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Substitution and complementarity of alcohol and cannabis: A review of the literature

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Abstract

Background—Whether alcohol and cannabis are used as substitutes or complements remains debated, and findings across various disciplines have not been synthesized to date.

Objective—This paper is a first step towards organizing the interdisciplinary literature on alcohol and cannabis substitution and complementarity.

Method—Electronic searches were performed using PubMed and ISI Web of Knowledge. Behavioral studies of humans with 'alcohol' (or 'ethanol') and 'cannabis' (or 'marijuana") and 'complement*' (or 'substitut*') in the title or as a keyword were considered. Studies were organized according to sample characteristics (youth, general population, clinical and community-based). These groups were not set *a priori*, but were informed by the literature review process.

Results—Of the 39 studies reviewed, 16 support substitution, ten support complementarity, 12 support neither and one supports both. Results from studies of youth suggest that youth may reduce alcohol in more liberal cannabis environments (substitute), but reduce cannabis in more stringent alcohol environments (complement). Results from the general population suggest that substitution of cannabis for alcohol may occur under more lenient cannabis policies, though cannabis-related laws may affect alcohol use differently across genders and racial groups.

Conclusions—Alcohol and cannabis act as both substitutes and complements. Policies aimed at one substance may inadvertently affect consumption of other substances. Future studies should collect fine-grained longitudinal, prospective data from the general population and subgroups of interest, especially in locations likely to legalize cannabis.

Keywords

Cannabis; alcohol; substitutes; complements

INTRODUCTION

Alcohol and cannabis are two of the most commonly used drugs in the world (Substance Abuse and Mental Health Services Administration, 2012). However, the question of whether the two substances are consumed as substitutes or complements remains debated.

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Furthermore, findings across various disciplines (e.g., economics, epidemiology) have never been synthesized.

Generally, a "substitute" is something that takes the place of something else and a "complement" is something that completes something else or makes it better. These definitions can be applied to categorize how two drugs interact with one another such that they are "substitutes" if one drug can pharmacologically replace the other; "complements" if the effects of one drug are enhanced by the other; and "independent" if the effects of one drug are unaltered by the other (Hursh et al., 2005).

There are myriad individual and/or societal factors that may influence one's substance use and thus one's tendency to substitute or complement substances. For example, patterns of substance use can vary across income levels and social classes, and can be connected to social inequality and marginalization (Room, 2005). Similarly, the prevalence of substance use varies across countries due to differences in drug policies or cultures (Degenhardt et al., 2008). Social setting and networks can also influence use patterns, for example through developing a risk/reward tradeoff for substance use (Hunt, Evans, & Kares, 2007). All of these individual and societal factors could affect one's propensity to substitute/complement.

The goal of this paper is to review behavioral studies that explicitly examined substitution/complementarity of alcohol and cannabis with empirical data. The recent movements towards cannabis legalization in the US call for a better understanding of whether cannabis and alcohol act like substitutes or complements in the general population and among important subgroups (e.g., youth), especially if cannabis use becomes more prevalent as a result. Identifying subgroups prone to using the two as complements is particularly important because combined use can lead to greater impairment than ingestion of either substance alone (Ronen et al., 2010). Furthermore, understanding how a policy aimed at reducing the consumption of one substance (e.g., cannabis criminalization laws) affects consumption of another substance (e.g., alcohol) is crucial for developing optimal policies and recognizing potential unintended consequences (e.g., cannabis laws may inadvertently affect alcohol use).

METHOD

Electronic searches were performed using PubMed and ISI Web of Knowledge. Articles written in English with '*alcohol*' (or '*ethanol*') and '*cannabis*' (or '*marijuana*") and '*complement**' (or '*substitut**') in the title or as a keyword were considered. The Web of Knowledge is the world's largest accessible citation database and allows for in-depth exploration of specialized sub-fields within social science disciplines (Thompson Reuters, 2016). Although "co-use" is a relevant term that was considered for searches, co-use is a much broader concept that does not necessarily reflect the mechanisms of how individuals use alcohol and cannabis together (or separately); thus "co-use" was not used as a search term. Inclusion criteria were: 1) empirical studies of humans, and 2) if the independent variable was cannabis-related, the study needed to include an alcohol-related dependent variable; if the independent variable was alcohol-related, the study needed to include a cannabis-related dependent variable. Based on the title and abstract, articles were considered

for inclusion, then read and organized according to sample characteristics (i.e., adolescents and young adults, general population, clinical and community-based; please see Tables 1–3). These three groups were not set *a priori*, but were informed by the literature review process. This study was approved by the Institutional Review Board of the Public Health Institute.

RESULTS

Searches of '*complement**' yielded 69 results; 21 met inclusion criteria. Searches of '*substitut**' yielded 48 results; 27 met inclusion criteria. Nine studies overlapped between searches for a total of 39 studies reviewed. Of the 39 studies, 17 were conducted among youth/young adults, nine were conducted using the general population, and 13 were conducted with clinical samples. Twenty-one studies relied on cross-sectional designs and 17 utilized longitudinal data. The majority of studies (29/39) used individual-level outcomes, while 10 studies employed aggregate-level outcomes. In terms of independent/exposure variables, almost half (16/39) used cannabis-related policies as the primary independent variable. For details pertaining to each study, please see Tables 1–3.

DISCUSSION

Adolescents and young adults

Almost all studies of substitution/complementarity in youth involve cannabis- or alcohol-related policy. The strongest results come from these "natural experiments" of policy changes using longitudinal data (Angrist & Pischke, 2010), which account for both cross-sectional variation (e.g., differences in laws across states) and variation across time (e.g., changes in laws within a state over time).

