



Relationships between cannabis use and mental disorders: assessing the coherence of evidence from studies with different methodologies



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See [Comment](#) page 538

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See Online for appendix

Cannabis use often begins in adolescence and young adulthood, when anxiety, depression, psychosis, and bipolar disorder typically first develop. Young people aged in their mid-teens to mid-twenties who engage in daily cannabis use and develop a cannabis use disorder have a higher prevalence of these mental disorders. We assessed the coherence of evidence from epidemiological, genetic, experimental, and preclinical studies to assess relationships between daily cannabis use and the increased incidence, prevalence, and persistence of psychosis, bipolar disorder, anxiety, depression, and suicidal behaviours. We found credible evidence that daily cannabis use is a contributory cause of psychosis. There were fewer high quality epidemiological and genetic studies of bipolar disorder. The role of cannabis use in depression, anxiety, and suicidality was less certain because associations were modest and could reflect self-medication, shared risk factors, or bidirectional relationships. A high priority should be given to developing effective interventions for cannabis use disorders in people with mental disorders.

Introduction

Anxiety and depression are the most common mental disorders among young adults globally.¹ Psychotic disorders are less prevalent globally (23·6 million) than anxiety (301·4 million) and depression (279·6 million), but all of these disorders affect the lives of people who develop them.¹ Anxiety, depression, and psychotic disorders typically have their onset during late adolescence and early adulthood,² at the same time that cannabis use often begins.

Search strategy and selection criteria

We systematically searched for evidence following the National Academy of Sciences' two-step method, prioritising the findings of high quality systematic reviews and meta-analyses before including primary research published in English since the most recent review. Searches were performed in PubMed, Google Scholar, and Elicit in March, 2025, using search terms related to prospective evidence, cannabis use, and the mental health outcomes ("psychosis or schizophrenia", "bipolar disorder", "anxiety disorders", "depression", and "suicidality") and their prevention, harm reduction, and treatment. Studies were included if they examined prospective associations between cannabis use and mental health outcomes, reported quantitative effect sizes with measures of uncertainty, and employed clear methodological approaches. We prioritised the most recent and comprehensive systematic reviews with meta-analyses. We initially searched between Jan 28, 2015, and March 21, 2025, and then updated the search up to April 4, 2026. Two independent reviewers conducted study selection and data extraction (appendix p 2). In assessing the strength of evidence for a causal effect we looked for a coherence of findings in the extent to which different study approaches—each with different and ideally unrelated sources of bias—pointed to the same conclusions.

Cannabis use disorder comprises a problematic pattern of cannabis use that produces clinically significant impairment or distress (definition of key terms in the appendix p 9). Cannabis use disorder is more likely to develop when cannabis use is initiated during adolescence than adulthood and when the person uses daily or near-daily into young adulthood. A systematic review of six longitudinal studies estimated the risk of cannabis use disorder as 27% (95% CI 25–28) in young people who have ever used cannabis and 33% (22–44) among young people who used cannabis at least weekly.³ This Review prioritises evidence on frequent or regular cannabis use, defined as daily or near-daily use, because it is the pattern most strongly associated with the development of cannabis use disorders and with anxiety, depression, and psychotic disorders.

Potential roles of cannabis use in mental disorders

There are several ways frequent cannabis use could influence the risk of developing anxiety, depression, and psychotic disorders. First, it could bring forward the onset of disorders in people who were at high risk of developing them. Second, it could increase the incidence of mental disorders, ie, produce disorders that would not have developed in the absence of cannabis use. Third, frequent cannabis use could increase the chronicity of these mental disorders and thereby their prevalence in the population. Studies that follow representative samples of adolescents into adulthood are best designed to assess these possibilities, because they often measure exposure to cannabis use before symptoms of mental disorders develop and provide evidence on the course of these disorders.

These potential pathways are particularly relevant in the context of increasing cannabis availability and product potency in many high-income countries. As outlined by Freeman and colleagues elsewhere in this collection, the legalisation of medical and adult non-medical cannabis in

