Review

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Comparative harms assessments for cannabis, alcohol, and tobacco: Risk for psychosis, cognitive impairment, and traffic accident

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Abstract

Researchers have associated cannabis use with risk for psychosis, cognitive impairment, and traffic accident. However, this review shows that the association between moderate cannabis use and psychosis is no stronger, and often considerably weaker, than the corresponding association for moderate tobacco use. The same holds for associations with cognitive impairment. For the risk of traffic accident, the review confirms that the risk from alcohol use is substantially stronger than the risk from cannabis use, while the corresponding risk from tobacco use appears to be almost as strong as that from cannabis use. It thus appears that the risk for psychosis, cognitive impairment, and traffic accident associated with cannabis use is generally comparable to that from tobacco use. The article discusses different interpretations of these comparative harms assessments and presents two points of methodological critique to argue that the risks associated with cannabis and other generally criminalized drugs are probably exaggerated. First, any measurement of harms associated with high escapist activities such as drug abuse will be affected by the general dysfunction associated with the underlying reason why a person settles for frequent escapism. From this perspective, cannabis and tobacco use disorder are probably both associated with underlying problems and life issues that are, in and of themselves, associated with psychopathology, and researchers should be careful not to conflate the selection effect from belonging to the population segment that opts for high escapist lifestyles with any (putative) harmful effect from drug use itself. Second, criminalization probably shifts the composition of the user population in the direction of more dysfunctional users. From this perspective, the association between substance use disorder and underlying problems and life issues is stronger for criminalized substances, since people who live troubled lives are less likely to be deterred by the prospect of legal problems.

Keywords

cannabis, tobacco, alcohol, psychosis, cognitive impairment, traffic accident, selection effects

Review

Psychosis

The association between cannabis use and psychosis has been a major concern for cannabis researchers. The issue has been investigated for decades, with one early study of male Swedish conscripts finding that cannabis users were up to six times as likely as non-users to develop schizophrenia (Andréasson et al., 1987). Among the respondents this study regarded as high cannabis users, however, there was also an increased risk for schizophrenia associated with cigarette smoking (relative risk 6.1) and alcohol consumption (relative risk 6.5). This points to a challenge for such epidemiological studies, namely that it is difficult to separate the effects from cannabis, tobacco, and alcohol because of extensive overlaps in use. In one study by Goodwin et al. (2018), for instance, it was found that not only is cannabis use more common among people who smoke cigarettes, but daily cannabis users also predominantly tend to be cigarette smokers. As we will see in the following review, epidemiological studies of drug-related psychosis risk that provided odds ratios for both cannabis and tobacco have tended to find that the risk from

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tobacco use is at least as high as the risk from cannabis use. In this review, I have included all recent studies (from 2000 onwards) in relevant review articles (Gage et al., 2016; Large et al., 2011; Marconi et al., 2016; Murray et al., 2017; Patel et al., 2020; Ragazzi et al., 2018; van der Steur et al., 2020; van Winkel and Kuepper, 2014; Zammit et al., 2008) that reported separate risk or odds ratios for both cannabis and tobacco, as well as all newer studies I have been able to find, excluding only studies related to age of onset for psychosis. See the discussion below for an overview of studies that either did not include tobacco use in the analysis at all, or controlled for tobacco but did not report comparable figures for it.

Table 1. Risk for psychosis associated with cannabis and tobacco use.

	Cannabis	Tobacco
Degenhardt and Hall (2001)	4.15	3.97
Wiles et al. (2006)	0.72/1.47[a]	1.67
Compton et al. (2009)	1.14	1.03
Saha et al. (2011)[b]	1.13/1.35[c]	1.39/1.66[c]
Auther et al. (2012)[d]	3.94	6.09
Rössler et al. (2012)	1.59	1.52
Buchy et al. (2014)[d]	0.54	0.42
Gage et al. (2014)	1.48	1.61
Hartz et al. (2014)	3.47	5.11
Buchy et al. (2015)[d]	2.96	4.00
Carney et al. (2017)	1.4	1.5
Mustonen et al. (2018a)	1.53	2.00
Mustonen et al. (2018b)	2.85	2.17
Bhavsar et al. (2018)	3.00	1.89
Di Forti et al. (2019)[d]	2.34	3.73
Ferraro et al. (2020)	1.61	3.47
Corsi-Zuelli et al. (2021)[d]	0.70/4.15[e]	3.02
Quattrone et al. (2021)[d]	0.27/2.35[f]	3.48
Moore et al. (2007)[g]	1.41	
Myles et al. (2012)[g]		6.04
Linscott and van Os (2013)[g]	2.51/1.77[h]	
Gurillo et al. (2015)[g]		2.18/3.22[i]
Gage et al. (2016)[g]	1.8	
Kraan et al. (2016)[g]	1.14/1.75[j]	
Marconi et al. (2016)[g]	1.97	
Farris et al. (2020)[g]	1.11	
Hunter et al. (2020)[g]		1.99
Kiburi et al. (2021)[g]	1.71	

