilic nature of THC, which results in substantial body stores in some persons after periods of heavy use. Some users who have debilitating withdrawal symptoms realize they can no longer control their drug use and seek help. In hospital settings, acute cannabis withdrawal is almost universally missed by health care staff, yet it contributes to insomnia, anxiety, and irritability for regular users who suddenly stop active use. Protracted cannabis withdrawal symptoms, especially anxiety and insomnia, can persist for weeks or even

months beyond the last use of cannabis, much longer than most clinicians realize.

What is hyperemesis syndrome?

Cannabinoid hyperemesis syndrome has become more widely recognized in the past few years given increased rates of heavy use of high-strength cannabis. Patients may report taking an excessive number of hot showers, which can provide temporary symptom relief (23). Acute presentations may or may not involve intoxication on presentation; often include intractable nausea and vomiting lasting days to months; and may be especially difficult to control among patients with comorbid or poorly controlled migraine, psychiatric disorders, or opioid use disorders (7). Few controlled studies have been done, and case reports are mixed with regard to effective treatment (23). Short-term treatment often relies on a sedative-hypnotic, such as lorazepam, and antipsychotics with an antiemetic, such as promethazine or ondansetron for breakthrough nausea. Some patients further benefit from nonopioid pain medications, such as nonsteroidal anti-inflammatory drugs, when their presentation is accompanied by abdominal pain. Ongoing treatment to prevent recurrent episodes may include long-term use of tricyclic antidepressants (such as amitriptyline) but otherwise relies primarily on avoidance of known triggers, including emotional stress, sleep

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Table 4. Cannabis Withdrawal and Onset of Symptoms

Symptom	Onset	Persistence
Anxiety	4-96 h	Weeks to months (can persist for the long term)
Insomnia	1-2 d	4-12 wk
Restlessness	1-2 d	Days to weeks
Irritability	1-2 d	Days to weeks
Depression (alterations in mood)	1-2 d	Weeks to months
Anorexia or diminished appetite	1-2 d	Days to weeks
Pain	1-2 d	Depends on patient history of chronic pain syndromes and comorbidity

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deprivation, and prolonged fasting in addition to avoidance of further cannabis consumption (7).

Is cannabis use safe during pregnancy?

Patients should not use cannabis during pregnancy or while breastfeeding. However, data show that rates of cannabis use among pregnant women have increased dramatically in recent years after expanded legalization (24).

What is the relationship between cannabis use and psychiatric disorders?

Cannabis use can have a complex relationship with psychiatric disorders. Although there is no moderate- or high-quality evidence that cannabis can effectively treat any psychiatric condition, many patients with anxiety, depression, insomnia, and post-traumatic stress disorder report short-term symptom relief with cannabis use. Similar to long-term use of alcohol or benzodiazepines, these persons may find that their psychiatric symptoms worsen over time, in part due to withdrawal or rebound symptoms between episodes of cannabis use. *Amotivational syndrome* refers to the lack of motivation, declines in functioning and activity levels, apathy, depersonalization, and derealization that are common among heavy cannabis users (25).

Although evidence on causality is mixed, it is apparent that use of cannabis at younger ages among patients predisposed to schizophrenia is associated with earlier onset and more severe courses of psychotic illness—and yet, concerning, adolescent and young adult patients with attention deficit-hyperactivity disorder often report cannabis use despite its negative effect on executive functioning. In general, those who use cannabis are more likely to develop psychiatric disorders, such as depression and opioid use disorder, later in life (26). Yet

studies have also shown that self-reported cannabis use for psychiatric conditions is higher in states with medical cannabis laws, raising concerns about long-term complications (27).

What are the other health consequences of cannabis use?

Common health consequences of cannabis use are presented in **Table 3**. Severe but rare physiologic effects can include respiratory depression (28, 29); nephrotoxicity (30); gastrointestinal disruptions, such as hyperemesis, nausea, and abdominal pain (19); rhabdomyolysis; hyperthermia (31); seizures (16); acute cerebral ischemia (32); and cardiotoxicity, including dysrhythmia (33). The FDA recently warned that CBD can be hepatotoxic. Less severe but more frequent effects of cannabis use include tachycardia, bradycardia, hypotension, and arrhythmias (16). Among heavy, long-term users, upper respiratory infections are the most likely physical health problems. More recently, strong associations have been found between e-cigarette use and e-cigarette or vaping product use-associated lung injury among persons using black market cannabinoid cartridges.

