



INTERNATIONAL CENTRE
FOR SCIENCE IN DRUG POLICY

STATE OF THE EVIDENCE
CANNABIS USE
AND REGULATION



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The International Centre for Science in Drug Policy (ICSDP) is a network of scientists and academics from all global hemispheres committed to improving the health and safety of communities and individuals affected by illicit drugs by working to inform illicit drug policies with the best available scientific evidence. By conducting research and public education on best practices in drug policy while working collaboratively with communities, policy makers, law enforcement and other stakeholders, the ICSDP seeks to help guide effective and evidence-based policy responses to the many problems posed by illicit drugs.

The ICSDP strives to be a primary source for rigorous scientific evidence on the impacts of illicit drug policy on community health and safety. To this end, the ICSDP produces publications which adhere to the highest standards of peer-reviewed scientific research. The ICSDP also conducts public education campaigns about the need for evidence-based drug policies. The objective of these campaigns is to inform policymakers, affected communities, key stakeholders, and the general public on pressing current issues surrounding illicit drugs and drug policy.

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This report reflects the current evidence on cannabis up to its release in August 2015.

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INTRODUCTION

Since inception, the International Centre for Science in Drug Policy (ICSDP) has sought to ensure that policy responses to the many problems posed by illicit drugs are informed by the best available scientific evidence.

State of the Evidence: Cannabis Use and Regulation is the ICSDP's contribution to the growing global conversation on cannabis. This report should be read in tandem with *Using Evidence to Talk About Cannabis*, a complementary guide to having evidence-based discussions on cannabis use and regulation.

The regulation of recreational cannabis markets has become an increasingly important policy issue in a number of jurisdictions. Colorado and Washington State made headlines in 2012 when they became the first jurisdictions in the world to legalize and regulate the adult use and sale of cannabis for non-medical purposes. In 2013, Uruguay became the first country to legalize and regulate recreational cannabis markets. Momentum towards regulation continued in the United States in 2014 with successful ballot initiatives in Alaska, Oregon, and the District of Columbia. Globally, the issue of cannabis regulation is front and center in a growing number of jurisdictions, including Canada, Jamaica, Italy, Spain, several Latin American countries, and a number of additional U.S. states, including California, set to vote on legalization initiatives in 2016.

Unsurprisingly, given the robust global conversation around the regulation of recreational cannabis markets, claims about the impacts of cannabis use and regulation are increasingly part of the public discourse. Unfortunately, though, these claims are often unsupported by the available scientific evidence. Another reoccurring problem in the public discourse

is the selective inclusion of research studies based on their support for a predetermined narrative. The intentional exclusion of studies with contradictory findings does not allow for an objective review and analysis of all the evidence. This "cherry picking" of the evidence is a routine practice that distorts public understanding. By outlining the current state of all the scientific evidence on common cannabis claims, *State of the Evidence: Cannabis Use and Regulation* strives to ensure that evidence, rather than rhetoric, plays a central role in policy-making around this important issue.

The harms of misrepresenting the scientific evidence on cannabis should not be overlooked. Given that policy decisions are influenced by public opinion and media reports, public discourse needs to be well informed. By addressing knowledge gaps with scientific findings, the ICSDP hopes to dispel myths about cannabis use and regulation, and ensure that the scientific evidence on these topics is accurately represented. Only then can evidence-based policy decisions be made.

Readers of this report will notice three repeating themes emerge through the discussion of the scientific evidence on common cannabis claims.

First, many of the claims confuse correlation and causation. Although scientific evidence may find associations between two events, this does not indicate that one necessarily caused the other. Put simply, correlation does not equal causation. This is a commonly made mistake when interpreting scientific evidence in all fields, and is unsurprisingly a recurring source of confusion in the discourse on cannabis use and regulation.

Second, for several of these claims, the inability to control for a range of variables ("confounders") means that in many cases, we cannot conclude that a particular outcome was caused by cannabis use or regulation. Unless scientists can remove all other possible explanations, the evidence cannot conclusively say that one specific explanation is true.

Third, many of the claims cannot be made conclusively as there is insufficient evidence to support them. Findings from a single study or a small sample cannot be generalized to entire populations. This is especially pronounced for claims related to cannabis regulation, as not enough time has passed since the regulation of recreational cannabis in Colorado, Washington State, and Uruguay to examine many of the impacts of these policy changes.

These three common pitfalls are important to take into account when reading media reports and advocacy materials that suggest scientists have conclusively made some finding related to cannabis use or regulation. In many cases, due to the reasons outlined above, this will actually result in a misrepresentation of the scientific evidence.

State of the Evidence: Cannabis Use and Regulation is comprised of two sections: *Common Claims on Cannabis Use* and *Common Claims on Cannabis Regulation*.

Common Claims on Cannabis Use presents evidence on frequently heard claims about cannabis use, including claims on the addictive potential of cannabis, cannabis as a "gateway" drug, the potency of cannabis, and the impact of cannabis use on the lungs, heart, and brain (in terms of IQ, cognitive functioning, and risk of schizophrenia).

Common Claims on Cannabis Regulation presents evidence on frequently heard claims about the impacts of cannabis regulation, including the impact of regulation on cannabis availability, impaired driving, the use of cannabis, drug crime, drug tourism, and "Big Marijuana."

For each claim, the relevant available scientific evidence is presented and the strength of the scientific evidence in support of the claim is determined. Readers will notice that none of the claims are strongly supported by the scientific evidence, reinforcing the significant misrepresentation of evidence on cannabis use and regulation.

We hope that the evidence contained in this report meaningfully contributes to the global conversation around cannabis policy and helps policymakers, as well as general readers, separate scientific evidence from conjecture.

METHODS

We undertook a review of the available scientific literature on the topic of cannabis use and regulation. First, two co-authors (DW, TMW) identified common claims about cannabis put forward by media outlets, government agencies, political leaders, and third-party advocacy organizations. For each claim, two authors (TMW, DW) undertook a thorough review of all scientific peer-reviewed studies, as well as non-peer reviewed scientific studies (i.e., ‘grey literature’) on these topics. This process included searching major online academic databases, the Internet, medical library databases, and the citation lists of relevant scientific studies to identify the most up-to-date scientific evidence on cannabis use and regulation. All authors (DW, TMW, NM) then undertook a quality assessment process for the scientific literature related to each claim to determine the overall strength of the scientific evidence. Finally, all authors (DW, TMW, NM) contributed to the drafting of these findings in the text of this report and two authors (DW, NM) drafted the response sheets contained in *Using Evidence to Talk About Cannabis*.

The complete methodology for this report, including specific databases searched, keywords used, and quality assessment protocols, are available online at http://www.icsdp.org/cannabis_claims_methods.



COMMON CLAIMS ON CANNABIS USE

COMMON CLAIMS ON CANNABIS USE

CLAIM	STRENGTH OF SUPPORTING EVIDENCE	BOTTOM LINE
“Cannabis [is] as addictive as heroin.”	Weak	A lifetime of cannabis use carries a low risk of dependence (9%), while the risk of cannabis dependence is very low among those who report using it for one year (2%) or even 10 years (5.9%). This is much lower than the estimated lifetime risk of dependence to heroin (23.1%).
“[D]id you know that marijuana is on average 300 to 400 percent stronger than it was thirty years ago?”	Moderate	Although this claim overstates the existing evidence, studies do suggest that there have been increases in THC potency over time in some jurisdictions.
“I’m opposed to legalizing marijuana because it acts as a gateway drug.”	Weak	Evidence to date does not support the claim that cannabis use causes subsequent use of “harder” drugs.
Cannabis use “can cause potentially lethal damage to the heart and arteries.”	Weak	There is little evidence to suggest that cannabis use can cause lethal damage to the heart, nor is there clear evidence of an association between cannabis use and cancer.
Cannabis use lowers IQ by up to 8 points.	Weak	There is little scientific evidence suggesting that cannabis use is associated with declines in IQ.
Cannabis use impairs cognitive function.	Moderate	While the evidence suggests that cannabis use (particularly among youth) likely impacts cognitive function, the evidence to date remains inconsistent regarding the severity, persistence, and reversibility of these cognitive effects.
“[Cannabis] is a drug that can result [in] serious, long-term consequences, like schizophrenia.”	Weak	While scientific evidence supports an association between cannabis use and schizophrenia, a causal relationship has not been established.

CLAIM: “Cannabis [is] as addictive as heroin.” – *Daily Telegraph* (Fox, 2014)

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: A lifetime of cannabis use carries a low risk of dependence (9%), while the risk of cannabis dependence is very low among those who report using it for one year (2%) or even 10 years (5.9%). This is much lower than the estimated lifetime risk of dependence to heroin (23.1%).

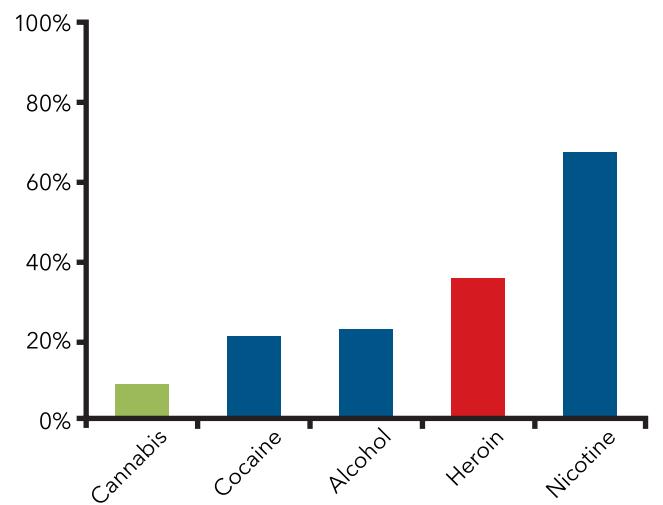
STATE OF THE EVIDENCE:

Drug dependence, also commonly referred to as addiction, can be a serious consequence of drug use. However, not all drugs have the same addictive potential, meaning that some drugs – like heroin – are more likely to lead to addiction than others. With respect to cannabis, this drug is associated with a lower risk of dependence compared to so-called “harder” illicit drugs, such as cocaine and heroin, as well as two regulated substances – nicotine and alcohol.

