



## King's Research Portal

DOI:

[10.1177/0269881120919970](https://doi.org/10.1177/0269881120919970)

*Document Version*

Peer reviewed version

[Link to publication record in King's Research Portal](#)

*Citation for published version (APA):*

Risso, C., Boniface, S., Subbaraman, M. S., & Englund, A. (2020). Does cannabis complement or substitute alcohol consumption? A systematic review of human and animal studies. *Journal of Psychopharmacology*, *34*(9), 938-954. <https://doi.org/10.1177/0269881120919970>

### **Citing this paper**

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

### **General rights**

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

### **Take down policy**

If you believe that this document breaches copyright please contact [librarypure@kcl.ac.uk](mailto:librarypure@kcl.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.

**Does cannabis complement or substitute alcohol consumption? A systematic review of human and animal studies**

Constanza Risso\* (1) (4), Sadie Boniface (1), Meenakshi Sabina Subbaraman (2), Amir Englund (1) (3)

(1) Addictions Department, Institute of psychiatry, psychology & neuroscience, Kings College London constanzarissod@gmail.com

(2) Alcohol Research Group, Public Health Institute, Emeryville, CA, United States of America

(3) Department of Psychosis Studies, Institute of psychiatry, psychology & neuroscience, Kings College London

(4) Clínica las Condes, Santiago, Chile.

**Key words:** Cannabis, alcohol, substitution, and complementarity.

## **ABSTRACT**

**Background:** Whether alcohol and cannabis complement or substitute each other has been studied for over two decades. In the changing cannabis policy landscape, debates are moving rapidly and spill over effects on other substances are of interest.

**Aims:** update and extend a previous systematic review, by; a) identifying new human behavioural studies reporting on substitution and/or complementarity of alcohol and cannabis, and b) additionally including animal studies

**Methods:** We replicated the search strategy of an earlier systematic review, supplemented with a new search for animal studies. Search results were cross checked against the earlier review and reference lists were hand searched. Findings were synthesised using a narrative synthesis.

**Results:** Sixty-five articles were included (64 in humans, one in animals). We synthesised findings into categories: patterns of use, substitution practices, economic relationship, substance use disorders, policy evaluation, others and animal studies. Overall, 30 studies found evidence for substitution, 17 for complementarity, 14 did not find evidence for either, and four found evidence for both.

**Conclusions:** Overall the evidence regarding complementarity and substitution of cannabis and alcohol is mixed. We identified stronger support for substitution than complementarity, though evidence indicates different effects in different populations and to some extent across different study designs. The quality of studies varied and few were designed specifically to address this question. Dedicated high quality research is warranted.

**Declaration of interest:** SB works at the Institute of Alcohol Studies which receives funding from the Alliance House Foundation. The other authors have no conflict of interest to declare.

## **BACKGROUND**

One aspect of the increasing liberalisation of medicinal and recreational cannabis taking place in many jurisdictions worldwide that remains poorly understood is the impact that potential increases in cannabis use will have on alcohol use, and whether alcohol and cannabis use substitute or complement one another. Substitution refers to the act of using something instead of another thing, and a complement is something which combines well with or improved something else.

A prominent argument in this issue is whether full or partial legalisation of cannabis will have beneficial or harmful effects on the population. Pro legalisation groups have highlighted the benefits of increased tax revenue, lower law enforcement costs, and the possible medical benefits of cannabinoids for the treatment of certain diseases (McGinty et al., 2017; Sznitman and Bretteville-Jensen, 2015). Contrarily, groups that favour criminalization argue on the harms caused to youth due to increased availability, increased motor vehicle accidents, and are sometimes also sceptical of the possible medical benefits (McGinty et al., 2017; Sznitman and Bretteville-Jensen, 2015).

A key component of the debate has been the harms due to these substances. By 2015, 63.5 million people were estimated to have alcohol use disorder worldwide, and 19.8 million cases of cannabis use disorder were estimated (Degenhardt et al., 2013; Peacock et al., 2018). Alcohol has been ranked as one of the most harmful psychoactive substances, and has been linked to a number of acute and chronic health harms such as cancer and cirrhosis, and is correlated with harms to others, as well as social and economic consequences (Nutt et al., 2010; Van Amsterdam et al., 2010). Some rank cannabis as a medium to low risk substance (Nutt et al., 2010; Van Amsterdam et al., 2010). However, research throughout the past

twenty years has evidenced that regular cannabis use is correlated to significant health and psychosocial harms, and has been linked to poorer school performance, psychosis and cognitive impairment in adulthood, and cardiovascular disease among vulnerable individuals (Hall, 2015).

Several reviews have looked at the relationship between cannabis and alcohol. While some have found evidence of increased co-use of cannabis and other substances upon cannabis liberalisation, they also concluded further research was needed on this subject (Yurasek et al., 2017). The current changing legal landscape has brought this debate to the forefront with some US states, Canada, and Uruguay, legalising recreational cannabis. Therefore, it is urgently pressing to better understand the relationship between alcohol and cannabis.

The present study is an update and extension of a systematic review completed by Subbaraman (2016), which concluded that alcohol and cannabis act as both complements and substitutes (Subbaraman, 2016). Given the rapidly changing policy landscape, a number of studies have been published since the previous was published. In the present study, we update and expand on the previous review on substitution and complementarity of alcohol and cannabis by identifying new behavioural studies in humans and adding a systematic review of experimental animal studies.

## **METHODS**

PRISMA-P 2015 Guidelines were used to report findings from this study.

## Search Strategy

MEDLINE, PsychINFO, and Embase were searched through OVID on the 28th of May 2018 replicating the search strategy of Subbaraman's 2016 review. The ISI Web of Science (WoS) was also searched using the Web of Science Core Collection. Additionally, articles found through hand searching reference lists on other sources that were found to be relevant were also included. Search terms were used as key words in the title and/or abstract, or as Medical Subject Heading Terms. The search terms used in OVID "alcohol.mp" OR "exp ALCOHOLS" AND "cannabis.mp" OR "exp CANNABIS" AND "complement\*.tw" OR "substitut\*.tw". For the ISI WoS, the search terms used were screened across titles and abstracts and where the following, "alcohol" OR "ethanol" AND "cannabis" OR "marijuana" AND "complement\*" OR "substitut\*"

For the additional review of animal studies, MEDLINE, PsychINFO, and Embase were searched through OVID on the 20th of May 2018. The search was performed simultaneously through the three databases. The search terms used were chosen because of their similarity to the ones used in the update of the Subbaraman review. The terms "complement" and "substitute" were not included. The search terms were filtered for title and abstract. The search strategy used in Ovid was "alcohol.tw" OR "ethanol.tw" AND "cannabis.tw" OR "marijuana.tw" and filters were used to limit the results to animal studies.

Additional records identified through hand searching and through expert recommendations were also included.

## **Inclusion Criteria**

In this systematic review, the inclusion criteria were the same as the Subbaraman (2016) review; (1) they had to be behavioural studies, (2) with a human population, and (3) if the independent variable was cannabis related, the dependent variable had to be alcohol related, or vice versa. For the animal studies, studies were eligible for inclusion if (1) they were experimental studies, (2) had an animal population, and (3) if the independent variable was cannabis-related, the dependent-variable had to be alcohol related, or vice versa.

## **Data selection**

All results were exported into Refworks ProQuest. Titles and abstracts were screened independently by two reviewers to assess eligibility for inclusion. The data extracted was; (a) country, (1) study design, (2) population, (3) sample size, (4) type of measure, (5) measurement tool, (6) independent variable, (7) dependent variable, (8) statistical analysis, (9) control variables, (10) conclusion (substitution, complementarity, both, or neither), and (11) quality assessment. The data was extracted into a data extraction template in Microsoft Excel.

## **Quality Assessment**

Quantitative studies were assessed using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies (EPHPP), as recommended in the Cochrane Handbook (Higgins and Green, 2011). However, the tool does not address individual limitations for each study, thus independent qualitative assessment was additionally

conducted by the reviewers to better assess the quality. Qualitative studies were assessed using the Critical Appraisal Skills Programme Checklist for Qualitative Studies (CASP). Animal studies were assessed using the SYRCLE's Risk of Bias tool for Animal Studies (Hooijmans et al., 2014).

### **Narrative Synthesis of Study Findings**

Due to the broad inclusion criteria in terms of study design and population, a meta-analysis was not feasible, and a narrative synthesis was more appropriate (Cheung and Vijayakumar, 2016; Jahan et al., 2016).

Findings were synthesised narratively under seven topics. Patterns of use; studies analysing how different populations use alcohol and cannabis in their daily life. Substitution practices; studies exclusively exploring self-reported substitution of cannabis for alcohol or alcohol for cannabis in specific populations. Economic relationship; Studies that evaluate if a monetary-related change in one substance affects the use or demand of another substance. Substance use disorders; studies evaluating changes in substance use in a population attempting to stop or reduce the use of another substance. Policy evaluation; studies that analyse the impact that a cannabis or alcohol related policy has in the use of alcohol or cannabis. Animal studies; experimental studies that analyse the relationship between alcohol and cannabis in animal models. Others; Studies that analyse substitution and complementarity between alcohol and cannabis but do not fit into any of the above-named groups



