

Can Cannabis be Considered a Substitute Medication for Alcohol?

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Abstract — **Aims:** Substituting cannabis for alcohol may reduce drinking and related problems among alcohol-dependent individuals. Some even recommend prescribing medical cannabis to individuals attempting to reduce drinking. The primary aim of this review is to assess whether cannabis satisfies the seven previously published criteria for substitute medications for alcohol [e.g. ‘reduces alcohol-related harms’; ‘is safer in overdose than alcohol’; ‘should offer significant health economic benefits’; see [Chick and Nutt \(2012\)](#) Substitution therapy for alcoholism: time for a reappraisal? *J Psychopharmacol* **26**:205–12]. **Methods:** Literature review. **Results:** All criteria appear either satisfied or partially satisfied, though studies relying on medical cannabis patients may be limited by selection bias and/or retrospective designs. Individual-level factors, such as severity of alcohol problems, may also moderate substitution. **Conclusions:** There is no clear pattern of outcomes related to cannabis substitution. Most importantly, the recommendation to prescribe alcohol-dependent individuals cannabis to help reduce drinking is premature. Future studies should use longitudinal data to better understand the consequences of cannabis substitution.

INTRODUCTION

Substitute therapies for tobacco (e.g. nicotine replacement therapy) and heroin (e.g. methadone) have been available for some time, while analogous substitutes for alcohol have been more elusive. A recent review of medication substitutes for alcohol defines seven criteria for substitution therapy ([Chick and Nutt, 2012](#)). At the same time, a growing number of studies suggest that cannabis could be considered as a substitute therapy for alcohol ([Mikuriya, 2004](#); [Charlton, 2005](#); [Reiman, 2009](#)). Some even suggest that medical cannabis be prescribed to individuals attempting to reduce alcohol use ([Mikuriya, 2004](#); [Charlton, 2005](#)). In light of the recent movements toward cannabis legalization in the USA, which imply that cannabis use may become more commonplace, especially among heavy drinkers ([Clements and Daryal, 2005](#)), we need to better understand whether cannabis can substitute for alcohol among individuals who are trying to reduce drinking.

This paper assesses whether cannabis satisfies conditions for substitution therapy according to the seven criteria outlined by [Chick and Nutt \(2012\)](#). Please note that although the impetus is to assess the viability of cannabis as a substitute treatment or medication, the majority of the studies cited do not necessarily regard medically prescribed cannabis. However, this is not a limitation *per se* because naturalistic cannabis use is probably more generalizable to ‘real-life’ conditions.

Criteria for substitution treatment and common substitution medications

[Chick and Nutt \(2012\)](#) recent review of medication substitutes outlined the following criteria for any substitution treatment:

- (1) It should reduce alcohol use and related harms.
- (2) It should ideally be free of harms, or at least less harmful than alcohol.
- (3) Misuse should be less than that of alcohol.
- (4) It should be shown that it can substitute for alcohol and not be used along with alcohol.

- (5) It should be safer in overdose than alcohol.
- (6) It should ideally not potentiate the effects of alcohol especially if either drug is taken in overdose.
- (7) It should offer significant health economic benefits.

Benzodiazepines and γ -aminobutyric acid (GABA) agonists have been considered the most promising substitutes for alcohol ([Chick and Nutt, 2012](#)). However, results from a series of studies by [Zack et al.](#) implied that benzodiazepines may prolong the risk of relapse ([Zack et al., 1999, 2006](#); [Poulos and Zack, 2004](#)). Furthermore, the American Psychiatric Association Task Force has cautioned against prescribing benzodiazepines to patients with a history of substance abuse or dependence because of their high-addiction potential.

Drugs such as sodium oxybate and baclofen also affect the GABAergic system and therefore have some pharmacological properties similar to alcohol. GABA agonists like baclofen may suppress cravings, reduce drinking and improve liver function ([Addolorato et al., 2002, 2005, 2007a, b](#)), but also increase alcohol-induced sedation and can severely impact daily functioning if not carefully titrated. Sodium oxybate, a drug similar to the street drug γ -hydroxybutyric acid (GHB), has also met controversy due to its addiction potential ([Chick and Nutt, 2012](#)). Other GABA-acting drugs (e.g. clomethiazole) were used in the 1970–1980s and found to cause less liver damage than alcohol; however, these drugs can be fatal when mixed with alcohol ([Chick and Nutt, 2012](#)).