Lopez-Quintero and colleagues examined multi-wave data from the National Epidemiologic Survey on Alcohol and Related Conditions, a U.S. nationally representative survey of people aged 18 and over (sample size: 7,389 cannabis users) (Lopez-Quintero et al., 2011). These authors found that the probability of dependence after the first year of use was about 2% (i.e., very low) for nicotine, alcohol, and cannabis users; for cocaine users, the probability was 7.1%. After a decade of use, the probabilities for dependence were higher for users of nicotine (15.6%), cocaine (14.8%), and alcohol (11%) compared to cannabis users (5.9%). The lifetime probability of becoming cannabis dependent was estimated at 8.9%; that is, fewer than 9% of lifetime cannabis users report drug dependence. This 9% probability of cannabis dependence is most often cited in the literature, most recently in two major scientific review articles on the impact

of cannabis (Hall, 2014; Volkow et al., 2014). This figure is considerably lower than estimated lifetime probabilities for users of nicotine (67.5%), alcohol (22.7%), and cocaine (20.9%) (Lopez-Quintero et al., 2011). The lifetime probability of becoming heroin-dependent has previously been estimated at 23.1% and 35.5% (Anthony et al., 1994).

FIGURE 1. Lifetime Probabilities of Drug Dependence



One other claim regarding cannabis dependence that has been frequently cited is that the probability of dependence may increase to 1 in 6 for those who initiate cannabis use in adolescence, and that this risk may increase to 25-50% among people who use cannabis daily (Hall, 2009; Volkow et al., 2014). This suggests that the age of onset of cannabis use and the frequency or regularity of use influences the

risk that an individual will become dependent. The source of this ‘1 in 6’ estimate is a paper by Wagner et al., which reported findings from the National Comorbidity Survey (NCS) that included 8,098 participants who comprised a nationally representative sample of the U.S. population aged 15-54 (Wagner and Anthony, 2002). These authors reported that 4.2% of participants qualified for “lifetime diagnosis of cannabis dependence” based on DSM-III-R criteria. While approximately 46% of the sample had ever used cannabis, approximately 9% had developed dependence. Wagner et al. conducted additional statistical analyses to find age- and time-specific estimates of use initiation for cannabis (as well as alcohol and cocaine). The authors reported that most cases of cannabis dependence occur at younger ages (between 15-25 years of age), with peak values at age 17-18. However, the developmental window of risk for cannabis dependence was nearly closed by age 30 (Wagner and Anthony, 2002). Further, after 10 years since the first use of cannabis, the risk of dependence dropped to near zero (meanwhile, the risk of progression to alcohol dependence lasts many more years since first alcohol use).

While data from large cross-sectional surveys like those mentioned here are valuable in estimating levels of cannabis dependence, cross-sectional data do not allow for causal interpretations. Therefore, we must be very cautious regarding any blanket statement that cannabis *leads* to addiction. The evidence shows that the vast majority – over 90% – of cannabis users do *not* become dependent. Indeed, Anthony and colleagues (1994) even stated their findings in the following way: “For every user with a history of cannabis dependence, there were 10 users who had not become dependent” (Anthony et al., 1994). Again, compared to users of nicotine and

alcohol, fewer users of cannabis will become dependent over time.

The common understanding of addiction – simply requiring a substance to function – is an oversimplification. There are multiple working definitions of drug addiction (also called substance use disorder); in one definition, drug addiction is defined as the compulsive use of a drug despite adverse consequences (Nestler, 1992). With this in mind, addiction to different substances is not necessarily related to equivalent harms. For example, many people meet the criteria for caffeine addiction, but this is generally not seen as a major public health problem. The symptoms for cannabis withdrawal have been characterized as primarily psychological (rather than physical), and include non-life threatening symptoms (craving, irritability, nervousness/tension, restlessness, depression, anger, sleep difficulty, strange dreams, decreased appetite, and headache) (Copersino et al., 2006; Kouri and Pope Jr, 2000). By comparison, withdrawal symptoms for addiction to alcohol or heroin have been shown to be severe (Olmedo and Hoffman, 2000; Redmond Jr and Krystal, 1984; Swift and Stout, 1992) and, in the case of alcohol, life-threatening (Trevisan et al., 1997). This implies that cannabis dependence is less severe than that associated with other major illegal and legal drugs.

CLAIM: “[D]id you know that marijuana is on average 300 to 400 percent stronger than it was thirty years ago?” – *Health Canada advertisement*¹

STRENGTH OF SUPPORTING EVIDENCE: Moderate

BOTTOM LINE: Although this claim overstates the existing evidence, studies do suggest that there have been increases in THC potency over time in some jurisdictions.

STATE OF THE EVIDENCE:

Tetrahydrocannabinol (THC) is the main psychoactive element in cannabis and thus THC levels have been studied as the primary marker of cannabis potency. There is evidence to support the claim that cannabis potency in some regions has increased in recent decades.

McLaren and colleagues found noticeable variation in cannabis potency between samples and within years (McLaren et al., 2008). For instance, while they found that potency in the U.S. seemed to have doubled (2% in 1980 to 4.5% in 1997) based on testing THC in confiscated cannabis, significant increases were not reported for European countries other than the United Kingdom and the Netherlands. Slight increases have also been reported in Australia (Hall and Swift, 2000).

In a more recent study, Mehmedic and colleagues reported U.S. data from 46,211 cannabis samples seized and analyzed between 1993 and 2008 (Mehmedic et al., 2010). They found that during this timeframe THC content across cannabis preparations increased from 3.4% to 8.8%, and that the increase appeared due to increases in nondomestic cannabis (i.e., an increase in the supply of cannabis imported into the U.S.).

In a review, Volkow and colleagues (2014) cited that THC content detected in samples of can-

nabis confiscated in the U.S. increased from approximately 3% to 12% (i.e., 300%) from the 1980s up to 2012 (Volkow et al., 2014). Given that this review from the U.S. is the only evidence for a 300% increase in potency, the claim that cannabis potency has increased by 300% to 400% on average across all jurisdictions overstates the existing scientific evidence. It is noteworthy that the observed increases of 300% in the United States occurred during a period of massive budgets allocated towards a primarily enforcement-based drug supply reduction approach (Miron, 2008). This suggests that enforcement-based approaches to reducing cannabis supply are likely limited. Moreover, trends towards increasing potency are not merely demand-driven, but are primarily a result of criminal market economics. Given that stronger strains provide higher profits per unit weight, and that criminal markets have no regulatory structures to set potency limits, the illicit nature of cannabis likely played a role in driving up potency.

As with all estimates of illicit products, there is the potential that methodological issues may be at play when determining estimates. McLaren and colleagues (2008) mention, for example, that cannabis samples that are tested tend to be small and that it is not always clear which part of the plant has been tested (McLaren et al., 2008). This is important given

that parts of the cannabis plant have higher reservoirs of THC. The extent to which police seizures of cannabis are representative of the larger market is also unclear (Arkes et al., 2008), suggesting that we may not be able to make market wide generalizations based on seized samples.

Other factors beyond THC content are important when considering the impact of potency. For example, mixing cannabis with tobacco – a common practice when smoking cannabis in many parts of the world – dilutes THC potency. The amount of active THC actually absorbed can also vary considerably based on the mode by which cannabis is consumed. Simply assessing THC levels paints an incomplete picture of the impact of cannabis potency.

A related issue is the actual health impact of any increases in THC content. Experts have suggested that increased THC potency may be linked to adverse health and/or mental health effects and consequences, including visits to emergency rooms (Hall, 2014; Volkow et al., 2014); however, this evidence is preliminary and highly equivocal at present. Indeed, McLaren and colleagues also report in their review that claims about “adverse mental health effects of cannabis contamination” were unsupported by the available evidence (McLaren et al., 2008). Briefly, this suggests that increases in cannabis potency and subsequent toxicity (i.e., contamination) lack unequivocal evidence. By contrast, there is burgeoning (though preliminary) evidence that some cannabis users may respond to higher THC content by reducing the volume of cannabis that they consume, which may in turn lessen potential adverse effects (Van der Pol et al., 2014).

¹ Accessed March 6th 2015 from www.youtube.com/watch?v=VEuCvUdHDNA



CLAIM: “I’m opposed to legalizing marijuana because it acts as a gateway drug.” – *Enrique Peña Nieto, President of Mexico*²

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: Evidence to date does not support the claim that cannabis use causes subsequent use of “harder” drugs.

STATE OF THE EVIDENCE:

The claim that cannabis acts as a “gateway drug” has been debated and tested by scientists in various ways across settings. To date, studies have shown relatively strong support for the use of cannabis generally preceding the use of other illicit drugs. However, studies have *not* shown that the “gateway” explanation is supported by the scientific evidence. Put another way, research has not established a causal relationship between using cannabis and the increased risk of using “harder” drugs such as cocaine and heroin.

Degenhardt and colleagues conducted a study to test the “gateway” theory using data on the initiation of use of alcohol, tobacco, cannabis, and other illicit drugs from a consistent set of epidemiological surveys from 17 countries (Degenhardt et al., 2010). These authors found variation across countries and cohorts regarding the strength of the association between so-called “gateway” substances and the use of other drugs. So, for example, the authors found that in some countries, alcohol/tobacco use was more strongly linked to later use of other illicit drugs than cannabis. They also observed so-called “gateway violations”; trends whereby “harder” illicit drugs were used before cannabis.

Although we cannot derive causal explana-

tions from this study, these data cast serious doubt on claims that cannabis is a “gateway” drug, especially when we consider different contexts across the globe. That being said, the widely observed sequence or ordering of drug use – i.e., alcohol/tobacco before cannabis, and cannabis before other illicit drugs – does seem to hold with few exceptions. In a review, Hall (2014) stated that the order of use with cannabis and other illicit drugs is one of “the most consistent findings in epidemiological studies of drug use in young adults” (p. 7). In another review, Volkow and colleagues included some studies that used animal subjects and found evidence that cannabis use can prime the brain for “enhanced responses to other drugs” (Volkow et al., 2014); however, these authors also mentioned that other substances, like nicotine and alcohol, have been linked to similar effects. It is important to note that despite these findings, the authors of these two recent reviews (as well as many scientists working on these issues) are very cautious regarding the validity of the “gateway” theory. Both reviews noted that interpretations of available data on cannabis and other drug use have been contested and that there are multiple interpretations for the general pattern of cannabis use before “harder” drugs.

Hall and Lynskey highlighted drug use pat-

terns documented in the literature that could support a “gateway” role for cannabis, but also outlined key competing explanations for these observed patterns (Hall and Lynskey, 2005). These include:

1. cannabis and other drugs being part of a shared illicit drug market;
2. certain characteristics of cannabis users (e.g., risk-taking) explaining the patterns of both cannabis and other drug use (i.e., factors like mental health confounding the relationship between cannabis use and other drug use); and
3. use of cannabis altering brain function in a way that increases the likelihood of other drug use.