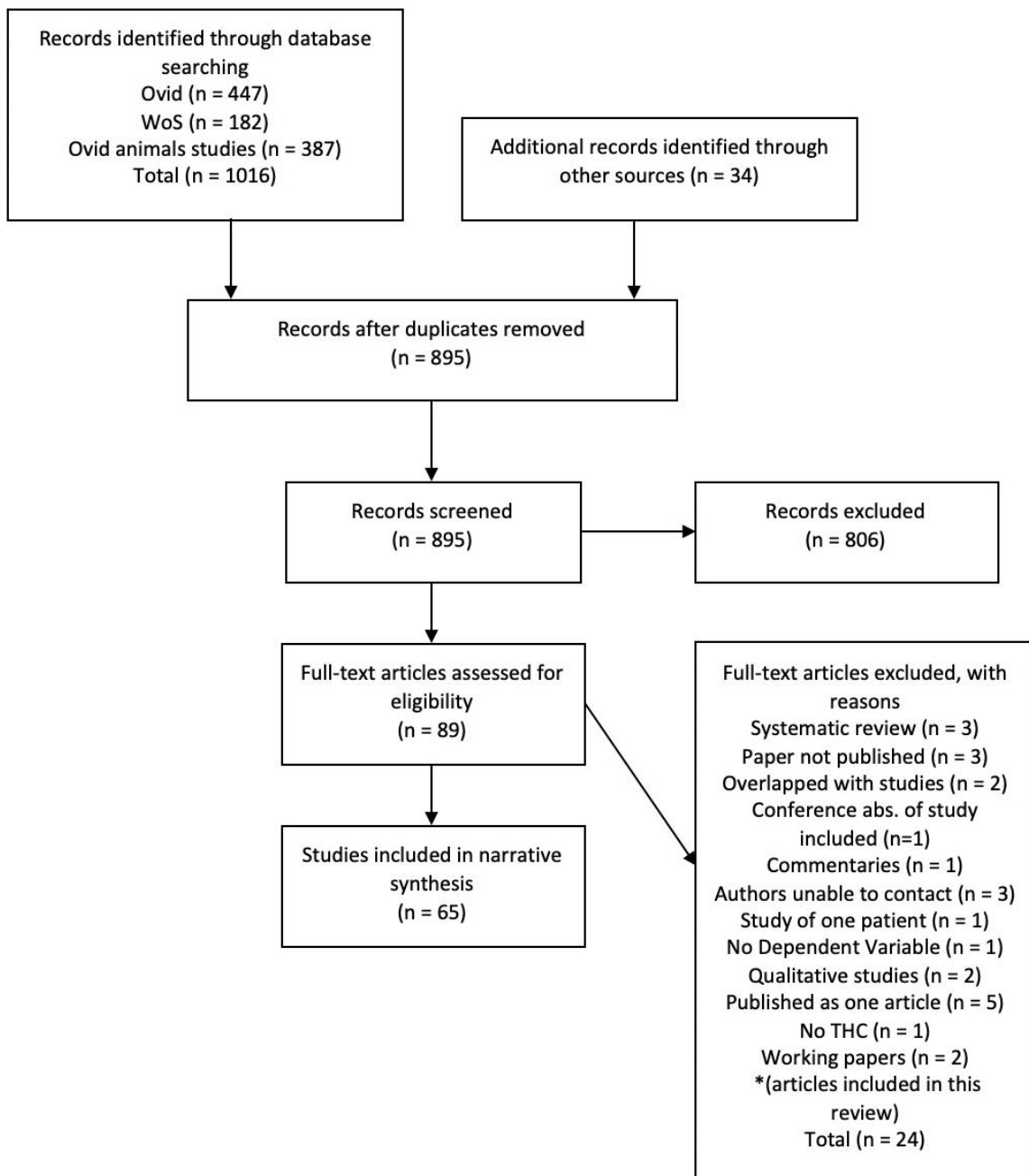
## **Terminology**

The word substitution and complementarity are used as shorthand throughout the article to describe the results of included studies. These terms are well suited to describing the majority of the individual-level data studies. However, they may be less adequate when addressing ecological studies which use population level data, where population level changes in alcohol or cannabis use do not necessarily reflect individuals switching from one substance to another, for example. However, for ease of understanding, and for consistency with the existing literature and search strategy, we use the same terminology for population-level studies.

## **RESULTS**

### **Included studies**

In total, 1046 articles were identified [FIGURE 1]. In total, 65 articles were included in the final review. Of these, 39 are the papers found in the Subbaraman (2016) review, and 26 additional articles were included in this review.



## General characteristics of the studies

Studies included were published between 1970 and 2019. Studies were conducted in USA (n=49), Canada (n=4), Australia (n=5), Norway (n=2), UK (2), Brazil (n=1), Sweden (n=1), and one was conjointly conducted in USA, The Netherlands, and Canada. The sample sizes ranged from 8 to 5,428,399. Twenty-six longitudinal studies, 34 cross sectional studies, one randomised controlled trial (RCT), one secondary analysis of an RCT, one experimental study in animals, one qualitative study, and one economic analysis study were identified.

Measures were also grouped into categories. The type of measure used was defined as the main unit or units of measurement explaining the dependent variable (outcome). Eight types of measure were identified (Table 1).

*Table 1. Types of measures*

|                            |   |
|----------------------------|---|
| Consumption                | Units of quantity and/or frequency of alcohol and/or cannabis, or participation in use measured by a dichotomous variable |
| Toxicological              | Toxicological measures  |
| Self-reported use          | Self-report of cannabis and/or alcohol use  |
| Self-reported substitution | Self-report of substituting one substance for another   |
| Fatalities                 | Quantity of traffic fatalities and of cannabis positive drivers involved in traffic fatalities                            |
| Monetary                   | Measures of drug prices   |
| Qualitative interview      | Reported through patient's interviews.  |
| Locomotor activity         | Distance moved by mice.   |
| Unspecified                | Does not specify the unit of measure used   |

## **1. Policy evaluation studies**

This section contains ecological studies on changes in cannabis policy. “Substitution” and “complementarity” are used as shorthand to describe any changes in alcohol use which were measured on a population level. Where studies used individual level data, this is noted in the text.

### *1.1 Minimum Legal Drinking Age (MLDA)*

Six studies looked at the effects of MLDA on cannabis and alcohol use, looking at the changes in substance use after a MLDA of 21 years had been applied in the USA. Two studies found evidence for substitution, one for complementarity, and three did not find evidence for either. Five studies used measures of consumption and one study used fatality measures. Four studies, and two were rated as moderate.

Regarding substitution, one study conducted in the 1980s in 43 US States, found that increased legal drinking age was associated with reduced alcohol use, but increased cannabis use (DiNardo and Lemieux, 2001). Another study using data from the early 2000s found that turning 21 years, and thus having legal access to purchase and drink alcohol, was linked to decreased cannabis use but increased alcohol use (Crost and Guerrero, 2012). This study analysed consumption data from individuals just below and above 21 years of age, therefore it did not rely on cross sectional state variations in alcohol prices and policies.

Contrarily, a study that used individual level data and also looked at cannabis and alcohol use just upon turning 21 years of age, found evidence for complementarity, with a 7% and 7.6% increase in cannabis and alcohol use respectively upon turning 21 in a MLDA-21 (Yörük and Yörük, 2011). Later on, the authors stated using a restricted sample in their original study, and

in a newer analysis found that in the full sample, the effect of the MLDA-21 was similar for alcohol but smaller and statistically insignificant for cannabis (Yörük and Yörük, 2013).

### *1.2 Medical Marijuana Laws (MML)*

Six studies assessed the impact of new MMLs on alcohol use. Four concluded substitution, one concluded complementarity, and one did not conclude either of the two. Four studies used measures of consumption and two used traffic fatality measures. Two studies were rated as strong, three as moderate, and one as weak.

Regarding substitution, a study looking at individual level data found that cannabis use and binge drinking decreased in 8<sup>th</sup> graders, but not in 10<sup>th</sup> and 12<sup>th</sup> graders, upon MML enactment, accounting for policies that could have affected the price of different substances (Cerda et al., 2018). Anderson (2013) conducted a study evaluating the impact of MMLs on traffic fatalities and alcohol use, and found that legalisation was associated with a decrease in alcohol involved traffic fatalities after a full the law came into effect (Anderson et al., 2013). Another study looked at border alcohol sales from Retail scanner data in 38 contiguous counties in Washington, and found that legalisation was associated with a 12% reduction in alcohol sales (Baggio et al., 2018).

One study found weak evidence for complementarity, stating that MMLs were associated with increased frequency of binge drinking in adults (21+), but this finding was not seen in adolescents (Wen et al., 2014). This study used individual level substance use and binge drinking.

### 1.3 Cannabis and alcohol related policies

Nine studies looked at cannabis related policies on alcohol and cannabis use. Seven studies found evidence for substitution and two for complementarity. Seven studies used consumption measures, one used a monetary measure, and one used fatality measures. Three studies were rated as strong, four as moderate, and two as weak.

Regarding substitution, one study that used a survey to simulate cannabis legalization on Australian college students found a 4% increase in cannabis use and a 1-4% reduction in alcohol use (Clements and Daryal, 2005). Another study evaluated the impact of cannabis decriminalisation in 11 US states, in an all-male sample, and found weak evidence that fewer individuals drank “*six or more drinks*” on a single drinking occasion (Thies and Register, 1993). Another study compared one London borough (Lambeth), where small quantities of cannabis were depenalised, to other London boroughs and found that cannabis depenalisation was associated with a reduction in alcohol-related hospital admissions in 15-24 years old, but no effect in older adults (Kelly and Rasul, 2014). A study that followed a small regional sample of two cohorts of 8<sup>th</sup> grade students in Tacoma, Washington, looking at individual-level alcohol and marijuana use, found that the cohort that did not experience recreational cannabis legalisation enactment had higher rates of cannabis use and the cohort that did experience the law enactment had higher rates of alcohol use (Mason et al., 2016).

In a study comparing different countries it was found that stricter alcohol policies were associated with reduced alcohol use among 6<sup>th</sup> and 10<sup>th</sup> graders but did not find evidence of changes in cannabis use (Simons-Morton et al., 2010). Another study found an increase in the price of alcohol was associated with a reduced probability of cannabis use in the youngest cohort (15-20 years), analysing individual level past month cannabis use (Farrelly et al., 1999).

## **2. Substance use disorders studies**

### *2.1 Cannabis cessation or reduction*

Twelve studies were identified. Four studies found evidence for substitution, one for complementarity, one for both, and six for neither. Seven studies used consumption measures, one used self-reported use of substance, one used toxicological data, and three did not specify the measure. One study was rated as strong, six as moderate, and five as weak.

Studies that found evidence for substitution were all conducted on non-treatment seeking cannabis users reducing their use (Allsop et al., 2014; Copersino et al., 2006a, 2006b; Peters and Hughes, 2010). One study found a 52% increase of alcohol use at follow-up (alcohol drinks/day), among participants with former alcohol abuse/dependence problems, when they abstained from cannabis use (Peters and Hughes, 2010). Another study identified a greater increase of alcohol use during cannabis abstinence among baseline light drinkers (21 Standard Units/week), compared to those who were heavier drinkers at baseline (Allsop et al., 2014).

### *2.2 Alcohol cessation or reduction*

Five studies were identified. One study found evidence for substitution and two studies concluded on complementarity and two did not conclude on neither. Four studies used measures of consumption measures and one used self-report use. Two were rated as moderate, and three as weak.

Regarding substitution, one study looked at records of 92 patients that reported using cannabis to treat their alcohol use problems and found that 83 patients reported cannabis as

effective, while nine said to use cannabis to achieve total abstinence (Mikuriya, 2004). As to complementarity, one study found that participants who used cannabis at post discharge from alcohol dependence treatment were associated with a higher risk of relapsing and returning to alcohol use (Aharonovich et al., 2005).