Although benzodiazepines and GABA agonists may be medically acceptable substitutes for alcohol, they can have unpleasant side effects for many people. In addition, these drugs can lead to dependence and health risks if alcohol is ingested simultaneously ([US Food and Drug Administration, 2013](#)). Based on these premises, [Charlton \(2005\)](#) suggested that cannabis might be ‘a safer and less anti-social substitute’ for drinking. Charlton claimed that most people use alcohol to achieve certain psychological effects, and that they will choose equally effective substitutes as long as they are available, legal and socially acceptable. Charlton stated that alcohol policy should aim to reduce related medical and social harms and that ‘lifestyle drug substitution’ or substituting

safer but equally effective agents, could be one way to reduce harms (Charlton, 2005).

Charlton admitted that cannabis substitution may be a radical idea. But whether radical or not: does cannabis satisfy the seven criteria for substitution therapies?

MATERIALS AND METHODS

Electronic searches were performed using PubMed, Google Scholar and ISI Web of Knowledge. Articles including 'alcohol' (or 'ethanol') and cannabis [or 'marijuana' or ' Δ^9 -tetrahydrocannabinol (THC)', the predominant psychoactive compound in cannabis] in the title or as a keyword were considered for this review. Only studies with humans were included. Based on the title and in some cases the abstract, articles were considered for inclusion, then read and organized according to each of the seven criteria. For example, articles regarding health economic costs were discussed and cited under Criterion #7 ('should offer significant health economic benefits'). The objective here is not to provide an exhaustive literature review; for example, genetic and neurobiological studies would certainly supplement the studies cited. Instead, the current goal is to present representative behavioral studies as a step toward determining cannabis' feasibility as a substitute for alcohol.

RESULTS

Results are summarized in Table 1. The first column states each criterion. The second column summarizes the studies for and against substitution. The third column states notable study design flaws for studies cited in column 2.

Criterion #1: it should reduce alcohol use and related harms

The earliest published account of cannabis substitution is a case study of a 49-year-old female alcoholic who found that with Antabuse and smoking cannabis helped her to quit drinking (Mikuriya, 1970). Within 5 months, the patient's physical and mental health markedly improved, and within 2 years, her liver and general health returned to normal. As her physician, Dr Mikuriya noted that although alcohol and cannabis differ greatly, they can both instill euphoria and detachment. But while alcohol seriously affected his patient physically and emotionally, cannabis did not produce the same negative consequences (Mikuriya, 1970). Mikuriya recommended clinical trials of cannabis among selected patients while cautioning that cannabis is not a panacea.

Mikuriya went on to lead two-additional cannabis substitution studies demonstrating cannabis' potential efficacy for both substitution and alleviation of alcohol-related harms. In a 2001 observational study, Mikuriya reviewed records from his medical practice and counted 104 patients who reported using

Table 1. Summary of how cannabis satisfies the seven criteria for substitute therapies