North America and other high-income countries such as Germany has reduced criminalisation-related harms.⁴ Legalisation has enabled the regulation of cannabis products, to which young adults now have legal access, many with high levels of delta-9-tetrahydrocannabinol (THC), which are sold at substantially lower prices than under prohibition.⁴⁻⁶ The increasing accessibility of more potent cannabis products make it important to explore whether frequent cannabis use is associated with the occurrence of mental disorders; the temporal relationships between frequent cannabis use and mental disorders and if they are bidirectional; and whether common factors such as shared genetic vulnerabilities or unmeasured confounding by psychosocial risk factors contribute to these associations. We systematically searched for evidence to assess the coherence of evidence from prospective observational studies, genetically informed epidemiological studies, clinical trials, and experimental tests of the biological plausibility of a causal relationship (key research questions are outlined in panel 1). We used evidence from multiple study designs, each with different strengths and limitations, to make more informed assessments of potential causal effects on the assumption that coherent findings in study designs, subject to different sources of bias, support more robust conclusions.⁷

Cannabis use and psychosis

Prospective studies in Germany, the Netherlands, New Zealand, Sweden, and the UK have assessed associations between daily or near-daily cannabis use in adolescence and young adulthood and the likelihood of receiving a diagnosis of psychosis or reporting psychotic symptoms (table).⁸ A 2024 meta-analysis found that any measure of recreational cannabis use (eg, current use, use ever, lifetime frequency of use) was associated with a three-fold increase in the incidence of psychosis.⁹ Before we can conclude that cannabis use plays a causal role in psychoses, we need to assess two alternative explanations of the association: the self-medication hypothesis and unmeasured confounding.

The self-medication hypothesis

According to the self-medication hypothesis, people who experience early symptoms of psychosis, such as depressed mood, use cannabis to relieve their symptoms.¹⁰ This hypothesis could explain why regular cannabis use is more common among people with newly incident cases of psychosis than their age-matched peers without psychosis.¹¹ However, evidence for the self-medication hypothesis is weak.^{8,12} First, people with psychosis who use cannabis have reported doing so for many of the same reasons as people who do not have psychosis, namely, to feel good, to have fun, and to fit in with their peers.¹³ Second, epidemiological studies have found that cannabis use more often precedes than follows the onset of psychotic symptoms, and that the relationship persists after controlling for a personal

history of psychotic symptoms.^{8,9,11} Third, people with psychosis who used cannabis before diagnosis and continue to do so after diagnosis have higher rates of relapse and more positive psychotic symptoms than peers who discontinue cannabis use.¹⁴⁻¹⁶ These results are consistent with the hypothesis that THC exacerbates symptoms of psychosis and might produce psychotic symptoms in susceptible individuals.¹²

Unmeasured confounding

Associations between frequent cannabis use and the risk of psychosis could also be explained by unmeasured factors that increase the risks of developing both cannabis use disorder and a psychotic disorder.¹⁷ These factors could be environmental (eg, childhood abuse) or

Panel 1: Key questions

- Is there evidence that cannabis use can increase the incidence, prevalence, and chronicity of anxiety, depression, psychosis, bipolar disorders, and suicidal behaviours?
- Are there biological and genetic mechanisms that would explain potential causal roles of cannabis use on these mental disorders and symptoms?
- What are the implications for interventions addressing cannabis use disorders among people with these mental disorders?
- Are there effective interventions to prevent the initiation of cannabis use and reduce progression to cannabis use disorder in people who have or are at risk of these mental disorders?
- How should we treat people with these mental disorders who have comorbid cannabis use disorders?
- Can we reduce cannabis-related harm among people with these mental disorders who use cannabis or have a cannabis use disorder and who may not be willing to cease using cannabis, by providing evidence-based guidelines on less harmful patterns of use?

	Evidence for association	Understanding of temporal relationship	Potential confounding factors
Psychosis	Strong evidence from multiple study designs	Clear temporal relationship	Adjustment for confounders attenuates but does not eliminate the association
Bipolar disorders	Modest association with less consistent evidence	Unclear temporal relationship	Might be explained by common factors (few genetically informed studies)
Depressive disorders	Modest association in prospective studies	Unclear temporal relationship	Association could be explained by confounding factors
Anxiety disorders	Modest association with mixed findings	Unclear temporal relationship	Uncertain
Suicidal behaviours	Modest to moderate association	Unclear temporal relationship	Uncertain

See the appendix (pp 3, 4) for studies that informed this table.

Table: Epidemiological evidence on possible causal roles of cannabis use in mental disorders

genetic risk factors for cannabis use and psychosis.¹⁷ Since the association between cannabis use and psychosis becomes stronger with the frequency of cannabis use, any shared risk factors must show a similar relationships to both cannabis use and psychosis risk.¹² Burke and colleagues⁹ reported an E value of 5·95, indicating that an unmeasured confounder would need to be associated with both cannabis use and psychosis by risk ratios of at least 5·95 each, independent of measured factors, to fully explain the observed association.