Note: Figures represent odds ratios or risk ratios, but are not necessarily comparable across studies.
[a]Odds for cannabis use reflect non-dependent and dependent use.
[b]Figures reflect daily tobacco use versus cannabis use disorder.
[c]Odds for cannabis and tobacco use reflect screen and probe items.
[d]Unadjusted odds ratios calculated by me based on information supplied in the original article.
[e]Odds for cannabis use reflect lifetime use of cannabis but no other illicit drugs and current use of cannabis.
[f]Odds for cannabis use reflect less than daily use and current use.
[g]Overall or median values in review articles.
[h]Odds for cannabis use reflect prevalence and incidence of psychotic experience.
[i]Odds for tobacco reflect prospective studies and case-control studies.
[j]Odds for cannabis use reflect use and abuse/dependence.

Table 1 provides an overview of odds ratios for psychosis related to tobacco and cannabis use. In this overview, I have focused on comparing moderate patterns of cannabis and tobacco use. As will be discussed in more detail in the methodological critique below, heavy or chronic drug use is often related to escapism, which in turn is related to underlying socioeconomic or health issues, making it hard to disentangle negative health outcomes associated with these life issues from outcomes that may result from the drug use itself. Some of the reviewed studies (e.g. Di Forti et al., 2019) found higher risk from more intensive cannabis use, but while these results may indicate that heavy cannabis use incurs increased risk for psychosis, there may also be a selection effect at play related to being the sort of person who opts for near-constant intoxication. For this reason, research into drug harms should preferably focus on moderate use. For tobacco, light to moderate use could be defined as daily use of about 5–10 cigarettes (Boulos et al., 2009; Schane et al., 2010). Daily use of cannabis would constitute heavy use, however, whereas a moderate pattern of cannabis might be defined as one or two use occasions per week (Ellingson et al., 2021; Watson et al., 2021). However, different studies report divergent statistics, and I have used the figures available, noting in the text what forms of use patterns they refer to. Note that the figures in Table 1 are not necessarily directly comparable across studies. In this discussion, terms such as "abuse" mirror the terminology employed in the reviewed articles.

The following paragraphs of text review the findings from the studies presented in Table 1. This review does not attempt to evaluate the quality of these studies: with two exceptions, the association between psychosis and tobacco use is at the same level or stronger than that between psychosis and cannabis use in all these studies, regardless of quality assessments. The text discussing these studies is included to facilitate quality control; readers who are not interested in critically reviewing the figures provided in Table 1 might prefer to skip the following paragraphs.

An early study by Degenhardt and Hall (2001) found that regular tobacco use was associated with psychosis at an unadjusted odds ratio of 3.97, whereas (any) cannabis use, weekly cannabis use, and cannabis use disorder had odds ratios of 3.98, 4.15, and 5.86, respectively. This indicates that regular tobacco use has a slightly weaker association with psychosis than regular cannabis use. They also reported odds ratios of 1.71 and 3.93 for daily alcohol use and alcohol use disorder. Wiles et al. (2006) found that, after controlling for confounding variables, non-dependent cannabis had a reduced risk for psychosis (odds ratio 0.72), while cannabis-dependent users had increased risk (odds