Criterion	Satisfied?	Caveats
1. Reduces alcohol use and related harms	Mixed: Yes: Mikuriya (1970); Mikuriya and Mandel, 2001, 2004), DiNardo and Lemieux (2001), Clements and Daryal (2005), Peters and Hughes (2010), Metrik <i>et al.</i> (2011), Crost and Guerrero (2012) No: Bickel <i>et al.</i> (1995), Pacula (1998), Aharonovich <i>et al.</i> (2005), Moore (2010)	Studies in favor are limited by focus on medical cannabis patients Behavioral economic studies are conducted among individuals without AUD. Aggregate-level studies must be contextualized with individual-level studies
2. Less harmful than alcohol	Yes: Room (2006), Nutt <i>et al.</i> (2007)	But also not harm free (Room, 2006)
3. Misuse is less than that of alcohol	Mixed: Nutt <i>et al.</i> (2007) ranks both psych and physical dependence risks lower. Cannabis use disorders are less prevalent than AUD [US National Institute of Drug Abuse (2013), Hasin <i>et al.</i> (2007), Falk <i>et al.</i> (2008)]	The prevalence of cannabis use disorders among those with AUD is much higher than those without AUD (Stinson <i>et al.</i> , 2006)
4. Can substitute for alcohol	Mixed: Yes: Reiman (2000, 2009), Vaillant <i>et al.</i> (1982), Clements and Daryal (2005), Saffer and Chaloupka (1999), Alter <i>et al.</i> (2006), Lucas <i>et al.</i> (2012) No: Bickel <i>et al.</i> (1995), Pacula (1998), Booth and Kirchner (2001), Aharonovich <i>et al.</i> (2005), Midanik <i>et al.</i> (2007), Magill <i>et al.</i> (2009), Moore (2010)	Studies of med cannabis patients are limited by self-report and possible selection bias. Also, none examine (a) <i>prospective</i> shift from drinking to substituting or (b) whether substituting cannabis for alcohol leads to reduced harms or improved quality of life
5. Is safer in overdose than alcohol	Yes: Nutt <i>et al.</i> (2007), SAMHSA (2004)	
6. Does not potentiate the effects of alcohol especially if either drug is taken in overdose	Mixed: Some studies have concluded that cannabis potentiates the effects of alcohol, while others report no synergistic or additive effects in terms of impairment Does not potentiate: Liguori <i>et al.</i> (2002), Lenne <i>et al.</i> (2010), Ballard and de Wit (2011) Does potentiate: Chait and Perry (1994), Ramaekers <i>et al.</i> (2000), Bramness <i>et al.</i> (2010), Ramaekers <i>et al.</i> (2011), Ronen (2010), Downey <i>et al.</i> (2013)	Most driving impairment studies have small samples ($n < 20$) and do not include individuals with AUD In overdose, fatality would be more likely due to alcohol (SAMHSA, 2004)
7. Offers significant health economic benefits	Only if considering aggregate-level costs. However, because these figures apply to the aggregate, they do not necessarily mean that health economic benefits would be seen in individuals (Harwood <i>et al.</i> , 1998; Nutt <i>et al.</i> , 2007)	Studies of post-substitution drinking patterns and alcohol-related harms and problems are needed, since the health economic benefits can only be calculated relative to these issues

cannabis to replace hazardous alcohol use. All of these patients claimed that cannabis relieved both craving for and symptoms masked by alcohol use (Mikuriya and Mandel, 2001). Most recently, another observational record review of 92 patients who substituted cannabis for alcohol showed that 100% reported cannabis as a very effective (50%) or effective (50%) substitute for alcohol. Ten percent of patients reported a year or more of alcohol abstinence and attributed their success to cannabis, while 21% reported return to unsafe drinking when stopping cannabis use (Mikuriya, 2004).

Mikuriya's studies suggest that cannabis substitution for alcohol can improve overall health (Mikuriya, 1970; Mikuriya and Mandel, 2001; Mikuriya, 2004), as well as alleviate pain resulting from alcohol-related injury in medical cannabis users (Mikuriya and Mandel, 2001). Importantly, the Mikuriya studies were observational and published in non-peer-reviewed journals, so the methodological rigor of the studies is not certain. Even so, reports from 1746 medical cannabis users in California corroborated that cannabis can alleviate anxiety and may help sleep (Reinarman *et al.*, 2011). Similarly, data from the large ($n=43,093$), nationally representative US National Epidemiologic Study on Alcohol and Related Conditions (NESARC) showed that 43% of those with a lifetime anxiety disorder self-medicated with alcohol (Bolton *et al.*, 2009). Thus some individuals may use cannabis in similar contexts as alcohol.

Although the results from the above studies are provocative, they rely on retrospective designs and often focus on medical marijuana users without alcohol use disorders (AUD). Furthermore, medical marijuana patients may be dealing with illnesses that affect their drinking regardless of cannabis use. Peters and Hughes (2010) circumvented these study design problems by following 28 daily cannabis users who were not trying to reduce their cannabis consumption. Participants were asked to abstain from cannabis for 2 weeks; alcohol substitution occurred for participants with a past alcohol abuse or dependence diagnosis. The authors speculated that although cannabis and alcohol belong to different drug classes (i.e. cannabinoids versus sedatives) these participants were substituting 'pharmacologically similar' substances for one another in order to achieve similar effects (Peters and Hughes, 2010). A larger prospective study of 236 heavy drinkers similarly showed that cannabis users reduced alcohol consumption faster than non-users (Metrik *et al.*, 2011).