### **3. Economic relationship**

#### *3.1 General population*

Three studies were included in this group. One study concluded complementarity, and two studies found evidence for both complementarity and substitution. All studies used consumption measures and were rated as strong.

Comparing cross price effects in eight demographic samples, one study found that alcohol and cannabis were associated as economic complements in the full sample, in white-male-non-Hispanics, in blacks, and in Native Americans (Saffer and Chaloupka, 1999a). This study also found evidence of substitution in Hispanics, and no effect in women, Asians, and young people (Saffer and Chaloupka, 1999a).

A study conducted in Australia found that a 10% increase in the price of alcohol could be related to a 4.17% increase in the probability of cannabis use, suggesting economic substitution (Cameron and Williams, 2001). They also found that cannabis decriminalisation, as an indicator of price, could increase alcohol participation, suggesting complementarity (Cameron and Williams, 2001). In South Australia, the only state that decriminalised cannabis, individual-level alcohol drinking was 3% higher than in the rest of the country (Cameron and Williams, 2001).



### *3.2 Young people*

Two studies found evidence for complementarity, one for substitution, and one for both. All used measures of consumption and were rated as strong.

Regarding complementarity, a study from the USA among 14-21-year olds found that doubling beer tax could result in a 11.4% reduction in the probability of using marijuana and a 13.3% reduction in the demand for marijuana, compared to a 3.2% reduction in the probability of using alcohol and an 8.1% reduction in the demand for alcohol (Pacula, 1998).

Another study on college students found that higher beer tax was associated with lower prevalence of alcohol and cannabis use, and cannabis prices were negatively related to alcohol and marijuana participation (Williams et al., 2004). Results from Williams (2004) are difficult to weight as the tool used (CAS) is nationally representative of fulltime students in four-year colleges only, and provides self-reported data. Both studies rely on cross sectional data and price policies (Pacula, 1998; Williams et al., 2004).

A study from the 1980s that used decriminalisation as an indicator of cannabis price (cannabis in decriminalised states is expected to be cheaper) found that youth consumed alcohol less frequently and were less likely to engage in heavy drinking in decriminalized states (Chaloupka and Laixuthai, 1997). Furthermore, they found that a state that moved from criminalisation to decriminalisation, the number of drinking abstainers could increase by 12%, frequent drinkers could reduce by 11%, and heavy drinking episode could reduce by 12% (Chaloupka and Laixuthai, 1997). In a sample of 12th graders, one study found that a 1% increase in liquor prices was associated with reduced odds of frequent marijuana use by 2.4%

(complementarity), but decriminalisation of marijuana was linked to reduced odds of frequent drinking by 7% (substitution) (Yamada et al., 1996).

### *3.3 Drug users*

Of the two studies, one concluded on substitution and one on complementarity. One study used measures of consumption, and the other used monetary measures. One study was rated as strong, and the other as weak.

A study on a sample of 80 polydrug users found an increase in alcohol purchases when the perceived quality of cannabis dropped to average or poor (Cole et al., 2008).

A study in Australia found evidence for complementarity showing that the price of alcohol and the fine for exceeding the Blood Alcohol Concentration limit for driving was negatively related to cannabis use. This was stronger in participants that used alcohol and cannabis concomitantly (Williams and Mahmoudi, 2004).

### *3.4 Other*

This study analysed the changes in cannabis prices in Australia and found that, for the period of 1990, cannabis prices dropped an average of 20 percent, while cannabis consumption increased 2,8 percent and alcohol consumption dropped an average of 6,05 percent, supporting substitution (Clements, 2004).

## **4. Patterns of use**

### *4.1 General population*

This study found evidence for complementarity, used consumption measures, and was rated as moderate. The study compared the use and transition of substances in different types of cannabis users, in two periods of time, and found that participants who continued to use cannabis from Wave 1 to Wave 2 had higher odds of reporting alcohol use problems, compared to participants who stopped using cannabis (Choi et al., 2018).

### *4.2 Young people*

Four studies found evidence for complementarity, and one found evidence for neither. All studies used consumption measures. One study was rated as strong, one as moderate, and three as weak.

A Norwegian study on high school students found that those who drank more alcohol were more likely to use both substances, and that in 80% of cannabis events, drinking had also occurred (Pape et al., 2009). An earlier Norwegian study found that regular cannabis users showed greater alcohol use, compared to those who only tried cannabis occasionally (Hammer and Vaglum, 1992). A study that assessed a cohort of college students in the USA found that one more drink in the month duration of the study was associated with 40% increased odds of using cannabis (O'Hara et al., 2016).

## **5. Substitution practices**

### *5.1 Medical cannabis patients*

All studies found evidence of substitution. All studies used self-reported substitution as the main measure unit and were rated as weak.

The three studies conducted in Canada were funded by the dispensaries whose costumers made up the study populations, and found a 25%, 52%, and 41% substitution rate of medical cannabis for alcohol (Lucas et al., 2013, 2016; Lucas and Walsh, 2017). Another study was conducted across three dispensaries in USA and found that 42% of participants reported a reduction in alcohol use since they started using medical cannabis (Piper et al., 2017). The last study was conducted in the USA and found that 40% of the participants reported substituting alcohol for cannabis.

### *5.2 Cannabis users*

This was the only qualitative study identified in the review. The conclusion was substitution. Participants reported that they substituted alcohol for cannabis because it was “safer” and had less adverse effects.

## **6. Other**

Studies in this category did not fit within the other categories for the narrative synthesis. Two studies concluded substitution and two concluded complementarity. Three studies used consumption measures and one used self-reported substitution. One study was rated as strong, one as moderate, and two as weak.

Considering substitution, one study found that participants who reported no alcohol use were more likely to report cannabis use (Alter et al., 2006). Another study used a sub sample of

(Reiman, 2009), and found that 50% of participants reported substituting alcohol for cannabis (Reiman, 2007).

Regarding complementarity, one study analysing the impact of Methadone Maintenance Therapy (MMT) enrolment on the onset of heavy drinking, in injectable heroin users, found that cannabis use was related to heavy drinking onset, and not MMT (Klimas et al., 2016). Another study from the USA found that there were twice as many Simultaneous Users (using cannabis and alcohol concomitantly) as there were Concurrent Users (cannabis and alcohol use separately), and simultaneous users had higher levels of frequency and quantity of alcohol use, and had higher likelihood of drunk driving (Subbaraman and Kerr, 2015).

## ***7. Animal studies***

This study was conducted on a rodent model exploring the roll of cannabinoids in alcohol related problems using locomotor activity as the main unit of measurement. The study was rated with low risk of bias. It used a twelve-day acquisition period of daily ethanol injections, followed by four-days of injections of cannabinoid treatment, and found that THC or THC + CBD was effective at reducing alcohol sensitisation, but CBD alone was not effective (Filev et al., 2017).

## **DISCUSSION**

Sixty-five eligible articles were identified and included in this review. Thirty studies found evidence for substitution, 17 for complementarity, four found evidence for both, and 14 did not find evidence for either. Overall, the conclusions of this review and Subbaraman (2016) are very similar. However, whereas Subbaraman (2016) found that decriminalisation suggests some evidence of substitution, this review found mixed evidence for cannabis decriminalisation, depending on the population being studied. Our findings were synthesised into seven groups in a narrative synthesis. This showed that the evidence differs based on the population studied, on the type of study, and the quality of data.

### ***Main results***

The largest number of studies were on alcohol and cannabis related policies. This review found that in MML-jurisdictions, there is some evidence of a substitution effect among adolescents, which is similar to a review by Schlienz and Lee (2018). Other types of cannabis policies showed mixed findings. The evidence on the impact of alcohol related policies was inconclusive. However, there are studies that show that increasing the price of alcohol can result in a reduction of both, alcohol and cannabis use in adolescents. Overall, we find that a large number of policy studies address individual policies and are limited to cross sectional data and self-reported surveys, which makes analysis of results difficult as evidence may not be sufficiently strong.

Substitution of one substance for another has been a major concern among clinicians. One study found that even though the prevalence of co-use of alcohol and cannabis is high among

people in drug treatment, the literature does not show clear direction of substitution or complementarity (Yurasek et al., 2017). However, an interesting finding is that the few studies that show increased drinking during cannabis abstinence were all conducted on cannabis-users who were not seeking treatment, while those that showed evidence of reduced drinking during cannabis abstinence were all conducted on users who were seeking treatment. This shows there may be wider factors to additionally consider, such as motivation to stop substance use.

Regarding how cannabis and alcohol relate to each other economically, the findings were less consistent. Some studies suggested young people were more responsive to increased alcohol prices, compared to cannabis prices, given that two studies show that increased beer tax reduced alcohol and cannabis use in college students. Nevertheless, these studies are limited to cross sectional data and self-reported surveys, which could be highly biased.

There was some evidence that medical cannabis patients use cannabis to substitute alcohol. Still, these findings must be interpreted with caution, as most of these studies were funded by the same medical cannabis dispensaries who provided the cannabis to the study participants. These studies also did not assess complementarity, and therefore, the risk of bias is high in this group of studies.

Only one study in animals was identified. This study showed evidence of potential for cannabinoids in the treatment for alcohol use disorders, either in managing alcohol withdrawal or for relapse prevention.

This review has several strengths. Firstly, the quantity of papers included provides a large body of evidence which allows to expand our understanding as well as identifying gaps in the literature. Following the search strategy of the previous systematic review replicates and

expands on its findings. The addition of quality assessment tools provides more nuance of the studies included in this review, which allows for a greater understanding of the issue and highlights where more high-quality research is needed. The review of animal studies adds a new perspective to the debate and highlights potential medical benefits of cannabinoids in the treatment of alcohol use disorders. Finally, using a narrative synthesis of study allows for findings to be differentiated based on study design is another strength of the study as it may be the case that cannabis can be a substitute in some instances and a complement in others.

We also identified several limitations. First, most studies have been conducted on the impact of policies, leaving large gaps of evidence in other areas. Also, a large portion of the studies were assessed as weak, thus, much of the evidence is based on poor quality studies, making it difficult to draw strong conclusions. All studies on medical cannabis patients were found weak to be weak with a high likelihood of bias, thus providing little reliable evidence. Most studies also used self-report measures, which are known to be biased and somewhat less reliable. Some of the studies did not clearly state how they measured outcomes, making comparison to other studies difficult. Lastly, many studies have shown the potency of cannabis has drastically increased over the last few decades, which may lead different results between newer and older studies (Chandra et al., 2019; Freeman et al., 2019).