To investigate these potential pathways, Morral and colleagues built a statistical model based on U.S. population drug use survey data. They tested data on the risk, order, and dose-response relationships related to cannabis use and other drugs. While they could not unequivocally disprove the cannabis “gateway” theory, they nevertheless demonstrated “that the primary evidence supporting gateway effects is equally consistent with an alternative model of adolescent drug use initiation in which use, *per se*, of marijuana has no effect on the later use of hard drugs” (Morral et al., 2002).

Studies like that by Degenhardt and colleagues have consistently shown that there are few exceptions to an age-of-onset relationship (Degenhardt et al., 2010). In other words, the earlier one tries drugs, the more likely they are to subsequently use other drugs. A key implication of this finding is to focus prevention efforts not so much on one particular type of drug such as cannabis, but on addressing the risk of early use, as the age of onset appears to

have much more of an impact on the future drug-related harms that an individual experiences compared with the impact of cannabis use.

² Reported in The Washington Post. Accessed March 6th 2015 from <http://www.washingtonpost.com/blogs/worldviews/wp/2013/02/06/mexicos-president-opposes-legalizing-marijuana-calls-it-a-gateway-drug/>



CLAIM: Cannabis use “can cause potentially lethal damage to the heart and arteries.” – *World Federation Against Drugs*³

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: There is little evidence to suggest that cannabis use can cause lethal damage to the heart, nor is there clear evidence of an association between cannabis use and cancer.

STATE OF THE EVIDENCE:

There is little research regarding the impact of cannabis use on the heart and cardiovascular functioning. A recent review reported that the mechanisms behind cannabis effects on the cardiovascular system are “complex and not fully understood” (Volkow et al., 2014). Although cannabis use has been found to be associated with acute effects that can trigger events like heart attack and stroke (Jouanlus et al., 2014; Thomas et al., 2014), clear causal linkages have not been established. Research has also tended to suggest that potentially risky cardiovascular effects from cannabis smoking are more likely to occur in older adults (Hall, 2014). In sum, there is a need for ongoing research on these health effects, but claims purporting “lethal damage” related to cannabis use are overstating the scientific research.

With respect to the impact of cannabis on physical health, studies have reported that smoking cannabis is associated with various respiratory-related problems, including injury to the large airways and symptoms of chronic bronchitis (Gordon et al., 2013; Tashkin, 2013; Tashkin et al., 2002). However, Tashkin also reported no evidence of a strong association between cannabis smoking and chronic obstructive pulmonary disease or several other

pulmonary conditions (Tashkin, 2013). Interestingly, a 20-year study involving a cohort of 5,115 participants found that low, occasional cannabis use was actually associated with increased, rather than decreased, pulmonary function (Pletcher et al., 2012). In a recent review, Hall summarized the current evidence on the effects of long-term cannabis smoking on respiratory function as “unclear” (Hall, 2014).

The measurement of respiratory risks associated with cannabis use are substantially complicated by the routine practice of smoking cannabis and tobacco together. The respiratory harms and carcinogenic risks of tobacco are not contested, and certainly remain when combined with cannabis. Importantly, potential respiratory harms can be minimized or eliminated by consuming cannabis using methods other than smoking. Vaporizing, for example, is thought to reduce these harms significantly, and ingesting cannabis (via edibles) eliminates them entirely (Abrams et al., 2007; Earlywine and Barnwell, 2007; Hazekamp et al., 2006).

The impact of cannabis smoking on the development of lung cancer also remains unclear. While Hashibe and colleagues (2006) ob-

served an association between long-term cannabis smoking and lung cancer, this association was non-significant when the results were adjusted for the impact of cigarette smoking and several other confounders (Hashibe et al., 2006).

It is worth noting that risks of morbidity and mortality associated with use of tobacco and alcohol are much higher than those associated with cannabis use. For example, evidence has found far greater risk of lung problems among tobacco users compared to regular cannabis users (Tashkin, 2013).

³ From the title of a post on the World Federation Against Drugs website, linking to a study on cannabis smoking and cardiovascular problems. Accessed March 8th 2015 from <http://wfad.se/latest-news/1-articles/4724-smoking-cannabis-can-cause-lethal-damage-to-heart>



CLAIM: Cannabis use lowers IQ by up to 8 points.

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: There is little scientific evidence suggesting that cannabis use is associated with declines in IQ.

STATE OF THE EVIDENCE:

In recent years, the claim that cannabis use leads to significantly lower IQ has often been repeated, with an 8-point drop in IQ sometimes mentioned. One study in particular authored by Meier and colleagues (2012) is frequently cited as supporting evidence (Meier et al., 2012). However, the strength of this study's findings has been questioned and newer evidence suggests that other substance use may have a greater impact on IQ. Indeed, a re-review of the data presented by Meier and colleagues, conducted by Rogeberg (Rogeberg, 2013), suggests that the association between cannabis use and IQ decline can actually be explained (i.e., confounded by) by the socio-economic status of participants, rather than by cannabis use itself.

The article by Meier and colleagues was based on data from participants in the Dunedin Study, a longitudinal investigation that followed a cohort of individuals ($n = 1,037$) born in 1972/1973 in New Zealand until the age of 38 (Meier et al., 2012). One of the main results reported was that "persistent cannabis dependence" was associated with decline on most IQ subtests. By contrast, people who initiated cannabis use in adulthood did not show the same IQ declines. It was also reported that quitting cannabis use "did not fully restore neuropsychological functioning" among adolescent-onset former persistent users. While these are intriguing findings, basing general claims regarding the impact of cannabis use on IQ on the results of one study – even a rela-

tively well-designed prospective cohort study – is problematic, particularly when the major claim (i.e., an 8-point drop in IQ as a result of cannabis use) was observed among only a very small subsample ($n = 38$) of participants, representing 3.7% of the total sample.

Indeed, findings from a more recent prospective cohort study with a larger sample suggest an alternative explanation to these findings. Mokrysz and colleagues examined IQ test scores at ages 8 and 15 among participants (born 1991/1992) in the Avon Longitudinal Study of Parents and Children cohort in the United Kingdom (Mokrysz et al., 2014). Out of the full sample ($n = 2,612$; over twice as large as the Dunedin cohort), 24% reported using cannabis at least once by age 15. While those who used cannabis more than 100 times saw a significant IQ decline of over 3 points compared to people who never used the drug, this effect disappeared after other key factors (e.g., sex, socioeconomic status, and other substance use) were taken into account. Additionally, alcohol use was associated with IQ decline and actually explained most of the variance in the IQ changes that had been linked to cannabis use (i.e., the association between cannabis and IQ decline was confounded by alcohol use). Mokrysz and colleagues concluded that the age of substance use, rather than cannabis use per se, may be responsible for poorer neuropsychological outcomes. These authors also stated the following (emphasis added):

The findings do not support the hypothesis that cannabis use in adolescence leads to persistent decline in cognitive functioning, once other possible confounding variables are accounted for. The finding that moderate but not heavier alcohol use was associated with IQ decline may relate to a detrimental effect of alcohol use in adolescence, warranting further investigation. (Mokrysz et al., 2014)



CLAIM: Cannabis use impairs cognitive function.

STRENGTH OF SUPPORTING EVIDENCE: Moderate

BOTTOM LINE: While the evidence suggests that cannabis use (particularly among youth) likely impacts cognitive function, the evidence to date remains inconsistent regarding the severity, persistence, and reversibility of these cognitive effects.

STATE OF THE EVIDENCE:

There are concerns that cannabis use, especially when initiated in adolescence, may lead to various forms of cognitive impairment. For example, a recent Health Canada advertisement flashed “loss of memory” and “learning problems” on the screen (Health Canada, 2014). The U.S. National Institute on Drug Abuse has warned parents that cannabis use “has negative effects on attention, motivation, memory, and learning that can persist after the drug’s immediate effects wear off – especially in regular users” (NIDA, 2014). While there is moderate evidence to support a general claim that early-onset and sustained cannabis use is associated with certain cognitive deficits, there remain important gaps in our knowledge regarding the full range of effects and their reversibility.

There is a fairly large though quite mixed literature about the effects of cannabis use on cognitive functioning and related outcomes. Recent reviews by Volkow and Hall summarize a number of studies that report associations between heavy, long-term cannabis use and cognitive impairments in memory, attention, and verbal learning (Hall, 2014; Volkow et al., 2014). Crane and colleagues also conducted a comprehensive review and noted that recent and previous literature has shown that the acute effects of cannabis intoxication (i.e., currently ‘high’) are associated with short-term decreases in learning and memory; an unsurprising finding given that these effects occur

of twins (Verweij et al., 2013). Hall et al. summarize as follows:

An analysis of twins who were discordant for early cannabis use [e.g., one used while the other didn't] found no difference in risk of early school-leaving between the twins who did and did not use cannabis, suggesting that the association was explained by shared genetic and environmental risk factors. These findings are supported by two earlier analyses of US twin-study data. (Hall, 2014)

The inconsistency across the scientific literature on this topic is likely related to methodological differences in the studies (e.g., samples, doses, cannabis use histories), as well as the lack of adequate adjustment for confounders. Both Hall and Crane note that, over time, studies in this field have become more systematic and methodologically sound (Crane et al., 2013; Hall, 2014). At present, though, there is little evidence that cannabis use causes long-term, irreversible declines in cognitive function, as opposed to the inevitable impairment related to intoxication.



CLAIM: “[Cannabis] is a drug that can result [in] serious, long-term consequences, like schizophrenia.” – Kevin Sabet, *Smart Approaches to Marijuana* (Baca, 2015)

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: While scientific evidence supports an association between cannabis use and schizophrenia, a causal relationship has not been established.

STATE OF THE EVIDENCE:

On balance, the evidence has established an association between cannabis use and psychotic symptoms associated with schizophrenia. However, the scientific literature does not suggest that there is a causal relationship between cannabis use and schizophrenia.

Importantly, if cannabis use caused schizophrenia, we would expect to see increases in incidence as rates of cannabis use have increased, but this trend has not been observed (Hall, 2014). To that end, one UK-based study reported that, given that cannabis use has increased fourfold among the UK population between the early 1970s to 2002, there should be a corresponding 29% increase in cases of schizophrenia among men, and 12% increase among women between 1990 and 2010 (Hickman et al., 2007). Instead, in the period during which these increases were estimated to increase the most (1996–2005), it was found that annual cases of schizophrenia in the UK were either stable or declining (Frisher et al., 2009). These findings strongly suggest that cannabis use does not cause schizophrenia.