Prospective studies have statistically controlled for the effects of measured confounders, such as other drug use, personal characteristics, and a history of psychotic symptoms.^{16,18–21} Some studies have controlled for the effects of unmeasured confounders by using fixed effects regression to assess relationships between cannabis use and psychotic symptoms within the same individuals when they are and are not using cannabis.^{20,22} The largest of these studies showed that cannabis use was a stronger predictor of later psychotic symptoms (odds ratio [OR]=7·03 [95% CI 2·39–20·69]) than were psychotic symptoms of cannabis use (OR=0·59 [0·21–1·71]).²²

Tobacco smoking is a key potential confound because cannabis and tobacco smoking are strongly associated.²³ Systematic reviews of epidemiological studies suggest that cigarette smoking could play a causal role in schizophrenia.^{23,24} Some studies have found that the association between cannabis use and psychosis is greatly attenuated after controlling for cigarette smoking,²⁵ but other studies have found that the association persists after controlling for smoking.^{26,27} It is unclear how best to control statistically for tobacco smoking when it might play a causal role in the initiation of cannabis smoking.

Shared genetic risks

Genetically informed studies can assess whether the association between frequent cannabis use and psychosis could be explained by shared genetic factors.^{28,29} These studies assess whether the strength of the association between frequent cannabis use and psychosis varies with the degree of genetic relationship between people (eg, twins, parents, siblings, cousins, and people who are unrelated). Some studies have used polygenic risk scores to assess whether the association between cannabis use and psychosis is explained by shared genetic risk. Mendelian randomisation uses genetic variants associated with the exposure of interest (cannabis use) in an instrumental variable analysis to test whether cannabis plays a causal role in psychosis.²⁹ In their review of these studies, Gillespie and Kendler found evidence that there were shared genetic risks for cannabis use and psychosis, and that emerging symptoms of psychosis increased the risks of a person using cannabis.²⁸ They concluded that after controlling for these relationships, cannabis use was still likely to be a contributory cause of psychosis.

Trends in psychosis incidence and prevalence

If there is a causal relationship between cannabis use and psychosis, then one would expect the incidence or prevalence of schizophrenia to increase as the prevalence of cannabis use increases among young adults.³⁰ It has been difficult to decide whether this is the case, because psychosis incidence would increase only modestly if the relationship were causal.³⁰ Some studies suggest that the incidence of psychoses has increased in locations where the prevalence of cannabis use has increased.^{12,31} Other studies show increased treatment of psychoses in jurisdictions that have legalised cannabis, although these associations could be confounded by differences in treatment provision.^{32,33} Analysis of a Danish population-based psychiatric case registry also found that the attributable risk of cannabis use for schizophrenia increased since 2010, probably reflecting a higher prevalence of cannabis use since then.³⁴

Assessing the coherence of the evidence on cannabis use and psychosis

The coherence of evidence supports the hypothesis that regular cannabis use is a contributory cause of psychosis, ie, a factor that acts in conjunction with other risk factors to produce psychotic symptoms.^{11,35–39} First, cannabis use seems to precede more often than follow the onset of psychosis. The earlier cannabis use begins, the more frequently it is used, the higher its THC content, and the longer the period of daily use, the greater the risk appears to be that the person will experience psychotic symptoms or develop a psychotic disorder.^{11,35,39,40} Second, the principal psychoactive ingredient in cannabis, THC, acts upon CB1 cannabinoid receptors in the brain, and these receptors have been implicated in the pathophysiology of psychosis (appendix p 5).^{41–43} Third, THC given under double-blind conditions produces dose-related increases in positive and negative psychotic symptoms in people who do and who do not have a psychotic disorder.^{44–46} Fourth, people who use cannabis who develop a psychotic disorder and continue to use cannabis have poorer outcomes than people with psychotic disorders who cease using cannabis.^{14,15} Fifth, epidemiological and genetic studies find that adjustment for plausible confounding variables attenuates but does not eliminate the association between regular cannabis use and psychotic symptoms. Sixth, preclinical studies of rodent analogues of psychosis phenotypes provide support for the biological plausibility of a causal relationship. A systematic review found a significant association between the exposure of adolescent animals to THC and impaired schizophrenia-related behavioural phenotypes, such as cognitive deficits, sensorimotor gating, and pronounced behavioural changes relevant to negative symptoms of schizophrenia.⁴⁷