Should clinicians screen for cannabis use, and if so, how?

Clinicians should ask patients whether they are using cannabis. In the summer of 2020, the U.S. Preventive Services Task Force revised its official guidance and now encourages all physicians in primary care settings to screen for drug use among adult patients when referrals to evidence-based treatment are available. Validated screening tools are recommended. The 2 most commonly used tools for adolescents are the Screening to Brief Intervention (S2BI) and the Brief Screener for Tobacco, Alcohol, and other Drugs (BSTAD), both of which are available on NIDAMED. Patients who report cannabis use in the past month

should be asked simple screening questions, such as whether they use more than they intend; whether they have difficulty reducing their use; and whether use interferes with their activities, health, or social commitments. The SBIRT (Screening, Brief Intervention, and Referral to Treatment) model developed by the Substance Abuse and Mental Health Services Administration can help to distinguish between problematic use, which benefits from a brief clinical intervention with motivational interviewing techniques, and more severe

cannabis use disorder, which requires specialized treatment. Urine toxicologic testing in most general clinical settings is not a preferred way to screen for cannabis use or cannabis use disorder, although it may help with clinical management for patients attempting to sustain abstinence from cannabis. The American Academy of Pediatrics and the National Council for Behavioral Health now provide tailored screening recommendations for pediatric and adult populations, respectively.

Health Consequences of Cannabis Use... Cannabis use, especially heavy or daily use, is risky, and this should be clearly communicated to patients. Although some light or intermittent users may experience pleasurable effects, such as relaxation, euphoria, and creativity, a significant minority, especially those with daily use or use of high-potency products, are likely to develop addiction, worsening of psychiatric symptoms, amotivational syndrome, or vulnerabilities to upper respiratory infection.

CLINICAL BOTTOM LINE

Is cannabis useful for treating pain?

For many years, there have been anecdotal reports of pain relief from regular cannabis use. Chronic pain is the most common qualifying condition for medical cannabis reported by patients nationwide (34). However, the evidence for cannabis and cannabinoids as treatment for pain is mixed. Beyond the indications for which cannabinoids are FDA-approved, multiple randomized controlled trials and systematic reviews support their use for chronic pain, including neuropathic pain. The National Academies of Sciences, Engineering, and Medicine Committee on the Health Effects of Marijuana concluded that there is "conclusive or substantial evidence" that cannabis is effective for the treatment of chronic pain

in adults, based on the expert committee's assessment that the literature on chronic pain has many supportive findings from good-quality studies with no credible opposing findings (35). In addition, a meta-analysis of 28 studies found moderate-quality evidence supporting the use of cannabinoids in treatment of chronic pain (36). Other reviews describe the evidence for cannabinoids in chronic pain as weaker. A 2017 meta-analysis of 27 studies examining the effectiveness of cannabis as pharmacotherapy for chronic pain found weak evidence that it alleviates neuropathic pain and no evidence that it was useful for other types of pain (37). Another meta-analysis of 91 publications that specifically examined the use of cannabis to treat non-cancer-related chronic pain found that cannabinoids reduce pain 30%

Medical Benefits of Cannabis

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more than placebo (odds ratio, 1.46 [95% CI, 1.16–1.84]), but the number needed to treat to achieve a 50% reduction in pain was 24 (CI, 15–61), whereas the number needed to harm for any adverse effect of cannabis was 6 (CI, 5–8), suggesting that the benefits of cannabis use were outweighed by possible harm (38). Another important factor to consider is the patient's prior use of opioid medication and whether a trial of a cannabinoid may mitigate additional side effects from opioids.

Does cannabis prevent seizures?