Longitudinal studies of adolescents and young adults

Two longitudinal studies have focused on youth. First, Pacula (1998) used annual data from the National Longitudinal Survey of Youth (NLSY) 1979 cohort (N=8,008) to examine the effects of state-level beer taxes on past 30-day number of drinks and cannabis frequency (Pacula, 1998). The NLSY79 data showed complementary between cannabis and alcohol: doubling the beer tax reduced the probability of cannabis use by 11.4%, while only reducing the probability of drinking by 3.2%. Pacula (1998) also assessed effects of cannabis decriminalization using a dichotomous indicator and controlling for aggregate factors such as alcohol and cannabis prices and the ratio of crimes: officers in each state; decriminalization appeared to significantly predict a higher prevalence of alcohol consumption, also suggesting complementarity. The only other longitudinal study of youth focused on the effects of Medical Marijuana Laws (MMLs) and showed that time-varying state-level MML indicators were not significantly related to past 30-day alcohol use (Anderson, Hansen, & Rees, 2012). Thus, results from studies with the strongest designs are mixed, perhaps due to differences in samples and variables examined.

Cross-sectional studies of adolescents and young adults

The majority of studies on youth rely on cross-sectional surveys. In terms of aggregate-level outcomes, the earliest published study of substitution occurred in response to Operation

Intercept, an anti-drug measure headed by President Nixon in May 1969. Operation Intercept involved closing the Mexican/American border, which reduced the cannabis supply in the US (McGlothlin, Jamison, & Rosenblatt, 1970). Among a sample of students and free clinic patients who had used cannabis ≥ 10 times, 44–51% reported reduced cannabis frequency as a result of cannabis unavailability between May and October 1969. Although results rely on self-report, the vast majority of those reporting a cannabis shortage (76–84%) reported increasing use of alcohol and other drugs because of the shortage (McGlothlin et al., 1970).

Cross-national studies, on the other hand, appear to support complementarity. In a cross-national comparison (USA, Canada, Netherlands) of 4,858 10th graders, alcohol and cannabis laws were examined in relation to use. With USA as the referent (because it has the strictest drug laws), relative risks of drinking were 1.30–2.0 for both Dutch and Canadian boys and girls, though rates of cannabis use did not differ. Although it is impossible to tell if laws preceded prevalence, the results show that alcohol use is higher among 10th graders in countries with more liberal cannabis policies (Simons-Morton, Pickett, Boyce, ter Bogt, & Vollebergh, 2010). Population-level analyses of adolescents from 35 European countries (European School Project on Alcohol and Drugs/ESPAD) similarly indicated complementarity: most cannabis users combined with alcohol at least once, and population-level drinking and cannabis use correlated positively (Pape, Rossow, & Storvoll, 2009). Pape and colleagues also analyzed individual-level data from a survey of 14–20 year-olds in Norway (N=16,813), which showed a that 82% of cannabis users had used in combination with alcohol, and 80% of cannabis use incidents involved alcohol (Pape et al., 2009). Thus, cannabis appears to be used as a complement to alcohol in both cross-national studies.

Alcohol-related policies and substitution/complementarity among youth

Cross-sectional studies of beer taxes also show complementarity among youth. On the aggregate level, findings from the 1993–1999 Harvard SPH College Alcohol Study surveys (N=48,174) showed that higher beer taxes were related to lower alcohol and cannabis use, and that the price of cannabis was negatively related to alcohol and cannabis use, though decriminalization did not significantly affect either (Williams, Pacula, Chaloupka, & Wechsler, 2004). On the individual-level, Farrelly and colleagues examined effects of state-level cannabis fines/penalties among youth (age 12–20) and younger adults (age 21–30) in the 1990–1996 National Household Survey of Drug Abuse (NHSDA); again, higher beer prices led to decreased probability of cannabis use. Importantly, most effects disappeared when including state effect indicators, implying possible endogeneity by unaccounted state factors. Still, the authors concluded that increasing the price of alcohol would decrease cannabis use among youths (Farrelly, Bray, Zarkin, Wendling, & Pacula, 1999). Importantly, these studies depend on cross-sectional variation in beer taxes, which could be driven by unobserved variables such as cultural attitudes or preferences within states. However, the results are similar to what was found in Pacula's longitudinal study (Pacula, 1998), which suggests that the relationship between beer taxes and cannabis use among youth may be robust. Furthermore, because youth generally have lower income levels than adults, the reduced cannabis use associated with increased alcohol costs may reflect true economic substitution, i.e., the limited financial capacity of younger respondents may influence their

substance use patterns more than (or in addition to) the psychoactive associations between alcohol and cannabis.