An older study with a large sample ($n = 45,570$) of Swedish male conscripts found that participants who had tried cannabis by 18 years of age were 2.4 times more likely to receive a diagnosis of schizophrenia over the following 15 years compared to those who had not tried the drug (Andréasson et al., 1987). However, this study was not able to deter-

mine the direction of causality with respect to cannabis use and schizophrenia. Instead, the authors state: “Whether cannabis abuse preceded psychiatric symptoms in these cases or vice-versa cannot be determined” (Andréasson et al., 1987). Another follow-up of the Swedish cohort by Zammit and colleagues revealed a dose-response relationship between cannabis use at age 18 and schizophrenia risk (i.e., those who used the drug more frequently had higher risk), and the effect remained after controlling for various confounders including other substance use and certain features of family history and personality traits (Zammit et al., 2002). Notably, because this study only measures drug use at baseline, it is impossible to determine the patterns of drug use among study participants in the decades between the study’s baseline and emergence of schizophrenia. This introduces the potential for misclassification bias into the study.

Volkow and colleagues have noted the difficulty of establishing causality in studies regarding cannabis use and mental illness, as a number of factors could predispose individuals to both (Volkow et al., 2014). For example, in a systematic review that included longitudinal and population-based studies on cannabis use and risk of psychotic outcomes, Moore and colleagues also found a dose-response effect of cannabis use on any psychotic outcomes, independent of other confounders and acute intoxication (Moore et al., 2007). However, they also noted

that observational studies cannot eliminate all confounders and that the uncertainty regarding a direct causal relationship between cannabis use and psychosis is “unlikely to be resolved in the near future” (Moore et al., 2007). In an article that examined different hypotheses about cannabis use and psychosis, Pierre notes that there are numerous factors that may increase the risk of psychosis; that the magnitude of risk from cannabis use appears “modest”; and that evidence is “equivocal” regarding the assumption that cannabis use “can cause schizophrenia” (Pierre, 2011). Scientific findings are inconsistent on the magnitude of risk posed by cannabis use, as well as the frequency or timing of use that is associated with mental illness (Andréasson et al., 1987; Caspi et al., 2005; Moore et al., 2007).

As Caspi and colleagues (2005) have noted, “the vast majority of young people who use cannabis do not develop psychosis” (Caspi et al., 2005). These authors and other available research have suggested that increased risk of psychosis from cannabis use may be most pronounced among people who are already genetically susceptible to such symptoms and schizophrenia (Henquet et al., 2008). Indeed, a recent study compared individuals who did and did not use cannabis (Proal et al., 2014). All participants then provided information about their family history of schizophrenia. The authors of the study found that while family history of schizophrenia predicted participant schizophrenia, cannabis use had no impact on increasing this risk. In short, the authors concluded that cannabis use by itself did not increase the risk of schizophrenia.

Out of all the evidence reviewed here in relation to claims about cannabis use and health effects, some of the strongest evidence (e.g., based on well-designed studies, etc.) supports

an association between cannabis use and a risk of schizophrenia. However, as summarized above, a causal relationship between cannabis use and schizophrenia is not supported by the evidence (Advisory Council on the Misuse of Drugs, 2008).





COMMON CLAIMS ON CANNABIS REGULATION

COMMON CLAIMS ON CANNABIS REGULATION

CLAIM	STRENGTH OF SUPPORTING EVIDENCE	BOTTOM LINE
Legalization / regulation increases the availability of cannabis.	Weak	Evidence suggests that the supply of illegal cannabis has increased under a prohibition model, and that availability has remained high among youth. Evidence does not suggest that cannabis availability among youth has increased under regulatory systems.
"[I]f marijuana was legalized, the increase in users would be both large and rapid..."	Weak	Evidence suggests that the policy environment (specifically legal status and enforcement policy) has at most a marginal impact on the prevalence of drug use, thereby suggesting that regulating cannabis markets will not inevitably cause higher levels of cannabis use.
Regulation will not reduce drug crime.	Weak	Given that the prohibition of cannabis has not been shown to reduce illegal supply, it is likely that cannabis regulation is more effective at minimizing criminal markets for cannabis, despite the fact that criminal markets will continue to represent a proportion of the total market.
"We are going to have a lot more people stoned on the highway and there will be consequences."	Weak	While experimental studies suggest that cannabis intoxication reduces motor skills and likely increases the risk of motor vehicle collisions, there is not sufficient data to suggest that cannabis regulation would increase impaired driving, and thereby traffic fatalities.
Regulation promotes drug tourism.	Weak	While evidence suggests that, depending on the use of regulatory controls and geographic setting, regulation may in some cases lead to an increase in drug tourism, the data do not suggest that this is an inevitable consequence of regulation.
Regulation leads to a "Big Marijuana" scenario.	Weak	Available evidence regarding "Big Marijuana" is currently lacking, though regulatory controls can be introduced within regulatory systems to reduce the potential of profit maximization by cannabis retailers.

CLAIM: Legalization / regulation increases the availability of cannabis.

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: Evidence suggests that the supply of illegal cannabis has increased under a prohibition model, and that availability has remained high among youth. Evidence does not suggest that cannabis availability among youth has increased under regulatory systems.

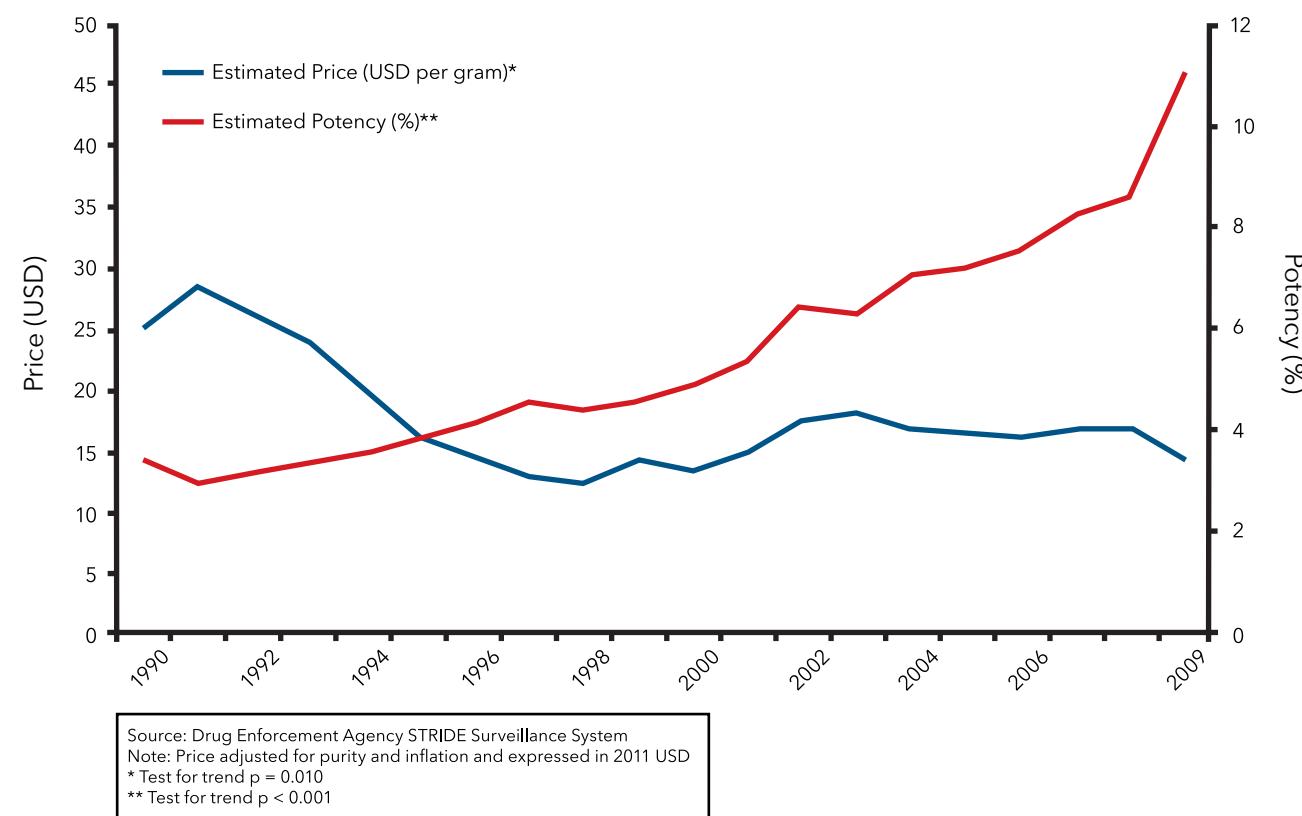
STATE OF THE EVIDENCE:

Over three decades of drug law enforcement, there is no evidence to suggest that the availability of cannabis has declined. Indeed, the opposite appears to be true. The availability of illegal cannabis is difficult to quantify, given the obvious challenges in assessing the size and composition of illegal drug markets, and the fact that “availability” is a poorly and inconsistently defined variable. As such, governments, law enforcement, and experts in the field have prioritized the use of two measures – price and purity – to assess changes in illicit

drug markets. Assuming a constant demand, if the price of a drug drops and the purity of a drug increases, this suggests that the available supply has increased.

The United States provides a useful case study in this regard. Data suggest that the use of cannabis has remained relatively stable in the U.S. (UNODC, 2014). At the same time, as shown in Figure 2 below, the price of cannabis has dropped significantly in the U.S., while its potency has increased (Werb et al., 2013a).

FIGURE 2. Estimated Price and Potency of Cannabis in the United States, 1990-2009



These trends in price and potency suggest that the supply of illicit cannabis has overwhelmed government supply reduction efforts, and indeed that it likely increased during this period, given that use remained relatively constant or increased (UNODC, 2014).

Importantly, the ineffectiveness of enforcement-based approaches for controlling cannabis supply in the U.S. affect young people in particular. The Monitoring the Future study is an annual surveillance study of drug and alcohol use among American youth. Every year since the beginning of the study in 1975, over 80% of American grade 12 students – and in some years, over 90% – have consistently reported that cannabis was “fairly easy” or “very easy” to obtain (Monitoring the Future, 2014). Similarly, in the European Union, research from 2014 indicates that 58% of young people aged 15 to 24 believe it would be either very easy or fairly easy to obtain cannabis within 24 hours (European Commission, 2014).