We identified a number of newer studies (17) published since the previous review, suggesting that ongoing monitoring of the literature would be of value. The evidence base may evolve as interest grows in this area and more studies are published. Comprehensive research of drug policy implementation across different populations should be subject of future studies. The recent enactment of cannabis legalisation in Canada will provide a natural experiment to



evaluate the changes in cannabis and alcohol use. Research into clinical populations is inconclusive with overall study quality being low.

Evidence from animal studies is recent and scarce and no early conclusions should be drawn. Also, these findings are difficult to generalise to humans as results from animal studies are often not replicated in humans.

Finally, most studies were conducted in the USA. Research is needed in other jurisdictions to study how findings vary in systems that differ politically, economically and culturally.

## **CONCLUSION**

This review found evidence for both, substitution and complementarity, between cannabis and alcohol. Across the different groups assessed in this review, we find that the largest amount of research has been conducted on policy studies substitution, with evidence leaning towards substitution. Otherwise, findings do not show a clear tendency to either substitution or complementarity, and suggest that alcohol and cannabis are used differently and have different effects in different populations. Moreover, to our knowledge, this is the first review that explores the effects of alcohol and cannabis use in animal models, with some novel findings. We find the evidence base on this topic expanding rapidly. Overall, there is a need of high-quality research designed to address the topic, for example, through experimental studies and capitalising opportunities to conduct ecological studies as a result of the current rapidly changing policy landscape around cannabis in some parts of the world.

**Table 2.** Policy Evaluation Studies (20 studies)

| <i>Paper</i>   | <i>Country</i> | <i>Study design</i>      | <i>Population</i>   | <i>Sample size</i>                                 | <i>Measure Category</i> | <i>Measurement tool</i>                    | <i>Independent variable</i>   | <i>Dependent variable</i>  | <i>Conclusion</i> | <i>Quality assessment</i> |
|--|----------------|--------------------------|---|--|-------------------------|--|---|--|-------------------|---------------------------|
| <i>Medical Marijuana Laws studies (7 studies)</i>        |                |                          |   |  |                         |  |   |  |                   |                           |
| Baggio, 2018 (Baggio et al., 2018)                       | USA            | Pre/post                 | Nielsen Retail Scanner database 2006-2015                       | 52 market areas in 48 contiguous states            | Consumption             | Nielsen Retail Scanner database            | County-level MML  | County-level alcohol sales   | Substitution      | Moderate                  |
| Cerda, 2018 (Cerda et al., 2018)                         | USA            | Pre/post                 | MTF 1991-2015   | 1,179,372  | Consumption             | Monitoring The Future Data                 | State-level MML   | Individual-level past 30-day cannabis use, and past two-week binge drinking                        | Substitution      | Weak                      |
| Sabia, 2017 (Sabia et al., 2017)                         | USA            | Repeated cross sectional | Behavioral RISK Factor Surveillance System 1990-2012 population | 5,428,399  | Consumption             | Behavioral Risk Factor Surveillance System | State-level MML   | Past 30-day alcohol consumption  | Substitution      | Moderate                  |
| Salomonsen-Sautel, 2014 (Salomonsen-Sautel et al., 2014) | USA            | Longitudinal Pre/post    | Fatality Analysis Reporting System (FARS)                       | 36-six-month intervals of motor vehicle fatalities | Fatality                | FARS                                       | Indicator of commercial availability of medical cannabis in Colorado (2009) | State-level proportions of drivers in fatal crashes who were alcohol-impaired or cannabis-positive | Neither           | Strong                    |

|   |     |                        |  |                                |             |  |   |   |  |          |
|---|-----|------------------------|--|--------------------------------|-------------|--|---|---|--|----------|
| Wen, 2014<br>(Wen et al., 2014)           | USA | Cross sectional Survey | National Survey on Drug use and Health                       | 183.600 (12-20), 219.400 (20+) | Consumption | National Survey on Drug Use and Health (NSDUH) | State-level MML indicator                               | Individual-level alcohol, cannabis, and other drug use, binge-drinking                      | Weak complements among those older than 21 | Moderate |
| Anderson, 2013<br>(Anderson et al., 2013) | USA | Longitudinal Pre/post  | National Survey on Drug Use and Health (NSDUH) and FARS BRFS | Varies by dataset              | Fatality    | NSDUH, High Price Magazine, FARS               | State-level MML & cannabis decriminalisation indicators | State-level alcohol-related traffic fatality rate, monthly # drinks, prevalence of bingeing | Substitutes                                | Strong   |

---

*Cannabis and alcohol related policies studies (7 studies)*

---

|   |     |                        |  |                        |             |                                |   |  |   |          |
|---|-----|------------------------|--|------------------------|-------------|--------------------------------|---|--|---|----------|
| Subbaraman, 2019<br>(Subbaraman and Kerr, 2019) | USA | Cross sectional survey | Washington residents aged 18 and over              | 5492                   | Consumption | Self-report survey             | Legalisation of recreational cannabis               | Individual-level past 30 days number of drinking days, number of drinks per drinking day, frequency of 5 or more drinks, alcohol related harms | Some evidence of substitution for (decrease in alcohol related harms) | Strong   |
| Miller, 2018<br>(Miller and Seo, 2018)          | USA | Longitudinal           | Nielsen Retail Scanner database                    | 37 Washington counties | Monetary    | Nielsen Retail Scanner Dataset | State-level marihuana legalisation                  | State-level alcohol sales  | Substitution  | Moderate |
| Mason, 2016<br>(Mason et al., 2016)             | USA | Cohort                 | Adolescents in Washington (two cohorts, before and | 238                    | Consumption | Self-report surveys            | State-level pre/post non-recreational marijuana law | Individual-level past 30 days rate of alcohol, marijuana and cigarette use   | Substitution  | Moderate |

|  |                          |                        |   |                                       |             |  |   |   |                  |          |
|--|--------------------------|------------------------|---|---------------------------------------|-------------|--|---|---|------------------|----------|
|  |                          |                        | after non-recreational marijuana law)                           |                                       |             |  |   |   |                  |          |
| Kelly, 2014 (Kelly and Rasul, 2014)              | UK                       | Pre/post               | Quarterly hospital admissions from 1997-2009 in London, England | <1 million public hospital admissions | Fatality    | Hospital records                                       | Depenalisation of cannabis possession in Lambeth, London, England | Hospitalizations related to alcohol use                 | Substitutes      | Strong   |
| Simons-Morton, 2010 (Simons-Morton et al., 2010) | Canada, USA, Netherlands | Cross sectional Survey | Health Behaviour in School Age Children (15 years old)          | 4858                                  | Consumption | Health Behaviour in School-Aged Children Survey (HBSC) | Restrictiveness of country-level alcohol and cannabis prices      | Country-level frequency alcohol, cannabis use           | Complement       | Strong   |
| Clements, 2005                                   | Australia                | Cross sectional survey | First year college economics students                           | 281                                   | Consumption | Self-report survey                                     | Hypothetical (simulation) cannabis legalisation                   | Individual-level beverage specific alcohol use          | Substitution     | Weak     |
| Farrelly, 1999 (Farrelly et al., 1999)           | USA                      | Cross sectional survey | National Household Survey on Drug Abuse (12-20 years old)       | 49,311                                | Consumption | National Household Survey on Drug Abuse (NHSDA)        | State-level cannabis penalties, county-level # cannabis arrests   | Individual-level past month cannabis use                | Complement       | Moderate |
| Thies, 1993 (Thies and Register, 1993)           | USA                      | Cross sectional Survey | National Longitudinal Survey of Youth (1979)                    | 12,686                                | Consumption | National Longitudinal Survey of Youth (1984 and 1988)  | State-level cannabis decriminalisation indicator, MLDA arrests    | Individual-level cannabis and alcohol use and frequency | Weak substitutes | Moderate |

|   |     |                        |   |     |             |                    |   |  |              |      |
|---|-----|------------------------|---|-----|-------------|--------------------|---|--|--------------|------|
| McGlothlin, 1970<br>(McGlothlin et al., 1970) | USA | Cross sectional survey | College students and free clinic patients | 594 | Consumption | Self-report survey | Occurrence of operation intercept (1969) (Marijuana blockage) | Prevalence of self-reported substitution of alcohol for cannabis | Substitution | Weak |
|---|-----|------------------------|---|-----|-------------|--------------------|---|--|--------------|------|

*Minimum Legal Drinking Age studies (6 studies)*

|  |     |                              |  |                               |             |  |                     |  |              |          |
|--|-----|------------------------------|--|-------------------------------|-------------|--|---------------------|--|--------------|----------|
| Keyes, 2015<br>(Keyes et al., 2015)    | USA | Pooled cross sections        | 15-25-year olds from the 1999-2011 FARS      | 7191                          | Fatality    | FARS   | Turning MLDA of 21  | Individual-level fatal injury due to alcohol use, marijuana use, or alcohol and marijuana use              | Neither      | Moderate |
| Krauss, 2015<br>(Krauss et al., 2015)  | USA | Cross sectional Survey       | NSDUH 2004-2012 (Born 1949-1972)             | 110,300                       | Consumption | National Survey on Drug Use and Health       | State-level MLDA-21 | Individual-level past month and past year cannabis use and meeting criteria for marijuana abuse/dependence | Neither      | Strong   |
| Crost, 2013<br>(Crost and Rees, 2013)  | USA | Cross sectional panel survey | National Longitudinal Survey of Youth        | 28,089                        | Consumption | National Longitudinal Survey of Youth (1997) | Turning MLDA of 21  | Individual level past 30-day cannabis use and frequency  | Neither      | Strong   |
| Yoruk, 2013<br>(Yörük and Yörük, 2013) | USA | Cross sectional survey       | National Longitudinal Survey of Youth (1997) | ~9000                         | Consumption | National Longitudinal Survey of Youth (1997) | Turning MLDA of 21  | Individual-level past 30-day cannabis and alcohol use and frequency  | Neither      | Moderate |
| Crost, 2012<br>(Crost and              | USA | Cross sectional Survey       | National Survey on                           | 71 (State-level observations) | Consumption | National Survey of Drug use and Health       | Turning MLDA of 21  | Population level past month cannabis and alcohol frequency   | Substitution | Strong   |

|   |     |                        |                             |          |             |                            |   |  |              |        |
|---|-----|------------------------|-----------------------------|----------|-------------|----------------------------|---|--|--------------|--------|
| Guerrero, 2012)                           |     |                        | Drug Use and Health         |          |             |                            |   |  |              |        |
| DiNardo, 2001 (DiNardo and Lemieux, 2001) | USA | Cross sectional Survey | Monitoring the Future Study | >156,000 | Consumption | Monitoring the Future Data | MLDA, State-level cannabis decriminalisation indicator, alcohol price | State level prevalence of past day 30-day cannabis & alcohol frequency | Substitution | Strong |