In terms of other alcohol-related policies, a number of analyses have examined the minimum legal drinking age (MLDA) with mixed results. Using the 1982–1989 Monitoring the Future (MTF) samples, DiNardo and Lemieux (2001) examined raising the MLDA from 18 to 21, cannabis decriminalization and the price of alcohol on past 30-day cannabis and alcohol consumption; increasing the MLDA from 18 to 21 decreased alcohol use by 4.5 percentage points but increased the prevalence of cannabis use by 2.4 percentage points (DiNardo & Lemieux, 2001). Based on these findings, the authors built an economic model of consumption showing that the increase in cannabis use was attributable to standard substitution. A separate analysis of the MLDA using the 2002–2007 National Survey on Drug Use and Health (NSDUH) showed a sharp decrease in cannabis use at the age of 21: the probability of past 30-day drinking increased from 60% to 70%, while the probability of cannabis use decreased by two percentage points from a baseline of about 20% (Crost & Guerrero, 2012). The opposing effects suggest substitution; instrumental variable models showed that a 9.8 percentage point increase in the probability of alcohol consumption led to a two percentage point decrease in cannabis use, with stronger effects for women. The authors concluded that policies limiting alcohol access might increase cannabis consumption in young adults, especially women. Importantly, the authors noted that the results' external validity best applies to alcohol policies aimed at individuals who are close to 21 years old and likely to comply with regulations like the MLDA (Crost & Guerrero, 2012). These findings contradicted an earlier study reported that turning 21 was associated with an increase in cannabis use in most model specifications in the NLSY97, consistent with complementarity (Yörük & Yörük, 2011). However, in a re-analyses of the NLSY97, Crost and Rees applied the same regression discontinuity design and found no evidence of complementarity (Crost & Rees, 2013), perhaps because Yörük (2011) restricted the sample to respondents who had used cannabis at least once since last interviewed. Applying the same design to all respondents, Crost and Rees found no significant changes in cannabis use at age 21; thus current cannabis users may complement more than the sample as a whole, which would be expected. Most recently, a study of fatal accidents among 16–25 year olds (N=7,191), which also used a regression discontinuity approach, showed that the prevalence of cannabis-related accidents did not change significantly at the MLDA of 21 (Keyes, Brady, & Li, 2015). While alcohol use did increase, cannabis use did not change at the MLDA of 21, which corroborates what Yörük and Yörük (2011) and Crost and Guerrero (2012) had found with similar methods. Still, taken as a set, results from studies of the MLDA are mixed.

Cannabis-related policy and substitution/complementarity among youth

On the other hand, results from studies of youth focused on cannabis-related policy as the independent variable support substitution. In the 1982–1989 MTF samples, simulating the effects of uniform cannabis criminalization (e.g., cannabis use is a criminal offense in all US states across time) versus uniform decriminalization (e.g., cannabis use is not a criminal offense in any US states across time) suggested that cannabis could substitute for alcohol (Chaloupka & Laixuthai, 1997): moving from total criminalization to total decriminalization

would increase the number of alcohol abstainers in the past year by 12%, while reducing the number of frequent drinkers by 11%. In addition, simulations using the pooled time-series of state cross-sections (1975–1988) for the Fatality Analysis Reporting System, (FARS, an annual census of fatal motor vehicle accidents in the 48 contiguous US states) demonstrated that changing total criminalization to decriminalization would reduce the fatal accident rate by 6% among 15–24 year olds. This is consistent with Model's (1993) findings that substitution can result from reductions in the “full price” of cannabis due to decriminalization because the full price includes monetary costs related to criminality, e.g., lost wages (Model, 1993). Importantly, the results suggest that substitution resulting from decriminalization may yield overall reductions in drug and alcohol-related consequences, such as accidents (Chaloupka & Laixuthai, 1997). Furthermore, the findings support those found in MTF using aggregate-level outcomes (DiNardo & Lemieux, 2001).

Another study of hypothetical legalization (N=281) showed differential effects according to beverage preference: consumption of spirits decreased most with hypothetical legalization. The largest anticipated reduction in drinking was for the daily cannabis users, suggesting that they would be most likely to substitute in legal environments (Clements & Daryal, 2005). Similarly, data from the 1979, 1984, and 1988 NLSY cohorts (N=12,686 14–21 year olds) showed that the frequency of drinking 6+ drinks in an episode went down in states that had decriminalized cannabis, again supporting substitution (Thies & Register, 1993).

Other studies of adolescents and young adults

Similarly, results potentially supporting substitution have been observed in a more recent MTF subsample (N=11,542): students who reported no alcohol use were more likely to report cannabis use (Alter, Lohrmann, & Greene, 2006). Although the study focused on perceived access harms, the authors concluded that cannabis may substitute for alcohol among individuals who choose to completely abstain from alcohol (Alter et al., 2006); however, this conclusion may be over-reaching since substitution implies previous use of a substance with subsequent changes in its usage patterns because of concurrent changes in usage patterns of another substance

Finally, an 8-week trial of naltrexone for alcohol dependence in 18–25 year olds (N=122) showed that cannabis use did not affect alcohol use, alcohol-related consequences, or motivation to reduce drinking in bivariate tests. The authors did not examine alcohol outcomes in multivariate regressions as the focus of the study was medication adherence (Peters et al., 2012). Thus, the single clinical study is not particularly informative here.

Summary of studies of adolescents and young adults

Overall, more than half (9/17) of the studies among adolescents and young adults used cannabis policy as the primary independent variable; six of these concluded that alcohol and cannabis are substitutes, indicating that youth may use less alcohol in environments with more liberal cannabis policies (Alter et al., 2006; Chaloupka & Laixuthai, 1997; Clements & Daryal, 2005; Crost & Guerrero, 2012; DiNardo & Lemieux, 2001; McGlothlin et al., 1970; Thies & Register, 1993). Of the six studies concluding that alcohol and cannabis are complements, three were based on beer tax associations (Farrelly et al., 1999; Pacula, 1998;

Williams et al., 2004); this includes both longitudinal and cross-sectional studies that examined both individual and aggregate-level outcomes, which suggests that higher beer taxes are associated with less cannabis use among youth. Overall, alcohol and cannabis are used as both substitutes and complements among youth and young adults, and policies aimed at one substance appear to affect consumption of the other. Results are summarized in Table 1.

General population

Similarly to the studies of youth, the majority of the general population studies examined cannabis policy relative to substance use in order to assess substitution/complementarity. Specifically, most studies used indicators of MMLs or cannabis decriminalization as the independent variable; results have been mixed.