Large, US nationally representative behavioral economics studies have reported that aggregate drinking may decrease if cannabis were legalized (Clements and Daryal, 2005), and that substitution is common in young adults (DiNardo and Lemieux, 2001). Results from the 2002–2007 National Survey of Drug Use and Health similarly showed that individual-level alcohol consumption increased and cannabis use significantly decreased at the minimum legal drinking age of 21, especially among women (Crost and Guerrero, 2012); the authors performed several sensitivity tests and concluded that alcohol and cannabis are substitutes, at least from an economic standpoint, and that the actual substitution effect is likely stronger than that shown due to potential under-reporting of cannabis use.

Conversely, other behavioral economic studies have found alcohol and cannabis to be complements in that the use of one substance increases use of the other (Bickel *et al.*, 1995; Pacula, 1998; Moore, 2010). The discrepancies within behavioral economics imply that results from aggregate-level studies

must be contextualized with individual-level studies. Furthermore, behavioral economic laboratory studies are conducted among individuals without AUD.

Although most of the above studies suggest that cannabis use can reduce alcohol use and related harms, many of the studies cited are limited by retrospective designs and selection bias. Furthermore, few focus on individuals with AUD. Findings from behavioral economics are mixed, with some calling cannabis and alcohol substitutes, and others calling them complements. Thus, cannabis only partially satisfies Criterion #1.

Criteria #2: it should ideally be free of harms, or at least less harmful than alcohol

Cannabis is certainly not free of harms (Room, 2006). However, two-independent groups of experts, including the British National Group of Consultant Psychiatrists registered on the Royal College of Psychiatrists as specialists in addiction, ranked cannabis as less harmful than both alcohol and benzodiazepines in terms of physical harm, dependence and social harm (i.e. accounting for factors such as toxicity and related health care costs; Nutt *et al.*, 2007). Another possibly more objective comparison of harm may be the 'safety ratio' between the usual effective dose (for non-medical purposes) and the usual lethal dose: 10–20 for GHB and alcohol versus >100 for cannabis (Room, 2006). This again implies that cannabis may be safer than both alcohol and previously examined medication substitutes. Room (2006) also offered a short comparison of both individual and societal harms related to various psychoactive substances. He ranked alcohol, tobacco and cannabis as causing most to least harm. Specifically, he cited European studies that classify 'general toxicity' as very strong for alcohol and very weak for cannabis, and 'social dangerousness' as strong for alcohol and weak or none for cannabis.

Withdrawal from cannabis is also less severe than withdrawal from alcohol (and potentially benzodiazepines). Withdrawal from alcohol can lead to seizures or even death (Bayard *et al.*, 2004). Similarly, withdrawal from benzodiazepines can lead to seizures or psychosis in extreme cases (Schweizer and Rickels, 1998). On the other hand, withdrawal from cannabis is much less severe, though it can lead to dysphoria or irritability (Budney *et al.*, 2001). Although sometimes clinically ambiguous, cannabis withdrawal has been documented; a recently developed scale shows that cannabis withdrawal can correlate with trouble sleeping, nightmares/strange dreams and angry outbursts (Allsop *et al.*, 2011, 2012).

Smoking cannabis, which is the most common way to ingest it, can lead to health problems such as impaired respiratory function. Furthermore, both incident and continued cannabis use have been linked to increased risk of incident psychotic symptoms (Kuepper *et al.*, 2011), though cannabis use is not considered a sufficient cause for psychosis in itself (Arseneault *et al.*, 2004). In sum, the above studies show that cannabis is safer than alcohol. Thus, cannabis satisfies the second criterion.

Criteria #3: misuse should be less than that of alcohol

Nutt *et al.* (2007) ranked both psychological and physical dependence risks for cannabis as lower than those for alcohol

(Nutt *et al.*, 2007). According to the US National Institute of Drug Abuse, 9% of those who use cannabis go on to develop dependence (US National Institute of Drug Abuse, 2013). On the other hand, NESARC results show that the lifetime prevalence of alcohol dependence is almost twice as high at 17.8% (Hasin *et al.*, 2007). Among those with alcohol problems, a prevalence study of past 12-month alcohol use disorders showed that 9.9% of those with alcohol use disorders also had a cannabis use disorder (as defined by the diagnostic and statistical manual of mental disorders, 4th edition) compared with only 0.67% of those without alcohol use disorders (Stinson *et al.*, 2006).