ratio 1.47); by comparison, current cigarette smoking had an odds ratio of 1.67 for psychosis, and heavy alcohol use had an odds ratio of 2.21. Compton et al. (2009) found non-significant hazard ratios for onset of psychosis at 1.14 and 1.25 for weekly/daily use of cannabis and 1.06 and 1.03 for weekly/daily use of tobacco; they also reported significantly reduced hazard ratios for weekly/daily alcohol use. The fully adjusted models by Saha et al. (2011) found that daily cigarette smoking was significantly associated with delusional-like experiences with odds ratios of 1.39 for screen items and 1.66 for probe items. They provided no directly comparable figures for regular cannabis use, but cannabis use disorder had non-significant odds ratios of 1.13 for screen items and 1.35 for probe items, while cannabis dependence disorder had significant odds ratios of 1.76 and 2.39. This study therefore indicated that cannabis use disorder seems to be associated with lower risk for psychosis-like symptoms than daily cigarette smoking. The odds ratios for alcohol use disorder were both non-significant at 1.01 and 1.09, while alcohol dependence disorder was associated with odds ratios of 1.85 and 1.93, only the former of which was significant. Auther et al. (2012) reported that conversion to psychosis was not significantly related to lifetime cannabis use or abuse in their sample, as adjusted for potential confounders, but unadjusted odds ratios for lifetime use of cannabis and tobacco could be calculated on the basis of their sample overview (Auther et al., 2012: 2490, Table 2). These figures indicated a stronger association for tobacco (odds ratio 6.09) than for cannabis (odds ratio 3.94). The findings by Rössler et al. (2012), on the other hand, indicated that casual cannabis use in adulthood had an odds ratio of 1.59 and for schizophrenia nuclear symptoms, while the corresponding odds ratios for alcohol misuse and cigarette use (measured as lifetime use of 20+ cigarettes) were 1.53 and 1.52. Regular cannabis use had odds ratios of 1.77 in adulthood and 2.29 in adolescence, but there was no corresponding figures for regular or adolescent tobacco use. A study by van Gastel et al. (2013; not shown in Table 1) declared that "[c]igarette smoking and cannabis use are equally strongly associated with psychotic-like experiences" (2393), although their figures especially for the level of distress from such experiences were substantially higher for daily cigarette use than for monthly cannabis use. A previous study by van Gastel et al. (2012; not shown in Table 1) trended in the opposite direction.

Table 2. Risk for traffic accident associated with cannabis and alcohol use.

	Cannabis	Alcohol
Longo et al. (2000)	0.82	8.0
Lowenstein and Koziol-McLain (2001)	1.1	3.2
Mura et al. (2003)	2.5	3.8
Drummer et al. (2004)	2.7	6.0
Kuypers et al. (2012)	13.40	6.77
Hels et al. (2013)	1.91	9.79
Poulsen et al. (2014)	1.3	13.7
Li et al. (2017)	1.62	5.37
Martin et al. (2017)	1.65	17.8
Brubacher et al. (2019)	1.74[a]	6.00[b]
Drummer et al. (2020)	1.9	16

Note: Numbers represent adjusted odds ratios combined for all dosage levels, if provided in the original publications. Figures are not necessarily directly comparable across studies.

[a]Non-significant odds ratio for drivers with THC of at least 5 ng/ml; the study found no increased risk of crash responsibility in drivers with THC below 5 ng/ml.

[b]Odds for blood alcohol concentrations of at least 0.08%.

The findings obtained by Buchy et al. (2014) were somewhat anomalous, as unadjusted odds ratios for lifetime use of cannabis and tobacco calculated on the basis of their sample overview indicated reduced odds for conversion to psychosis (Buchy et al., 2014: 279, Table 2). The odds ratios were 0.54 for cannabis and 0.42 for tobacco, although in both cases the 95% confidence interval spanned the null. A comorbidity study by Hartz et al. (2014) found that cannabis use (>21 times per year) had an odds ratio of 3.47 for psychosis, whereas daily cigarette smoking had an odds ratio of 5.11 and heavy alcohol use a ratio of 3.96. Gage et al. (2014) did not examine the odds ratio for alcohol, but their odds ratios for psychosis were 1.48 for cannabis and 1.61 for cigarettes, with frequency of use measured with four-level categorical variables. The effect from cannabis become non-significant when controlled for cigarettes, while the effect from cigarettes was attenuated but remained significant when controlled for cannabis. In the study by Buchy et al. (2015), no controls had abuse or dependence of either cannabis or tobacco, but by compiling all forms of use of either drug based on data from their Table 2 (2279), I calculated unadjusted odds ratios of 2.96 for cannabis and 4.00 for tobacco associated with risk of developing psychosis. Carney et al. (2017) found odds ratios for psychosis risk of 1.5 for daily tobacco use, 1.5 for daily alcohol use, and 1.2 for daily cannabis use, of which only the association for tobacco was significant. However, they also found significant associations for current and lifetime cannabis use, with odds ratios of 1.4 and 1.5, respectively. The study by Mustonen et al. (2018b) is an exception, however, with odds ratios for psychosis at 2.17 for daily tobacco use and 2.85 for any cannabis use. On the other hand, the fully adjusted model by Mustonen et al. (2018a) found that smoking ten or more cigarettes per day was associated with a significant risk for psychosis (odds ratio 2.00), while the odds ratio for lifetime cannabis use was non-significant at 1.53. Bhavsar et al. (2018) found odds ratios for psychotic experience of 1.76 for daily tobacco use and 1.89, 3.00, and 3.49 for less than weekly, between weekly and daily, and daily cannabis use, respectively, thus (arguably) constituting another exception. Di Forti et al. (2019)