Longitudinal studies of the general population

Data from the NSDUH and Behavioral Risk Factor Surveillance System (BRFSS) showed that MMLs were associated with a 1.51 reduction in mean number of drinks/month by males and a 0.65 reduction in females, with the strongest effects among 20–29 year olds (who are more likely to use medical cannabis than other age groups (Anderson & Rees, 2011)). Controlling for state-level traffic and alcohol laws and using neighboring states as controls, MMLs were associated with 8.7% decrease in the rate of fatal accidents, a 12% decrease in any-blood alcohol content (BAC) crashes, a 14% decrease in high BAC crashes, and 19% decrease in fatality among 20–29 year olds specifically in the 1990–2009 FARS data (Anderson & Rees, 2011). Comparable analyses of all 19 states with MMLs in 2013 supported these conclusions: one year after MMLs were passed, traffic fatalities tended to fall by 8–11% (Anderson, Hansen, & Rees, 2013).

Conversely, Salomonsen-Sautel and colleagues used 1994–2011 FARS data to examine whether MMLs in Colorado affected the proportion of drivers in fatal crashes who were alcohol-impaired (BAC ≥ 0.08%), and found no change in either Colorado or the 34 control states (Salomonsen-Sautel, Min, Sakai, Thurstone, & Hopfer, 2014). The mixed results from the FARS data may be due to differences in the subgroups examined, as well as potentially inconsistent testing and reporting across states and times.

The most recent longitudinal general population study looked at the effects of the depenalization of cannabis possession in Lambeth, London, England on drug-related hospital admissions. Using > 1 million public hospital records and difference-in-difference regressions, Kelly and Rasul (2014) found a significant reduction in alcohol-related admissions post-depenalization for the youngest cohort (15–24 years old), suggesting that cannabis could substitute for alcohol in this age group.

Cross-sectional studies of the general population

While 3/4 of the longitudinal studies support substitution, results from cross-sectional general population surveys support complementarity. First, Saffer and colleagues found that higher alcohol taxes decreased drug use in the 1988–1991 NHSDA; the relationship did not differ across races (Saffer & Chaloupka, 1998). Saffer (1999) used the same dataset to

examine effects of cannabis decriminalization on alcohol and other drug use; decriminalization was associated with more alcohol use (complementarity) for the full sample, white males and African-Americans (H. Saffer & F. J. Chaloupka, 1999). However, for Native Americans and Hispanics, alcohol and cannabis appeared to be economic substitutes. No effects were found for Asians, women or youth. The differences across different ethnic, gender and age groups are especially important in light of the fact that they are often ignored when general policies are being considered. Similarly, results from the Australian National Drug Strategy Household Survey (NDSHS; N=9,744) showed that the criminal status of cannabis did not appear to affect alcohol use (Cameron & Williams, 2001). An extension of the NDSHS study likewise concluded that cannabis decriminalization did not affect alcohol use (Williams & Mahmoudi, 2004). The strongest result from (Williams & Mahmoudi, 2004) was that cannabis use was inversely associated with fines for exceeding the legal BAC, implying complementarity; notably, this finding contradicts Cameron and Williams (2001), which concluded that higher alcohol prices were positively associated with cannabis use, implying substitution. Data from the 2004–2011 NSDUH surveys support complementarity as well: a dichotomous MML indicator was associated with a 6–9% increase in the frequency of binge-drinking among those 21 and older (Wen, Hockenberry, & Cummings, 2014). MMLs did not affect drinking behavior among those 12–20 years old; however, earlier MML changes (e.g., California) might have been missed due to the time-period analyzed.

Summary of studies of the general population

Table 2 summarizes results from the general population. Eight out of nine general population studies used indicators of cannabis policy as the independent variable; most notably, all five cross-sectional studies using individual-level consumption as the dependent variable concluded that cannabis and alcohol are complements while the longitudinal studies using state-level dependent variables concluded that they are substitutes. Importantly, cross-sectional data cannot adequately measure substitution/complementarity because substitution and complementarity inherently require the passage of time. Thus the discrepancy between individual- and aggregate-level results may be due to individuals who substitute over time but report both cannabis and alcohol use within a single cross-sectional time period. In addition, differential rates of substitution/complementarity may occur within subgroups; some of these general population studies begin to identify subgroups that may be more likely to substitute, such as Native Americans and Hispanics (H. Saffer & F. Chaloupka, 1999) as well as subgroups more likely to complement, such as whites, African Americans, males, and polysubstance users (H. Saffer & F. Chaloupka, 1999; Williams & Mahmoudi, 2004).

Clinical and community-based samples

General population studies of adults, which usually rely on cross-sectional or retrospective reports, are well supplemented by clinical and community-based studies, which tend to use prospective data (Table 3). In addition, clinical samples include the heaviest substance users and have more detailed measures of substance use, which may improve study validity.

Cannabis treatment seekers

The first set of clinical studies focuses on cannabis treatment seekers. In a prospective cohort (N=212) of individuals seeking treatment for cannabis, posttreatment increases in alcohol-related problems were not associated with reduced cannabis use (Stephens, Roffman, & Simpson, 1994). A similar study (N=291) showed significant increases in alcohol problems at every follow-up, though there were no changes in alcohol use (Stephens, Roffman, & Curtin, 2000). A study of 207 individuals wanting help quitting/reducing cannabis found that 73% increased drinking at the one-year follow-up. However, increased alcohol was not related to decreased cannabis, and those with lower baseline drinking were more likely to increase alcohol use than those with high baseline drinking (who were more likely to reduce drinking). The authors concluded that substitution was not occurring and that any increases in drinking could be attributed to regression to the mean (Kadden, Litt, Kabela- Cormier, & Petry, 2009). Overall, within studies of cannabis treatment-seeking individuals who reduce cannabis, neither alcohol substitution nor complementarity appears to occur.