Cannabis use and bipolar disorders

People with bipolar disorders can experience symptoms of mania (elated mood), depression, and psychotic

symptoms, including delusional beliefs.⁴⁸ These people are often included in studies of first episode psychosis and have higher rates of cannabis use than the general population.^{49,50} Longitudinal studies indicate that people who have used cannabis have a higher risk of developing bipolar disorders than those who have not.^{49,51}

In longitudinal studies of people with bipolar disorders, the frequency of cannabis use at the time of diagnosis predicts the frequency of manic symptoms at follow-up.⁴⁸ Cannabis use is also associated with a younger age of onset of mania, more frequent depressive or manic episodes, more severe bipolar symptoms, more rapid cycling or mixed episodes, and less improvement with treatment.⁴⁸ Systematic reviews find an association between cannabis use and poor outcomes in people with bipolar disorder.^{48,52}

Assessing the coherence of the evidence on cannabis use and bipolar disorders

Daily cannabis use might play a contributory causal role in precipitating and exacerbating bipolar disorders,⁴⁸ but the evidence is not as strong as that for daily cannabis use and schizophrenia. There are fewer prospective studies of daily cannabis use and bipolar disorders, their findings are less consistent, and few of these studies have controlled well for confounding variables or ruled out the hypothesis of reverse causation.⁴⁸ Few genetically informed studies exist to exclude the possibility that the association is explained by shared genetic risks for regular cannabis use and developing bipolar disorders.^{48,53,54}

Cannabis use and depressive disorders

People who have depressive disorders report higher rates of cannabis use disorder and of regular cannabis use than people without depressive disorders,^{52,55} but the strength of association is modest in longitudinal studies.⁵⁶ A systematic review estimated the OR of depression among people who use cannabis to be 1.29 (95% CI 1.13–1.46).⁵⁷ Although it appeared that people who used cannabis heavily were more likely to report symptoms of depression than non-heavy consumers, the CIs included the null value and thus, the difference was not significant. There was inadequate control of potential confounders related to the outcome of depression, and interpretation was complicated because different studies used different measures of cannabis use and depression.

Systematic reviews of prospective studies of the association between patterns of cannabis use and the clinical course of depressive disorders find that people who are depressed and have cannabis use disorder report more severe symptoms of depression than those without cannabis use disorder.⁵² A meta-analysis found a consistent association between cannabis use at baseline among young people and depression at follow-up, which persisted after adjusting for potential confounders.⁵⁸ It also found a stronger association between cannabis use

in adolescence and depression at follow-up (OR=1.33 [95% CI 1.19–1.49]) than between depression at baseline and later cannabis use (OR=1.03 [1.01–1.05]).⁵⁸

There is unclear evidence on the plausibility of a causal role for regular cannabis use in depression incidence or prevalence. Animal studies suggest that the endo-cannabinoid system interacts with the serotonergic system in ways that could affect symptoms of depression, but the relevance of this evidence to humans is uncertain.^{59–62} A few studies have used genetically informed designs, such as discordant twin studies,⁶³ to test the hypothesis that association between regular cannabis use and depression can be explained by shared genetic risk factors.⁵⁵ A Mendelian randomisation study has suggested that cannabis use disorder could play a causal role in depressive disorders.⁶⁴

Cannabis use and anxiety disorders

There are very few longitudinal studies of relationships between regular cannabis use and anxiety disorders, and meta-analyses of these studies have come to different conclusions. Gobbi and colleagues reported a meta-analysis of three longitudinal studies of anxiety in young adults in the USA.⁶⁵ They found no significant increase in the risk of anxiety disorders among people who used cannabis (OR=1.18 [95% CI 0.84–1.67]). Zimmerman and colleagues' review of four longitudinal studies found a small association between cannabis use and social anxiety disorders and symptoms of acute anxiety, but mixed results for generalised anxiety disorders.⁶⁶

Burke and colleagues⁹ conducted a systematic review and meta-analysis of longitudinal studies of general population samples that assessed cannabis use and anxiety disorders, including only studies that excluded participants with anxiety symptoms at baseline. Cannabis use was not associated with incident anxiety disorder in estimates from seven studies (risk ratio [RR]=1.10 [95% CI 0.99–1.22]).⁹ Lowe and colleagues⁶⁷ reported a systematic review and meta-analysis of prospective studies of population samples of individuals in early (age 13–16 years) or late (age 17–19 years old) adolescence who did not have a physical or mental health disorder at baseline. Quantitative analysis of six longitudinal studies found an association between adolescent cannabis use and the later development of an anxiety disorder (OR=2.14 [95% CI 1.37–3.36]). A sensitivity analysis restricted to five studies that controlled for comorbid substance use produced similar results (OR=2.38 [1.34–4.20]).⁶⁷

Overall, some studies have reported modest associations between cannabis use and anxiety disorders. Few have assessed the regularity of use. These modest associations might reflect shared risk factors for anxiety and cannabis use disorders, or reverse causation (eg, people with anxiety using cannabis to self-medicate and subsequently developing a cannabis use disorder). It also remains unclear whether cannabis use adversely affects the course of anxiety disorders or treatment compliance.

