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## Co-use of Alcohol and Cannabis: A Review

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### Abstract

**Purpose of Review**—The purpose of this review is to provide an overview of the existing literature on the relationship between the co-use of cannabis and alcohol including (1) epidemiology, comorbidity, and associated consequences of cannabis and alcohol use disorders; (2) preclinical and clinical laboratory studies examining behavioral pharmacology of cannabis and alcohol co-use; and (3) clinical outcomes related to co-use.

**Recent Findings**—Findings from the literature reviewed suggest that the co-use of alcohol and cannabis is associated with additive performance impairment effects, higher and more frequent consumption levels, increased social and behavioral consequences such as driving while impaired, and greater likelihood of the experiencing comorbid substance use and mental health disorders. Furthermore, co-use may be associated with worse clinical outcomes, yet there are few studies examining the development and evaluation of interventions on reducing the co-use of cannabis and alcohol.

**Summary**—There is a need for more rigorous and longitudinal research studies on the co-use of cannabis and alcohol to glean a more complete understanding of the relationship between the two substances. Findings can be used to develop and refine intervention strategies to successfully reduce cannabis and alcohol co-use.

### Keywords

Cannabis; Alcohol; Co-use; Behavioral pharmacology; Comorbidity; Clinical outcomes

### Introduction

Co-use of cannabis and alcohol is highly prevalent nationwide [1–3]. Among alcohol drinkers, cannabis is the most widely used drug [4] with about 58% of adolescent drinkers

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reporting marijuana use [14]. Similarly, over 75% of cannabis users also report consuming alcohol [5–7]. Approximately one half of young adult cannabis users report simultaneous use of alcohol and cannabis, in which users consume both substances during the same occasion [8, 9], placing them at increased risk to experience problems associated with their co-use [10]. Moreover, large-scale national surveys indicate that individuals with a lifetime cannabis use disorder (CUD) diagnosis are at an elevated risk for developing a comorbid alcohol use disorder (AUD) [1–3].

The use of both alcohol and cannabis concurrently (general use of both substances) and simultaneously (use of both substances at the same time) is of particular concern because it is associated with greater social consequences, higher rates of AUD, and increased prevalence of mental illness [11]. With ongoing policy changes surrounding the legalization of cannabis use, examining the influence of co-use on alcohol and cannabis use patterns, CUD and AUD severity, and associated cannabis and alcohol problems becomes increasingly important. Legislation in 28 states and the District of Columbia now authorizes use of medical and/or recreational cannabis use [12]. Consequently, it is imperative to gain a better understanding of how the effects of co-use influence behavior and the impact of co-use on public health. Hence, the purpose of this review is to provide an overview of the existing literature on the relationship between the co-use of cannabis and alcohol. Specifically, we will review (1) epidemiology, comorbidity, and associated consequences of CUD and AUD; (2) preclinical and clinical laboratory studies examining behavioral pharmacology of cannabis and alcohol co-use; and (3) clinical outcomes related to co-use. This review included studies across age groups and included both simultaneous use (alcohol and cannabis ingested during the same occasion) and concurrent use (use of both substances but not necessarily during the same episode). Because studies examining simultaneous use are rare and limited to adolescent and young adult populations [6, 9, 13–15], we will refer to both simultaneous and concurrent use as co-use throughout this review (unless the differentiation is relevant to study findings). Articles were identified using PsychINFO, PubMed, and Google Scholar with search terms cannabis, marijuana, alcohol, co-use, dual use, simultaneous use, and concurrent use.

## **Epidemiology, Comorbidity, and Associated Problems of Cannabis and Alcohol Use Disorders**

### **Prevalence and Comorbidity of Cannabis and Alcohol Use Disorders**

Rates of illicit drug/alcohol use disorders and treatment admissions are highest among co-users of cannabis and alcohol [16]. Individuals who have a current or lifetime diagnosis of cannabis use disorder (CUD) are at increased likelihood for the development of an AUD; [17–20] with approximately 68% of individuals with current CUD and over 86% of those with a history of CUD meeting current criteria for an AUD [17, 21]. Cannabis dependence doubles the risk for long-term persistent alcohol consequences [22] and among adults with no history of AUD, cannabis use was associated with increased incidence of AUD 3 years later compared to no cannabis use [23]. Similarly, a comorbid diagnosis of AUD and CUD is associated with riskier drinking patterns and increased cannabis-related problems than having a single diagnosis [10].