Abbreviations for measurement tool: FARS (Fatality Analysis Reporting System)

**Table 3.** Substance use disorders studies (17 studies)

| <i>Paper</i>  | <i>Country</i> | <i>Study design</i>                | <i>Population</i>  | <i>Sample size</i> | <i>Measure Category</i> | <i>Measurement tool</i>   | <i>Independent variable</i>                  | <i>Dependent variable</i>                  | <i>Conclusion</i>                                      | <i>Quality assessment</i> |
|---|----------------|------------------------------------|--|--------------------|-------------------------|---|--|--|--|---------------------------|
| <i>Cannabis cessation or reduction studies (13 studies)</i> |                |                                    |  |                    |                         |   |  |  |  |                           |
| Hodgins, 2017 (Hodgins et al., 2017)                        | Canada         | Cross sectional Survey             | Individuals recovered from Cannabis Use Disorder through treatment-assisted or self-directed efforts | 119                | Consumption             | Marijuana Problem Scale, Process of Change Questionnaire, researcher-led interview on substance use changes during recovery | Cannabis recovery (abstinence or moderation) | Self-reported changes in other alcohol use | Both   | Weak                      |
| Allsop, 2014 (Allsop et al., 2014)                          | Australia      | Prospective community-based cohort | Non-treatment seeking cannabis users   | 45                 | Consumption             | Cannabis withdrawal Scale (CWS) and urine toxicology  | Cannabis abstinence                          | Quantity of alcohol use                    | Substitution, especially among baseline light drinkers | Strong                    |

|  |     |                        |  |     |                   |  |                                 |  |   |          |
|--|-----|------------------------|--|-----|-------------------|--|---------------------------------|--|---|----------|
| Peters, 2010<br>(Peters and Hughes, 2010)    | USA | Prospective cohort     | Daily cannabis users not trying to stop or reduce cannabis | 28  | Consumption       | MWC, MCQ, CPQ, and PACS  | Cannabis abstinence             | Drinks per day   | Substitution                                      | Moderate |
| Kadden, 2009<br>(Kadden et al., 2009)        | USA | Prospective cohort     | Cannabis treatment seekers                                 | 207 | Consumption       | Time-line Follow-Back (TLFB), Addiction Severity Index, Marijuana Problem Scale, Coping Strategies Scale | Past 90 days cannabis frequency | Indicator of increased (>10%) past 90-day proportion days using alcohol, drinks per drinking day | Neither   | Moderate |
| Hughes, 2008<br>(Hughes et al., 2008)        | USA | Prospective cohort     | Daily cannabis users trying to stop or reduce on their own | 19  | Not specified     | Questionnaire for cannabis use and intentions to use   | Cannabis abstinence             | Alcohol use  | Neither   | Weak     |
| Copersino, 2006<br>(Copersino et al., 2006a) | USA | Prospective cohort     | Non-treatment seeking cannabis users                       | 104 | Self-reported use | Marijuana Quit Questionnaire   | None                            | Self-reported use of alcohol to relieve cannabis withdrawal during quit attempt                  | Substitution: Some evidence to relieve withdrawal | Weak     |
| Copersino, 2006<br>(Copersino et al., 2006b) | USA | Cross sectional survey | Non-treatment seeking adult cannabis smokers               | 104 | Consumption       | Marijuana Quit Questionnaire   | Cannabis abstinence             | Alcohol use  | Substitution                                      | Weak     |

|   |     |                    |  |     |               |  |                                |                                 |                  |          |
|---|-----|--------------------|--|-----|---------------|--|--------------------------------|---------------------------------|------------------|----------|
| Budney, 2003<br>(Budney et al., 2003)     | USA | Prospective cohort | 18 cannabis users; 12 past users in parallel | 30  | Not specified | MWC, MCQ, Brief Symptom Inventory,   | Cannabis abstinence            | Alcohol use                     | Neither          | Moderate |
| Budney, 2001<br>(Budney et al., 2001)     | USA | Prospective cohort | Daily cannabis users                         | 12  | Not specified | Substance use diary, MWC, the Brief Symptom Inventory, MCQ                               | Cannabis abstinence            | Alcohol use                     | Neither          | Weak     |
| Kouri, 2000<br>(Kouri and Pope, 2000)     | USA | Prospective cohort | Current and former cannabis users            | 60  | Toxicological | 14-item daily withdrawal diary, Hamilton Depression Rating Scale, Hamilton Anxiety Scale | Cannabis withdrawal symptoms   | Changes in alcohol use          | Neither          | Moderate |
| Stephens, 2000<br>(Stephens et al., 2000) | USA | Prospective cohort | Cannabis treatment seekers                   | 291 | Consumption   | Follow up questionnaires   | Past 90 days alcohol frequency | Monthly cannabis frequency      | Weak complements | Moderate |
| Stephens, 1994<br>(Stephens et al., 1994) | USA | Prospective cohort | Cannabis treatment seekers                   | 212 | Consumption   | DAST   | Weekly alcohol use             | Past 90 days cannabis frequency | Neither          | Moderate |

*Alcohol cessation or reduction (4 studies)*

|   |     |                           |  |      |             |   |  |   |                                   |          |
|---|-----|---------------------------|--|------|-------------|---|--|---|-----------------------------------|----------|
| Subbaraman, 2017<br>(Subbaraman et al., 2017) | USA | Secondary analysis of RCT | Newly alcohol-abstinent alcohol-dependant participants (COMBINE Study) | 1383 | Consumption | Follow-up medical assessments at week 8, 16, 26, 52, and 68 | Cannabis use and quartiles of cannabis use | Post treatment percentage of days abstinent, Drinks Per Drinking Day, and | Weak evidence for complementarity | Moderate |
|---|-----|---------------------------|--|------|-------------|---|--|---|-----------------------------------|----------|



---

|   |                             |                           |   |                       |                   |   |                                     | Percentage of Heavy Drinking Days                 |              |          |
|---|-----------------------------|---------------------------|---|-----------------------|-------------------|---|-------------------------------------|---|--------------|----------|
| Peters, 2012<br>(Peters et al., 2012)           | USA                         | RCT                       | 8-week RCT of naltrexone for alcohol use                              | 122 (18-21 years old) | Consumption       | Young Adult Consequence Questionnaire, The Contemplation Ladder, The Barrat Impulsivity Scale, Drinking-Induced Disinhibition Scale, Medication Adherence Questionnaire | Cannabis user                       | Individual-level alcohol use and related problems | Neither      | Weak     |
| Aharonovich, 2005<br>(Aharonovich et al., 2005) | USA                         | Prospective cohort        | Inpatient psychiatric/substance abuse treatment                       | 250                   | Self-reported use | Longitudinal Psychiatric Research Interview for Substance and Mental Disorders  | Post discharge cannabis use         | Alcohol use post treatment                        | Complements  | Weak     |
| Mikuriya, 2004<br>(Mikuriya, 2004)              | USA                         | Longitudinal cohort study | Seekers of physician's approval to use cannabis for alcohol treatment | 92                    | Consumption       | Examination of medical records follow up interview  | indicator, alcohol                  | Efficacy of treating alcoholism with cannabis     | Substitution | Weak     |
| Rosenberg, 1978                                 | Longitudinal Pre/post study | USA                       | Men experiencing difficulties with alcohol                            | 44                    | Consumption       | Not specified   | Cannabis or cannabis and disulfiram | Alcohol use during                                | Neither      | Moderate |

---

(Rosenberg et al., 1978)

alcohol treatment

Abbreviations for measurement tool: MTF (Monitoring The Future Survey), MWC (Marijuana Withdrawal Checklist), MCQ (Marijuana Craving Questionnaire), CPQ (Cannabis Problems Questionnaire), Penn Alcohol Craving Scale

**Table 4.** Economic relationship studies (ten studies)

| <i>Paper</i>                                  | <i>Country</i> | <i>Study design</i>    | <i>Population</i>                                   | <i>Sample size</i> | <i>Measure Category</i> | <i>Measurement tool</i>                              | <i>Independent variable</i>                      | <i>Dependent variable</i>                                | <i>Conclusion</i>   | <i>Quality assessment</i> |
|---|----------------|------------------------|---|--------------------|-------------------------|--|--|--|---|---------------------------|
| <i>General population studies (3 studies)</i> |                |                        |   |                    |                         |  |  |  |   |                           |
| Cameron, 2001 (Cameron and Williams, 2001)    | Australia      | Cross sectional survey | National Drug Strategy Household Survey (Australia) | 9,744              | Consumption             | Australian National Drug Strategy's Household Survey | State-level cannabis decriminalisation indicator | Individual-level past 12 months cannabis and alcohol use | Both: Decriminalisation increases alcohol use suggesting complements, price effects suggest substitution    | Strong                    |
| Saffer, 1999 (Saffer and Chaloupka, 1999a)    | USA            | Cross sectional survey | National Household Survey on Drug Abuse             | 49,802             | Consumption             | National Household Survey on Drug Abuse              | State-level cannabis decriminalisation indicator | Individual-level alcohol frequency, cannabis use         | Both<br>Complements for full sample, white males and blacks: substitutes for Native Americans and Hispanics | Strong                    |
| Saffer, 1998 (Saffer and Chaloupka, 1999)     | USA            | Cross sectional survey | National Household Survey on Drug Abuse             | 49,802             | Consumption             | National Household Survey of Drug Abuse              | State-level alcohol and drug prices              | Individual-level alcohol frequency, cannabis use         | Complements   | Strong                    |

*Young people studies (4 studies)*

|  |     |                        |  |   |             |   |  |  |   |        |
|--|-----|------------------------|--|---|-------------|---|--|--|---|--------|
| Williams, 2004<br>(Williams et al., 2004)          | USA | Cross sectional survey | Harvard School of Public Health's College Alcohol Study (CAS) (1993, 1997, 1999) | 15,479 expands (Cameron 2001) to polysubstance users & adds control for drunk driving | Consumption | Harvard School of Public Health's College Alcohol Study (CAS) | State-level cannabis decriminalisation indicators, fines for drunk driving, price for cannabis and alcohol | Individual-level past year cannabis use                          | Complements, especially among polysubstance users & males | Strong |
| Pacula, 1998<br>(Pacula, 1998)                     | USA | Longitudinal panel     | National Longitudinal Survey of Youth (1979)                                     | 8,008   | Consumption | National Longitudinal Survey of Youth                         | State-level beer tax   | Individual-level past 30 days # drinks, # of times used cannabis | Complement  | Strong |
| Chaloupka, 1997<br>(Chaloupka and Laixuthai, 1997) | USA | Cross sectional survey | Monitoring the Future  | 25,430  | Consumption | Monitoring the Future   | State-level cannabis decriminalisation indicator   | Individual-level alcohol frequency, heavy drinking accidents     | Substitution  | Strong |

|                                       |     |                        |   |     |             |                                       |  |   |      |        |
|---------------------------------------|-----|------------------------|---|-----|-------------|---------------------------------------|--|---|------|--------|
| Yamada, 1996<br>(Yamada et al., 1996) | USA | Cross sectional survey | 12th grade high school students in the academic year of 1981/1982 | 672 | Consumption | National Longitudinal Survey of Youth | State-level liquor price / marijuana decriminalisation | Individual-level marijuana use / Individual-level alcohol use | Both | Strong |
|---------------------------------------|-----|------------------------|---|-----|-------------|---------------------------------------|--|---|------|--------|