One of many cannabinoids found in the cannabis plant, CBD has been shown to prevent seizures. Two multicenter, international trials with 120 and 171 participants demonstrated the efficacy of CBD as an add-on medication to manage the pediatric seizure disorders Dravet syndrome and Lennox-Gastaut syndrome (39, 40). Over 14 weeks of treatment, 20 mg of CBD per kilogram of body weight significantly reduced the median frequency of convulsive seizures in children and young adults with Dravet syndrome as well as the estimated median difference in monthly drop seizures between CBD and placebo in participants with Lennox-Gastaut syndrome. On the strength of these rigorous trials, a CBD formulation was ap-

proved by the FDA for the treatment of Dravet syndrome and Lennox-Gastaut syndrome in 2018.

What are other medical benefits of cannabis?

Before the approval of a CBD formulation in 2018, 2 cannabinoids related to THC, dronabinol and nabilone, were approved by the FDA in 1985 for chemotherapy-induced nausea and vomiting, with dronabinol gaining an additional indication for appetite stimulation in wasting conditions, such as AIDS, in 1992. Evidence also supports use of cannabis and cannabinoids to treat spasticity associated with multiple sclerosis. A recent meta-analysis evaluated 17 randomized controlled trials of cannabis and cannabinoids that included more than 3000 participants, with aggregate data showing modest but statistically significant positive effects on spasticity as well as pain and bladder dysfunction in this population (41). Similarly, the American Academy of Neurology published guidelines that determined that nabiximols, a medication available in Europe but not the United States that contains THC and CBD in a nearly 1:1 ratio, has the highest level of empirical evidence supporting its use as pharmacotherapy for spasticity and pain associated with multiple sclerosis (42).

Medical Benefits of Cannabis... The medical benefits of cannabis are debated vigorously among those studying it in the medical community. Many health care professionals do not certify the use of medical cannabis in their patients for various reasons, including skepticism about the level of scientific evidence supporting its use, fear of jeopardizing licensure by recommending a federally illegal substance, and lack of permission from their employer. A small but growing body of evidence suggests efficacy of cannabis and cannabinoids beyond FDA indications, particularly for chronic pain and muscle spasticity related to multiple sclerosis. Thus, in some clinical scenarios where first- and second-line treatments have been exhausted, it is reasonable for a health care professional to engage in a risk-benefit conversation about cannabis and cannabinoids as pharmacotherapy for a limited number of medical conditions.

CLINICAL BOTTOM LINE

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What do clinicians need to know about medicolegal issues related to their patients' use of cannabis?

Medicolegal risks related to patients' use of cannabis have not been well described. No special protections are afforded to patients who use medical cannabis certified by a physician. Policies are left to the discretion of the employer, with cannabis use expressly forbidden in some

safety-sensitive positions. Certifying the use of cannabis, or cannabinoids in formulations that are not approved by the FDA, is a riskier proposition for health care professionals than prescribing standard FDA-approved medications. In such instances, the health care professional should have a thorough risk-benefit conversation with the patient and should document it.

What is cannabis use disorder?

Like much of the public, many clinicians believe that cannabis can be psychologically addictive but not physically addictive like other drugs. However, cannabis does predictably cause physical dependence—the hallmarks of which are tolerance and withdrawal—and heavy users may have great difficulty in attempting to reduce or quit their use, leading to addiction with compulsive, continued use and worsening consequences (22, 43). The symptoms and clinical correlates of cannabis use disorder are listed in **Table 5**.

The risk for cannabis use disorder has historically been considered to be 1 in 11 for adults (about 9%) and 1 in 6 for adolescents (about 17%). However, the potency of THC, the primary psychoactive cannabinoid in cannabis, has increased dramatically in recent decades, now often surpassing 12%–20% (11, 13). It is unclear how increased potency will affect the addictive liability of cannabis, especially among users who “dab” or use concentrates (“wax” or “shatter”) that can surpass 90% THC. Of great concern, recent large federally funded studies, such as the National Epi-

Treatment of Cannabis Use Disorder

demologic Survey on Alcohol and Related Conditions III (with data collected in 2012 and 2013), have suggested that among adults who have used cannabis in the past year, upward of 30% meet diagnostic criteria for cannabis use disorder (44), a dramatic increase to approximately 7 million affected adults (44).