### **Consumption Level Related to Co-use**

With respect to severity of use, recent studies show that when cannabis and alcohol are consumed during the same occasion, higher quantities of both substances are used and they are used more frequently compared to when either substance is consumed concurrently or alone [9, 13]. Generally, higher levels of consumption or an increase in consumption of one substance is related to higher levels of or an increase in use of the other substance. For example, individuals using higher levels of cannabis reported higher levels of alcohol relative to those using lower amounts of cannabis. Among college-aged drinkers, lifetime and past year use of cannabis increased as level of alcohol consumption increased [24, 25].

### **Problems and Behavioral Consequences Associated with Co-use**

The co-use of cannabis and alcohol is more harmful and associated with more overall consequences compared to the use of either substance alone [9, 26]. Studies have noted the association between alcohol consumption and alcohol-related problems is stronger among co-users than among those who use alcohol only [27]. Co-users consume higher levels of alcohol and experience more alcohol-related consequences [26, 28–32] and report increased cannabis use and cannabis-related consequences [33]. Additionally, heavier dual use of cannabis and alcohol during adolescence is associated with more negative outcomes in adulthood including substance use dependence, involvement in the criminal justice system, and low rates of high school graduation compared to no use or using either substance alone [26]. Co-use is associated with a variety of personal, academic, and social consequences [9, 13], including higher likelihood of arrest, depressive symptoms [34], and impulsivity [35]. Another study found that daily co-use of alcohol and cannabis places individuals at the highest risk of injuries and negative consequences compared to daily use of either alcohol or cannabis alone in combination with weekly use of the other substance [36]. In contrast, weekly use of both cannabis and alcohol was associated with the lowest risk [36]. High risk sex behavior has also been linked with co-use of cannabis and alcohol [37]. In women, alcohol exacerbates problems typically attributed to cannabis use [38] and women with low sexual assertiveness refusal were more likely to engage in risky sex on days when they had consumed both alcohol and cannabis prior to the sexual activity [39].

### **Prevalence and Impact of Driving Under the Influence of Alcohol and Cannabis**

Research suggests that co-use of alcohol and cannabis has synergistic effects over and above additive risk, as is evinced in the impaired driving literatures. As compared to alcohol drinkers, co-users exhibit twice the risk of driving under the influence [9]. One study conducted in France indicated that approximately 40% of sampled drivers under the influence of cannabis and involved in fatal accidents, also exceeded the legal limit for alcohol [40]. This is consistent with research demonstrating the combined effect of cannabis and alcohol compared to either alone may have the biggest influence on driving tasks [41]. High school seniors who used cannabis and alcohol together had the highest rates of unsafe driving compared to students who co-used the substances less frequently [15]. Bramness et al. [42] conducted a retrospective cross-sectional forensic database study examining drivers apprehended by the police suspected of driving under the influence of alcohol and other drugs. Researchers found that cannabis impairs driving ability in a dose-response manner,

though the effect was smaller than for alcohol. However, when THC and alcohol were both on board, the risk of being deemed impaired greatly increased. Research on the prevalence of driving under the influence of both alcohol and cannabis is particularly important of late as driving under the influence of cannabis has increased in states with cannabis legislation [43, 44] with concomitant increase in rates of driving under the influence of both alcohol and cannabis [45]. Risk of motor vehicle accident rises significantly with increasing cannabis dose and use frequency [44], and the influence of increasing dose is particularly disquieting as potency of recreationally available cannabis has increased significantly in recent years [46, 47].

### **Other Psychiatric Disorders and Mental Health Symptoms Related to Co-use**

The use of cannabis and alcohol concurrently and separately is also associated with higher rates of psychiatric disorders and symptom severity [48]. Having a CUD is associated with the occurrence of other substance use disorders (SUD), mood disorders, anxiety disorders, post-traumatic stress disorder (PTSD), and personality disorders [49••]. This is important because having a mental health diagnosis is a risk factor for the initiation of both alcohol and cannabis use, as well as drug and alcohol-related problems [50].

