ABSTRACT: Marijuana and its extracts are derived from Cannabis sativa, a type of hemp plant that contains active compounds called cannabinoids. As with many drugs, regular use of marijuana can result in dependence. Cannabis dependence is defined as a problematic pattern of use leading to clinically significant impairment or distress. Symptoms of dependence include using cannabis in larger amounts or over a longer period than was prescribed or intended, making unsuccessful efforts to cut down or control cannabis use, and spending time in activities necessary to obtain, use, or recover from cannabis effects. Signs and symptoms of withdrawal include irritability, anger, anxiety, difficulty sleeping, abdominal pain, fever, chills, and severe headache. Once an accurate diagnosis of marijuana dependence has been made, pharmacological and psychosocial treatment options can be considered. Although a literature review indicates insufficient evidence for a single broadly and consistently effective pharmacological treatment for cannabinoid dependence, adjunctive treatment for nausea, anxiety, and insomnia can be helpful. Replacement therapy and short-term dose tapering with synthetic cannabinoids may also be used to manage withdrawal symptoms. Studies of motivational enhancement therapy, cognitive-behavioral therapy, and contingency management for treating marijuana dependence have shown promising results.

Marijuana and its extracts are derived from Cannabis sativa, a type of hemp plant that contains active compounds called cannabinoids, which are categorized as psychoactive (e.g., cannabinol), non-psychoactive (e.g., cannabidiol), and inactive. Marijuana is the most common illicit drug in Canada and is used to manage symptoms of some health conditions. However, as with many drugs, regular use of marijuana can result in dependence.

In 2012, the prevalence of marijuana use among the general population in Canada was 10.2%, and the rate of past-year marijuana use among youth age 15 to 24 was 20.3%, with an average age of 16 years for first use. Although marijuana use is widespread among adolescents and young adults, dependence is often underdiagnosed.

The effects of cannabinoids come from the action of two major receptor subtypes: CB1 receptors (located mainly in the central nervous system but also found in the lungs, liver, and...
Diagnosis and treatment of marijuana dependence

The **DSM-5** defines cannabis dependence as a disorder characterized by a problematic pattern of use leading to clinically significant impairment or distress, as manifested by at least two of the following symptoms occurring within a 12-month period:

- Using cannabis in larger amounts or over a longer period than was prescribed or intended.
- Making unsuccessful efforts to cut down or control cannabis use.
- Spending a lot of time in activities necessary to obtain, use, or recover from cannabis effects.
- Craving cannabis or feeling an urge to use cannabis.
- Failing to fulfill major life obligations at work, school, or home.
- Continuing to use cannabis despite persistent or recurrent social or interpersonal problems.
- Giving up or reducing involvement in important social, occupational, or recreational activities.
- Using cannabis in physically hazardous circumstances.
- Continuing to use cannabis despite having a persistent or recurrent physical or psychological problem.
- Tolerance, as defined by a need for markedly increased amounts of cannabis or a markedly diminished effect with continued use of the same amount of cannabis.
- Withdrawal, as manifested by the characteristic withdrawal syndrome.

Individuals use cannabinoids for many reasons. Although the effects vary from person to person, users often report improved sleep, improved appetite, reduced anxiety, and better pain control. However, cannabinoids can have many other less desirable effects on organ systems, including cognitive effects (e.g., psychosis, memory and learning problems, cognitive impairment, amotivational syndrome), cardiovascular effects (e.g., unstable blood pressure, tachycardia), respiratory effects (e.g., heavy cough, frequent acute chest infections), and endocrine effects (e.g., reduced testosterone levels). Symptoms of intoxication with or withdrawal from cannabinoids can complicate management of other health conditions. In addition, cannabinoids can interact with commonly prescribed medications such as certain antidepressants, theophylline, fentanyl, zolpidem, lorazepam, and disulfiram. While cannabinoid overdose is unlikely, cannabinoids often produce unwanted effects such as sedation, intoxication, clumsiness, dizziness, dry mouth, lowered blood pressure, and increased heart rate.

Results from both human and animal studies of cannabis consumption indicate that regular use can lead to increased tolerance and dependence. Approximately 10% of individuals who regularly use cannabis will develop dependence. The potency of the cannabinoid as well as the amount used, the duration of use, and the route of administration will determine the severity of withdrawal symptoms. Withdrawal symptoms usually start within 24 to 48 hours of abstinence, reach a peak within 4 to 6 days, and can last up to 4 weeks.