NESARC results also showed that approximately one-quarter of cannabis users also had an AUD. The co-use of other drugs was less common, ranging from ~9.5% for opioids to <1% for inhalant/solvent, heroin or other drugs. The rate of drug-specific substance use disorders was the highest for cannabis at ~10% (Falk *et al.*, 2008). However, those with alcohol disorders also have higher rates of sedative misuse (Stinson *et al.*, 2006), which highlights the importance of weighing criteria relative to alternatives like benzodiazepines.

Thus from a strictly epidemiological point of view, the documented rate of cannabis dependence is less than the rate of alcohol dependence, suggesting that cannabis may fulfill Criterion #3. However, the increased likelihood of cannabis dependence among those with past or current alcohol problems dampens support for this criterion.

Criterion #4: it should be shown that it can substitute for alcohol and not be used along with alcohol

While some consider cannabis a complement to alcohol, a growing number of studies suggest that individuals actually substitute cannabis in place of alcohol. For example, 40% of 350 respondents reported substitution in a community-based survey of medical cannabis patients in Berkeley, CA, USA (Reiman, 2009). Although Reiman (2009) did not examine bivariate associations with past alcohol or drug treatment, 16% of participants reported formal substance abuse treatment and 2% reported involvement in a 12-step or other recovery program. In a similar study of 130 medical cannabis patients in the San Francisco Bay Area, half the sample reported using cannabis substitution for alcohol (Reiman, 2000). Within another community-based sample of medical marijuana patients in Canada ($n = 404$), 41% reported using cannabis as a substitute for alcohol (Lucas *et al.*, 2012); rates of substitution were very similar to those reported in Reiman (2009). A 30-year-prospective study that included 110 male alcohol abusers showed that among the 49 who eventually maintained a year of abstinence, half developed 'substitute dependencies', including two who used cannabis (Vaillant *et al.*, 1982). Though the above studies suggest that cannabis could be an alternative to alcohol, they are limited by small sample sizes, self-report and possible selection bias from medical cannabis patients. Furthermore, all studies besides Vaillant *et al.* (1982) rely on retrospective designs.

In addition, as discussed above, cannabis and alcohol can be considered complements in that combined use may lead to more substance use compared with the use of either alone (Bickel *et al.*, 1995; Pacula, 1998; Midanik *et al.*, 2007; Magill *et al.*, 2009; Moore, 2010). In a large probability community survey of 733 at-risk drinkers, those who also used cannabis

reported higher frequencies and quantities of alcohol use, as well as more negative alcohol-related consequences (Booth and Kirchner, 2001). Among 250 substance use disorder treatment seekers, cannabis use may have increased the hazard of alcohol relapse and decreased the likelihood of stable abstinence (Aharonovich *et al.*, 2005).

Furthermore, the odds of alcohol dependence are substantially higher among those with cannabis dependence (Stinson *et al.*, 2006), suggesting that hazardous alcohol use may increase as cannabis use increases. Similarly, the developmental literature shows that cannabis and alcohol use trajectories are related (Martin *et al.*, 1996; Windle and Wiesner, 2004; Schulenberg *et al.*, 2005; Pape *et al.*, 2009), and that conjoint use can be explained by either common risk factors or the nature of the substances causing use of one to lead to use of the other (Jackson *et al.*, 2008).

Thus, although a handful of studies claim that cannabis can substitute for alcohol, a number of others conclude that the two substances are complements: cannabis satisfies Criterion #4 only partially.

Criterion #5: it should be safer in overdose than alcohol

As noted under Criterion #2, the safety ratio for cannabis is >10 times higher than that of alcohol. Furthermore, the Substance Abuse and Mental Health Administration (SAMHSA) has explicitly stated: 'Cannabis is rarely the only drug involved in a drug abuse death... in most cases, the proportion of cannabis-involved cases labeled as "One drug" (i.e. cannabis only) will be zero or nearly zero' (Substance Abuse and Mental Health Services Administration, 2004). On the other hand, alcohol was deemed to be a cause of death for 3.5% of US mortalities in the year 2000 (Mokdad *et al.*, 2004). This criterion is satisfied.