A substantial body of research has identified many risk factors for cannabis use disorder, including vulnerable family environments and family history of substance use disorders (SUDs), sexual abuse (especially during childhood), antisocial behavior and impulsivity, early-onset anxiety disorders, and substance use (45). Risk factors are interconnected and unlikely to act in isolation; for example, childhood traumas are well known to be related to later mood and anxiety disorders, and these disorders may mediate their eventual effects on the progression of SUDs.

When should clinicians offer help with quitting?

Cannabis use disorder is treatable, and as with other disorders, outcomes are best with a multidisciplinary approach. Persons with cannabis use disorder are often unaware of their addiction

Table 5. Diagnostic Criteria for Cannabis Use Disorder and Clinical Correlates*

<i>DSM-5 Diagnostic Criterion†, by Symptom Domain</i>	<i>Clinical Correlates</i>
Excessive use	
Excessive amounts used	Smoking or vaping throughout the day Needing to “get high” to get out of bed or start the day Buying large quantities (i.e., several ounces to last weeks)
Excessive time obtaining/using/recovering	Stockpiling a supply of cannabis at home Always carrying cannabis when away from home Social activity requires cannabis use
Physical dependence	
Tolerance	Smoking or vaping the equivalent of 5, 10, or even 20 “joints” daily Using throughout the day, yet appearing “sober” or functioning
Withdrawal	Insomnia, anorexia, anxiety, irritability, restlessness, dysphoria, and/or physical pain and discomfort when using less than usual (may persist for weeks or months in attenuated form for long-time users)
Urges to keep using	
Cravings	Preoccupation with obtaining or using cannabis Uncontrollable urge to use that interferes with other pursuits, especially during stressful times
Unsuccessful attempts to cut down	Setting personal goals to use less/spend less on cannabis, but repeatedly failing to make progress
Problems from use	
Hazardous use	Using before driving or engaging in activities with risk for injury
Interpersonal trouble	Continuing to use despite concerns among family Prioritizing ongoing use over obligations to others Losing friends
Interference with occupation	Delaying job seeking or settling for lower-paying job while protecting time to get high or reduce responsibilities that would interfere with cannabis use
Medical issues	Heavy cannabis use despite frequent respiratory infections (e.g., bronchitis) and shortness of breath with physical activity Frequent binge eating of junk food despite presence of obesity or diabetes
Interference with former activities	Staying home to get high rather than meeting friends Giving up other hobbies to prioritize cannabis use, even if not a conscious decision

DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

** Adapted from reference 57.*

† Cannabis use disorder is specified as mild if it meets 2-3 of the 11 criteria, moderate if it meets 4-5 criteria, and severe if it meets ≥6 criteria.

for many years and may continue frequent use without the notice of others, including health care providers. Similar to declines in functioning associated with dementia, the slowly accumulating dysfunction resulting from cannabis use disorder can be hard to detect, especially by the index patient. It is not uncommon for patients seeking treatment to report that they did not realize they were addicted until they needed to pass a preemployment drug test or went on a trip without access to cannabis. For

these reasons, it is critical for physicians to proactively screen for cannabis use and its effect on patient health and functioning.

Similar to the management of other chronic diseases, such as hypertension and obesity, patients with cannabis use disorder should be comanaged with a therapist or psychiatrist who has experience in managing SUDs. Treatment begins with a comprehensive psychiatric assessment, ideally including collateral information from family, friends, co-

workers, or previous providers and from medical records. For cannabis use disorder, the clinician should primarily assess patterns of substance use (both cannabis and other substances) and the patient's reasoning for what he or she finds useful and problematic about these patterns. In general, best practices emphasize a long-term management model in the outpatient setting rather than residential treatment for acute and maintenance treatment of SUDs. Although some patients with severe cannabis use disorder may not be able to stabilize their use without being removed from their home environment, the outpatient setting is often the most appropriate level of care.

Addressing ambivalence is a universal aspect of management of SUDs. Once they receive treatment, patients often acknowledge spending an excessive amount of time and money on cannabis and a desire to reduce use despite an ongoing attachment to the drug. Starting with the initial assessment, the clinician can adopt the patient's vocabulary, perspectives, and verbalized priorities to facilitate motivational work to reinforce patient "change talk" in the framework of motivational interviewing (46).