Cannabis users not seeking treatment

In contrast, alcohol might substitute for cannabis among users who are not seeking treatment. Among 104 non-treatment-seeking cannabis smokers who reported at least one cannabis quit attempt without treatment, half reported increased tobacco, alcohol, and/or sleeping aids to cope with cannabis withdrawal (Copersino et al., 2006), suggesting some substitution, though very few initiated new substance use (N=6). The authors concluded that quitting cannabis spontaneously may lead to increases in legal substance use; however, the results rely on small sample and retrospective self-report, and analyses were deemed exploratory. Still, a community-based study of non-treatment-seeking, DSM-IV dependent cannabis users (N=45) similarly found that two-week cannabis abstinence was related to increases in alcohol that decreased once cannabis was resumed, especially among those with low baseline alcohol use; alcohol did not increase among those who remained abstinent through the one-month follow-up (Allsop et al., 2014).

Natural history descriptions

Prospective "natural history descriptions" of attempts to abstain from cannabis have also been used. Kouri and colleagues (2000) examined 28-day diary data from 30 users and 30 non/former cannabis users and found that cannabis abstinence was not related to alcohol, tobacco, or caffeine use (Kouri & Pope, 2000). Among a smaller (N=12) sample of daily users, alcohol use did not differ between using and abstinent study phases (Budney, Hughes, Moore, & Novy, 2001). A longer 50-day natural history study (N=18 users abstaining, 12 ex-users) documented withdrawal symptoms, and alcohol, cigarette and caffeine consumption: overall, alcohol use did not change (Budney, Moore, Vandrey, & Hughes, 2003). Although these results suggest that substitution is not occurring among cannabis users who abstain, participants in these three studies were asked not to change alcohol use, which substantially limits interpretation. In a natural history study of daily cannabis users in Vermont (N=19), neither cannabis abstinence nor reduction were related to changes in alcohol use (Hughes, Peters, Callas, Budney, & Livingston, 2008). Though participants did

not receive instructions about alcohol consumption, the sample was small and consisted of daily dependent users, which may also limit generalizability.

Similar one-month diaries completed by 28 daily cannabis users showed that those with past alcohol use disorders (AUD) significantly increased alcohol use during cannabis abstinence (52% increase), while those without past AUD did not (3% increase), suggesting that individuals with AUD may be more likely to substitute (Peters, 2010). On the other hand, among individuals with AUD in psychiatric treatment, cannabis use increased the hazard of alcohol relapse and decreased the likelihood of stable abstinence post-discharge, suggesting complementarity (Aharonovich et al., 2005). Thus, results from AUD samples are mixed.

Medical cannabis users

Substitution does appear common among medical cannabis users. In a cross-sectional survey of 350 medical cannabis patients, 40% reported substituting cannabis for alcohol (Reiman, 2009); 65% reported “less adverse side effects” as the reason for substitution. A similar Canadian study (N=404) stated that 75% of the sample claimed to have used cannabis as a substitute for some other substance, while 41% used cannabis as substitute for alcohol specifically (Lucas et al., 2013). Those who reported using cannabis as a substitute for alcohol were significantly more likely ($p < 0.05$) to be male, to make between $40,000 and $59,000 annually, to be current drinkers, and to report a history of alcohol and substance abuse than those who did not report substituting, suggesting other potential modifiers.

Summary of studies of clinical and community-based samples

Table 3 summarizes results from the 13 studies using clinical or community samples. Among cannabis users and treatment seekers, alcohol does not appear to substitute for cannabis during times of cannabis abstinence. Results from studies of individuals with AUD are inconclusive. Only cross-sectional studies of medical cannabis users support substitution, though those studies are limited by possible selection and recall bias. Thus, there is no clear pattern of substitution/complementarity among clinical and community samples.

Overall summary of findings

Of the 39 studies reviewed, 16 support substitution, ten support complementarity, 12 support neither and one supports both. Findings from longitudinal studies of youth lean towards complementarity while findings from general population studies support substitution. The inconsistent conclusions may be explained by 1) the examination of heterogeneous subgroups both across and within studies (e.g., youth vs. adults, heavy vs. light drinkers), 2) variation in independent and dependent variables (e.g., any vs. binge drinking), and 3) reliance on a binary model of cannabis and alcohol co-use (i.e., substitution vs. complementarity), especially because co-use patterns are more complex. In reality, “concurrently available reinforcers” (e.g., alcohol and cannabis) fall on a continuum such that they can be substitutes, complements, or independent of one another to different people at different times (Bickel, DeGrandpre, & Higgins, 1995) (Green & Freed, 1993). On one end, “substitutable reinforcers” can be easily traded for one another due to similar functionalities. At the opposite end “complementary reinforcers” are consumed together proportionately, and therefore cannot be traded for one another (Green & Freed, 1993). The

current results indicate that longitudinal studies of youth support complementarity while general population studies support substitution; this further corroborates the notion that as psychoactive reinforcers, alcohol and cannabis indeed fall on a substitution/complementarity spectrum.

Alcohol and cannabis policies

Studies of MMLs and cannabis decriminalization suggest that adolescents and young adults may reduce alcohol use in more liberal cannabis environments (substitute). Conversely, studies of beer taxes showed that youth reduced cannabis use when taxes were raised, suggesting complementarity in more stringent alcohol environments. Studies of the MLDA were mixed; whether changing the MLDA affects cannabis use among youth remains an open question.

In the general population, three of the four longitudinal studies concluded that alcohol and cannabis are substitutes, while all five cross-sectional studies using individual-level consumption as the dependent variable concluded that cannabis and alcohol are complements. Notably, all of these studies used cannabis decriminalization or MML indicators as the independent variable. As discussed above, cross-sectional data cannot capture the passage of time and are therefore suboptimal for assessing substitution/complementarity. The inconsistencies between the cross-sectional and longitudinal findings may be explained by individuals who actually do substitute over time but report both cannabis and alcohol use within a single cross-sectional time period. Thus, taken as a set, findings from the general population suggest that substitution may occur in more liberal cannabis environments.