Collectively, these data suggest that a system of drug prohibition has not been successful at reducing the availability of cannabis, which has been more than able to keep pace with changes in demand. By contrast, it is noteworthy that levels of cannabis use in the Netherlands, where cannabis has been *de facto* legalized for decades, are estimated to be less than half of those in the United States in the period prior to state cannabis regulation (20% vs. 42%) (Degenhardt et al., 2008), while it has similar or lower levels of use to neighbouring European countries (EMCDDA, 2015). This implies that prohibition-based cannabis policies do not in and of themselves lead to lower levels of cannabis use.

In short, the evidence does not suggest that the availability, supply, or use of cannabis is

meaningfully controlled by cannabis prohibition – at least not beyond marginal, localized and temporary impacts. Further, given that the regulatory systems for recreational cannabis have only recently been implemented in Colorado, Washington State, and Uruguay, it is too soon to tell what long-term impact these policy changes will have on cannabis availability. It is noteworthy, though, that drug regulation approaches provide a wide range of tools to policymakers – including bans on advertising, taxation, restrictions on licensing, and age restrictions – that have been shown to successfully limit access to tobacco among youth (Gutierrez and Pardo, 2015; Johnston et al., 2012).



CLAIM: “[I]f marijuana was legalized, the increase in users would be both large and rapid...” – Robert L. DuPont⁴

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: Evidence suggests that the policy environment (specifically legal status and enforcement policy) has at most a marginal impact on the prevalence of drug use, thereby suggesting that regulating cannabis markets will not inevitably cause higher levels of cannabis use.

STATE OF THE EVIDENCE:

Some observers point to alcohol and tobacco use statistics to support claims that these substances are widely used due to their availability, and that cannabis use would therefore increase under a regulatory system. While alcohol and tobacco are legally regulated and indeed commonly used substances in many countries including Canada and the U.S., this does not necessarily mean that the population will experience a surge in cannabis use if the drug were regulated.

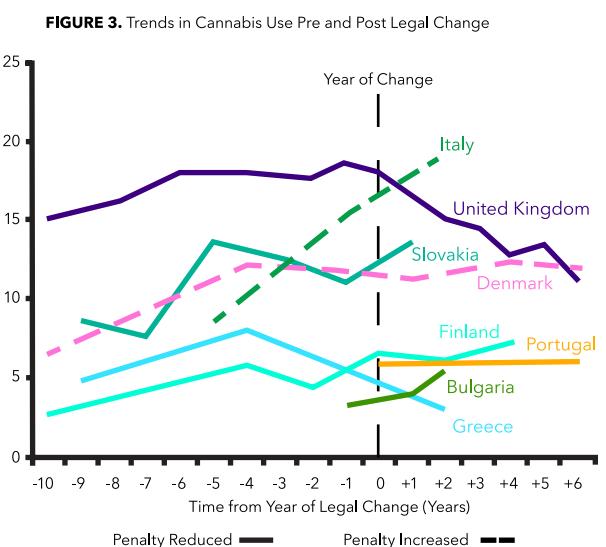
Counterevidence to claims that regulation leads to increased use comes from a large study that examined drug use data across 17 countries (combined sample size of 85,052 participants) that took part in World Health Organization World Mental Health Surveys. In this study, Degenhardt and colleagues looked at lifetime use and age of first use of tobacco, alcohol, cannabis, and cocaine (Degenhardt et al., 2008). The U.S. and New Zealand had the highest rates of cannabis use (42%) compared to other countries. The U.S. also stood out with greater levels of alcohol use and cocaine use, despite having a higher minimum legal drinking age and a more punitive illicit drug policy compared to many comparable developed nations. Compared to the U.S., the Netherlands has much lower levels of cannabis use,

especially among youth, despite having a *de facto* regulatory system for recreational cannabis. Overall, countries known to have stringent or punitive drug policies did not exhibit lower levels of drug use compared to countries with less stringent or more liberal policies. This pattern of findings led Degenhardt and colleagues to conclude that “by itself, a punitive policy towards possession and use accounts for limited variation in nation level rates of illegal drug use” (Degenhardt et al., 2008).

Various studies and surveillance reports comparing jurisdictions have highlighted the lack of correlation between legal status or harshness of law enforcement regimes, and levels of drug use (Degenhardt et al., 2008; EMCDDA, 2015; Reinarman, 2009). In addition, longitudinal studies show no clear association between changes in cannabis policy and levels of use. For instance, a large national 15-year research study in the United States reported that medical marijuana systems has not led to increases in recreational adolescent cannabis use (Hasin et al., 2015).

Over the last decade or so, several European countries have also changed their cannabis policies. Comparing prevalence estimates of cannabis use from before and after the policy

change can indicate whether there is an association between the legal changes and cannabis use.



Reproduced from the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA).

The graph above from the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) plots changes in cannabis prevalence among 15 to 34 year olds against time (with zero representing the year of a legal change in cannabis policy) (EMCDDA, 2011). The common legal hypothesis is that increased penalties will lead to a fall in drug use and reduced penalties to a rise in drug use. If this were true, countries where penalties increased (i.e., the dotted lines) would see decreases in cannabis use after the imposition of harsher legal sanctions, while countries where penalties decreased (i.e., the solid lines) would see rises in use after a reduction in legal sanctions. As can be seen in the graph, and according to the EMCDDA, “no simple association can be observed between legal changes and cannabis use prevalence” (EMCDDA, 2011).

Although the evidence that reducing penalties does not increase the prevalence of cannabis use is of significant importance, this does not necessarily predict that legal regulation will

⁴ From a post titled, “Why We Should Not Legalize Marijuana” on the Illinois Church Action on Alcohol and Addiction Problems website. Accessed March 18th 2015 from <http://ilcaaap.org/2011/06/22/why-we-should-not-legalize-marijuana/>

not lead to increases in use. Legal regulation necessarily opens up new sources of drug availability, and the way these sources are managed has the potential to generate sizeable changes in prevalence of use (Kilmer, 2010; Kilmer et al., 2010). The use of stringent and responsible regulatory controls, such as advertising bans and appropriate levels of taxation, are necessary to constrain any increases in consumption.

Some opponents to cannabis regulation have singled out use rates in U.S. states that have regulated recreational cannabis use. For example, commentators have noted that, based on recent National Survey on Drug Use and Health (NSDUH) data, cannabis use in Colorado has risen between 2011-2012 and 2012-2013, and that past-month and past-year cannabis use in the state has exceeded the national average, including use among adolescents. However, it is important to note that legal sales of recreational cannabis to adults officially opened in Colorado at the start of 2014 (Hopfer, 2014). Insufficient time has passed since the regulation of recreational cannabis use began in the state to adequately evaluate the impact of this policy shift on long-term cannabis use trends. It is also likely that individuals underreported their cannabis use prior to cannabis regulation given the stigma associated with engaging in illegal drug use. In the short term, data on cannabis use among youth in Colorado suggests that use has stayed the same or even declined (especially when comparing data from the 1990s until the present) among teenagers in the years prior to formal regulation, while post-regulation data from the Colorado Department of Public Health and Environment have demonstrated that the use of cannabis by teenagers in Colorado has continued to decline after the legal reform (CDPHE, 2014).

CLAIM: Regulation will not reduce drug crime.

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: Given that the prohibition of cannabis has not been shown to reduce illegal supply, it is likely that cannabis regulation is more effective at minimizing criminal markets for cannabis, despite the fact that criminal markets will continue to represent a proportion of the total market.

STATE OF THE EVIDENCE:

A commonly heard argument *in favour* of cannabis regulation is that it would reduce the violence associated with the illicit drug trade and the criminal justice resources spent on arresting and prosecuting drug offences. In response, opponents have countered that regulating cannabis will *not* reduce drug crime. To help bolster this claim, it has been reported that, for example, in recent years Colorado has witnessed significant increases in seizures of cannabis in mail parcels and other forms of transit that would have been diverted to other states (Rocky Mountain HIDTA, 2013). Media reports and groups like Smart Approaches to Marijuana have suggested that underground markets for cannabis thrive in Washington State and Colorado (Smart Approaches to Marijuana, 2015). As well, it has been estimated that Mexican drug cartels receive a minority of their revenue from cannabis and, as such, cannabis regulation would do little to reduce other illicit activities and crime related to other drugs (Kilmer et al., 2010a).

Although illegal drug crime is still likely to continue under a regulated market, under prohibition-based systems, criminal markets control 100% of the cannabis market. By contrast, regulatory markets will divert at least a proportion of revenue towards legal mechanisms.

Overall, there is a lack of high-quality empir-

ical investigations to substantiate how much drug crime thrives under regulatory systems for recreational cannabis. Unfortunately, the situation in Netherlands is not very instructive since, due to their unusual legal approach, whilst the sales of cannabis from the 'coffee shops' is tolerated, supply to the 'back door' remains via criminal producers and suppliers. In Colorado and Washington State, insufficient time has passed since cannabis regulation to adequately assess the situation. It is also difficult to study how much impact a change in drug legislation has on crime in general and even drug crime specifically, as shifts in crime are subject to *many* factors, including social-structural changes. Additionally, criminal markets are notoriously difficult to quantify. Nonetheless, regulated cannabis markets directly reduce some drug crime by removing the illegal nature of some forms of cannabis production, distribution, and consumption – assuming demand remains relatively constant.

While observers argue that cannabis regulation has not substantially reduced drug crime, evidence does not suggest that prohibition has been more effective. However, plenty of empirical evidence has accumulated demonstrating the failures of drug prohibition and law enforcement when it comes to reducing the size of underground drug markets and trafficking. Werb and colleagues examined illicit drug supply indicators from government

surveillance system data and found evidence of decreasing prices for and increasing purity of heroin, cocaine, and cannabis over the last two decades (Werb et al., 2013a). At the same time, seizures of these drugs had typically increased or remained stable across global regions.

Together these findings suggested a general *increase* in illegal supplies of these drugs, despite continued international efforts focused on supply reduction. Also under prohibition, the illicit cannabis trade represents a highly lucrative criminal market (Kilmer and Pacula, 2009). For a specific example, the domestic illicit cannabis trade in British Columbia is estimated to be between approximately \$400 million and \$600 million annually (Werb et al., 2012), while the pre-regulation illicit cannabis market in Washington State has been estimated at approximately \$300 million annually (Archambault et al., 2013). Regulation of recreational cannabis in Washington State has, at the very least, incorporated a substantial proportion of this illegal market into a regulated system.

Finally, the notion that enforcement-based responses to illicit drug markets reduce the violence associated with criminal activity appears to be false. A recent systematic review evaluated the impact of drug law enforcement on subsequent levels of drug-related and criminal violence (Werb et al., 2011). This review found that over 90% of scientific studies reported that violence increased as a result of drug law enforcement operations, and in many cases that this increase in violence was sustained for up to two years. These findings suggest that prohibition-based responses are unlikely to be more effective than regulatory approaches in reducing levels of violent drug crime.