Often, patients who use cannabis heavily report that it helps them with anxiety or insomnia regardless of whether they have a common comorbid diagnosis, such as an anxiety disorder. Although the short-term benefits of using cannabis may help with anxiolysis or treating early insomnia, in general cannabis, especially via rebound withdrawal symptoms, can worsen these underlying conditions over time (similar to how some patients with heavy alcohol use develop worsening anxiety). In addition to managing

these symptoms, identifying other patient goals, such as finding a new job or rebuilding relationships, is key to aligning with the patient.

What is the role of psychosocial interventions?

A combination approach of psychosocial and behavioral therapies with medication management is often ideal for cannabis use disorder. Given limitations in the efficacy of medications for treating patients with cannabis use disorder, intensive psychosocial approaches take on additional importance. Medications often help retain patients in care long enough for them to better respond to psychosocial and behavioral interventions for SUDs.

Psychotherapy for patients with cannabis use disorder should focus on reasons for change, goal commitments, emotion and impulsivity regulation, skills for coping with distress, and conquering denial and self-deception about the effects of drug use (47). A Cochrane Review found that cognitive behavioral therapy and motivational enhancement therapy, especially in combination, had the most consistent evidence for assisting with initial reductions in cannabis use and severity of dependence (48). High-intensity approaches, such as more than 4 sessions delivered over more than a month, were superior to lower-intensity treatment. Cognitive behavioral therapy techniques can be used to analyze different thought processes associated with different use situations, challenge automatic thoughts regarding reasons for continued use, enable a potential role transition to no longer being an active user, and reflect on what it means to be in recovery.

Additional behavioral approaches can help patients reengage

with old hobbies and find new distracting and stimulating activities to occupy their time. As with any SUD, working with patients to avoid the people, places, and things associated with drug use is key to minimizing environments and triggers for resuming use. This may include coaching patients on the importance of deleting and blocking numbers for drug dealers and distancing themselves from friends with whom they often used. Intensive work to develop distress tolerance skills is often critical to reducing the likelihood that patients will continue to resume drug use to manage uncomfortable feelings and thoughts, especially for patients with comorbid psychiatric illness, such as mood or anxiety disorders. Although some patients with cannabis use disorder may benefit from 12-step peer-support groups, such as Cannabis Anonymous, the literature on the effectiveness of these groups for persons whose primary drug of choice is cannabis is limited.

What is the role of pharmacologic treatment?

To date, no medications have been approved by the FDA for treatment of cannabis use disorder (49). However, several medication-based approaches (some off-label) target cravings, withdrawal symptoms, and comorbid psychiatric disorders (50).

Treatment of cravings

Several medications have anticraving properties in addition to their primary mechanisms (49). Naltrexone, a μ -opioid receptor antagonist, has been approved by the FDA for alcohol and opioid use disorders as well as (in combination with bupropion) binge eating disorder. A single daily dose of 50 mg of naltrexone can also generally help reduce cravings for other intoxicants and curb impulsive behaviors, such as gambling. Naltrex-

one is currently under investigation specifically as a possible medication for cannabis use disorder, although study results have thus far been mixed (51). Additional medications that have demonstrated anticraving properties for some patients are bupropion (labeled as Zyban for smoking cessation) and topiramate (50).

Several promising studies of adolescents have also been conducted with *N*-acetylcysteine (NAC), an anti-inflammatory supplemental amino acid that is hepatoprotective and a glutamate modulator in the central nervous system. In the first published, fully powered clinical trial with positive results for pharmacotherapy for cannabis use disorder, Gray and colleagues initially found that youths and young adults aged 15–21 years ($n = 116$) who received 1200 mg of NAC twice daily along with contingency management had 2.4 times the odds of cannabis-negative urine test results compared with those assigned to placebo with contingency management (52). However, a follow-up study did not replicate the initial results among adults (53).

Most specific to the primary treatment of cannabis use disorder are medications that are active at the CB1 receptor (51). Dronabinol, a Schedule III synthetic THC for treatment of nausea and cachexia, partially agonizes the CB1 receptor. In addition, a newer analogue of THC, nabilone (Schedule II), has even stronger activity at the CB1 receptor, potentially making it more subjectively reinforcing for patients (50, 54).