There is preclinical evidence that cannabis interacts with the endocannabinoid system. Cannabis use during adolescence could impair the endocannabinoid system, affecting brain development and neurotransmitter function, and high-potency cannabis could increase the risk of anxiety symptoms.⁶⁸ The preclinical evidence also suggests that low to moderate activation of CB1 receptors could reduce anxiety and hyperactivity in stress-related brain circuits, whereas high THC doses increase anxiety, and chronic THC exposure downregulates CB1 receptors and might produce rebound anxiety on cessation of use.

Cannabis and suicidal behaviour

Systematic reviews and meta-analyses addressing the relationship between cannabis use and suicidal behaviour are based on a small number of longitudinal studies. A meta-analysis of longitudinal studies of cannabis use by adolescents reported a modest association between cannabis use and later suicidal ideation (OR=1.50 [95% CI 1.11–2.03]) and a stronger association with suicide attempts (OR=3.46 [1.53–7.84]).⁶⁵ However, these estimates were based on only three studies in each case. Athey and colleagues conducted a meta-analysis of longitudinal studies and found that individuals with diagnosed cannabis use disorder had an elevated risk of suicide mortality (standardised mortality ratio=3.31 [1.42–7.70]).⁶⁹ Maviel and colleagues systematically addressed the evidence in 25 studies of adolescents and adults on the extent to which an association between regular cannabis use and suicidality was mediated by depression.⁷⁰ They reported that 12 of 25 studies found no association between cannabis use and suicidality after adjusting for depression, concluding there were too few well controlled studies to decide whether the relationship was moderated or mediated by depression.⁷⁰

Assessing the coherence of the evidence on cannabis and anxiety, depression, and suicidal behaviour

The associations between cannabis use and anxiety, depression, and suicidal behaviours are modest in prospective studies. For depression, the association might be explained by confounding factors that have not been well controlled in many studies.^{56,57,71} For anxiety disorders, systematic reviews showed mixed results, with some finding small positive associations⁶⁷ and others finding no significant associations after controlling for confounders.⁹ Self-medication is a possible explanation for the higher prevalence of depression and anxiety among people who use cannabis.⁵⁵ Associations have been reported for suicidal ideation, suicide attempts, and mortality with cannabis use disorder,^{65,69} but estimates are based on very few studies.

A bidirectional relationship is a plausible explanation of the associations between cannabis use and anxiety and depression. Cannabis use could alleviate low mood and

reduce anxiety through its positive subjective effects, but this might come at the cost of increasing the risk of cannabis use disorder. A cannabis use disorder might worsen depressive and anxiety symptoms by impairing the person's ability to cope with the demands of daily life or comply with treatments for their anxiety and depression, such as cognitive behaviour therapy or medication.

Interventions

Given the high rates of comorbidity between cannabis use disorder, psychosis, bipolar, anxiety, depression, and suicidal behaviour and evidence that cannabis use could worsen their clinical courses, it would be prudent for clinical services to screen for symptoms of cannabis use disorder among people with these mental disorders. The WHO screening instrument ASSIST is a short self-report scale that can alert clinicians to the possibility of high risk patterns of cannabis and other drug use, that could be exacerbating symptoms of these disorders.⁷² Given the consistent evidence that continued cannabis use worsens clinical outcomes,⁷³ it would also be prudent to encourage people with these mental disorders to cease using cannabis or reduce their frequency and amount of use and to use cannabis products with lower concentrations of THC. Clinicians should be aware that cannabis withdrawal symptoms can worsen the symptoms of people with severe mental disorders who cease using cannabis during mental health treatment.⁷³

Given the widespread availability of cannabis for medical use in increasing numbers of jurisdictions, patients with these disorders should be asked whether they have been recommended or prescribed cannabis as a medicine and assess how it interacts with their mental health. The efficacy and safety of cannabinoids for mental health and substance use disorders are covered in this collection by Wilson and colleagues.⁷⁴