Criterion #6: it should ideally not potentiate the effects of alcohol especially if either drug is taken in overdose

The proportion of deaths attributed to cannabis alone has been documented as 'zero or nearly zero' in a report from SAMHSA, implying that it cannot be taken in overdose itself. Furthermore, combining cannabis with alcohol does not lead to higher blood or breath alcohol levels (Chait and Perry, 1994; Liguori *et al.*, 2002). Although smoking cannabis may slow the absorption of ethanol, which subsequently reduces ethanol's psychoactive effects (Lukas *et al.*, 1992), plasma THC levels can be enhanced if alcohol is consumed immediately after smoking cannabis (Lukas and Orozco, 2001; Downey *et al.*, 2013). Thus cannabis combined with alcohol can lead to greater impairment than ingestion of either substance alone with the combination yielding additive (as opposed to multiplicative) effects on measures of impairment (Chait and Perry, 1994).

As noted in Ronen *et al.* (2010), the literature on combined cannabis/alcohol effects is small and with mixed results. While some studies have shown that combining cannabis and alcohol leads to greater impairment than either alone (Ramaekers *et al.*, 2000, 2011; Bramness *et al.*, 2010; Ronen *et al.*, 2010; Downey *et al.*, 2013), others have shown no differences (Liguori *et al.*, 2002; Lenne *et al.*, 2010; Ballard and de Wit, 2011). More recent studies have focused on the joint effects of cannabis and alcohol effects in regard to driving impairment. In a study of 18 healthy volunteers, Ramaekers *et al.*

(2000) concluded that combining cannabis and alcohol impaired driving performance more than either alone. A 2010 study of 12 participants similarly showed that the combination of alcohol and cannabis had the strongest effects (compared with either substance alone) in terms of impaired (a) driving tasks, (b) non-driving tasks, such as arithmetic calculations, (c) subjective sensations, such as feeling 'high' or 'sedated' and (d) physiological measures, such as heart rate (Ronen *et al.*, 2010). A similar, larger ($n = 80$) study of recreational cannabis and alcohol users also concluded that driving performance was worse for those under the influence of both cannabis and alcohol compared with either substance alone, and that THC-blood levels were higher for those who had consumed both substances (Downey *et al.*, 2013).

Among heavy cannabis users, the joint effects of cannabis and alcohol were shown to impair divided attention (but not other neurocognitive tasks) more than alcohol alone (Ramaekers *et al.*, 2011); importantly, these heavy users may have developed tolerance to cannabis that allowed them to perform better on these tasks than lighter users may perform. Furthermore, although the above driving simulation studies use double-blind, placebo-controlled designs, they were all rather small ($n < 100$), and not necessarily generalizable to heavy alcohol users. A larger ($n = 5042$), retrospective cross-sectional forensic database study of drivers apprehended for driving under the influence of alcohol showed that when THC and ethanol were both detected, the participant was more likely to be judged impaired; the risk of being judged impaired increased additively according to alcohol and cannabis dosages (Bramness *et al.*, 2010).

Conversely, a number of other driving impairment studies have yielded divergent results. A study of joint alcohol and cannabis' effects on driving impairment, body sway and mood showed no additive effects of taking both substances (Liguori *et al.*, 2002). A more recent study of 25 experienced and 22 inexperienced drivers similarly found no synergistic effects when combining alcohol and cannabis (Lenne *et al.*, 2010). Another study of 11-healthy participants reported that the combination of cannabis and alcohol was not synergistic, and that the combination appeared to have less than additive effects on working memory, psychomotor ability and simple reaction time, or subjective mood compared with either substance alone (Ballard and de Wit, 2011). Although these studies may provide evidence that cannabis does not potentiate the effects of alcohol, these driving impairment studies are small and not generalizable to heavy drinkers *per se*.

Thus some studies have concluded that cannabis potentiates the effects of alcohol, while others report no synergistic or additive effects in terms of impairment. These divergent results may be due to differences in study designs (e.g. measures of impairment differed across studies). In light of the mixed evidence, cannabis only partially satisfies the sixth criterion. However, we could again compare alternative substitutes: benzodiazepines are known to exacerbate alcohol's effects, and the interaction between benzodiazepines and alcohol can be fatal (Koski *et al.*, 2002).