### **Co-use and Adolescent Brain Development**

Research regarding the impact of cannabis and alcohol consumption on adolescent brain development is mixed. One study found that adolescent co-users evidenced less white matter abnormalities compared to just drinkers, suggesting the potential for cannabis to have some neuroprotective factors [51]. Other research, however, demonstrates that cannabis and alcohol use may contribute to atypical cortical development [52, 53] which may increase vulnerability to mental health difficulties and co-occurring SUDs in adulthood [54, 55] compared to use of either substance alone or non-users. These findings may be explained by a pre-existing vulnerability that is exacerbated by substance use. In addition to atypical brain development, patterns of elevated alcohol and cannabis use in adolescence may slow or diminish the natural development of psychosocial maturity from adolescence to young adulthood [56]. Hence, co-users may be less likely to develop the skills necessary to function independently and engage in appropriate social interactions compared to those who do not use during adolescence. Fortunately, decreased use is associated with increases in maturity [56].

## **Behavioral Pharmacology of Cannabis and Alcohol Co-use**

### **Preclinical Research**

Preclinical and experimental research can be utilized to better understand the complex relationship between the co-use of cannabis and alcohol and related consequences. Emerging preclinical evidence demonstrates that the endocannabinoid system, which regulates cannabis reinforcement, is also involved in alcohol reinforcement, motivation to consume alcohol, excessive alcohol consumption, and alcohol dependence [57–60]. Furthermore, preclinical studies show that antagonists of the cannabinoid receptors and inhibitors of the enzymatic degradation of endocannabinoids dampen both preference for and overall intake of alcohol [61, 62]. In contrast, cannabinoid receptor agonists and endocannabinoids serve to

escalate alcohol-seeking behavior and consumption [63, 64]. Over time, chronic exposure to alcohol contributes to elevated endocannabinoid levels, which in turn leads to downregulation of the cannabinoid receptor signaling [58, 64]. Overall, these findings from preclinical research support the existence of potential cross-tolerance between cannabis and alcohol and have important translational implications for clinical research. For example, involvement of the endocannabinoid system in alcohol reinforcement is particularly relevant for prevention and intervention studies, as well as research devoted to identifying biological and pharmacological pathways explicating potential reasons for co-use of cannabis and alcohol and the progression to problematic substance use.

### **Clinical Research on Behavioral Performance Impairment from Co-use**

Much clinical research has focused on behavioral performance impairment that results from co-use of both cannabis and alcohol. Chait and Perry [65] conducted a study wherein alcohol and cannabis were administered to participants (four conditions: alcohol, cannabis, alcohol and cannabis in combination, and no active treatment) and effects on mood and behavior the day after administration were investigated. Cannabis and alcohol alone produced moderate subjective intoxication and behavioral impairment, while weak evidence was obtained for subjective or behavioral effects the day after active drug treatments. Combined alcohol and cannabis yielded the greatest impairment levels on most tasks as well as higher subjective ratings of intoxication. Few significant interactions were observed between the two drugs, suggesting presence of additive effects. In another study by Chait and Perry [66], the effect of acute alcohol consumption on subsequent cannabis use was evaluated. Alcohol and cannabis users were administered alcohol beverages (0.0, 0.3, or 0.6 g/kg) 30 min prior to a 60-min ad libitum cannabis smoking session. Cannabis self-administration was not dose-dependently affected by the alcohol pretreatments. Thus, it appears that alcohol may not impact motivation to self-administer cannabis in a dose-dependent manner; however, more research is still required to determine the effect of cannabis administration on subsequent alcohol consumption.

Other laboratory research has been used to examine driving-related skills and performance following co-administration of both alcohol and cannabis. Perez-Reyes and colleagues [67] conducted an investigation examining the interaction between alcohol and cannabis on plasma concentrations, subjective intoxication, and psychomotor performance. Alcohol (0.42 g/kg, 0.85 g/kg, or placebo) was administered to participants over 30 min, and cannabis (2.4% THC or placebo) was administered 15 min later. Findings from this research suggested that the performance impairment of driving-related skills attributed to alcohol were potentiated by cannabis. However, alcohol administration before cannabis administration did not significantly impact subjective ratings of “high,” heart rate, or THC plasma concentration. Similarly, Ramaekers et al. [68] assessed the separate and combined effect of alcohol and cannabis administration on driving performance during a balanced, 6-way, crossover design investigation. During separate sessions, participants were administered cannabis (0, 100, or 200 µg/kg) with and without alcohol administration (0.04 g/dl) and subsequently completed actual driving tasks. Cannabis and alcohol alone significantly impaired performance in the driving tasks, and the combination of cannabis and alcohol impaired driving performance to a greater degree. In another study by Ramaekers et