CLAIM: “We are going to have a lot more people stoned on the highway and there will be consequences.” – Rep. John Mica (R-Fla.)⁵

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: While experimental studies suggest that cannabis intoxication reduces motor skills and likely increases the risk of motor vehicle collisions, there is not sufficient data to suggest that cannabis regulation would increase impaired driving, and thereby traffic fatalities.

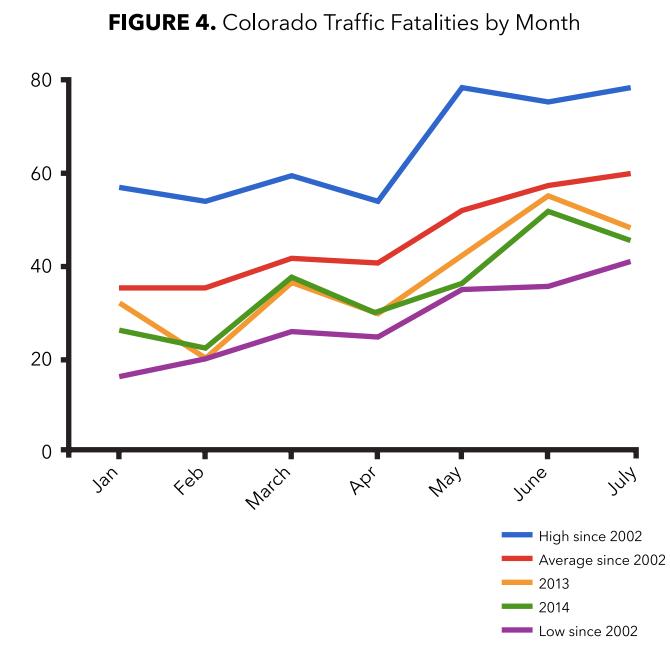
STATE OF THE EVIDENCE:

Although evidence shows that the risk of motor vehicle collisions increases for drivers during acute intoxication from cannabis use, evidence does not suggest that cannabis regulation leads to increases in the number of impaired drivers on the road.

A systematic review and meta-analysis of epidemiologic studies by Asbridge and colleagues is often cited to support the statement that cannabis use doubles the risk of a car crash (Asbridge et al., 2012). The Asbridge review included nine studies using control groups; all the studies were assessed as medium or high quality. Across most of these studies, driving under the influence of cannabis was associated with a significantly higher risk of crashing compared with driving unimpaired (Asbridge et al., 2012). Another meta-analysis of epidemiologic studies similarly found that cannabis use increases the risk of motor vehicle collisions by more than 2-fold and in a dose-response manner (i.e., increasing dose and frequency of use increases crash risk) (Li et al., 2012).

As such, while the evidence indicates that the risk of motor vehicle collisions increase for drivers during acute intoxication from cannabis use, there is no evidence to suggest

that regulation of recreational cannabis will lead to an increase in persons driving while under the influence of cannabis. For example, recent data from Colorado provides reason to question any general claims that cannabis regulation will necessarily lead to less safety on the road at the population-level. As shown in the figure below, since the introduction of a regulatory system in 2012, traffic fatalities have actually decreased across the state. If cannabis regulation increased the risk of motor vehicle collisions as a result of more widespread use of cannabis, then we would expect that this



Raw data from the Colorado Department of Transportation.

⁵ Reported in the Washington Post. Accessed March 18th 2015 from <http://www.washingtonpost.com/news/the-watch/wp/2014/08/05/since-marijuana-legalization-highway-fatalities-in-colorado-are-at-historic-lows/>

would be borne out by the data. However, the opposite appears to be the case, with the post-regulation period in Colorado associated with lower levels of traffic fatalities (Colorado Department of Transportation, 2015). While the levels of total traffic fatalities may not tell us about the specific role of cannabis use in car crashes, they do suggest that cannabis regulation in Colorado has not led to less safety on the road at the population level. The falling rates of alcohol impaired driving fatalities also indicate that it is possible to prevent impaired driving, even for a legal drug. For instance, public education and awareness campaigns that are possible in a legally regulated market can certainly be valuable prevention interventions, as has occurred with drunk driving (Hingson and Winter, 2003). Similarly successful initiatives could be used to prevent driving under the influence of cannabis.

Importantly, by comparison, the risk of *fatal* crashes involving drivers with a Blood Alcohol Content (BAC) at 0.08% or above (i.e., the legal limit in many jurisdictions) was estimated to carry a 6-fold to a 241-fold increased risk compared with non-impaired drivers (Zador et al., 2000). Clearly, the risk of not only motor vehicle collisions, but fatal collisions, associated with alcohol use is much higher than that associated with cannabis use. The impact of alcohol intoxication on driving therefore remains a far greater public health concern.

Finally, there are also some important limitations of studies assessing motor impairment risk related to cannabis use. First, laboratory or experimental studies involving driving simulators have reported that participants often compensate for impairment from cannabis use by driving more slowly (Hall, 2014; Hartman and Huestis, 2013). Some epidemiologic studies have only examined certain populations

(e.g., people treated for substance use) or have not used appropriate controls (Hartman and Huestis, 2013). Importantly, as Li and colleagues noted, polydrug use (i.e., use of more than one drug) creates challenges in determining the precise risk associated with cannabis use (Li et al., 2012). Many impaired drivers test positive for more than one drug (including alcohol), which creates difficulties in interpreting results in statistical models, given challenges in disentangling the impact of the use of multiple drugs.



CLAIM: Regulation promotes drug tourism.⁶

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: While evidence suggests that, depending on the use of regulatory controls and geographic setting, regulation may in some cases lead to an increase in drug tourism, the data do not suggest that this is an inevitable consequence of regulation.

STATE OF THE EVIDENCE:

Reports about “drug tourism” have often made reference to cannabis sales at coffee shops in the Netherlands. Although it is unclear how systematically the data was collected, it has been estimated that of the 4.5 million tourists who visit Amsterdam annually, approximately a quarter visit a coffee shop and 10% say that use of cannabis in a coffee shop was their reason for visiting the city (Kilmer, 2010). Reports have noted that the evidence on drug tourism in the Netherlands is “sparse” (MacCoun, 2010), though we caution that this may simply be a function of a lack of scientific data, rather than implying a lack of drug tourism. It is noteworthy that a proposal for a ‘wietpas’ (i.e., weed pass) put forward by the Dutch government would have restricted access to cannabis sales at Dutch coffee shops to residents (Rolles, 2014). However, this proposal was abandoned due to overwhelming opposition, with polling suggesting that 80% of Dutch residents believed that the proposal would increase the illegal drug trade. As of 2014, a small minority of Dutch municipalities (15%) have introduced restrictions that bar the sale of cannabis to non-residents (Rolles, 2014). It is also worth noting that drug tourism is not restricted to settings where cannabis has been regulated. Media reports suggest that Vancouver, Canada, for instance, is a cannabis tourism destination (Moore, 2012), though un-

der current drug laws, policymakers in Canada do not have access to regulatory controls to discourage cannabis tourism.

In a report about the potential impacts of cannabis legalization in California, Kilmer and colleagues stated that, “Marijuana legalization would likely be a high-profile action, noted by people around the United States and even abroad. Plausibly, it could influence decisions to vacation in California” (Kilmer, 2010b). In a more recent report cited by this group, the Colorado Department of Revenue published estimates of out of state visitor spending on cannabis using a sales tax receipt information, point-of-sale statistics, and data from county tourist offices (Light et al., 2014). They estimate that 44% percent of revenue from cannabis sales in metropolitan areas, and 90% of sales in rural communities, occurred from buyers residing out of state (i.e., drug tourists) (Light et al., 2014). Additionally, in a recent analysis assessing the likelihood of drug tourism related to cannabis regulation in the United States, Caulkins and colleagues note that the potential for cannabis tourism is related to the size and distance of neighboring populations in settings that have not regulated recreational cannabis use (Caulkins et al., 2015), meaning that certain settings (i.e., states in the country’s northeast) are likely to see

more drug tourists compared with others.

Importantly, drug tourism is not necessarily a negative side effect of regulation, and may in fact be desirable in some settings. As Caulkins and colleagues note, “Marijuana tourism is not all bad; it would generate revenues for hoteliers and restaurateurs just as fall leaves and ski slopes do. But with tourism comes traffic, congestion, and—for marijuana tourism—some risk of drivers who are impaired on their return journey. That could lead—as it has in a few Dutch towns—to problems with disorder.” (Caulkins et al., 2015). In a review article, Monshouwer and colleagues noted that some municipalities in the Netherlands have had to address nuisance issues related to “drug tourists” coming from Belgium, Germany, and France (Monshouwer et al., 2011). On the whole, while drug tourism has some benefits (revenue) and drawbacks (public disorder), there is little evidence suggesting that it has contributed to widespread negative health or social outcomes in settings that have regulated cannabis.

The review by Monshouwer and colleagues also highlighted the ways in which regulatory policies can be changed or tightened to discourage tourists (e.g., visitors would need a membership card to purchase cannabis, strict limits on sale quantities, age restrictions at coffee shops, or restricting sales of cannabis to home country citizens), while still avoiding an enforcement-based model to control cannabis, which is likely less effective in reducing supply and availability (Monitoring the Future, 2014; Werb et al., 2013b). Uruguay proactively took steps in this direction, as their regulations permit only residents to grow and purchase cannabis. This was an intentional policy decision made by the federal government to reduce the possibility that Uruguay would become a can-

nabis tourism destination (Gutierrez & Pardo, 2015).

⁶ For example, see CBC news story. Accessed March 19th 2015 from <http://www.cbc.ca/news/world/colorado-gets-high-on-pot-revenue-marijuana-tourists-1.2564410>



CLAIM: Regulation leads to a “Big Marijuana” scenario.

STRENGTH OF SUPPORTING EVIDENCE: Weak

BOTTOM LINE: Available evidence regarding “Big Marijuana” is currently lacking, though regulatory controls can be introduced within regulatory systems to reduce the potential of profit maximization by cannabis retailers.