*Drug user's studies (2 studies)*

|   |           |                        |  |        |             |  |  |   |              |        |
|---|-----------|------------------------|--|--------|-------------|--|--|---|--------------|--------|
| Cole, 2008<br>(Cole et al., 2008)               | UK        | Cross sectional survey | Polydrug users who illegally use controlled drugs    | 80     | Monetary    | AUDIT, DAST-A, SDS, HADS, simulation purchase of alcohol and drugs | Changes in the quality of cannabis                               | Individual-level purchase   | Substitution | Weak   |
| Williams, 2004<br>(Williams and Mahmoudi, 2004) | Australia | Cross sectional survey | Australian National Drug Strategies Household Survey | 48,174 | Consumption | Australian National Drug Strategy's Household Survey               | State-level cannabis decriminalisation indicator; cannabis price | State-level past month & past year alcohol and cannabis frequency | Complement   | Strong |

*Other (1 study)*

|                                    |           |                   |                        |    |          |  |                             |                     |              |         |
|------------------------------------|-----------|-------------------|------------------------|----|----------|--|-----------------------------|---------------------|--------------|---------|
| Clements, 2004<br>(Clements, 2004) | Australia | Economic analysis | Australian Drug market | NA | Monetary | Australian Bureau of Criminal Intelligence | Changes in marijuana prices | Alcohol consumption | Substitution | Unrated |
|------------------------------------|-----------|-------------------|------------------------|----|----------|--|-----------------------------|---------------------|--------------|---------|

*Abbreviations for measurement tool: AUDIT (Alcohol Use Disorder Identification Test), DAST-A (Drug Abuse Screening Test for Adolescents, SDS (Severity of Dependence Scale for cannabis), SDS (Hospital Anxiety and Depression Scale)*

**Table 5.** Patterns of use studies (six studies)

| <i>Paper</i>                                | <i>Country</i> | <i>Study design</i>       | <i>Population</i>  | <i>Sample size</i> | <i>Measure Category</i> | <i>Measurement tool</i>  | <i>Independent variable</i>                             | <i>Dependent variable</i>                          | <i>Conclusion</i> | <i>Quality assessment</i> |
|---|----------------|---------------------------|--|--------------------|-------------------------|--|---|--|-------------------|---------------------------|
| <i>General population studies (1 study)</i> |                |                           |  |                    |                         |  |   |  |                   |                           |
| Choi, 2018<br>(Choi et al., 2018)           | USA            | Longitudinal panel        | PATH study (wave 1 and 2) respondents  | 26,204             | Consumption             | Population Assessment of Tobacco and Health Study (PATH)             | Past 12 months and 30 days of frequency of cannabis use | Past 12 months and 30-day frequency of alcohol use | Complements       | Moderate                  |
| <i>Young people studies (5 studies)</i>     |                |                           |  |                    |                         |  |   |  |                   |                           |
| Gripe, 2018<br>(Gripe et al., 2018)         | Sweden         | Cross sectional survey    | Swedish Council for Information on Alcohol and Other Drugs Survey population | 149,603            | Consumption             | Swedish Council for Information on Alcohol and other Drugs Survey    | Individual-level alcohol use                            | Individual-level cannabis use                      | Neither           | Strong                    |
| O'Hara, 2016<br>(O'Hara et al., 2016)       | USA            | Longitudinal cohort study | College students   | 876                | Consumption             | COPE inventory. Daily diary study: 2-3 weeks after baseline using an | Quantity of daily drinks and overall alcohol 30-day use | Evening cannabis use                               | Complement        | Weak                      |

|   |        |                           |   |        |             |  |  |   |  |          |
|---|--------|---------------------------|---|--------|-------------|--|--|---|--|----------|
|   |        |                           |   |        |             | online website to report last night cannabis and alcohol use each day for 30 days. |  |   |  |          |
| Deza, 2015<br>(Deza, 2015)                | USA    | Longitudinal panel        | National Longitudinal Survey of Youth 1997        | 8,984  | Consumption | National Longitudinal Survey of Youth (1997)                                       | State-level medical marijuana laws   | State-level traffic fatalities, alcohol and cannabis use  | Complement   | Moderate |
| Pape, 2009<br>(Pape et al., 2009)         | Norway | Cross sectional survey    | European School Project on Alcohol and Drugs      | 16,813 | Consumption | Norwegian youth Survey and ESPAD   | None   | Proportion of cannabis/alcohol use occasions  | Complement   | Weak     |
| Hammer, 1992<br>(Hammer and Vaglum, 1992) | Norway | Longitudinal cohort study | Sample extracted from the 1985 NSYPASW aged 17-20 | 1,997  | Consumption | National Survey of Youngs People Adjustment to School and Work (NSYPASW)           | Total past frequency of cannabis use and past year frequency of cannabis use | Past four weeks and past year of alcohol use, quantity of alcohol use in the last drinking incident | Complement in young groups and young adult females | Weak     |

*Abbreviations for measurement tool: ESPAD (European School Survey on Alcohol and Other Drugs)*

**Table 6.** Substitution practices studies

| <i>Paper</i>                                 | <i>Country</i> | <i>Study design</i>    | <i>Population</i>                                    | <i>Sample size</i> | <i>Measure category</i>    | <i>Measurement tool</i>   | <i>Independent variable</i> | <i>Dependent variable</i>  | <i>Conclusion</i> | <i>Quality assessment</i> |
|--|----------------|------------------------|--|--------------------|----------------------------|---|-----------------------------|--|-------------------|---------------------------|
| <i>Medical Cannabis Patients (5 studies)</i> |                |                        |  |                    |                            |   |                             |  |                   |                           |
| Lucas, 2017<br>(Lucas and Walsh, 2017)       | Canada         | Cross sectional survey | Patients registered to purchase cannabis from Tilray | 271                | Self-reported substitution | Online 107-item questionnaire available in French and English                               | Medical cannabis use        | Participants reporting substituting cannabis for prescription drugs, alcohol tobacco, or illicit drugs | Substitution      | Weak                      |
| Piper, 2017<br>(Piper et al., 2017)          | USA            | Cross sectional survey | Members of dispensaries in New England               | 1,513              | Self-reported substitution | Online survey; items on self-reporting substitution of cannabis for alcohol and other drugs | Medical cannabis use        | Prevalence of self-reported substitution of alcohol for cannabis                                       | Substitution      | Weak                      |
| Lucas, 2016<br>(Lucas et al., 2016)          | USA            | Cross sectional survey | Cannabis Access for Medical Purpose Survey (CAMPS)   | 473                | Self-reported substitution | Cannabis access for Medical Purposes Survey (CAMPS)   | Medical cannabis use        | Prevalence of substituting cannabis for prescription drugs, alcohol tobacco, or illicit drugs          | Substitution      | Weak                      |

|                                     |        |                        |   |     |                            |   |      |  |              |      |
|-------------------------------------|--------|------------------------|---|-----|----------------------------|---|------|--|--------------|------|
| Lucas, 2013<br>(Lucas et al., 2013) | Canada | Cross sectional survey | Medical cannabis patients from dispensaries in British Columbia | 404 | Self-reported substitution | Adapted version of medical cannabis survey from Reiman, 2009                              | None | Self-reported substitution of cannabis for alcohol | Substitution | Weak |
| Reiman, 2009<br>(Reiman, 2009)      | USA    | Cross sectional survey | Medical cannabis patients from Berkeley Patient's Group (BPG)   | 350 | Self-reported substitution | Survey created by researcher with portions adapted from a Medical cannabis patient survey | None | Self-reported substitution of cannabis for alcohol | Substitution | Weak |

---

*Cannabis users (1 study)*

|                                 |     |                   |  |    |           |  |                           |   |              |  |
|---------------------------------|-----|-------------------|--|----|-----------|--|---------------------------|---|--------------|--|
| Lau, 2015<br>(Lau et al., 2015) | USA | Qualitative study | Baby Boomer marijuana users in San Francisco | 97 | Interview | Semi-structured in-depth life history interview, questionnaire and health survey | Recreational cannabis use | Self-reported substitution of cannabis for prescription drugs, alcohol, tobacco, or illicit drugs as a harm reduction measure | Substitution | Moderate<br>(Assessed using CASP Tool) |
|---------------------------------|-----|-------------------|--|----|-----------|--|---------------------------|---|--------------|--|

---



**Table 7. "Other" studies**

| <b>Paper</b>                                 | <b>Country</b> | <b>Study design</b>                             | <b>Population</b>  | <b>Sample size</b> | <b>Measure category</b>    | <b>Measurement tool</b>   | <b>Independent variable</b>                  | <b>Dependent variable</b>  | <b>Conclusion</b>                                    | <b>Quality assessment</b> |
|--|----------------|---|--|--------------------|----------------------------|---|--|--|--|---------------------------|
| Klimas, 2016 (Klimas et al., 2016)           | Canada         | Longitudinal prospective community-based cohort | Heroin users   | 357                | Consumption                | Self-report and 50.3 month follow up  | Enrolment in Methadone Maintenance Treatment | Initiation of heavy drinking   | Complement   | Weak                      |
| Subbaraman, 2015 (Subbaraman and Kerr, 2015) | USA            | Cross sectional survey                          | Current drinkers from the National Alcohol Study (NAS) 2005 and 2010 | 8,626              | Consumption                | National Alcohol Study (NAS)  | Current alcohol use                          | Past 12 months cannabis use frequency, drunk driving, alcohol related social consequences, alcohol related harms | Some evidence of complementarity in concurrent users | Moderate                  |
| Reiman, 2007 (Reiman, 2007)                  | USA            | Cross sectional survey                          | Medical cannabis patients  | 130                | Self-reported substitution | Qualitative interview, adapted from of the RAND 36-item Health survey, Patient Satisfaction Questionnaire III | None   | Self-reported substitution of cannabis for alcohol and other drugs   | Substitution   | Weak                      |

|                                     |     |                        |  |        |             |                                   |  |  |              |        |
|-------------------------------------|-----|------------------------|--|--------|-------------|-----------------------------------|--|--|--------------|--------|
| Alter, 2006<br>(Alter et al., 2006) | USA | Cross sectional survey | Monitoring the Future, Midwest subsample | 11,542 | Consumption | Survey like Monitoring the future | Perceived access and harms of alcohol and cannabis | Individual-level past month alcohol and cannabis frequency | Substitution | Strong |
|-------------------------------------|-----|------------------------|--|--------|-------------|-----------------------------------|--|--|--------------|--------|