Treatment of withdrawal

Aggressive management of withdrawal is key to minimizing risk for resumption of active drug use (50). Withdrawal symptoms, primarily anxiety and insomnia, can persist for weeks or even months beyond

the last use of cannabis. Familiar medications for anxiety that have limited addictive liability (selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, hydroxyzine, α -2 agonists) can be instrumental, especially in the first month or two of treatment. Medications for sleep are often needed for an even longer period of several months. Studies have been conducted on short-term use of sedating antidepressants and mood stabilizers, such as low-dose mirtazapine or quetiapine (50).

When should clinicians consider consulting a specialist for patients with cannabis use disorder?

The critical role of simultaneous treatment of comorbid psychiatric

conditions underscores the necessity of a comprehensive psychiatric evaluation when patients with cannabis use disorder first enter treatment. Paradoxically, patients with SUDs are often hesitant to take new medications while attempting to reduce or stop drug use, likely for reasons related to a desire to be completely drug-free, internalized stigma and shame, and unfamiliarity with the benefits of psychopharmacology. Working with this resistance can be an important part of treatment, and it requires the clinician's patience and may require a mental health specialist. Comprehensive care for cannabis use disorder should also always include evidence-based treatment of psychiatric comorbidity.

Treatment of Cannabis Use Disorder... Millions more adults now meet criteria for cannabis use disorder in a given year, and all clinicians, not just mental health professionals, have vital roles in improving clinical management, from screening and diagnosis to overseeing treatment plans. Despite a lack of FDA-approved medications, several evidence-based pharmacologic and psychotherapeutic treatments are available to practitioners.

CLINICAL BOTTOM LINE

Practice Improvement

What measures do stakeholders use to evaluate the quality of care for patients who use cannabis?

There has been a shift within the addiction treatment landscape to better emphasize measurement-based care. In keeping with accreditation standards in other areas of medicine, The Joint Commission now requires the use of standardized instruments for specialty treatment programs managing cannabis use disorder. However, no such validated scales exist in the outpatient office setting. Rather, the National Institute on Drug Abuse Principles of Drug Addiction Treat-

ment offer best practices emphasizing individualized care plans tailored to the patient after a comprehensive evaluation. In particular, the combination of medication and psychosocial approaches for an adequate duration of care (addiction treatment lasting <90 days is generally ineffective for changing long-term outcomes) is indicated for most patients.

What do scientific, clinical, and professional organizations recommend regarding the care of patients who use cannabis?

Just as there are a wide variety of opinions among physicians on

the care of patients who use cannabis, organizations have made a range of statements on this issue. All scientific, clinical, and professional organizations support treatment of patients with problematic cannabis use, especially those who meet criteria for cannabis use disorder. However, opinions diverge about therapeutic use of cannabis. All groups seem to support additional research into the safety and efficacy of cannabis and cannabinoids, and most organizations have encouraged evaluation of the Drug Enforcement Administration (DEA) Drug Scheduling in recent years,

although those conversations dwindled after the Farm Bill of 2018 relaxed the DEA status of CBD. Some organizations, such as the American College of Physicians and the Canadian Medical Association, acknowledge the possibility that cannabis and cannabinoids may offer necessary alternatives to medications available from pharmaceutical companies. Others, such as the American Psychiatric Association, the American Society of Addiction Medicine, the American Academy of Pediatrics, and the National Institute on Drug Abuse, oppose use of cannabinoids that are not approved by the FDA.

In the Clinic Tool Kit

Care of the Patient Using Cannabis

Patient Information

<https://medlineplus.gov/marijuana.html>

<https://medlineplus.gov/spanish/marijuana.html>

Information on cannabis in English and Spanish from the National Institutes of Health's MedlinePlus.

www.cancer.gov/about-cancer/treatment/cam/patient/cannabis-pdq

Information on cannabis and cannabinoids from the National Cancer Institute at the National Institutes of Health.

<https://easyread.drugabuse.gov/content/marijuana-weed-pot-facts>

<https://easyread.drugabuse.gov/es/content/datos-sobre-la-marihuana-hierba-porro>

Marijuana facts in English and Spanish from the National Institute on Drug Abuse.