did not report odds ratios for cigarette use, but my calculation of unadjusted odds ratios from the numbers provided in their article (Di Forti et al., 2019, Table 1) gives a ratio of 2.19 for lifetime cannabis use and a ratio of 3.73 for smoking more than ten cigarettes per day compared to not smoking at all. They also reported crude (minimally adjusted) odds ratios of 2.5 for cannabis use more than once per week and 6.2 for daily use, corresponding to fully unadjusted odds ratios of, respectively, 2.34 and 6.36.

More recent studies have also tended to find similar or higher psychosis-related risks from tobacco use than from cannabis use. Ferraro et al. (2020) found that first-episode psychosis patients had odds ratios of 1.61 for current cannabis use and 3.47 for current tobacco use. Quattrone et al. (2021) did not report odds ratios for cigarette use, but I calculated unadjusted odds ratios based on the data provided in the Supplementary Online Appendix. The odds ratios for their outcome variable (first-episode psychosis) were 2.18 for lifetime cannabis use, 2.35 for current cannabis use, and 3.48 for smoking more than ten cigarettes per day compared to non-smoking combined with moderate smoking. Cannabis use at a frequency of less than daily use was associated with substantially reduced risk (odds ratio 0.27), whereas daily use incurred an odds ratio of 3.96. The odds ratio for the use of potent cannabis (more than 10% THC) was 2.82. I also calculated unadjusted odds ratios based on the data in Corsi-Zuelli et al. (2021, Table 1), where any use of tobacco was associated with first-episode psychosis at an odds ratio of 3.02. Lifetime use of cannabis only (no other illicit drugs) had an odds ratio of 0.70, whereas the odds ratio for current cannabis use was 4.15.

It is also worth mentioning that a small study by Kristensen and Cadenhead (2007; not shown in Table 1) found a more strongly significant association between tobacco use and conversion to psychosis ($p = 0.005$) than between cannabis abuse and conversion to psychosis ($p = 0.012$). Thus, the overall picture that emerges is that cannabis users may have increased risk for psychosis-related disorders, but the risk appears to be either at about the same level as the corresponding risk from tobacco use, as found by seven studies (Buchy et al., 2014; Carney et al., 2017; Compton et al., 2009; Corsi-Zuelli et al., 2021; Degenhardt and Hall, 2001; Gage et al., 2014; Rössler et al., 2012), or substantially lower, as found by nine studies (Auther et al., 2012; Buchy et al., 2015; Di Forti et al., 2019; Ferraro et al., 2020; Hartz et al., 2014; Mustonen et al., 2018a; Quattrone et al., 2021; Saha et al., 2011; Wiles et al., 2006). Contrariwise, two studies found a substantially higher odds ratio for cannabis (Bhavsar et al., 2018; Mustonen et al., 2018b).