**Table 8. Animal studies**

| <b>Paper</b>                        | <b>Country</b> | <b>Study design</b>       | <b>Population</b> | <b>Sample size</b> | <b>Measure category</b> | <b>Measurement tool</b>  | <b>Independent variable</b>                                  | <b>Dependent variable</b> | <b>Conclusion</b>  | <b>Quality assessment</b> |
|-------------------------------------|----------------|---------------------------|-------------------|--------------------|-------------------------|--|--|---------------------------|--|---------------------------|
| Filev, 2017<br>(Filev et al., 2017) | Brazil         | Longitudinal experimental | DBA/2 Mice        | 84                 | Locomotor activity      | Sensitisation context for 15 minutes (wooden box painted with white acrylic) | Photo cannabinoid treatment (THC, THC+CBD, CBD) by injection | Locomotor activity        | Substitution in THC and THC+CBD treatment, no effect for CBD treatment alone | Low risk                  |

- Aharonovich E, Liu X, Samet S, et al. (2005) Postdischarge cannabis use and its relationship to cocaine, alcohol, and heroin use: a prospective study. *The American Journal of Psychiatry* 162(8): 1507–1514. DOI: 10.1176/appi.ajp.162.8.1507.
- Allsop DJ, Dunlop AJ, Saddler C, et al. (2014) Changes in cigarette and alcohol use during cannabis abstinence. *Drug and Alcohol Dependence* 138: 54–60. DOI: 10.1016/j.drugalcdep.2014.01.022.
- Alter RJ, Lohrmann DK and Greene R (2006) Substitution of marijuana for alcohol: The role of perceived access and harm. *Journal of Drug Education* 36(4). Baywood Publishing: 335–355. DOI: 10.2190/2780-G96W-J17N-R3H1.
- Anderson MD, Hansen B and Rees DI (2013) Medical Marijuana Laws, Traffic Fatalities, and Alcohol Consumption. *The Journal of Law and Economics* 56(2). The University of Chicago Press: 333–369. DOI: 10.1086/668812.
- Baggio M, Chong A and Kwon S (2018) Marijuana and Alcohol Evidence Using Border Analysis and Retail Sales Data. DOI: 10.2139/ssrn.3063288.
- Budney AJ, Hughes JR, Moore BA, et al. (2001) Marijuana abstinence effects in marijuana smokers maintained in their home environment. *Archives of General Psychiatry* 58(10): 917–924. DOI: 10.1001/archpsyc.58.10.917.
- Budney AJ, Moore BA, Vandrey RG, et al. (2003) The time course and significance of cannabis withdrawal. *Journal of Abnormal Psychology* 112(3): 393–402. DOI: 10.1037/0021-843x.112.3.393.
- Cameron L and Williams J (2001) Cannabis, Alcohol and Cigarettes: Substitutes or Complements? *Economic Record* 77(236): 19–34. DOI: 10.1111/1475-4932.00002.
- Cerda M, Sarvet AL, Wall M, et al. (2018) Medical marijuana laws and adolescent use of marijuana and other substances: Alcohol, cigarettes, prescription drugs, and other illicit drugs. *Drug and Alcohol Dependence* 183. Elsevier Ireland Ltd: 62–68. DOI: 10.1016/j.drugalcdep.2017.10.021.
- Chaloupka F and Laixuthai A (1997) Do Youths Substitute Alcohol and Marijuana? Some Econometric Evidence. *Eastern Economic Journal* 23(3). Eastern Economic Association: 253–276.
- Chandra S, Radwan MM, Majumdar CG, et al. (2019) New trends in cannabis potency in USA and Europe during the last decade (2008–2017). *European Archives of Psychiatry and Clinical Neuroscience* 269(1): 5–15. DOI: 10.1007/s00406-019-00983-5.
- Cheung MW-L and Vijayakumar R (2016) A Guide to Conducting a Meta-Analysis. *Neuropsychology Review* 26(2): 121–128. DOI: 10.1007/s11065-016-9319-z.
- Choi NG, DiNitto DM and Marti CN (2018) A longitudinal assessment of change in marijuana use with other substance use problems. *The American Journal of Drug and Alcohol Abuse* 44(6): 642–652. DOI: 10.1080/00952990.2018.1461879.
- Clements KW (2004) Three facts about marijuana prices. *Australian Journal of Agricultural and Resource Economics* 48(2). Australian Agricultural and Resource Economics Society: 271–300.

- Clements KW and Daryal M (2005) Exogenous shocks and related goods: Drinking and the legalisation of marijuana. *Economics Letters* 89(1). Elsevier: 101–106.
- Cole JC, Goudie AJ, Field M, et al. (2008) The effects of perceived quality on the behavioural economics of alcohol, amphetamine, cannabis, cocaine, and ecstasy purchases. *Drug and Alcohol Dependence* 94(1–3): 183–190. DOI: 10.1016/j.drugalcdep.2007.11.014.
- Copersino ML, Boyd SJ, Tashkin DP, et al. (2006a) Cannabis withdrawal among non-treatment-seeking adult cannabis users. *The American Journal on Addictions* 15(1): 8–14. DOI: 10.1080/10550490500418997.
- Copersino ML, Boyd SJ, Tashkin DP, et al. (2006b) Quitting among non-treatment-seeking marijuana users: reasons and changes in other substance use. *The American Journal on Addictions* 15(4): 297–302. DOI: 10.1080/10550490600754341.
- Crost B and Guerrero S (2012) The effect of alcohol availability on marijuana use: Evidence from the minimum legal drinking age. *Journal of Health Economics* 31(1): 112–121. DOI: 10.1016/j.jhealeco.2011.12.005.
- Crost B and Rees DI (2013) The minimum legal drinking age and marijuana use: new estimates from the NLSY97. *Journal of Health Economics* 32(2): 474–476. DOI: 10.1016/j.jhealeco.2012.09.008.
- Degenhardt L, Ferrari AJ, Calabria B, et al. (2013) The global epidemiology and contribution of cannabis use and dependence to the global burden of disease: results from the GBD 2010 study. *PloS One* 8(10): e76635. DOI: 10.1371/journal.pone.0076635.
- Deza M (2015) Is there a stepping stone effect in drug use? Separating state dependence from unobserved heterogeneity within and between illicit drugs. *Journal of Econometrics* 184(1). Elsevier: 193–207.
- DiNardo J and Lemieux T (2001) Alcohol, marijuana, and American youth: the unintended consequences of government regulation. *Journal of Health Economics* 20(6): 991–1010. DOI: 10.1016/s0167-6296(01)00102-3.
- Farrelly M, Bray J, Zarkin G, et al. (1999) *The Effects of Prices and Policies on the Demand for Marijuana: Evidence from the National Household Surveys on Drug Abuse*. w6940, February. Cambridge, MA: National Bureau of Economic Research. DOI: 10.3386/w6940.
- Filev R, Engelke DS, Da Silveira DX, et al. (2017) THC inhibits the expression of ethanol-induced locomotor sensitization in mice. *Alcohol (Fayetteville, N.Y.)* 65: 31–35. DOI: 10.1016/j.alcohol.2017.06.004.
- Freeman TP, Groshkova T, Cunningham A, et al. (2019) Increasing potency and price of cannabis in Europe, 2006–16. *Addiction (Abingdon, England)* 114(6): 1015–1023. DOI: 10.1111/add.14525.
- Gripe I, Danielsson A-K and Ramstedt M (2018) Are changes in drinking related to changes in cannabis use among Swedish adolescents? A time-series analysis for the period 1989–2016. *Addiction* 113(9): 1643–1650. DOI: 10.1111/add.14244.

- Hall W (2015) What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? *Addiction (Abingdon, England)* 110(1): 19–35. DOI: 10.1111/add.12703.
- Hammer T and Vaglum P (1992) Further course of mental health and use of alcohol and tranquilizers after cessation or persistence of cannabis use in young adulthood: a longitudinal study. *Scandinavian Journal of Social Medicine* 20(3): 143–150. DOI: 10.1177/140349489202000303.
- Higgins JP and Green S (2011) *Cochrane Handbook for Systematic Reviews*.
- Hodgins DC, Kim HS and Stea JN (2017) Increase and decrease of other substance use during recovery from cannabis use disorders. *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors* 31(6): 727–734. DOI: 10.1037/adb0000307.
- Hooijmans CR, Rovers MM, de Vries RBM, et al. (2014) SYRCLE’s risk of bias tool for animal studies. *BMC medical research methodology* 14: 43. DOI: 10.1186/1471-2288-14-43.
- Hughes JR, Peters EN, Callas PW, et al. (2008) Attempts to Stop or Reduce Marijuana Use in Non-Treatment Seekers. *Drug and alcohol dependence* 97(1–2): 180–184. DOI: 10.1016/j.drugalcdep.2008.03.031.
- Jahan N, Naveed S, Zeshan M, et al. (2016) How to Conduct a Systematic Review: A Narrative Literature Review. *Cureus* 8(11). DOI: 10.7759/cureus.864.
- Kadden RM, Litt MD, Kabela-Cormier E, et al. (2009) Increased Drinking in a Trial of Treatments for Marijuana Dependence: Substance Substitution? *Drug and alcohol dependence* 105(1–2): 168–171. DOI: 10.1016/j.drugalcdep.2009.05.024.
- Kelly E and Rasul I (2014) Policing cannabis and drug related hospital admissions: Evidence from administrative records. *Journal of Public Economics* 112: 89–114. DOI: 10.1016/j.jpubeco.2014.01.008.
- Keyes KM, Brady JE and Li G (2015) Effects of minimum legal drinking age on alcohol and marijuana use: evidence from toxicological testing data for fatally injured drivers aged 16 to 25 years. *Injury Epidemiology* 2(1). DOI: 10.1186/s40621-014-0032-1.
- Klimas J, Wood E, Nguyen P, et al. (2016) The Impact of Enrolment in Methadone Maintenance Therapy on Initiation of Heavy Drinking among People who Use Heroin. *European addiction research* 22(4): 210–214. DOI: 10.1159/000444513.
- Kouri EM and Pope HG (2000) Abstinence symptoms during withdrawal from chronic marijuana use. *Experimental and Clinical Psychopharmacology* 8(4). American Psychological Association: 483–492. DOI: 10.1037/1064-1297.8.4.483.
- Krauss MJ, Cavazos-Rehg PA, Agrawal A, et al. (2015) Long-Term Effects of Minimum Legal Drinking Age Laws on Marijuana and Other Illicit Drug Use in Adulthood. *Drug and alcohol dependence* 149: 173–179. DOI: 10.1016/j.drugalcdep.2015.01.043.
- Lau N, Sales P, Averill S, et al. (2015) A safer alternative: Cannabis substitution as harm reduction. *Drug and Alcohol Review* 34(6): 654–659. DOI: 10.1111/dar.12275.