Information for Health Professionals

www.drugabuse.gov/publications/drugfacts/marijuana

www.drugabuse.gov/es/publicaciones/drugfacts/la-marihuana

Marijuana drug facts in English and Spanish from the National Institute on Drug Abuse.

www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq

Information on cannabis and cannabinoids from the National Cancer Institute at the National Institutes of Health.

www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html

Information on cannabis and cannabinoids from the Government of Canada.

www.ncsl.org/research/health/state-medical-marijuana-laws.aspx

State medical marijuana laws from the National Conference of State Legislatures.

In the Clinic

WHAT YOU SHOULD KNOW ABOUT CANNABIS

In the Clinic
Annals of Internal Medicine

What Is Cannabis?

Cannabis, also known as marijuana, is a plant that contains chemicals that act on your brain. The most common chemicals are called “THC” and “CBD.” When you smoke, vape, eat, or drink parts of the plant, the chemicals can change your mood and behavior and give you a “high” feeling. During the “high,” you may:

- Feel relaxed and intensely happy
- Experience heightened senses
- Feel hungrier than usual

In recent years, many states have passed laws making it easier to use cannabis. With this increase in access, more people are using cannabis than ever before.



matic stress disorder by using cannabis, their symptoms may actually worsen over time. In fact, cannabis use has been connected with more severe psychiatric disorders later in life.

Does Cannabis Use Have Risks or Side Effects?

Unpleasant side effects of using cannabis may include:

- Paranoia and hallucinations
- Anxiety
- Impaired motor skills (including driving)
- Learning difficulties
- Memory loss
- Nausea and vomiting
- Red, bloodshot eyes
- Racing heartbeat

The strength of THC in cannabis has increased in recent years. This makes side effects and dependence more likely. Edible forms have especially unpredictable effects. Cannabis should not be used by pregnant or breastfeeding women.

People who use cannabis for a long time can require larger amounts. Some may struggle with addiction, feel unmotivated, and experience worsening psychiatric problems and more respiratory infections.

Can Cannabis Treat Certain Medical Conditions?

Two chemicals found in cannabis have been approved to treat the nausea caused by chemotherapy and to increase appetite in patients with AIDS. The chemical CBD has been shown to prevent some types of seizures.

Some research shows that the cannabis plant and products made from it might help with chronic pain and can alleviate muscle stiffness from multiple sclerosis. However, the U.S. Food and Drug Administration has not approved the plant as a medicine. It remains illegal at the national level.

If you have a condition that you think cannabis could help, and you have exhausted approved treatment options, talk with your doctor about the risks and benefits of cannabis.

There is no strong evidence that cannabis can treat mental illness. Although some people get relief from anxiety, depression, and posttrau-

What Should I Do if I Think I Have a Problem With Cannabis Use?

- Talk to your doctor if you think you have a problem with cannabis use. Contrary to popular belief, cannabis is both psychologically and physically addictive.
- There is a wide range of withdrawal symptoms, including insomnia, lack of appetite, anxiety, irritability, and restlessness.
- You may be at higher risk for cannabis use disorder if you have a family history of substance misuse, a personal history of substance use or sexual abuse, anxiety disorders, or antisocial behaviors.

How Is Cannabis Use Disorder Diagnosed and Treated?

- Your doctor will ask you when and how often you use cannabis and other substances and what you find positive or negative about these patterns.
- You will have a psychiatric assessment, which will ideally include input from selected family, friends, and previous medical providers.
- Treatment is best done as an outpatient, although some patients need more intense support.
- Treatment usually includes behavioral therapy combined with medication.
- Treatment works best when done with a therapist or psychiatrist who has experience in substance use disorders.
- During treatment, it is important to avoid people, places, and things associated with your cannabis use to minimize triggers.
- Medicines are available to treat cravings, withdrawal symptoms, insomnia, depression, and anxiety, but there is no medicine to treat the disorder directly.

Questions for My Doctor

- Is cannabis an option we should consider to safely treat my medical condition?
- What treatments are available to help me safely reduce or stop cannabis use?

For More Information



National Institute on Drug Abuse
www.drugabuse.gov/drug-topics/marijuana
MedlinePlus
<https://medlineplus.gov/marijuana.html>