al. [69], heavy cannabis users were recruited for a double-blind, placebo-controlled, three-way examination of tolerance and cross-tolerance to the neurocognitive effects of cannabis and alcohol. Subjects completed three alcohol conditions intended to sustain steady blood alcohol concentrations (0, 0.5, and 0.7 mg/ml) over 5 h. Three hours post-alcohol administration onset, participants were administered cannabis (400 µg/kg). Alcohol significantly impaired driving-related skills including critical tracking, divided attention, and stop-signal performance. While cannabis alone had minimal effect on performance, again the combined impact of cannabis and alcohol on divided attention were greater than those by alcohol alone.

Recent research has employed advanced simulated driving methods to assess the effects of cannabis and alcohol co-use. Hartman and colleagues [70] investigated the effect of cannabis on driving with and without alcohol on THC blood concentrations in a within-subject study with six conditions. Participants drank alcohol (placebo or low dose) and inhaled 500 mg vaporized cannabis (placebo, 2.9%, or 6.7% THC) ad libitum for 10 min before completing a driving simulation. An interaction between cannabis and alcohol was observed in time spent at high speed; thus, cannabis may have diminished the propensity to increase driving speed following alcohol consumption. Further complicating the relationships among cannabis, alcohol, and driving, while an alcohol breathalyzer can be used to measure approximate blood alcohol concentrations in potentially impaired drivers, no acceptable roadside test exists for assessing recent cannabis use. Taken together, research concerning the behavioral performance impairment that occurs from co-use of alcohol and cannabis suggests that users experience additive performance impairment above and beyond effects occurring after either substance alone.

### **Clinical Research on Pharmacokinetic Interactions of Co-use**

Much clinical research on co-use of cannabis and alcohol has been concerned with investigation of pharmacokinetic interactions between the two drugs. Lukas and colleagues [71] assigned casual cannabis and alcohol users to a cannabis dose group (placebo, 1.26% THC, or 2.53% THC). During three experimental sessions, participants consumed beverages with three separate alcohol doses (placebo, 0.35, and 0.7 g/kg) and smoked cannabis corresponding to their assigned cannabis group 30 min later. Cannabis slowed the absorption of alcohol, and subsequently reduced the psychoactive effects of alcohol, ultimately suggesting that cannabis may change the bioavailability of alcohol. Using similar methodology, a second study suggested that plasma THC levels were significantly increased when subjects first consumed alcohol [72]. Compared to placebo, the combination of a low cannabis dose (2.53% THC) and low alcohol dose (0.35 g/kg) increased the number and duration of positive subjective effects, and resulted in higher plasma levels of THC. In contrast, the low cannabis dose combined with a high alcohol dose (0.7 g/kg) dampened the rise in plasma alcohol levels and ultimately decreased the number and duration of positive subjective effects despite the high peak in THC plasma levels. Ballard and de Wit [73] also conducted a study assessing whether the combination of low alcohol doses (placebo, 0.1, or 0.2 g/kg) and oral THC (placebo and 2.5 mg THC capsules) produced synergistic effects on subjective, cognitive, and physiological measures. The effects of alcohol and THC were evaluated alone, and in combination, across separate sessions, in a within-subjects,



randomized, double-blind design. The authors reported no evidence for synergistic effects of acute combinations of very-low-dose alcohol and THC on subjective or physiologic response, or on cognitive performance. An interaction between ethanol and THC was observed, however, on ratings of desire to consume more of the administered drug. THC, when combined with ethanol, decreased the elevated ratings of wanting more ethanol after ethanol administration. Consequently, THC may either dampen ethanol's effects or replace desire for more. More laboratory work is needed to examine how cannabis affects motivation to use alcohol and vice versa.

More recent work has employed vaporized cannabis administration to investigate the effect of cannabis and alcohol co-use on subsequent cannabinoid plasma levels. Similar to findings reported by Lukas and Orozco [72], when alcohol was on board, significantly higher blood cannabinoid levels were detected [74••]. Similarly, blood THC concentration following cannabis vaporization and breath alcohol concentration were significantly associated with subjective drug effects with alcohol increasing the duration of the cannabis effects [75]. These findings may broaden our understanding of increased impairment typically observed following cannabis and alcohol co-administration relative to administration of either substance alone.