In reviews and meta-analyzes, Moore et al. (2007) found that the pooled adjusted odds ratios for the risk of any psychotic outcome in individuals who had ever used cannabis was 1.41. Linscott and van Os (2013) obtained odds ratios for the association of cannabis use and the prevalence and incidence of psychotic experience at 2.51 and 1.77, respectively, but warned that the effect from cannabis use was driven by a single study (Binbay et al., 2012) "which yielded unusually high odds" (Linscott and van Os, 2013: 1137). Without the inclusion of this study, the I^2 for cannabis decreased from 65% to 18%. The review by Gage et al. (2016) of longitudinal studies on cannabis and psychotic outcomes found a median odds ratio of 1.8 (disregarding one unadjusted odds ratio of 1.77), and a meta-analysis by Kraan et al. (2016) found that lifetime cannabis use had a non-significant odds ratio of 1.14 for transition to psychosis in individuals at ultra-high risk, while the odds ratio for cannabis abuse or dependence was significant at 1.75. Marconi et al. (2016) calculated an odds ratio of 3.90 for the risk of schizophrenia and psychosis among the most severe cannabis users, corresponding to a median odds ratio for any cannabis use at 1.97. Farris et al. (2020) obtained a non-significant pooled relative risk for the association between cannabis use and transition to psychosis among individuals at clinical high-risk of 1.11. Gage et al. (2017; not shown in Table 1) reported "some evidence in support of the hypothesis that cannabis initiation increases the risk of schizophrenia, although the size of the causal estimate is small" (975–976); their odds ratio was 1.04 per doubling odds of cannabis initiation. Finally, Kiburi et al. (2021) calculated an odds ratio for adolescent cannabis use for risk of psychosis at 1.71.

Correspondingly, a meta-analysis by Myles et al. (2012) found that tobacco use incurred an odds ratio of 6.04 for first-episode psychosis, and a meta-analysis by Gurillo et al. (2015) found that the odds ratios for psychosis in cigarette smokers had an overall value of 2.18 in prospective studies and 3.22 in case-control studies. In a meta-analysis of tobacco use and the risk of schizophrenia, Hunter et al. (2020) found that smokers had a significantly higher risk than nonsmokers (odds ratio 1.99). In sum, the risks associated with tobacco use appear to be at least as high as those associated with cannabis use, and especially if we ignore the anomalous results from Binbay et al. (2012) that strongly affected the meta-analysis by Linscott and van Os (2013). Taking the median values of these meta-analyzes (counting both values where two are provided in Table 1) gives an odds ratio of 1.75 for cannabis and 2.70 for tobacco, while the mean values are 1.69 for cannabis and 3.36 for tobacco. We should not infer from these figures that the risk from cannabis use is negligible, but they do seem to indicate that we can be somewhat less concerned with the risk for psychosis related to cannabis than we are with the apparently more serious risk for psychosis related to the more prevalent tobacco use.

However, many studies into the association between cannabis and psychosis-related disorders did not report separate results for alcohol and tobacco. A number of these studies also did not report that they have controlled for

tobacco use (Addington and Addington, 2007; Alemany et al., 2014; Arseneault et al., 2002; Auther et al., 2015; Brañas et al., 2016, 2017; Callaghan et al., 2012; Corcoran et al., 2008; Di Forti et al., 2014; Dragt et al., 2012; Ferdinand et al., 2005; Foti et al., 2010; Freeman et al., 2018; Grech et al., 2005; Harley et al., 2010; Houston et al., 2008; Konings et al., 2008, 2012; Kuepper et al., 2011; Levy and Weitzman, 2019; McGrath et al., 2010; Phillips et al., 2002; Ringen et al., 2016; Rognli et al., 2020; Schubart et al., 2011; Scott et al., 2009; Seddon et al., 2016; Skinner et al., 2011; Smith et al., 2009; Stefanis et al., 2004; Tien and Anthony, 1990; Tosato et al., 2013; Valmaggia et al., 2014; van Os et al., 2002; Verdoux et al., 2003; Vinkers et al., 2013; Wainberg et al., 2021; Weiser et al., 2002), while others did explicitly apply such controls, but did not report odds or risk ratios for tobacco (Arranz et al., 2020; Baeza et al., 2009; Bechtold et al., 2016; Binbay et al. 2012; Di Forti et al., 2009; D'Souza et al., 2020; Fergusson et al., 2003, 2005; Fonseca-Pedrero et al., 2020; Henquet et al., 2005; Hides et al., 2009; Karcher et al., 2019; Leadbeater et al., 2019; Mackie et al., 2013; Manrique-Garcia et al., 2012; McHugh et al., 2017; Miettunen et al., 2008; Sami et al., 2020a, 2020b; Setién-Suero et al., 2019; Spriggens and Hides, 2015; Zammit et al., 2002, 2011). Given that there is sufficient evidence for an association between tobacco use and psychosis (as per the above discussion and Beratis et al., 2001; Dickerson et al., 2013; Kelly and McCreadie, 1999; Mallet et al., 2017; Manzella et al., 2015; Quigley and MacCabe, 2019; Sørensen et al., 2011; Weiser et al., 2004) to allow Alderson and Lawrie (2015) to hypothesize that "the association of cannabis with psychosis could be attributable to the tobacco with which most cannabis is consumed" (673), the lack of statistical control for tobacco use in analyzes of associations between cannabis use and psychoses does not inspire confidence in their validity.