Cannabis withdrawal is defined in the **DSM-5** as clinically significant distress or impairment of social or occupational functioning seen approximately 1 week after cessation of heavy and prolonged use. Withdrawal will involve the development of three or more of the following signs and symptoms: irritability, anger or aggression, anxiety, difficulty sleeping (i.e., insomnia, disturbing dreams), decreased appetite, restlessness, depressed mood. In addition, withdrawal will involve at least one physical symptom: abdominal pain, shakiness/tremors, sweating, fever, chills, severe headache. Significant individual variation has been reported regarding the severity and duration of withdrawal symptoms.

Before an accurate diagnosis of marijuana dependence can be made, a comprehensive assessment is required. Such assessment must take into account the duration of use, amount used daily, route of administration, and other substances of abuse. Also, general health and mental health conditions must be assessed to differentiate between symptoms that could be attributable to other substances or other physical and mental health conditions. A urine drug screen (UDS) is needed to identify the type of substances being abused. It is common to hear from substance users that some drug dealers add addictive substances such as heroin or fentanyl to their marijuana for secondary gain. A baseline UDS can help health care providers identify other undiagnosed opioid dependencies among marijuana users.

Managing dependence

Once an accurate diagnosis of marijuana dependence has been made, treatment options can be considered. Both pharmacological and psychosocial options have been studied.

Although a comprehensive review of the published literature indi-
cates insufficient evidence for a single broadly and consistently effective pharmacological treatment for cannabinoid dependence,\(^\text{4}\) adjunctive treatment for nausea, anxiety, and insomnia can be helpful. Some studies have evaluated the effect of bupropion, divalproex, naltrexone, nefazodone, and oral THC in the management of cannabinoid withdrawal syndrome. Two randomized controlled trials found that replacement therapy and short-term dose tapering with synthetic cannabinoids was effective in reducing cravings, anxiety, feelings of misery, difficulty sleeping, and chills.\(^\text{4,6}\) Nefazodone has been found to reduce anxiety and muscle pain.\(^\text{6}\)

Psychosocial treatments of cannabinoid dependence have been tested in several studies. Motivational enhancement therapy (MET), cognitive-behavioral therapy (CBT), and contingency management (CM) have been carefully evaluated and have all shown promising results.

Motivational enhancement therapy uses principles of motivational psychology to produce a rapid change. MET consists of an initial assessment using various instruments followed by four individualized treatment sessions. The first two sessions focus on structured feedback from the initial assessment, future plans, and motivation for change. The final two sessions are for reinforcing progress, encouraging reassessment, and providing objective perspective on the process of change.\(^\text{7}\)

Cognitive-behavioral therapy was originally developed to treat depression and has since been used to prevent relapse when treating substance dependence. CBT helps individuals identify and change problematic behaviors by enhancing their self-control and teaching them to use effective coping strategies. Individuals using CBT explore the positive and negative consequences of substance use, self-monitor for triggers, and employ strategies for coping with triggers, cravings, and high-risk situations.

Contingency management interventions are based on principles of behavioral modification and operant conditioning. First, CM therapists arrange the environment so that target behaviors (e.g., abstinence from cannabis) are readily detected through frequent monitoring and urinalysis. Second, therapists provide tangible reinforcement such as a gift certificate whenever the target behavior is demonstrated. Third, when the target behavior does not occur, therapists systematically withhold rewards or administer small punishments (e.g., withdrawal of methadone carry privileges).\(^\text{8}\)

Findings indicate that although each of these interventions represents a reasonable and efficacious treatment approach, the combination of MET and CBT is more potent.\(^\text{9}\)

**Summary**

Despite widespread use among adolescents and young adults in Canada, cannabinoid dependence is often underdiagnosed and undertreated. While no single pharmacological treatment for dependence has been identified, adjunctive treatment for nausea, anxiety, and insomnia and replacement therapy and short-term dose tapering with synthetic cannabinoids may be used to manage withdrawal symptoms. Long-term behavioral therapies, including motivational enhancement therapy, cognitive-behavioral therapy, and contingency management, may also be used to treat marijuana dependence.

**Competing interests**

None declared.

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**References**