Individuals with a cannabis use disorder and a comorbid mental disorder face complex challenges in addressing both types of disorder. There is scarce research on the effectiveness of treatment, prevention, and harm reduction strategies, and there are major gaps in the research literature. A systematic review of clinical trials indicates that psychosocial treatments, such as cognitive behavioural therapy (CBT) and motivational enhancement therapy, can reduce the frequency of cannabis use and the severity of symptoms of cannabis use disorder.⁷⁵ However, the review excluded studies that recruited participants with comorbid disorders, a common practice in clinical trials of cannabis use disorder treatments. In a systematic review of people with co-occurring mental disorders, contingency management was effective in reducing cannabis use among individuals with psychotic-spectrum disorders or major depressive disorder, but the evidence was based on small samples with short follow-up periods, and treatment effect maintenance requires further research.⁷⁶

There is some evidence that co-occurring mental illness can reduce the efficacy of treatments for cannabis use

disorder and vice versa. Anxiety symptoms are associated with increased severity of withdrawal symptoms from using cannabis,⁷⁷ depression is associated with a lower likelihood of cannabis abstinence after a cessation attempt,⁷⁸ and people with psychosis who use cannabis have poorer clinical outcomes.^{14,79} Targeted treatments have been developed to address both cannabis use disorder and mental health comorbidity, and there is some evidence from RCTs (reviewed below) that they reduce cannabis use and symptoms of the mental health condition. Larger studies in more representative samples are needed to assess the effectiveness of these interventions.

Psychosis

A 2013 trial of targeted treatments for psychosis and cannabis use did not find motivational interviewing combined with CBT more effective than treatment as usual.⁸⁰ Contingency management also did not appear to improve the effects of psychoeducation.⁸¹ However, a subsequent RCT of individuals with first episode psychosis found that 16 weeks of specific CBT-cannabis cessation (CBT-CC) for a reduction in cannabis use was more effective than treatment as usual that included pharmacotherapy and general CBT.⁸² Reduction in the severity of cannabis use was significantly higher in the CBT-CC group than in those receiving treatment as usual over a 12-month period ($\chi^2=34.34$, $p<0.001$). Patients who reduced or stopped using cannabis showed significantly fewer psychotic symptoms ($\beta=-0.754$; $p=0.022$). A recent systematic review and meta-analysis of 35 RCTs of psychosocial interventions for people with schizophrenia and co-occurring substance use disorders found no significant effect on reducing symptoms (standardised mean difference=-0.11 [95% CI -0.27 to 0.05]) and substance use (SMD=-0.01 [-0.21 to 0.18]).⁸³ A pilot study of a smartphone application for self-guided psychosocial intervention focusing on behaviour change found that both the intervention and standard care control groups used more cannabis harm reduction strategies and increased motivation to change, and the intervention group had larger reductions in cannabis-related problems at 12-week follow-up.⁸⁴

Integrated treatment of cannabis use disorder and psychosis

Patients with schizophrenia and comorbid cannabis use disorder have traditionally been treated by different clinicians who work in separate psychiatric treatment and substance use services, but this approach is associated with poor treatment outcomes. Integrated approaches involve the same clinicians or care team providing coordinated substance misuse and mental health treatment. A review of 35 clinical trials found that comprehensive, integrated outpatient treatment programmes better engaged dually diagnosed patients in services and helped them reduce their substance use and reach remission more effectively than parallel treatment.⁸⁵

Other mental disorders

There have been few RCTs of treatments for cannabis use disorder in people who have comorbid anxiety, depression, or suicidality. Antidepressant treatments have not been shown to reduce comorbid cannabis use disorder and depression.^{86,87} Motivational interviewing combined with CBT tailored for cannabis use and depressive symptoms resulted in greater reductions in both types of symptoms than a brief intervention.⁸⁸

One RCT examined the efficacy of integrated CBT for individuals with cannabis use disorder and an anxiety disorder.⁸⁹ Participants who received the integrated treatment showed significantly greater reductions in cannabis use and anxiety symptoms than those who received standard treatments. An RCT with young adults aged 18–25 years with major depressive disorder and general anxiety disorder compared waitlist to a text message-delivered intervention informed by motivational interviewing for treating cannabis use disorder.⁹⁰ Cannabis use declined significantly in the treatment condition only among individuals with subthreshold depression or anxiety, not among those meeting disorder criteria. These results suggest that early and integrated intervention can lead to favourable outcomes for individuals with dual diagnoses, but it remains unclear whether treatment effects apply to those with more severe depressive or anxiety disorders. More RCTs are needed to strengthen the evidence base for treatment of cannabis use disorder with mental health comorbidities and guide the design of personalised psychosocial and pharmacological approaches.