It should also be remembered that tobacco and cannabis use are strongly correlated even when the latter is consumed separately from the former (Gage et al., 2014; Goodwin et al., 2018), so that the chain of causality posited by Alderson and Lawrie (2015) is only one of at least two possibilities. Furthermore, for those studies that have indicated that the use of stronger "skunk" variants of cannabis incurs an increased risk for psychosis (e.g. Di Forti et al., 2019; Freeman et al., 2018), it should be noted that such potent cannabis varieties are more commonly mixed with tobacco because they may be too potent to smoke undiluted. In addition, chronic cannabis use may be more prevalent among individuals from underprivileged backgrounds (Gripe et al., 2021; Legleye et al., 2012), and some studies that controlled for demographic and clinical variables found no significant association between cannabis use and various psychosis measures that was not accounted for by such variables (Barrowclough et al., 2015; Dragt et al., 2012; Proal et al., 2014; Sevy et al., 2010). Using the data presented in the article by Di Forti et al. (2019, Table 1), I calculated unadjusted odds ratios for psychotic disorder of 2.92 for unemployment and 3.80 for their lowest education level (school with no qualifications), both of which are substantially higher than their ratios for cannabis use. If we consider the fact that tobacco use (more than ten cigarettes per day) is also strongly associated with psychotic disorder in these data, the overall picture might seem to indicate that such disorder is most importantly associated with factors such as underprivilege, marginalization, and distress, which are in turn associated with the use of both tobacco, cannabis, and many other drugs (Barros et al., 2018; Borges et al., 2019; Cho and Kogan, 2016; Coley et al., 2018; Cooper et al., 2013; Gage et al., 2020). Di Forti et al. (2019) seem to have controlled for education and unemployment in their analysis, but not for other causes of distress such as poverty, childhood abuse, living in a community with high levels of violent crime, social exclusion, general psychological trauma, and so forth; other researchers were even less rigorous.

Thus, one interpretation of the observed association between cannabis/tobacco use and psychosis, which I will discuss in more detail in my methodological critique below, is that the relationship is spurious. This interpretation would be strengthened by the identification of associations between psychosis and other behaviors related to underprivilege, marginalization, and so forth, such as high use of fast food, soda, and television. Such associations have not yet been intensively studied, but one recent study by Zhang et al. (2022) found that time spent watching TV was related to psychosis at an odds ratio of the same magnitude as the median ratio for cannabis use in the above review. Another interpretation is that both cannabis and tobacco use are causally related to risk of psychosis (e.g. Quigley and MacCabe, 2019). One issue that seems to speak against this interpretation, however, is that cigarette smoking has declined substantially in western countries over the past decades. According to the American Lung Association (2022), cigarette smoking among U.S. adults has fallen from 42.6% in 1965 to 13.7% in 2018, while previous research found that smoking prevalence among white males reached 80% for cohorts born between 1900 and 1929 (Burns et al., 1997). If cigarette smoking roughly doubles the risk for psychosis in a causal sense, this very substantial decline in smoking would presumably have translated into a substantial drop in psychosis rates. This argument is an antiparallel to a similar argument about increasing cannabis use (e.g. Ksir and Hart, 2016), although the increase in cannabis use is substantially smaller in magnitude than the decrease in tobacco use. Since the association between cannabis and psychosis also appears to be weaker than the association between tobacco and psychosis, increasing cannabis use cannot compensate for decreasing tobacco use.