## **Treatment and Intervention of Cannabis and Alcohol Co-use**

### **The Influence of Co-use on Successful Treatment**

Although cannabis use is strongly linked with alcohol use, the direction of this relationship is unclear. For example, abstinence from cannabis has been associated with elevated alcohol craving and consumption of alcohol among individuals with AUD [76], suggesting initial preliminary evidence of substitution. Yet, individuals with more than one SUD tend to have an especially severe clinical course [77] and poor prognosis [78]. With the exception of a few studies that do not show cannabis use to negatively influence alcohol or smoking cessation outcomes in non-dependent drinkers [28, 79], many studies have demonstrated that using cannabis during alcohol treatment is associated with negative alcohol treatment outcomes at follow-up [80–83]. For example, among alcohol-dependent individuals, those who used cannabis during alcohol treatment reported fewer days abstinent from alcohol 1 year following treatment than those who did not use cannabis [83]. Thus, cannabis use may have a negative impact on alcohol treatment outcomes and individuals who use both substances seem to have poorer alcohol treatment response.

### **Treatment and Intervention for Co-use**

There is a substantial body of research examining the efficacy of pharmacotherapy and behavioral treatments for alcohol [84–88] or cannabis use disorders [78, 89–92]. To date, however, there is little research evaluating the efficacy of interventions specifically for the co-use of cannabis and alcohol. In the general adolescent population, family, individual, and group-based interventions have been shown to be efficacious in reducing substance misuse (alcohol, marijuana, and other illicit substances) among adolescents [93] with family-based models being the most frequently tested and supported. In emergency department patients, both standard care and a brief motivational intervention reduced cannabis and alcohol use

among co-users; however, only patients in the brief motivational intervention group sustained those reductions in the simultaneous use of alcohol and cannabis across time [94]. In college students, a behavioral economic supplemental session on alcohol consumption and cannabis use found no effect of treatment on alcohol consumption outcomes but did find a decrease in cannabis use days compared to an educational control condition [95].

With the intervention research on co-use of alcohol and cannabis lacking, some studies have begun to examine the secondary effects of alcohol-specific interventions on changes in cannabis use. A recent meta-analysis indicated that alcohol BMIs may not facilitate changes in cannabis use among college students [96]; instead, regardless of treatment condition, college students who successfully reduced their drinking at short- and long-term follow-ups were more likely to be non-users of cannabis or reduce their cannabis use at follow-up. This complementary relationship between cannabis and alcohol use is also supported by research indicating that the risk factors for initiation and maintenance of problematic use are similar across substances [97], and together suggest that individuals and interventions that successfully reduce alcohol consumption may lead to secondary changes in cannabis use. In the college setting, BMIs that target multiple substances have also been associated with reductions in poly-drug use [98–100].

## Discussion and Conclusion

This review is intended to be a synopsis of significant clinical and public health areas related to the co-use of cannabis and alcohol. In concert, findings from the literature reviewed suggest that the co-use of alcohol and cannabis is highly prevalent across age groups and is associated with higher and more frequent consumption levels, as well as increased risk for comorbid SUDs and mental health disorders (see Table 1 for summary of key findings). There has been an increase in driving under the influence of both alcohol and cannabis, as well as other social consequences. Furthermore, most clinical laboratory research on co-use or co-administration of cannabis and alcohol has found additive performance impairment effects with pharmacological interactions that impact impairment, absorption, bioavailability, and subjective effects. Although the co-use of cannabis and alcohol is related to worse clinical outcomes, the literature in this area is mixed. Furthermore, although co-use may negatively impact the treatment of other substances, interventions targeting both cannabis and alcohol use is scarce.

## Limitations of the Literature and Future Recommendations

Findings from preclinical research support the existence of potential cross-tolerance between cannabis and alcohol that may have important translational implications for clinical research. Although clinical studies consistently demonstrate increased cognitive and behavioral impairment from co-use at varying doses, interpretation of blood THC levels is complex due to rapidly decreasing concentrations immediately following smoking. With driving under the influence for example, blood THC concentrations obtained from drivers may be lower than set limits despite greatly exceeding them while driving. Further complicating interpretation, blood concentrations during driving cannot be back-extrapolated due to unknown time after cannabis use and individual variability in THC blood concentration trajectories [101].



