American Society of Clinical Psychopharmacology Corner Leslie L. Citrome, MD, MPH, Editor

It is illegal to post this copyrighted PDF on any website. Psychiatric Disorders and Comorbid Cannabis Use:

How Common Is It and What Is the Clinical Impact?

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Cannabis use is increasingly visible as policy shifts toward legalization in many states, and the potential impact of cannabis use on patients is an important issue for mental health providers to understand. As of early 2018, 9 US states have laws allowing recreational cannabis use,1 and fewer adults now perceive cannabis as risky than ever before.2 Yet, the degree to which cannabis use can be harmful is often unclear to clinicians. In the absence of a complete research base or clear recommendations from medical societies, clinicians are often left wondering how they should address cannabis use. This article, the first of a 2-part series, reviews recent findings regarding the extent of cannabis use among individuals with mental health problems as well as the potential impact of cannabis use on both symptoms and treatment. This article does not distinguish between patients' intended recreational use versus use recommended by a doctor, given the large overlap in formulations and paucity of data on medical use alone. Rather, we focus on what is known regarding the prevalence of cannabis use and cannabis use disorders (using DSM-IV criteria, the most widely used definitions in epidemiologic studies) among individuals with psychiatric disorders, user characteristics, impact on psychiatric symptoms, and adverse effects on mental health treatment. In the forthcoming companion article, we examine cannabis screening, assessment, and intervention strategies.

PREVALENCE OF CANNABIS USE AND CANNABIS USE DISORDERS

Studies have consistently found that cannabis use is common among individuals with psychiatric disorders. According to results from the National Survey on Drug Use and Health, 18% of adults in the US had a mental illness in 2015-2016, and 24% of those used cannabis in the prior year.³ A cohort study of outpatient adults with major depression showed that 37% used cannabis within 30 days prior to enrollment. 4 In a multisite study of inpatients with serious mental illness (eg, schizophrenia, major depression, and bipolar disorder), 30% reported cannabis use 30 days prior to admission.⁵

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To share: https://doi.org/10.4088/JCP.18ac12267 © Copyright 2018 Physicians Postgraduate Press, Inc. Among adults aged 60 and over in depression treatment, cannabis use in the prior 30 days was reported by 12% of men and 4% of women.⁶ Although individuals with psychiatric disorders who use cannabis are generally more likely to be younger and male, clinicians can anticipate seeing cannabis use among patients across a variety of age ranges and demographic groups.

Studies show that mood and anxiety disorders co-occur at higher levels in individuals with cannabis use disorder than in the general population.⁷ Similarly, adolescent cannabis use disorder has been associated with an increased risk of attention-deficit/hyperactivity disorder, mood and anxiety disorders, and other substance use disorders. In a large study of 471 individuals with bipolar disorder and 1,761 controls, individuals with bipolar disorder were 6.8 times more likely to report lifetime history of use. 9 The rate of cannabis use disorders in those with bipolar disorder was 29%, and these disorders independently associated with suicide attempts as well as disability.9 Analysis of the National Epidemiologic Survey on Alcohol and Related Conditions data, gathered in 2 waves from nearly 35,000 respondents, found strong associations between cannabis use and increased risk of future cannabis use and other substance use disorders, 10 demonstrating the potential for cannabis use problems to become more severe over time.