STATE OF THE EVIDENCE:

Moves towards cannabis regulation in multiple U.S. states have prompted claims about regulation ushering in a so-called “Big Marijuana” (less commonly, “Big Cannabis” or “Cannabis Inc.”) scenario. The basic premise is that cannabis regulation necessarily leads to a large, for-profit cannabis industry that features little oversight and lack of concern about public health and safety (Lopez, 2015) – echoing the negative influence of “Big Tobacco,” “Big Alcohol,” or “Big Pharma.” This claim is largely unsubstantiated by evidence, but reflects a reasonable concern that the implementation of for-profit systems for cannabis regulation incentivize the entry of aggressive private interests seeking to maximize profit by selling as much cannabis as possible with little concerns for potential negative public health impacts.

Tobacco was, in previous decades in North America, heavily advertised, and became a commonly used substance as well as a major source of preventable health conditions and mortality (Richter and Levy, 2014). Given this experience, it has been assumed that cannabis regulation will lead to a similar situation involving advertising (especially to youth) and industry deception about the health risks associated with cannabis use. These concerns, however, generally discuss “Big Marijuana” as a potential, rather than current, concern. This is a result of a lack of existing data from American states that have regulated cannabis. It is noteworthy that in the Netherlands, a state

with longstanding de facto cannabis regulation, few if any major concerns about “Big Marijuana” have been reported – though this may also be related to the fact that cannabis production is still technically criminalized in the Netherlands.

Concerns that regulation will inevitably lead to a “Big Marijuana” scenario imply a weaker level of government control than is possible under cannabis regulation. However, restrictions on advertising, requirements for product labelling on health harms, and investments in public education are regulatory controls that do not foster a large commercialized industry and can be adopted. In a comparative policy analysis of Colorado, Washington State, and Uruguay, Pardo briefly summarized numerous laws and regulations that place restrictions on, for example, retail quantities, age of purchase, commercial cultivation practices and processing, advertising and promotion, and internet sales (Pardo, 2014). Uruguay, for example, has prohibited cannabis advertising (Pardo, 2014). In addition to the use of strict regulatory controls, limiting market players can also diminish the likelihood of a “Big Marijuana” scenario. For instance, the size of markets in Spain and Belgium have been limited through the “cannabis social club” model, in which non-commercial organizations are only legally allowed to cultivate and distribute cannabis to their members (Decorte, 2015).



REFERENCES

- Abrams, D.I., Vizoso, H.P., Shade, S.B., Jay, C., Kelly, M.E., Benowitz, N.L., 2007. Vaporization as a smokeless cannabis delivery system: a pilot study. *Clinical Pharmacology & Therapeutics* 82, 572-578.
- Advisory Council on the Misuse of Drugs, 2008. Cannabis: Classification and public health. UK Home Office, London.
- Andréasson, S., Engström, A., Allebeck, P., Rydberg, U., 1987. Cannabis and schizophrenia: A Longitudinal Study of Swedish Conscripts. *The Lancet* 330, 1483-1486.
- Anthony, J.C., Warner, L.A., Kessler, R.C., 1994. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey. *Experimental and Clinical Psychopharmacology* 2, 244-268.
- Archambault, M., McNeilly, E., Roe, P., 2013. Benefit-cost analysis of Initiative 502: Legalization of marijuana in Washington. *Evans School Review* 3, 10.
- Arkes, J., Pacula, R.L., Paddock, S.M., Caulkins, J.P., Reuter, P., 2008. Why the DEA STRIDE data are still useful for understanding drug markets. National Bureau of Economic Research.
- Asbridge, M., Hayden, J.A., Cartwright, J.L., 2012. Acute cannabis consumption and motor vehicle collision risk: Systematic review of observational studies and meta-analysis. *British Medical Journal* 344.
- Baca, R., 2015. Here's anti-legalization group Project SAM's response to CNN's 'Weed 3'. <http://www.thecannabist.co/2015/04/20/weed-3-cnn-project-sam-kevin-sabet/33728/>
- Caspi, A., Moffitt, T.E., Cannon, M., McClay, J., Murray, R., Harrington, H., Taylor, A., Arseneault, L., Williams, B., Braithwaite, A., Poulton, R., Craig, I.W., 2005. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene X environment interaction. *Biological Psychiatry* 57, 1117-1127.
- Caulkins, J.P., Kilmer, B., Kleiman, M.A.R., MacCoun, R.J., Midgette, G., Oglesby, P., Pacula, R.L., Reuter, P.H., 2015. Considering marijuana regulation: Insights for Vermont and other jurisdictions. RAND Corporation.
- CDPHE, 2014. Colorado teen marijuana use continues to decrease post legalization. Colorado Department of Public Health and Environment.
- Colorado Department of Transportation, 2015. Historical fatal crashes graphs for Colorado since 2002 https://www.codot.gov/library/traffic/safety-crash-data/fatal-crash-data-city-county/historical_fatals.pdf/view. Accessed on July 23 2015.
- Copersino, M.L., Boyd, S.J., Tashkin, D.P., Huestis, M.A., Heishman, S.J., Dermand, J.C., Simmons, M.S., Gorelick, D.A., 2006. Cannabis withdrawal among non-treatment-seeking adult cannabis users. *American Journal on Addictions* 15, 8-14.
- Crane, N.A., Schuster, R.M., Fusar-Poli, P., Gonzalez, R., 2013. Effects of cannabis on neurocognitive functioning: Recent advances, neurodevelopmental influences, and sex differences. *Neuropsychology Review* 23, 117-137.
- Decorte, T., 2015. Cannabis social clubs in Belgium: Organizational strengths and weaknesses, and threats to the model. *International Journal of Drug Policy* 26, 122-130.
- Degenhardt, L., Chiu, W.-T., Sampson, N., Kessler, R.C., Anthony, J.C., Angermeyer, M., Brufaerts, R., de Girolamo, G., Gureje, O., Huang, Y., Karam, A., Kostyuchenko, S., Lepine, J.P., Mora, M.E.M., Neumark, Y., Orel, J.H., Pinto-Meza, A., Posada-Villa, J., Stein, D.J., Takeshima, T., Wells, J.E., 2008. Toward a global view of alcohol, tobacco, cannabis, and cocaine use: Findings from the WHO World Mental Health Surveys. *PLoS Medicine* 5, 1053-1067.
- Degenhardt, L., Dierker, L., Chiu, W.T., Medina-Mora, M.E., Neumark, Y., Sampson, N., Alonso, J., Angermeyer, M., Anthony, J.C., Bruffaerts, R., de Girolamo, G., de Graaf, R., Gureje, O., Karam, A.N., Kostyuchenko, S., Lee, S., Lépine, J.P., Levinson, D., Nakamura, Y., Posada-Villa, J., Stein, D., Wells, J.E., Kessler, R.C., 2010. Evaluating the drug use "gateway" theory using cross-national data: Consistency and associations of the order of initiation of drug use among participants in the WHO World Mental Health Surveys. *Drug and Alcohol Dependence* 108, 84-97.
- Earlywine, M., Barnwell, S.S., 2007. Decreased respiratory symptoms in cannabis users. *Harm Reduction Journal* 4, 11.
- EMCDDA, 2011. Looking for a relationship between penalties and cannabis use. European Monitoring Centre for Drugs and Drug Addiction, Lisbon.
- EMCDDA, 2015. 2015 European drug report: Trends and developments. European Monitoring Centre for Drugs and Drug Addiction, Luxembourg.
- European Commission, 2014. Young People and Drugs Flash Eurobarometer 401. Directorate-General for Communication, European Commission.
- Fergusson, D.M., Boden, J.M., 2008. Cannabis use and later life outcomes. *Addiction* 103, 969-976.
- Fox, E., 2014. Where the Telegraph and Daily Mail get it wrong on cannabis. Huffington Post UK. Huffington Post, London.
- Frisher, M., Crome, I., Martino, O., Croft, P., 2009. Assessing the impact of cannabis use on trends in diagnosed schizophrenia in the United Kingdom from 1996 to 2005. *Schizophrenia Research* 113, 123-128.
- Gordon, A.J., Conley, J.W., Gordon, J.M., 2013. Medical consequences of marijuana use: A review of current literature. *Current Psychiatry Reports* 15.
- Gutierrez, A., Pardo, B., 2015. A Comparison of the world's first three jurisdictions to legally regulate marijuana: Colorado, Washington and Uruguay. Drug Policy Alliance, Washington, D.C.
- Hall, W., 2009. The adverse health effects of cannabis use: What are they, and what are their implications for policy? *International Journal of Drug Policy* 20, 458-466.
- Hall, W., 2014. What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? *Addiction* 110, 19-35.
- Hall, W., Swift, W., 2000. The THC content of cannabis in Australia: Evidence and implications. *Australian and New Zealand Journal of Public Health* 24, 503-508.
- Hall, W.D., Lynskey, M., 2005. Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. *Drug and Alcohol Review* 24, 39-48.
- Hartman, R.L., Huestis, M.A., 2013. Cannabis effects on driving skills. *Clinical Chemistry* 59, 478-492.