Prevention and harm reduction

Preventive interventions delivered in schools or via the internet have been found to be effective at reducing cannabis uptake in young people.^{91,92} The effectiveness of these interventions in reducing cannabis use disorders in young people with mental health vulnerabilities who might use cannabis to self-medicate symptoms of anxiety and depression needs to be investigated.

Conrod and colleagues⁹³ recently reported a 5-year follow-up of a programme that aimed to prevent the development of substance use disorders in school-aged children by matching cognitive behavioural interventions to four personality traits associated with an increased risk of early use of cannabis and other substances, namely, impulsivity, sensation seeking, anxiety sensitivity, and hopelessness. They found a 35% reduction in the annual prevalence of substance use disorder in the intervention condition relative to the control condition. Molina noted that this translated into a reduction in substance use disorder risk of one student for every 52 at-risk students who received the intervention.⁹⁴ The programme had no significant intervention effects on anxiety, depression, or an overall index of mental health difficulties.⁹³

Harm reduction approaches aim to reduce the likelihood that a young person who uses cannabis will

Panel 2: Lower-Risk Cannabis Use Guidelines⁹⁵**General precautions**

- People who use cannabis (PWUC) need to know that there is no universally safe level of cannabis use; thus, the only reliable way to avoid any risk for harm from using cannabis is abstinence
- Frequent cannabis use, and especially intensive use over long periods, can lead to a cannabis use disorder or cannabis dependence that could require treatment
- PWUC should exercise social consideration and responsibility in avoiding cannabis use that could result in harm to others

Recommendations

- 1 The initiation of cannabis use should be delayed until after late adolescence to reduce development-related vulnerabilities for harm
- 2 PWUC should use low potency cannabis products
- 3 All main available modes of use come with some risk for harm; PWUC should refrain from cannabis smoking and employ alternative options for pulmonary health protection
- 4 If use occurs by inhalation, PWUC should avoid deep inhalation or prolonged breath holding
- 5 PWUC should refrain from frequent or intensive cannabis use
- 6 Where circumstances allow, PWUC should use legal and quality controlled cannabis products
- 7 PWUC who experience impaired cognitive performance should consider suspending or substantially reducing the intensity of their cannabis use
- 8 PWUC should avoid driving a motor vehicle or operating machinery under the influence of cannabis
- 9 People planning to have children, as well as people who are pregnant or breastfeeding, should avoid cannabis to reduce risks to reproduction and child health
- 10 PWUC should exercise general caution in combining other psychoactive substances with cannabis
- 11 Specific groups of people who are at elevated risk for cannabis use-related health problems should avoid or adjust their cannabis use
- 12 The combination of risk factors for adverse health outcomes from cannabis use further amplifies the likelihood of experiencing severe harms and should be avoided

develop a cannabis use disorder or experience other harms. A widely disseminated set of guidelines are the Lower-Risk Cannabis Use Guidelines⁹⁵ (panel 2). Specific advice is available on how to reduce psychosis risk.⁹⁶ Research is needed on how best to use these guidelines to reduce cannabis use disorders among people with mental health conditions.

There is a large evidence gap on effective prevention and harm reduction in people with comorbid mental

Panel 3: Priorities for research on cannabis use disorders and mental disorders

- Epidemiological studies with longer follow-ups and larger sample sizes than current studies are needed to assess the role that cannabis use disorders play in the onset and outcomes of anxiety, depression, psychosis, bipolar disorders, and suicidal behaviours
- These studies should measure cannabis use precisely to determine dose-dependent risks
- Given the high rates of comorbidity, we urgently need research on how best to screen for cannabis use disorders in patients with anxiety, depression, psychosis, and bipolar disorders
- Integrated treatment approaches for cannabis use disorders and mental disorders show promise, but we need larger trials to replicate their findings and assess the feasibility of their routine clinical use
- There is an urgent need to develop practical treatment models and to provide clinicians with the resources and training to manage these cases
- We need to develop more effective methods to prevent cannabis use disorders in people with mental disorders and reduce the harms experienced by those who have cannabis use disorders

health disorders. More effective interventions could substantially reduce the incidence and prevalence of mental disorders and cannabis use and their burden on the people who have these disorders.