ADVERSE CONSEQUENCES OF CANNABIS USE

Cannabis use has been linked to increased anxiety, depression, and psychoses, especially among youth, 11 with increasing concern about adverse psychiatric effects in older adult populations.¹² Studies have identified associations between cannabis use and decreased cognition and amotivation, particularly among youth and frequent or heavy users (ie, use multiple times a day or for extended periods of time).¹³ Given that brain development continues into a person's mid-20s, cannabis use in adolescence can have greater addiction potential and more severe behavioral or social outcomes than use in adulthood. Risks of early, heavy cannabis use include a greater risk of development of a cannabis use disorder (approximately 9% of adults and 16% of youth who use cannabis eventually develop a cannabis use disorder), ^{13,14} risk of developing addiction to other drugs or alcohol, 13,15 and altered brain development and impaired critical cognitive functions (eg, memory, processing speed, reasoning, and IQ), making it difficult to learn and retain information.¹³ Moreover, cannabis use among youth, when combined with greater potency and frequent use, may advance the time of first onset of psychotic episode by 2 to 6 years. 16 Further, social consequences of greater use in adolescence in conjunction with mental health symptoms include problems in school performance and vocational advancement, car accidents, and risk behaviors (eg, condomless sex).

Despite growing numbers of older-adult cannabis users with psychiatric comorbidities, research with these populations has only started to emerge to inform clinical practice. In recent years, there has been an increase in the number of cannabis users with mental health conditions aged 50 and older. 17 Studies have suggested that

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It is illegal to post this copyrighted PDF on any website adults in this age group may be more vulnerable to the adverse disability exacted by these illnesses. In a study of adults with

adults in this age group may be more vulnerable to the adverse effects of cannabis use, since older adults experience changes in brain plasticity and age-related cognitive decline, processes that cannabis use has been found to negatively affect in other age groups. ¹³ Cannabis users aged 50 and older have been found to exhibit more psychological distress ¹⁸ and suicidal thoughts ¹² and higher rates of opioid use disorder ¹⁷ when compared to nonusers. These findings suggest a potential vulnerability of older adults with psychiatric disorders to adverse effects of cannabis use.

RELATIONSHIP OF CANNABIS USE TO THE ONSET AND COURSE OF PSYCHIATRIC DISORDERS AND COGNITIVE FUNCTION

Cannabis use is associated with both anxiety and depression, ¹⁹ especially among regular users, but causality has not been established.¹¹ A recent twin study found that frequent cannabis use was associated with significantly greater risk of major depression and suicidal ideation after adjusting for other factors. ²⁰ Longitudinal studies have reported conflicting evidence regarding the impact of cannabis on the course of psychiatric symptoms among individuals with depression. For example, some studies have reported that cannabis use worsens depressive symptoms over time, 4,21 while others have shown that cannabis users and nonusers are equally likely to have depression at follow-up.²² Individuals with depression also tend to be at increased risk of both initiating²³ and continuing to use cannabis over time.^{5,21} Social anxiety may motivate some individuals to use cannabis to manage uncomfortable feelings, yet it also may lead to worsening of symptoms and greater impairment over time. 24,25 Together, these findings suggest that cannabis may play a contributory role in depressive and anxiety disorders and imply that symptoms may increase with use. Research involving the use of cannabinoids to treat or lessen symptoms of depression and anxiety is extremely limited and has shown that cannabidiol, a cannabinoid, could have some possible anxiolytic or antidepressant effects in animal and human studies.²⁶ Although a small case series of patients with severe chronic schizophrenia (N=6) found that patients experienced symptom reduction following dronabinol (synthetic cannabinoid) administration,²⁷ we are aware of no other evidence that demonstrating that THC forms of cannabis are effective at reducing psychiatric symptoms in humans.

Cannabis use increases risk of developing psychosis, especially in those with a preexisting genetic vulnerability and those who initiated cannabis use at a young age. ²⁸ Young adults with psychoses who use cannabis have an earlier age of first-episode psychosis,²⁹ but young adults in a first episode of psychosis who stop using cannabis have better clinical outcomes than those who persist in using, as measured by fewer psychotic symptoms and better social functioning.30 Cannabis use in adulthood worsens the course of illness in schizophrenia, 11 and persistent use over time contributes to poorer functional outcomes as measured by the Global Assessment of Functioning scale.⁵ A review of 35 studies concluded that cannabis use is associated with increased, dose-dependent risk of psychotic outcomes, paranoia, hospitalizations, and lower brain volume.²⁸ Among those with bipolar disorder, cannabis use has been associated with an increased risk of subsequent manic symptoms.³¹ These findings highlight the particular risks of cannabis use among individuals with severe mental illness.