Therefore, more laboratory research is needed on pharmacokinetic interactions between cannabis and alcohol and performance impairments from co-use. To date, research in this area has been constrained by a relatively low dose of cannabis administered relative to cannabis with much higher THC potency commonly in use today [46]. This increased potency has been implicated in worse behavioral outcomes including increased alcohol intoxication, yet has been largely left unstudied. This type of research is difficult to conduct, however, due to the classification of cannabis as a Schedule I substance that restricts researcher access to cannabis products [102].

One consistent finding from the literature is that co-use of cannabis and alcohol is associated with increased likelihood of current and future cannabis and/or alcohol use disorders. What is less certain is the directionality of cannabis and alcohol consumption on mental health disorders. Despite this ambiguity, what can safely be gathered from this body of research is that early and frequent use and co-use of cannabis and alcohol is associated with the development of more psychiatric-related problems than occasional use or nonuse. Until there is greater clarity in this area, however, clinicians should continue to screen patients for cannabis and alcohol use as well as mental health issues. This may be especially important with early adolescents whose co-use is linked to abnormal brain development [55] and may be at risk of increasing their cannabis use following current and upcoming changes in legalization [103]. The clinical significance of these associations illustrates the need for more longitudinal research on cannabis and alcohol co-use among adolescents such as the ongoing Adolescent Brain Cognitive Development (ABCD) study which is examining the brain and cognitive development, substance use, and behavioral and other health outcomes of over 10,000 children over the course of 10 years [104]. Similarly, the incorporation of advanced longitudinal data collection techniques like ecological momentary assessment will address the directionality issues concerning the co-use of cannabis and alcohol use on behaviors and clinical outcomes.

From a clinical standpoint, it appears co-use of cannabis and alcohol may negatively impact the successful intervention of both substances, yet there are few studies examining the development and evaluation of interventions on reducing their co-use. Motivational and brief interventions appear promising, but this may vary depending on population [28, 79, 96]. An added clinical concern is the association between co-use and psychiatric comorbidity. Hence, researchers and clinicians must consider ways to incorporate efficacious substance use intervention approaches with mental health treatments. Ultimately, there is a need for more rigorous and specific research methodology on the co-use of cannabis and alcohol to glean a more complete understanding of the relationship and clinical implications of the two substances. Findings from which can be used to better develop and refine intervention techniques that will result in the reduction of the public health issues associated with the co-use of cannabis and alcohol.

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**Table 1**

## Summary table

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Key research findings	
1	Co-use of cannabis and alcohol is highly prevalent across age groups
2	Clinical laboratory research on co-use or co-administration of marijuana and alcohol has found additive performance impairment effects
3	Co-use of cannabis and alcohol results in pharmacological interactions that impact impairment, absorption, bioavailability, and subjective effects
4	Co-use is associated with greater behavioral and social consequences
5	There has been an increase in rates of driving under the influence of both alcohol and cannabis in several states
6	Co-use is related to higher rates of cannabis and alcohol use disorders and increased prevalence of mental health disorders
7	Adolescents may be at increased risk for abnormal brain development from co-use
8	Co-use appears to negatively impact successful intervention and treatment of both substances
9	Despite a surplus of research evaluating interventions and treatments for each substance separately, few studies have examined interventions to reduce co-use
Limitations of prior research	
1	Research has been constrained by low THC doses available and permitted for administration in laboratory studies relative to cannabis with higher THC potency commonly in use today
2	Lack of longitudinal and methodologically rigorous studies that examine the influence of co-use on behavior, mental health symptoms, and other clinical outcomes
3	Few studies have examined the efficacy of treatments/interventions to reduce co-use of cannabis and alcohol
Recommendations for future research	
1	Research examining the influence of alcohol or marijuana on motivation to use the other substance and vice versa
2	Laboratory investigations investigating administration of THC doses comparable to potencies commonly used to date
3	Future longitudinal research examining long-term effects of co-use on development and outcomes in both adolescents and adults
4	Develop and evaluate integrated treatments for comorbid CUD/AUD and psychiatric disorders
5	Future clinical trials examining interventions on the reduction of co-use

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