- Hashibe, M., Morgenstern, H., Cui, Y., Tashkin, D.P., Zhang, Z.F., Cozen, W., Mack, T.M., Greenland, S., 2006. Marijuana use and the risk of lung and upper aerodigestive tract cancers: Results of a population-based case-control study. *Cancer Epidemiology Biomarkers and Prevention* 15, 1829-1834.
- Hasin, D.S., Wall, M., Keyes, K.M., Cerdá, M., Schulenberg, J., O'Malley, P.M., Galea, S., Pacula, R., Feng, T., 2015. Medical marijuana laws and adolescent marijuana use in the USA from 1991 to 2014: Results from annual, repeated cross-sectional surveys. *The Lancet Psychiatry* 2, 601-608.
- Hazekamp, A., Ruhaak, R., Zuurman, L., van Gerven, J., Verpoorte, R., 2006. Evaluation of a vaporizing device (Volcano®) for the pulmonary administration of tetrahydrocannabinol. *Journal of Pharmaceutical Sciences* 95, 1308-1317.
- Health Canada, 2014. Drug Prevention - Marijuana Use - TV Ad. Accessed on July 20 2015.
- Henquet, C., Di Forti, M., Morrison, P., Kuepper, R., Murray, R.M., 2008. Gene-environment interplay between cannabis and psychosis. *Schizophrenia Bulletin* 34, 1111-1121.
- Hickman, M., Vickerman, P., Macleod, J., Kirkbride, J., Jones, P.B., 2007. Cannabis and schizophrenia: Model projections of the impact of the rise in cannabis use on historical and future trends in schizophrenia in England and Wales. *Addiction* 102, 597-606.
- Hingson, R., Winter, M., 2003. Epidemiology and consequences of drinking and driving. *Alcohol Research and Health* 27, 63-78.
- Hopfer, C., 2014. Implications of marijuana legalization for adolescent substance use. *Substance Abuse* 35, 331-335.
- Johnston, L.D., O'Malley, P.M., Bachman, J.G., Schulenberg, J.E., 2012. Monitoring the Future: Overview of key findings, 2011. *Monitoring the Future*. Institute for Social Research/National Institute on Drug Abuse, Ann Arbor.
- Jouanlus, E., Lapeyre-Mestre, M., Micallef, J., 2014. Cannabis use: Signal of increasing risk of serious cardiovascular disorders. *Journal of the American Heart Association* 3.
- Kilmer, B., 2010. Insights on the effects of marijuana legalization on prices and consumption. RAND Corporation.
- Kilmer, B., Caulkins, J.P., Bond, B.M., Reuter, P.H., 2010a. Reducing drug trafficking revenues and violence in Mexico: Would legalizing marijuana in California help? RAND Corporation.
- Kilmer, B., Caulkins, J.P., Pacula, R.L., MacCoun, R.J., Reuter, P.H., 2010b. Altered state? Assessing how marijuana legalization in California could influence marijuana consumption and public budgets. RAND Drug Policy Research Center.
- Kilmer, B., Pacula, R.L., 2009. Estimating the size of the global drug market: A demand-side approach Report 2. RAND Corporation.
- Kouri, E.M., Pope Jr, H.G., 2000. Abstinence symptoms during withdrawal from chronic marijuana use. *Experimental and Clinical Psychopharmacology* 8, 483.
- Li, M.C., Brady, J.E., DiMaggio, C.J., Lusardi, A.R., Tzong, K.Y., Li, G., 2012. Marijuana use and motor vehicle crashes. *Epidemiologic Reviews* 34, 65-72.
- Light, M.K., Orens, A., Lewandowski, B., Pickton, T., 2014. Market size and demand for marijuana in Colorado (prepared for the Colorado Department of Revenue). Marijuana Policy Group.
- Lopez, G., 2015. The best argument against marijuana legalization. Vox.com.
- Lopez-Quintero, C., Pérez de los Cobos, J., Hasin, D.S., Okuda, M., Wang, S., Grant, B.F., Blanco, C., 2011. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: Results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug and Alcohol Dependence* 115, 120-130.
- MacCoun, R.J., 2010. What can we learn from the Dutch Cannabis Coffeeshop experience? RAND Drug Policy Research Center.
- Macleod, J., Oakes, R., Copello, A., Crome, P.I., Egger, P.M., Hickman, M., Oppenkowski, T., Stokes-Lampard, H., Smith, G.D., 2004. Psychological and social sequelae of cannabis and other illicit drug use by young people: A systematic review of longitudinal, general population studies. *The Lancet* 363, 1579-1588.
- McLaren, J., Swift, W., Dillon, P., Allsop, S., 2008. Cannabis potency and contamination: A review of the literature. *Addiction* 103, 1100-1109.
- Mehmedic, Z., Chandra, S., Slade, D., Denham, H., Foster, S., Patel, A.S., Ross, S.A., Khan, I.A., ElSohly, M.A., 2010. Potency trends of Δ9-THC and other cannabinoids in confiscated cannabis preparations from 1993 to 2008. *Journal of Forensic Sciences* 55(5), 1209-1217.
- Meier, M.H., Caspi, A., Ambler, A., Harrington, H., Houts, R., Keefe, R.S.E., McDonald, K., Ward, A., Poulton, R., Moffitt, T.E., 2012. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proceedings of the National Academy of Sciences* 109, E2657-E2664.
- Miron, J.A., 2008. The budgetary implications of marijuana prohibition. Harvard University, Cambridge.
- Mokrysz, C., Gage, S., Landy, R., Munafò, M.R., Roiser, J.P., Curran, H.V., 2014. Neuropsychological and educational outcomes related to adolescent cannabis use, a prospective cohort study. *European Neuropsychopharmacology* 24, S695.
- Monitoring the Future, 2014. Monitoring the Future: a continuing study of American youth. <http://monitoringthefuture.org/data/data.html>.
- Monshouwer, K., Van Laar, M., Vollebergh, W.A., 2011. Buying cannabis in 'coffee shops'. *Drug and Alcohol Review* 30, 148-156.
- Moore, D., 2012. Vancouver marijuana 'Vansterdam' tours gaining popularity. Canadian Press.
- Moore, T.H., Zammit, S., Lingford-Hughes, A., Barnes, T.R., Jones, P.B., Burke, M., Lewis, G., 2007. Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review. *The Lancet* 370, 319-328.
- Morral, A.R., McCaffrey, D.F., Paddock, S.M., 2002. Reassessing the marijuana gateway effect. *Addiction* 97, 1493.
- Nestler, E.J., 1992. Molecular mechanisms of drug addiction. *Journal of Neurosciences* 12, 2439-2450.
- NIDA, 2014. Talking to your kids - communicating the risks. <http://www.drugabuse.gov/publications/marijuana-facts-parents-need-to-know/talking-to-your-kids-communicating-risks>. Accessed on July 13 2015.
- Olmedo, R., Hoffman, R.S., 2000. Withdrawal syndromes. *Emergency medicine clinics of North America* 18, 273-288.
- Pardo, B., 2014. Cannabis policy reforms in the Americas: A comparative analysis of Colorado,

- Washington, and Uruguay. *International Journal of Drug Policy* 25, 727-735.
- Pierre, J.M., 2011. Cannabis, synthetic cannabinoids, and psychosis risk: What the evidence says. *Current Psychiatry* 10, 49.
- Pletcher, M.J., Vittinghoff, E., Kalhan, R., Richman, J., Safford, M., Sidney, S., Lin, F., Kertesz, S., 2012. Association between marijuana exposure and pulmonary function over 20 years. *Journal of the American Medical Association* 307, 173-181.
- Proal, A.C., Fleming, J., Galvez-Buccolini, J.A., DeLisi, L.E., 2014. A controlled family study of cannabis users with and without psychosis. *Schizophrenia Research* 152, 283-288.
- Redmond Jr, D.E., Krystal, J.H., 1984. Multiple mechanisms of withdrawal from opioid drugs. *Annual Review of Neuroscience* 7, 443-478.
- Reinarman, C., 2009. Cannabis policies and user practices: Market separation, price, potency, and accessibility in Amsterdam and San Francisco. *International Journal of Drug Policy* 20, 28-37.
- Richter, K.P., Levy, S., 2014. Big marijuana - Lessons from big tobacco. *New England Journal of Medicine* 371, 399-401.
- Rocky Mountain High Intensity Drug Trafficking Area, 2013. The legalization of marijuana in Colorado: The impact.
- Rogeberg, O., 2013. Correlations between cannabis use and IQ change in the Dunedin cohort are consistent with confounding from socioeconomic status. *Proceedings of the National Academy of Sciences* 110, 4251-4254.
- Rolles, S., 2014. Cannabis policy in the Netherlands: moving forwards not backwards. Transform Drug Policy Foundation, London. p. 2.
- Smart Approaches to Marijuana, 2015. Lessons after two years of marijuana legalization. Smart Approaches to Marijuana.
- Swift, R.M., Stout, R.L., 1992. The relationship between craving, anxiety, and other symptoms in opioid withdrawal. *Journal of Substance Abuse* 4, 19-26.
- Tashkin, D.P., 2013. Effects of marijuana smoking on the lung. *Annals of the American Thoracic Society* 10, 239-247.
- Tashkin, D.P., Baldwin, G.C., Sarafian, T., Dubinett, S., Roth, M.D., 2002. Respiratory and immunologic consequences of marijuana smoking. *Journal of Clinical Pharmacology* 42, 71S-81S.
- Thomas, G., Kloner, R.A., Rezkalla, S., 2014. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: What cardiologists need to know. *American Journal of Cardiology* 113, 187-190.
- Townsend, L., Flisher, A.J., King, G., 2007. A systematic review of the relationship between high school dropout and substance use. *Clinical Child and Family Psychology Review* 10, 295-317.
- Trevisan, L.A., Boutros, N., Petrakis, I.L., Krystal, J.H., 1997. Complications of alcohol withdrawal: pathophysiological insights. *Alcohol Health and Research World* 22, 61-66.
- UNODC, 2014. World Drug Report 2014. United Nations Office on Drugs and Crime, Vienna.
- Van der Pol, P., Liebregts, N., Brunt, T., van Amsterdam, J., de Graaf, R., Korf, D.J., van den Brink, W., van Laar, M., 2014. Cross-sectional and prospective relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: An ecological study. *Addiction* 109, 1101-1109.
- Verweij, K.J., Huizink, A.C., Agrawal, A., Martin, N.G., Lynskey, M.T., 2013. Is the relationship between early-onset cannabis use and educational attainment causal or due to common liability? *Drug and Alcohol Dependence* 133, 580-586.
- Volkow, N.D., Baler, R.D., Compton, W.M., Weiss, S.R.B., 2014. Adverse effects of marijuana use. *New England Journal of Medicine* 370, 2219-2227.
- Wagner, F.A., Anthony, J.C., 2002. From first drug use to drug dependence: Developmental periods of risk for dependence upon marijuana, cocaine, and alcohol. *Neuropsychopharmacology* 26, 488.
- Werb, D., Kerr, T., Nosyk, B., Strathdee, S., Montaner, J., Wood, E., 2013a. The temporal relationship between drug supply indicators: An audit of international government surveillance systems. *British Medical Journal Open* 3.
- Werb, D., Kerr, T., Nosyk, B., Strathdee, S., Montaner, J., Wood, E., 2013b. The temporal relationship between drug supply indicators: an audit of international government surveillance systems. *British Medical Journal Open* 3, 8.
- Werb, D., Nosyk, B., Kerr, T., Fischer, B., Montaner, J., Wood, E., 2012. Estimating the economic value of British Columbia's domestic cannabis market: Implications for provincial cannabis policy. *International Journal of Drug Policy* 23, 436-441.
- Werb, D., Rowell, G., Guyatt, G., Kerr, T., Montaner, J., Wood, E., 2011. Effect of drug law enforcement on drug market violence: A systematic review. *International Journal of Drug Policy* 22, 87-94.
- Zador, P.L., Krawchuk, S.A., Voas, R.B., 2000. Alcohol-related relative risk of driver fatalities and driver involvement in fatal crashes in relation to driver age and gender: an update using 1996 data. *Journal of Studies on Alcohol* 61, 387-395.
- Zammit, S., Allebeck, P., Andreasson, S., Lundberg, I., Lewis, G., 2002. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: Historical cohort study. *British Medical Journal* 325, 1199-1201.



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