Cannabis use has been linked to deficits in cognitive function among those with mental health problems³² and in the general population.³³ Neurocognition is one of the strongest predictors of functional outcome recovery in schizophrenia and bipolar disorder, with cognitive deficits accounting for much of the psychosocial

schizophrenia, the largest predictor of underreported cannabis use was neurocognitive deficits, suggesting underidentified service use needs among them.³⁴ Overall, the magnitude of neuropsychological deficits among cannabis users may depend on several factors, including presence of mental illness, duration of cannabis use, length of abstinence, and age at onset of use. Research on adolescent cannabis use has indicated that early, frequent, and heavy use of cannabis is associated with poorer cognitive and psychiatric outcomes,³⁵ although it remains unclear whether lower levels of exposure are harmful.

Longitudinal research among clinical samples has shown that cannabis use is associated with worse overall psychopathology and poorer functioning among psychiatric patients with depression and other severe mental illnesses and that these adverse clinical outcomes persist over time.⁵ Among adolescents, studies show an age- and dose-dependent association between cannabis use and high school completion, attainment of university degrees, welfare dependence, substance use, depression, and suicide attempts.³⁶ Individuals with posttraumatic stress disorder often use cannabis to help manage their symptoms and improve sleep, yet this puts them at risk for cannabis-related problems.³⁷ Reductions in cannabis use among those with cannabis use disorder have been associated with improvements in anxiety, depression, and sleep quality.³⁸ Thus far, research findings suggest that reduction in problematic cannabis use may have a beneficial impact on patients with a range of mental health symptoms, while the research on cannabis as a treatment for mental health symptoms is limited by a notable lack of randomized trials.

IMPACT OF CANNABIS USE ON MENTAL HEALTH TREATMENT ADHERENCE AND EFFICACY

An important question for providers is the extent to which cannabis use impacts mental health care. Strong evidence regarding one of the most well-researched aspects of this issue indicates that cannabis use contributes to worse adherence to antipsychotic medications.³⁹ One study of adults suffering from first-episode psychosis found that between 20% and 36% of the adverse effects of continued cannabis use on outcomes in psychosis treatment were mediated through the effects of cannabis use on medication adherence. 40 One study of young adult heavy drinkers found that those who used cannabis had worse adherence to naltrexone.⁴¹ No studies to our knowledge have examined if cannabis use affects antidepressant or anxiolytic adherence, although use of cannabis as self-medication for mood and anxiety symptoms suggests that this is a possibility. However, there is some evidence that cannabis use has the potential to interfere with depression and anxiety treatment by decreasing adherence to behavioral interventions.⁴² Since most behavioral interventions for anxiety are exposure-based, use of cannabis to reduce anxiety may render the mechanism of treatment ineffective. Interventions focused on medication and behavioral treatment adherence could partially mitigate the harm from cannabis use on patients with psychiatric disorders. Further, monitoring of cannabis use throughout the course of treatment should be prioritized, in conjunction with ongoing assessment of mental health symptoms.

CONCLUSIONS

Cannabis use is prevalent and often clinically problematic for patients with psychiatric disorders. Much of the current evidence stems from studies of association, not causation, linking cannabis use to adverse medical and psychiatric outcomes. Since prospective It is illegal to post this copyrighted PDF on any website.

severity in patients with major mental health conditions (especially schizophrenia and depression), perhaps if patients were more aware that ongoing symptom distress is linked to cannabis use, they might be more likely to consider treatment options to reduce use. Cannabis prevention and treatment strategies should especially target younger age groups, since use among adolescents and young adults is high and associated with adverse consequences. Older adults and those with a history of psychosis are also important and vulnerable populations. In a companion piece that will follow this article, we address strategies for effective cannabis use screening and intervention in the context of mental health treatment.

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