Criterion #7: it should offer significant health economic benefits

From a strictly economic standpoint, the US Department of Justice states that in 1992, the total economic cost of alcohol

abuse and alcoholism cost ~\$148 billion, while drug abuse/dependence cost ~\$98 billion (Harwood *et al.*, 1998). This implies that the costs of cannabis on the aggregate level are probably much lower than the costs of alcohol. In terms of health care expenditures, the independent experts from Nutt *et al.* (2007) similarly ranked the costs of cannabis use lower than the costs of alcohol use (Nutt *et al.*, 2007). However, these figures apply to the aggregate and do not necessarily mean that health economic benefits would be seen in individuals.

At the aggregate level, cannabis appears to satisfy Criterion #7. Yet because no studies to date have compared individual health economic outcomes for those who substitute cannabis versus those who do not, prospective studies of long-term drinking patterns, alcohol-related harms and problems and changes in quality of life are needed.

DISCUSSION

Summary of criteria

All criteria except #6 appear either satisfied or partially satisfied (Table 1). Besides the overall paucity of literature on the topic, major gaps include prior focus on medical cannabis patients and retrospective designs. Furthermore, studies that support substitution have not assessed subsequent harms, problems or related issues like health economic benefits or quality of life. Most importantly, no study has prospectively examined, (a) whether individuals with alcohol use disorders can effectively use cannabis to help reduce drinking and (b) longer term problems and health economic outcomes among those who substitute.

Cannabis and active substance abuse treatment

An exploratory study of medical cannabis users in substance abuse treatment suggested that medical cannabis use does not hinder drug treatment participation or adversely affect treatment outcomes (Swartz, 2010). In fact, results imply that those using medical cannabis may have had better treatment completion, employment and alcohol use outcomes compared with their non-medical cannabis using counterparts.

Similarly, Raby *et al.* (2009) showed that cannabis use may enhance treatment retention and improve outcomes for opiate-dependent individuals. Intermittent cannabis use predicted greater treatment retention and adherence to naltrexone pill taking. The authors speculate that cannabis may improve tolerability of naltrexone, perhaps because naltrexone enhanced the intoxicating effects of cannabis; this may have implications for naltrexone compliance among alcohol-dependent individuals, even though the study only included opiate-dependent individuals who did not drink much alcohol (Raby *et al.*, 2009).

Legalization movements in USA

Regardless of cannabis's candidacy as a substitute, the recent movements toward cannabis legalization in the USA make substance substitution especially relevant. A 2005 study of college students reported that they might reduce their drinking if cannabis were legalized, especially among daily drinkers and those who drank spirits (Clements and Daryal, 2005). A study of alcohol and cannabis policy effects on drug use similarly suggested lower alcohol use in states, where cannabis

was decriminalized (Saffer and Chaloupka, 1999). Furthermore, when the minimum legal drinking age was raised in the 1980s, cannabis consumption went up among American students in 43 states (DiNardo and Lemieux, 2001). A similar substitution effect has been observed in high school students (Alter *et al.*, 2006). Interestingly, Alter *et al.* also found that students who reported no alcohol use were more likely to report cannabis use. Although Alter *et al.* (2006) focus on perceived access to cannabis and perceptions of related harms, the findings may imply that cannabis can substitute for alcohol among individuals who choose to completely abstain from alcohol.

Next steps

The mixed evidence for all criteria besides #2 and #5 highlight areas for future research. For example, future studies should prospectively assess both alcohol-related (Criteria #1 and #4) and health economic (Criterion #7) outcomes for those who substitute and those who do not; although a randomized control trial is ideal, this involves substantial practical barriers due to cannabis' legal status. One alternative design would be to follow those in treatment and compare outcomes for those who substitute versus those who do not. Another would be to randomly assign individuals with AUD who also use cannabis to quit using cannabis and compare alcohol use outcomes to those not assigned to quit cannabis. In addition to longitudinal assessments, future studies should gather data regarding THC content and cannabis strains consumed by cannabis users as these factors likely impact cannabis' efficacy as a substitute.

While more research and improved study designs are needed to better identify the extent and impact of cannabis substitution on those affected by AUD, cannabis does appear to be a potential substitute for alcohol. Perhaps more importantly, cannabis is both safer and potentially less addictive than benzodiazepines and other pharmaceuticals that have been evaluated as substitutes for alcohol.

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