

Cannabis Use Disorder Presentation and Treatment

Cannabis Use Disorder Criteria (DSM-5-TR)

A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

- **Loss of Control:** Using more or for longer than intended
- **Inability to Quit:** Persistent desire or failed attempts to cut down
- **Time Commitment:** Spending excessive time getting, using or recovering from cannabis
- **Cravings:** Intense urges or desires to use
- **Role Neglect:** Use causes failure to meet work, school or home duties
- **Social Conflict:** Continued use despite related interpersonal/social problems
- **Loss of Interest:** Giving up important social, work or hobbies
- **Hazardous Use:** Use in physically dangerous situations
- **Physical/Psychological Risk:** Use despite knowing it causes/worsens health or mental issues
- **Tolerance:** Needing more for the same effect, or getting less effect from the same amount
- **Withdrawal:** Physical/mental symptoms upon stopping (e.g., irritability, insomnia, additional symptoms listed below) or using to avoid those symptoms. Withdrawal onset is typically within 24-72 hours; peaks as days 2-6; lasts 1-2 weeks

Note: Mild = 2-3 symptoms; moderate = 4-5 symptoms; severe = \geq 6 symptoms

Signs of Cannabis Intoxication and Withdrawal

	Cannabis Intoxication*	Cannabis Withdrawal
Physical Effects	Conjunctival injection, tachycardia, palpitations, orthostatic hypotension, dry mouth; poor motor coordination, head jerks	Gastrointestinal distress, diaphoresis, chills, nausea, shakiness, muscle twitches, hypertension. (less common compared to psychological and behavioral effects)
Psychological and Behavioral Effects	Relaxation, euphoria, slowed time perception, altered/intensified sensory perception, increased awareness of environment, impaired concentration, anterograde amnesia, and increased appetite; higher doses/repeated use/use in stressful settings are associated with hypervigilance, anxiety, paranoia, derealization, depersonalization, altered time sense, panic, hallucinations, psychosis, and delirium.	Irritability, anxiety, depression, restlessness, anorexia, insomnia/disturbed sleep

*Cannabis intoxication is mediated by delta-9-tetrahydrocannabinol (THC) interaction at cannabinoid 1 (CB1) receptors on neuronal membranes.

Note: Delta-8-THC exists in negligible amounts in the cannabis plant and has about 80% of the psychoactive properties of delta-9-THC.

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Relationship Between Cannabis Use and Psychosis

Cannabis products have increased in potency and concentration. There is growing evidence that rising cannabis use, coupled with higher potency cannabis, may be contributing to higher rates of psychotic disorders. Cross-sectional studies suggest that persons who use cannabis have a two to three-fold increased prevalence of schizophrenia and schizophrenia spectrum disorders compared with those who do not use cannabis. Out of all substance-induced psychotic disorders, cannabis-induced psychotic disorder is the most likely to progress to schizophrenia, with case conversion rate estimates as high as 34%. Factors associated with an increased risk of developing cannabis-induced psychotic disorders include genetic polymorphisms (in genes that modulate dopamine pathways), earlier age of cannabis use initiation, higher potency cannabis, and more frequent cannabis use. Among people with schizophrenia, cannabis use has been associated with increased risk of illness recurrence and hospitalization, and poorer functioning and treatment adherence. It is crucial to assess for a co-occurring psychotic disorder given the link between cannabis use and psychosis. It is often challenging to distinguish substance-induced psychosis from an additional, co-occurring psychotic disorder.

Clues that the person may have a co-occurring psychotic disorder include:

- Psychotic symptoms that persist for ≥ 1 month after abstinence from drugs
- Presence of prodromal psychotic symptoms before the onset of cannabis use
- Family history of a psychotic disorder

Pharmacotherapy Interventions for Cannabis Use Disorder

There is no well-established role for pharmacotherapy in cannabis use disorder treatment; no medication is FDA-approved for cannabis use disorder. Many studies assessing pharmacotherapy for cannabis use disorder are small and of lower quality.

Medication	Cannabis Intoxication*
$\Delta 9$-tetrahydrocannabinol containing preparations (e.g., dronabinol)	Did not increase abstinence from cannabis
Bupropion (sustained release 150 mg po BID)	Little to no difference compared with placebo in achieving abstinence from cannabis. (Often abused and/or diverted in forensic settings).
Cannabidiol (CBD) (dosed at 400 mg po BID)	Associated with significantly reduced cannabis use in adults (but larger studies and replication are needed)
Mood stabilizers (lithium, divalproex) and anticonvulsants (gabapentin, topiramate)	Little to no difference compared with placebo in achieving abstinence from cannabis
N-acetylcysteine (NAC) (dosed at 1200 mg po BID)	Little to no difference compared with placebo in achieving abstinence from cannabis
Selective serotonin reuptake inhibitors (SSRIs)	Fluoxetine, vilazodone, and escitalopram had little effect on cannabis abstinence.
Varenicline (dosed at 0.5-1 mg po BID)	Associated with significantly reduced cannabis use in adults (but larger studies and replication are needed)

Psychosocial Interventions for Cannabis Use Disorder

Cognitive-behavioral therapy (CBT) and motivational enhancement therapy (MET), alone or in combination, have the strongest evidence base for effectiveness. Contingency management (CM) may be used alone or as an augmentation to CBT and MET. Dialectical behavioral therapy (DBT) and acceptance and commitment (ACT) have some evidence for use but may be considered as second-line options.

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