- Lucas P and Walsh Z (2017) Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. *The International Journal on Drug Policy* 42: 30–35. DOI: 10.1016/j.drugpo.2017.01.011.
- Lucas P, Reiman A, Earleywine M, et al. (2013) Cannabis as a substitute for alcohol and other drugs: A dispensary-based survey of substitution effect in Canadian medical cannabis patients. *Addiction Research & Theory* 21(5). Taylor & Francis: 435–442. DOI: 10.3109/16066359.2012.733465.
- Lucas P, Walsh Z, Crosby K, et al. (2016) Substituting cannabis for prescription drugs, alcohol and other substances among medical cannabis patients: The impact of contextual factors. *Drug and Alcohol Review* 35(3): 326–333. DOI: 10.1111/dar.12323.
- Mason WA, Fleming CB, Ringle JL, et al. (2016) Prevalence of marijuana and other substance use before and after Washington State’s change from legal medical marijuana to legal medical and nonmedical marijuana: Cohort comparisons in a sample of adolescents. *Substance Abuse* 37(2): 330–335. DOI: 10.1080/08897077.2015.1071723.
- McGinty EE, Niederdeppe J, Heley K, et al. (2017) Public perceptions of arguments supporting and opposing recreational marijuana legalization. *Preventive Medicine* 99: 80–86. DOI: 10.1016/j.ypmed.2017.01.024.
- Mcglathlin W, Jamison K and Rosenblatt S (1970) Marijuana and the use of other drugs. *Nature* 228(5277). Nature Publishing Group: 1227–1229. DOI: 10.1038/2281227a0.
- Mikuriya TodH (2004) Cannabis as a Substitute for Alcohol: A Harm-Reduction Approach. *Journal of Cannabis Therapeutics* 4(1). Taylor & Francis: 79–93. DOI: 10.1300/J175v04n01\_04.
- Miller K and Seo B (2018) Tax Revenues When Substances Substitute: Marijuana, Alcohol, and Tobacco.: 48.
- Nutt DJ, King LA, Phillips LD, et al. (2010) Drug harms in the UK: a multicriteria decision analysis. *Lancet (London, England)* 376(9752): 1558–1565. DOI: 10.1016/S0140-6736(10)61462-6.
- O’Hara RE, Armeli S and Tennen H (2016) Alcohol and cannabis use among college students: Substitutes or complements? *Addictive Behaviors* 58: 1–6. DOI: 10.1016/j.addbeh.2016.02.004.
- Pacula RL (1998) Does increasing the beer tax reduce marijuana consumption? *Journal of Health Economics* 17(5): 557–585. DOI: 10.1016/s0167-6296(97)00039-8.
- Pape H, Rossow I and Storvoll EE (2009) Under double influence: assessment of simultaneous alcohol and cannabis use in general youth populations. *Drug and Alcohol Dependence* 101(1–2): 69–73. DOI: 10.1016/j.drugalcdep.2008.11.002.
- Peacock A, Leung J, Larney S, et al. (2018) Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. *Addiction (Abingdon, England)* 113(10): 1905–1926. DOI: 10.1111/add.14234.
- Peters EN and Hughes JR (2010) Daily marijuana users with past alcohol problems increase alcohol consumption during marijuana abstinence. *Drug and Alcohol Dependence* 106(2–3): 111–118. DOI: 10.1016/j.drugalcdep.2009.07.027.

- Peters EN, Leeman RF, Fucito LM, et al. (2012) Co-occurring marijuana use is associated with medication nonadherence and nonplanning impulsivity in young adult heavy drinkers. *Addictive Behaviors* 37(4): 420–426. DOI: 10.1016/j.addbeh.2011.11.036.
- Piper BJ, DeKeuster RM, Beals ML, et al. (2017) Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep. *Journal of Psychopharmacology (Oxford, England)* 31(5): 569–575. DOI: 10.1177/0269881117699616.
- Reiman A (2007) Medical Cannabis Patients: Patient Profiles and Health Care Utilization Patterns. *Complementary health practice review* 12(1). SAGE Publications: 31–50. DOI: 10.1177/1533210107301834.
- Reiman A (2009) Cannabis as a substitute for alcohol and other drugs. *Harm Reduction Journal* 6(1): 35. DOI: 10.1186/1477-7517-6-35.
- Rosenberg CM, Gerrein JR and Schnell C (1978) Cannabis in the treatment of alcoholism. *Journal of Studies on Alcohol*. Rutgers University Piscataway, NJ. DOI: 10.15288/jsa.1978.39.1955.
- Sabia J, Swigert J and Young T (2017) The Effect of Medical Marijuana Laws on Body Weight. *Health economics* 26. DOI: 10.1002/hec.3267.
- Saffer H and Chaloupka F (1999a) Demographic Differentials in the Demand for Alcohol and Illicit Drugs. *The Economic Analysis of Substance Use and Abuse: An Integration of Econometric and Behavioral Economic Research*. University of Chicago Press: 187–212.
- Saffer H and Chaloupka F (1999b) The Demand for Illicit Drugs. *Economic Inquiry* 37(3). Western Economic Association International: 401–11.
- Salomonsen-Sautel S, Min S-J, Sakai JT, et al. (2014) Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado. *Drug and Alcohol Dependence* 140: 137–144. DOI: 10.1016/j.drugalcdep.2014.04.008.
- Simons-Morton B, Pickett W, Boyce W, et al. (2010) Cross-national comparison of adolescent drinking and cannabis use in the United States, Canada, and the Netherlands. *The International journal on drug policy* 21(1): 64–69. DOI: 10.1016/j.drugpo.2009.02.003.
- Stephens RS, Roffman RA and Simpson EE (1994) Treating adult marijuana dependence: a test of the relapse prevention model. *Journal of Consulting and Clinical Psychology* 62(1): 92–99. DOI: 10.1037//0022-006x.62.1.92.
- Stephens RS, Roffman RA and Curtin L (2000) Comparison of extended versus brief treatments for marijuana use. *Journal of Consulting and Clinical Psychology* 68(5): 898–908.
- Subbaraman MS (2016) Substitution and complementarity of alcohol and cannabis: A review of the literature. *Substance use & misuse* 51(11): 1399–1414. DOI: 10.3109/10826084.2016.1170145.
- Subbaraman MS and Kerr W (2019) Subgroup trends in alcohol and cannabis co-use and related harms during the rollout of recreational cannabis legalization in Washington state. *The International Journal on Drug Policy* 75. DOI: 10.1016/j.drugpo.2019.07.003.

- Subbaraman MS and Kerr WC (2015) Simultaneous versus concurrent use of alcohol and cannabis in the National Alcohol Survey. *Alcoholism, Clinical and Experimental Research* 39(5): 872–879. DOI: 10.1111/acer.12698.
- Subbaraman MS, Metrik J, Patterson D, et al. (2017) Cannabis use during treatment for alcohol use disorders predicts alcohol treatment outcomes. *Addiction (Abingdon, England)* 112(4): 685–694. DOI: 10.1111/add.13693.
- Sznitman SR and Bretteville-Jensen AL (2015) Public opinion and medical cannabis policies: examining the role of underlying beliefs and national medical cannabis policies. *Harm Reduction Journal* 12(1): 46. DOI: 10.1186/s12954-015-0082-x.
- Thies CF and Register CA (1993) Decriminalization of marijuana and the demand for alcohol, marijuana and cocaine. *The Social Science Journal* 30(4): 385–399. DOI: 10.1016/0362-3319(93)90016-O.
- Van Amsterdam J, Opperhuizen A, Koeter M, et al. (2010) Ranking the harm of alcohol, tobacco and illicit drugs for the individual and the population. *European Addiction Research* 16(4): 202–207. DOI: 10.1159/000317249.
- Wen H, Hockenberry J and Cummings JR (2014) *The Effect of Medical Marijuana Laws on Marijuana, Alcohol, and Hard Drug Use*. NBER Working Papers 20085, May. National Bureau of Economic Research, Inc. Available at: <https://ideas.repec.org/p/nbr/nberwo/20085.html> (accessed 6 March 2020).
- Williams J and Mahmoudi P (2004) Economic Relationship Between Alcohol and Cannabis Revisited. *Economic Record* 80(248): 36–48. DOI: 10.1111/j.1475-4932.2004.00123.x.
- Williams J, Liccardo Pacula R, Chaloupka FJ, et al. (2004) Alcohol and marijuana use among college students: economic complements or substitutes? *Health Economics* 13(9): 825–843. DOI: 10.1002/hec.859.
- Yamada T, Kendix M and Yamada T (1996) The impact of alcohol consumption and marijuana use on high school graduation. *Health Economics* 5(1): 77–92. DOI: 10.1002/(SICI)1099-1050(199601)5:1<77::AID-HEC184>3.0.CO;2-W.
- Yörük BK and Yörük CE (2011) The impact of minimum legal drinking age laws on alcohol consumption, smoking, and marijuana use: evidence from a regression discontinuity design using exact date of birth. *Journal of Health Economics* 30(4): 740–752. DOI: 10.1016/j.jhealeco.2011.05.010.
- Yörük BK and Yörük CE (2013) The impact of minimum legal drinking age laws on alcohol consumption, smoking, and marijuana use revisited. *Journal of Health Economics* 32(2): 477–479. DOI: 10.1016/j.jhealeco.2012.09.007.
- Yurasek AM, Aston ER and Metrik J (2017) Co-use of Alcohol and Cannabis: A Review. *Current Addiction Reports* 4(2): 184–193. DOI: 10.1007/s40429-017-0149-8.



