# Psychiatric Disorders and Comorbid Cannabis Use:
## When Should We Be Concerned and What Can We Do About It?

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Cannabis use is common among individuals with psychiatric disorders, including those seeking treatment in mental health care settings. Yet, not all cannabis use is harmful, and providers are often unsure how to determine which patients are at risk for cannabis use–related problems and how to help. As cannabis use becomes more widely accepted in some regions of the US and many states move toward legalization, it is crucial for mental health providers to be well equipped to identify, assess, and treat problems of a range of possible severity, including cannabis use disorders. The first article in this 2-part series reviewed the prevalence of cannabis use and related problems among individuals with psychiatric disorders.[1] This companion article describes strategies for cannabis use screening, assessment, and intervention in the context of mental health care.

### SCREENING AND ASSESSMENT

It is important to screen individuals seeking mental health services for any use of potentially problematic substances, including cannabis. Brief, validated self-report questionnaires such as the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST)[2] are useful and can be integrated into self-administered computerized screening systems.[3,4] Key questions on the ASSIST include frequency of use; presence of health, social, legal, or financial cannabis-related problems; and symptoms of cannabis and other substance use disorders. Although some uncertainties remain regarding the impact of cannabis use on mental health, more frequent use and use at younger ages are consistently associated with worse mental health outcomes than occasional use or nonuse.[5] Therefore, it is essential to determine the age at which patients began regular use and current frequency of use. It is also important to ask about newer forms of use including vaping and THC concentrates.[6] Urine drug screens, used often in outpatient addiction treatment, court, and workplace settings, may not be needed in addition to validated self-report measures.[7] However, if used in a psychiatric setting, drug screens should be used consistently with all patients to reduce stigma.

Several brief scales have been developed for adolescents and adults to help assess severity and interest in reducing use. Examples include the 5-item Severity of Dependence Scale,[8] the 8-item Cannabis Use Disorders Identification Test-Revised (CUDIT-R),[9] and the 6-item Cannabis Abuse Screening Test (CAST).[10] The CUDIT-R and the CAST also include useful items on difficulties with memory or concentration. In a review of these measures, results of validation studies varied depending on population and standards for validity, but sensitivity, specificity, and predictive power in identifying cannabis use disorder were generally acceptable.[11] Regardless of the measure used, providers should be attuned to patients' own sense of how cannabis use may cause problems and what might motivate reduction in use.

Cannabis use disorder in the *DSM-5* is coded as F12.10 (mild) or F12.20 (moderate or severe) and is defined as "a problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least 2 or more symptoms occurring within a 12-month period."[12(p509)] *DSM-5* also includes diagnoses for withdrawal as well as cannabis-induced psychotic, anxiety, and sleep disorders. There is considerable potential for patients with more extensive use to exhibit withdrawal symptoms if they stop altogether.[13] In a sample of 170 adolescents and young adults with depression and cannabis use and/or dependence (using *DSM-IV* criteria), withdrawal was found in 92% of participants with dependence, and the most common withdrawal symptoms were craving (82%), irritability (76%), restlessness (58%), anxiety (55%), and depression (52%).[14] Thus, providers should be mindful of withdrawal in differential diagnosis and in planning intervention strategies.

### BEHAVIORAL INTERVENTIONS

Given the extent of cannabis use and potential adverse effects, there is a need to initiate treatment efforts in mental health treatment contexts. Many adults with depression and other psychiatric disorders try to stop using,[15] suggesting that patients may be willing to engage with interventions. In determining approach, providers should consider the extent of cannabis problems, psychiatric severity, willingness of patients to reduce use, and availability of specialty addiction treatment services.

The National Institute on Drug Abuse recommends 3 behavioral approaches for treatment of cannabis use disorders (applicable to both *DSM-IV* and *DSM-5* definitions): motivational interviewing (MI), cognitive-behavioral therapy (CBT), and contingency management.[16,17] There is strong evidence for the effectiveness of MI in helping to reduce

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cannabis use,[12] including among psychiatry outpatients.[18] MI is a patient-centered "collaborative conversation style for strengthening a person's own motivation and commitment to change."[19(p12)] Using MI, which can be integrated into other mental health services, providers can evoke (and ideally resolve) personal ambivalence about reducing use. In a study of 97 individuals with major depression and cannabis use and/or hazardous drinking, intensive MI/CBT was significantly better than a brief intervention alone at reducing cannabis use and hazardous substance use, with computer-based therapy showing the largest effect.[20] This finding is consistent with research indicating that the combination of MI and CBT seems to be more effective than either intervention alone.[16] The incorporation of MI can be especially effective with patients experiencing current problems yet expressing little desire or motivation to reduce or stop use.

Traditionally, cannabis use disorder and comorbid psychiatric disorders have been addressed either sequentially (the resolution of cannabis use before treating psychiatric disorders, or vice versa) or in parallel (treating both disorders concurrently but with different providers).[21] Over time, there has been more acceptance of an integrated approach to addressing cannabis use and psychiatric disorders such as PTSD,[22] anxiety,[23] depression,[24] and psychosis.[25] In particular, integrated pharmacologic and psychological treatments can reduce cannabis use in individuals with psychosis or depression.[26] Therefore, cannabis use should be assessed throughout mental health treatment with an explicit focus on the link between cannabis use and treatment effectiveness. For example, use of cannabis during exposure treatment for PTSD or anxiety can interfere with the hypothesized mechanisms of action (habituation to feared stimuli or traumatic events). Cannabis use can then be conceptualized and collaboratively addressed as a safety behavior rather than ignored. Another consideration is whether cannabis is used recreationally or medically (either prescribed or perceived to have medical benefits by the patient), as research indicates that medical cannabis users report worse physical and mental health than recreational users.[27–29] Therefore, medical users may be hesitant to reduce or stop cannabis use without alternative coping strategies for physical (eg, chronic pain) and psychiatric distress.