Notable subgroups

Numerous individual and/or societal factors influence individual substance use and the propensity to substitute/complement. The studies reviewed here suggest that cannabis-related laws may affect alcohol use differently across genders and races (H. Saffer & F. Chaloupka, 1999; Williams & Mahmoudi, 2004). For example, white males and African Americans were found to complement in more liberal cannabis environments, while Native Americans and Hispanics were found to substitute (H. Saffer & F. Chaloupka, 1999). Polysubstance users and males were also found to complement under cannabis decriminalization (Williams & Mahmoudi, 2004). Finally, substitution appeared to occur among medical cannabis users.

Common study limitations

Many of the studies cited used dichotomous measures of cannabis laws as their primary independent variable, which may overlook variations due to nuances, e.g., many non-decriminalized states have conditional discharges for first offenders (Pacula, Powell, Heaton, & Sevigny, 2013). Some studies may have under-sampled risky consumers as well. Within the general population studies, early studies exclude the price of cannabis, which may lead to omitted variable bias (Williams & Mahmoudi, 2004). Furthermore, the use of pooled cross-sectional data in many of the studies reviewed here might mask heterogeneity of effects over time and across subgroups. Finally, based on the search criteria, relevant studies

that did not explicitly refer to “substitution” and/or “complementarity” may have been missed; a broader review of the literature regarding alcohol/cannabis co-use would supplement the current findings and possibly explain some of what was found here.

Implications for future research and practice

Event-level data are crucial to understanding how individuals substitute/complement alcohol and cannabis; future studies should collect detailed data regarding alcohol and cannabis quantity and frequency, as well as regarding the order in which the substances are consumed. For example, individuals may substitute cannabis for alcohol if using cannabis first, but complement the two if drinking first. Whether cannabis can substitute for alcohol among individuals with AUD also remains an important open question (Subbaraman, 2014), especially because AUD treatment programs often expel patients for testing positive for other drugs; current and future studies are investigating whether cannabis use during AUD treatment affects post-treatment alcohol outcomes. In terms of policy, future studies should collect fine-grained longitudinal, prospective data from the general population and subgroups of interest, especially in locations that are likely to legalize cannabis in the near future. These data will help us understand how various groups along the co-use continuum respond to policy changes, and allow us to continue identifying high-risk groups and consequences associated with various co-use patterns. Understanding whether laws aimed at a particular substance have spillover effects on other substance use will help us develop optimal policies, while identifying groups associated with particular co-use patterns will inform prevention and intervention strategies.

Conclusion

Alcohol and cannabis act as both substitutes and complements, and policies aimed at one substance may inadvertently affect consumption of other substances. Results from studies of youth suggest that youth may reduce alcohol in more liberal cannabis environments (substitute), but reduce cannabis in more stringent alcohol environments (complement). Results from the general population suggest that substitution of cannabis for alcohol may occur under more lenient cannabis policies, though cannabis-related laws may affect alcohol use differently across genders and racial groups. Policymakers should consider spillover effects when crafting legislation.

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Table 1

Summary of studies examining cannabis/alcohol substitution and/or complementarity among **adolescents and young adults**

Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
				Longitudinal Studies					
Pacula, 1998	8,008	Longitudinal panel	National Longitudinal Survey of Youth (1979)	State-level beer tax	Individual-level past 30-day # drinks, # times used cannabis	Probit & OLS regression	Personal & family characteristics	Complements	Collinearity of crime/ officer ratio and state decriminalisation
Anderson, 2012	*Varies by dataset*	Pre/post	Youth Risk Behavior Surveillance System, National Longitudinal Survey of Youth (1997) Treatment Episode Data Set	State-level MML indicator	Individual-level past 30-day cannabis & alcohol use[a] & frequency; State-level cannabis-related treatment admissions	Fixed effects regression	Individual & state-level demo's; state-level taxes, BAC[b] law	Neither	Inconsistencies across states in YRBSS
				Cross-sectional Studies (Aggregate-level Outcomes)					
McGlothlin, 1970	594	Cross-sectional survey	College students, free clinic patients	Occurrence of Operation Intercept (1969)	Prevalence of self-reported substitution of alcohol for cannabis	Crude prevalence	None	Substitutes	Subject-specific definition of "substitution," no comparison group
DiNardo, 2001	>156,000	Cross-sectional survey	Monitoring the Future	MLDA[b], state-level cannabis decriminalisation indicator, alcohol price	State-level prevalence of past 30-day cannabis & alcohol frequency	Random effects regression	State-year demo's & policies	Substitutes	No agreement on controls, MTF excludes non-HS grads
Crost, 2012	71 (state-level obs)	Cross-sectional survey	National Survey on Drug Use and Health	Turning MLDA of 21	Population-level past month cannabis & alcohol frequency	Regression discontinuity, instrumental variables (IV)	None	Substitutes	Age might not be precise; IV estimates apply to 21 year olds likely to comply with laws like MLDA
Simons-Morton, 2010	4,858	Cross-sectional survey	Health Behavior in School Age Children (15 year olds from USA, Canada, Netherlands)	Restrictiveness of country-level alcohol & cannabis policies	Country-level alcohol frequency, cannabis use	Crude prevalence comparison	None	Complements	Cross-sectional; Potential endogeneity (laws could precede prevalence)
Pape, 2009	16,813	Cross-sectional survey	European School Project on Alcohol	None	Proportion of cannabis/alcohol use occasions	Crude prevalence comparison	None	Complements	Cross-sectional

Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
			& Drugs						
Williams, 2004a	48,174	Cross-sectional survey	Harvard School of Public Health College Alcohol Study	State-level cannabis decriminalisation indicator; cannabis price	State-level past month & past year alcohol & cannabis frequency	Fixed effects regression	Individual-level demo's; state-level prices & policies; college-level fines, penalties, miles from DEA	Complements	Measurement error in cannabis price (one of main IVs)
Cross-sectional Studies (Individual-level outcomes)									
Farrelly, 1999	49,311	Cross-sectional survey	National Household Survey on Drug Abuse (12–20 year olds)	State-level cannabis-related penalties, county-level # cannabis arrests	Individual-level past month cannabis use	Probit regression	Individual-level demo's, state-level cigarette & alcohol prices	Complements	Effects disappear when including state-level indicators
Chaloupka, 1997	25,430	Cross-sectional survey	Monitoring the Future	State-level cannabis decriminalisation indicator	Individual-level alcohol frequency, heavy drinking, accidents	Probit regression	Individual-level demo's, alcohol prices, MLDA, cannabis price	Substitutes	Measurement error in prices, accidents
Clements, 2005	281	Cross-sectional survey	First-year college economics students	Hypothetical cannabis legalization	Individual-level beverage-specific alcohol use[b]	Regression	Sex, intensity of cannabis use	Substitutes	Hypothetical; price elasiticities unclear
Thies, 1993	12,686	Cross-sectional survey	National Longitudinal Survey of Youth (1979)	State-level cannabis decriminalisation indicator, MLDA, arrests	Individual-level alcohol & cannabis use & frequency	Multiple regression	Individual-level demo's	Weak substitutes	Possible measurement in error in drug use frequency
Alter, 2006	11,542	Cross-sectional survey	Monitoring the Future: Midwest subsample	Perceived access & harms of alcohol & cannabis	Individual-level past month alcohol & cannabis frequency	Multiple regression	Individual-level demo's, academics	Substitutes	Pooled cross-sections; variation in surveys
Yörük, 2011	~9,000	Cross-sectional panel survey	National Longitudinal Survey of Youth (1997)	Turning MLDA of 21	Individual-level past 30-day alcohol & cannabis use & frequency	Regression discontinuity	Individual-level demo's	Complements	Only included respondents who had used cannabis at least once since last interviewed
Keyes, 2015	7,191	Pooled cross-sections	16–25 years olds from the 1999–2011 Fatality Analysis Reporting System	Turning MLDA of 21	Individual-level fatal injury due to alcohol use	Regression discontinuity; Joinpoint permutation	Sex, race/ethnicity, # vehicle occupants, # deaths in incident, year, state, whether state has MML	Neither	Missing data, inconsistent reporting/testing across states,

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Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
Crost, 2013	28,089	Cross-sectional panel survey	National Longitudinal Survey of Youth (1997)	Turning MLDA of 21	Individual-level past 30-day cannabis use & frequency	Regression discontinuity	Individual-level demo's	Neither	Age might not be precise (exact birthdays are unknown)
				Other Relevant Studies					
Peters, 2012	122 (18–25 year olds)	RCT	8-week randomized control trial for naltrexone for alcohol use	Cannabis user	Individual-level alcohol use & related problems	MANCOVA	None	Neither	Focus was not on alcohol, did not examine in regression

[a] Use is dichotomous yes/no

[b] BAC = Blood Alcohol Content

[c] MLDA = Minimum legal drinking age

[d] MML = Medical marijuana law

Table 2

Summary of studies examining cannabis/alcohol substitution and/or complementarity among the **general population**

Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
				Longitudinal Studies					
Anderson, 2011	*Varies by dataset*	Pre/post	National Survey on Drug Use and Health, Fatality Analysis Reporting System, BRFSS	State-level MML & cannabis decriminalisation indicators	State-level alcohol-related traffic fatality rate; monthly # drinks, prevalence of bingeing	Difference-in-difference; fixed effects regression	State-level BAC laws, demo's, driving characteristics	Substitutes	Ignores nuances of laws (as do most studies); Does not look at traffic fatalities involving cannabis
Anderson, 2013	*Varies by dataset; Expands* (Anderson, 2011) *to 19 states with MMLs*	Pre/post	National Survey on Drug Use and Health, Fatality Analysis Reporting System, BRFSS	State-level MML & cannabis decriminalisation indicators	State-level alcohol-related traffic fatality rate; monthly # drinks, prevalence of bingeing	Difference-in-difference; fixed effects regression	State-level BAC laws, demo's, driving characteristics	Substitutes	Ignores nuances of laws (as do most studies)
Salomonsen-Sautel, 2014	36 six-month intervals of motor vehicle fatalities	Pre/post	Fatality Analysis Reporting System	Indicator of commercial availability of medical cannabis in Colorado (2009)	State-level proportion of drivers in fatal crashes who were alcohol-impaired or cannabis-positive	Generalized least squares with AR(1)	34 states without MMLs through 2011; Proportion of male drivers, proportion of drivers age 21–24, proportion tested for drugs/alcohol	Neither	Inconsistent testing and reporting across states and time
Kelly, 2014	<1 million public hospital admissions	Pre/post	Quarterly hospital admissions from 1997–2009 in London, England	Depenalization of cannabis possession in Lambeth, London, England	Hospitalizations related to alcohol use	Difference-in-difference regressions	Admission age and gender; models also include time and neighborhood fixed effects	Substitutes	Changes in ICD coding over time; potential selection bias due to use of hospitalizations
				Cross-sectional Studies					
Saffer, 1998	49,082	Cross-sectional survey	National Household Survey on Drug Abuse	State-level alcohol & drug prices	Individual-level alcohol frequency, cannabis use[b]	Regression	Individual-level demo's, cost of living, state-level cannabis decriminalisation indicator	Complements	Measurement error in prices

Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
Saffer, 1999	49,082	Cross-sectional survey	National Household Survey on Drug Abuse	State-level cannabis decriminalisation indicator	Individual-level alcohol frequency, cannabis use	Regression	Individual-level demo's, cost of living, state-level alcohol & drug prices	Complements for full sample, white males & blacks; substitutes for Native Am's & Hispanics	Under-sampled risky consumers (a potential concern of numerous studies); pooled cross-sections
Cameron, 2001	9,744	Cross-sectional survey	National Drug Strategy Household Survey (Australia)	State-level cannabis decriminalisation indicator	Individual-level past 12-month alcohol & cannabis use	Probit regression	Individual-level demo's; State-level income, alcohol, cannabis, cigarette prices	Both: decriminalisation increases alcohol use suggesting complements; price effects suggest substitution	Only decriminalized state is South Australia, so decriminalisation effect might really be SA effect
Williams, 2004b	15,479 *Expands* (Cameron, 2001) *to polysubstance users & adds control for drunk driving*	Cross-sectional survey	National Drug Strategy Household Survey (Australia)	State-level cannabis decriminalisation indicator, fines for drunk driving, price of cannabis & alcohol	Individual-level past year cannabis use	Probit regression	Individual-level demo's	Complements, especially among polysubstance users & males	Results depend on inclusion of year effects
Wen, 2014	Not stated	Cross-sectional survey	National Survey on Drug Use and Health	State-level MML [b] indicator	Individual-level alcohol, cannabis, & other drug use, binge-drinking	Fixed effects regression	Individual & state-level demo's	Weak complements among those older than 21	Short time-frame (2004–2011) might miss effects of earlier MMLs (e.g., CA)

[a] MML = Medical marijuana law

[b] Use is dichotomous yes/no

Table 3

Summary of studies examining cannabis/alcohol substitution and/or complementarity among **adult clinical and community samples**

Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
Longitudinal Studies—Cannabis Treatment Seekers									
Stephens, 1994	212	Prospective cohort	Cannabis treatment-seekers	Weekly alcohol use	Past 90-days cannabis frequency	Bivariate MANOVA, correlations	None	Neither	Focus is cannabis treatment outcomes; generalizability
Stephens, 2000	291	Prospective cohort	Cannabis treatment-seekers	Past 90-day alcohol frequency	Monthly cannabis frequency	Partial correlations	Corresponding pre-treatment use measures	Weak complements	Cross-sectional; Generalizability
Kadden, 2009	207	Prospective cohort	Cannabis treatment-seekers	Past 90-day cannabis frequency	Indicator of increased (≥10%) past 90-day proportion days using alcohol, drinks per drinking day	Logistic regression	Individual-level demo's, psychiatric status, substance use severity	Neither	Cross-sectional; Generalizability
Longitudinal Studies—Cannabis Users/Non-Treatment Seekers									
Copersino, 2006	104	Prospective cohort	Non-treatment-seeking cannabis users	None	Self-reported use of alcohol to relieve cannabis withdrawal during quit attempt	Crude prevalence	None	Some evidence of substitution to relieve withdrawal	No comparison group
Allsop, 2014	45	Prospective community-based cohort	Non-treatment-seeking cannabis users	Cannabis abstinence	Alcohol use, quantity	Mixed models for repeated measures with AR(1)	Individual-level demo's, past use	Substitutes, especially among baseline light drinkers	Generalizability
Longitudinal "Natural History" Studies									
Kouri, 2000	60	Prospective cohort	Current & former cannabis users	Cannabis withdrawal symptoms (e.g., cravings)	Changes in alcohol use (not clear)	Within-subject ANOVA	None	Neither	Participants asked not to drink more than 2 drinks/day during study
Budney, 2001	12	Prospective cohort	Daily cannabis users	Cannabis abstinence	Alcohol use	Within-subject ANOVA	None	Neither	Participants asked not to change drinking; Small sample
Budney, 2003	30	Prospective cohort	18 cannabis users, 12 ex-users in parallel	Cannabis abstinence	Alcohol use	Within-subject ANOVA	None	Neither	Participants asked not to change drinking; Small sample; Generalizability

Study	Sample size	Study design	Population	Independent variable(s)	Dependent variable(s)	Method	Control variable(s)	Conclusion	Validity concerns
Hughes, 2008	19	Prospective cohort	Daily cannabis users trying to stop or reduce cannabis on their own	Cannabis abstinence	Alcohol use	Bivariate tests, Wilcoxon rank test	None	Neither	Small sample; Generalizability
Longitudinal Studies—Individuals with Alcohol Use Disorders									
Peters, 2010	28	Prospective cohort	Daily cannabis users not trying to stop or reduce cannabis	Cannabis abstinence	Drinks/day	Within-subject ANOVA	Individual-level demo's, past use	Substitution among those with past AUD	Small sample; Generalizability
Aharonovich, 2005	250	Prospective cohort	Inpatient psychiatric/ substance abuse treatment	Postdischarge cannabis use	Alcohol use post-treatment	Survival analysis	Individual-level demo's, psychiatric status, severity	Complements	Generalizability
Cross-sectional Studies—Medical Cannabis Users									
Reiman, 2009	350	Cross-sectional survey	Medical cannabis patients	None	Self-reported substitution of cannabis for alcohol	Descriptive	None	Substitutes	Subject-specific definition of substitution, medical cannabis patients may not generalize
Lucas, 2012	404	Cross-sectional survey	Medical cannabis patients	None	Self-reported substitution of cannabis for alcohol	Descriptive	None	Substitutes	Subject-specific definition of substitution, medical cannabis patients may not generalize

[a]MML = Medical marijuana law

[b]Use is dichotomous yes/no

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