The value of lived experience

It is crucial to consider the lived experience of people with comorbid cannabis use and mental disorders when designing treatment, prevention, early intervention, and harm reduction. This Review's lived experience expert author, AG, provides an autobiographical account of developing psychotic symptoms following regular cannabis use as a young adult in the appendix (pp 6–8). He describes the short-term perceived benefits of cannabis, including enhanced social identity and confidence, before gradually becoming increasingly withdrawn, fearful, and preoccupied with persecutory ideas. His experiences illustrate the difficulty many individuals face in recognising the role of cannabis in the development or worsening of symptoms and the powerful social and psychological meanings attached to cannabis use. This pattern is consistent with qualitative studies in which people report using cannabis to cope with distress, improve mood, reduce voices or anxiety, and manage difficult life experiences, despite emerging harms.^{97–99}

AG describes years of recurrent hospitalisation, persistent hallucinations, and severe psychological distress, including suicidal thoughts. Similar lived experience research has documented paranoia, altered perceptions, unusual beliefs, anxiety, and social

withdrawal associated with use of cannabis or synthetic cannabinoids.^{98,100} Individuals often report that cannabis provides only temporary relief, with symptoms returning or worsening after intoxication, and describe the effects as unpredictable and context dependent.⁹⁹

A central turning point in AG's recovery was recognising a consistent pattern of symptom exacerbation following cannabis use ("for me, weed meant hospital"; appendix p 7). This insight, together with family support, enabled him to stop using cannabis, after which he reported substantial improvement in psychotic symptoms, increased treatment engagement, and gradual rebuilding of functioning. Similar trajectories are described in other lived experience accounts, where understanding the cannabis–symptom relationship and reducing or ceasing use are associated with clinical improvement.¹⁰¹

Overall, lived experience evidence highlights the need for non-judgemental, collaborative care that acknowledges both the perceived benefits and harms of cannabis, supports insight into use and symptom patterns, and involves families where appropriate.

Conclusions

There is credible evidence that regular cannabis use plays a contributory causal role in psychosis. There is a consistent association between the frequency and duration of cannabis use and psychosis risk, and a causal relationship is biologically plausible. The evidence is less clear for anxiety, depressive and psychotic disorders (table). Cannabis use is associated with poorer clinical outcomes in people with bipolar disorder and depression. Associations with the onset of anxiety, depression, and suicidality are modest and could reflect self-medication, shared risk factors, or bidirectional relationships.

Higher quality studies with longer follow-ups and larger sample sizes are needed to assess rare outcomes such as suicide (panel 3). Standardised measurement of cannabis use and mental disorder symptoms should be used, and cannabis use should be measured more precisely to establish dose-dependent risks. Better quality in control for potential confounding is needed, with further efforts to triangulate evidence across different study designs with non-overlapping sources of bias.

Large evidence gaps remain in prevention, harm reduction, and treatment for co-occurring cannabis use disorders and mental disorders. Many health-care settings do not adequately address these comorbid conditions. Given the high comorbidity between cannabis use disorder and common mental disorders, it would be prudent for clinicians to screen for cannabis use disorder in patients with mental health conditions. Integrated treatment approaches show promise, but these trials require replication and studies of the feasibility of implementing this approach in routine clinical practice. There is an urgent need to develop practical treatment models and clinicians should be

provided with the resources and training to manage patients with comorbid cannabis use disorders so that they no longer experience avoidable worsening of mental health outcomes.

Contributors

Conceptualisation: WH, EH, YLH, JL, JW, and TPF. Investigation: WH, TMY, RLT, EH, CB, AG, YLH, JL, JW, and TPF. Methodology: WH, TMY, RLT, EH, CB, YLH, JL, JW, and TPF. Project administration: WH, TMY, and TPF. Supervision: WH, JL, and TPF. Validation: AG (lived-experience input). Visualisation: WH, TPF, and JL. Writing original draft: WH, TMY, RLT, EH, CB, AG, YLH, JL, and TPF. Writing review and editing: WH, TMY, RLT, EH, CB, AG, YLH, JL, JW, and TPF. Final approval and accountability for the work: WH, TMY, RLT, EH, CB, AG, YLH, JL, JW, and TPF.

Declaration of interests

WH reports providing expert advice to WHO on the adverse health effects of cannabis and providing expert testimony in a criminal trial on the harms of adolescent cannabis use. EH reports royalties from a treatment manual (CANDIS), funding from the European Council for training on the treatment of cannabis use disorders, and an unpaid leadership role as President of the German Association of Addiction Research and Therapy. YLH reports grant support from the US National Institutes of Health (DA055434) to the Icahn School of Medicine at Mount Sinai, and honoraria for a presentation at the Wisconsin Emotion Symposium. All other authors declared no conflicts of interest.

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