Depending on psychiatric severity, adaptations to behavioral interventions may be necessary. For example, Martino and colleagues[30,31] made specific recommendations for implementing MI with dually diagnosed patients (substance use and psychotic disorders), such as using simple and concise language; reflecting often; providing frequent summary statements, affirmations, and metaphors; and avoiding reflections on despair or negative life events. These MI modifications are straightforward and can enhance intervention effectiveness.

## MEDICATIONS

There are no currently approved medications for treating cannabis use disorder, and trials to date generally have not shown efficacy. Medication development efforts have (1) targeted initial abstinence (time-limited approach), (2) tried to replicate the success of opioid replacement therapy by offering legal cannabinoid receptor agonists, or (3) examined antidepressant treatment outcomes of patients with cannabis use disorder and co-occurring major depressive disorder.

Medications that have targeted initial abstinence include zolpidem, *N*-acetylcysteine (NAC), lofexidine, multiple serotonergic antidepressants, gabapentin, lithium, quetiapine, baclofen, divalproex, and oxytocin. Most of these studies were done in a controlled human laboratory, and the medication (or combination of medications) did not show dose-dependent decreases in self-administration of cannabis and/or self-reported withdrawal symptoms during a quit attempt. Insomnia is one of the most distressing withdrawal symptoms and can lead to relapse. Zolpidem has been shown to improve subjective sleep quality and objective sleep markers on polysomnogram in persons suddenly stopping daily cannabis use.[32] NAC is an over-the-counter dietary supplement that can improve dysregulated glutamatergic activity that occurs in cannabis use disorder. A phase 2 study of NAC 1,200 mg by mouth daily combined with contingency management and brief weekly cessation counseling demonstrated a significant doubling of the odds of abstinence over placebo in treatment-seeking adolescents (aged 15–21 years).[33] A larger multisite trial of the same dose of NAC in adults with cannabis use disorder showed no benefit over placebo,[34] indicating NAC at this dose may be effective only in persons aged 15–21.

Other targets have included the cannabinoid receptors, most notably the cannabinoid type 1 receptor ($CB_1$). Dronabinol, nabilone, and nabiximols have been investigated in studies investigating $CB_1$ agonist replacement therapy. Dronabinol and nabilone are synthetic THC analogs that are FDA approved for the treatment of nausea/vomiting associated with cancer chemotherapy. In a phase 2 outpatient clinical trial, dronabinol 40 mg/d combined with behavioral therapies did not result in reduction in cannabis use compared with placebo.[35] However, Phase 1 studies have shown that higher dronabinol doses (up to 120 mg/d) may show different results.[36,37] Nabilone has higher oral bioavailability compared to dronabinol and has shown promise in suppressing withdrawal and reducing risk for relapse in phase 1 studies.[38,39] Lastly, a recently published phase 1 trial of nabiximols, a mixture of THC and cannabidiol plant extracts approved in several European countries for multiple sclerosis treatment, did not show improvements in abstinence compared to placebo but did show reduction in cannabis use frequency.[40]

Prescribing antidepressants for cannabis use has yielded mixed results. In one small study, individuals with both depression and alcohol dependence who were frequent cannabis users who were prescribed fluoxetine had greater reduction in cannabis use than a control group.[41] Another study found no effect for vilazodone on reducing cannabis use, among those with cannabis dependence.[42] Similarly, venlafaxine was not effective in a recent trial among individuals with both depression and cannabis dependence.[43]

In considering which medications to use, clinicians may prescribe NAC for adolescent patients and zolpidem extended release for adult patients reporting sleep difficulties while trying to stop using cannabis. Off-label nabilone may be offered to adults who are unable to quit using zolpidem or are not good candidates for this medication due to co-occurring alcohol or benzodiazepine use. To increase intervention efficacy, clinicians should use medication as part of a comprehensive treatment program involving the behavioral therapies described above.

## SPECIALTY ADDICTION TREATMENT

Although there is much that mental health providers can do to address cannabis use, not all patients can be managed effectively in the context of outpatient psychiatric services (eg, weekly psychotherapy and/or periodic medication management), and lower-intensity treatment may not be effective for patients with higher severity cannabis use disorder and significantly reduced functioning.[26] These patients could benefit from referral to specialty addiction medicine programs in which inpatient and/or intensive outpatient care is provided. In practice, such higher-severity patients are likely to use other substances in addition to cannabis.

Treatment options and referral processes vary depending on the type of insurance coverage available to patients. Studies show that a majority of individuals diagnosed with substance use disorders fail to initiate specialty addiction treatment,[44] although data on referrals from psychiatry are lacking. It is critical for providers to help facilitate a patient's initiation and engagement with such programs as much as possible, depending on the context of clinical practice, eg, the extent to which mental health services are integrated with addiction medicine. Follow-up at subsequent mental health visits regarding specialty addiction treatment is also essential to addressing barriers to engagement in care.

## CONCLUSIONS

Cannabis use by patients in treatment for psychiatric disorders can present significant challenges to providers. This review highlights key strategies for screening, assessment, and intervention that can be effectively integrated into mental health services. Several brief measures are valuable for screening and measurement of cannabis problem severity, in addition to the *DSM-5* diagnostic criteria. Although there is a need for additional intervention development, behavioral strategies such as MI and CBT can help reduce cannabis use in those with mental health problems. For those with more severe cannabis use disorders, it is important for providers to assist patients in getting connected to specialty addiction services. Given the high rate of cannabis use prevalence and its adverse effects on psychiatric treatment, addressing cannabis use in the context of psychiatric services can make a positive impact on patient care.

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