Reviews and reviews of reviews (Campeny et al., 2020; Gage et al., 2016; Large et al., 2011; Marconi et al., 2016; Murray et al., 2017; Patel et al., 2020; Ragazzi et al., 2018; Sideli et al., 2020; van der Steur et al., 2020; van Winkel and Kuepper, 2014; Zammit et al., 2008) of the research on the association between cannabis and psychosis have sometimes concluded that the relationship is robust, but these conclusions are based on individual studies that have not always taken the possibly confounding effects from tobacco or demographics into account. Furthermore, other reviewers have found that the causal connection may point as much from psychosis to cannabis use as in the opposite direction (Haney and Evins, 2016; Hill, 2015; Ksir and Hart, 2016). Thus, while people who use cannabis may be at increased risk for psychosis-related disorders, people with vulnerability to such disorder may also be at increased risk for cannabis use.

Cognitive impairment

Cannabis has sometimes been found to be associated with cognitive impairment, usually as measured by IQ or working memory capacity. In one study by Becker et al. (2014), participants who smoked an average of 10 cannabis hits per day 333 days per year experienced "numerous cognitive deficits, most notably in verbal memory, engagement, and use of efficient strategies with complex tasks, and motivated decision making" (395). Similar findings of cognitive impairment have been reached in other studies of cannabis users (review in Broyd et al., 2016), although moderate cannabis use has not been associated with the same impairments (Schweinsburg et al., 2008). As with the question of psychosis, however, it seems likely that besides whatever impairing effect chronic cannabis use may have in and of itself, there is also a selection effect at play here, which I will discuss in more detail in the methodological critique below.

Some twin studies have found that cannabis-using twins did not show greater impairment in cognitive functioning than their abstinent siblings (Jackson et al., 2016; Meier et al., 2018; Ross et al., 2020; Schaefer et al., 2021), and the same has been found for educational attainment (Verweij et al., 2013). Jackson et al. (2016) concluded that "observed declines in measured IQ may not be a direct result of marijuana exposure but rather attributable to familial factors that underlie both marijuana initiation and low intellectual attainment" (E500). At least one other study disagreed, but did not control for tobacco use (Ellingson et al., 2021). It should also be noted that cotwin control models do not account for nongenetic differences between twins.

In studies of cognitive impairment that controlled for cigarette smoking, the effect from cannabis was often strongly attenuated, sometimes to the point of losing statistical significance, while the effect from tobacco use remained significantly negative even when controlled for cannabis use (McCaffrey et al., 2010; Mokrysz et al., 2016; Stiby et al., 2015). Stiby et al. (2015) noted that the effect from cigarettes was consistently stronger than the effect from cannabis, with daily cigarette smoking being associated with a negative effect on grades that was more than twice the magnitude of the effect from an indicator of cannabis abuse. However, some studies showing negative effects from cannabis use did not control for cigarette or alcohol use, even when their sample characteristics show that the cannabis users included in their study had consistent and significant higher use of cigarettes and alcohol than controls (Becker et al., 2014; Wadsworth et al., 2006). At least one other study that found a negative effect from cannabis did not offer any data on cigarette or alcohol use (Tait et al., 2011), which is unfortunate given the repeated findings of an association between cigarette use and cognitive impairment (Chamberlain et al., 2012; Weiser et al., 2010). It is also noteworthy that the cognitive impairment that may result from cannabis use seems to disappear after a month-long period of abstinence (Curran et al., 2016; Iversen, 2008).

Recent reviews of the relationship between cannabis use and cognitive impairment have found that there was sufficient evidence for an impairment effect in current heavy users, but insufficient evidence for a lasting effect after abstinence; however, these reviews did not discuss the possible confounding effect from tobacco use (Bourque and Potvin, 2021; Kroon et al., 2021; Scott et al., 2018). Scott et al. (2018) concluded that "[a]ssociations between cannabis use and cognitive functioning in cross-sectional studies of adolescents and young adults are small and may be of questionable clinical importance for most individuals" (585).

Finally, while there are some indications that cannabis use is associated with alterations of brain morphology, studies indicating such effects are not consistent in controlling for tobacco use (e.g. Crane et al., 2013; Jacobus et al., 2019), which Rocchetti et al. (2013) noted as a likely confounder. However, Gilman et al. (2014) did control for tobacco and alcohol use to find greater gray matter density in cannabis users, while a large-scale MRI study by Scott et al. (2019) found "no significant differences by cannabis group in global or regional brain volumes, cortical thickness, or gray matter density" (1362). Furthermore, brain damage possibly resulting from cannabis use appears to be less extensive than the damage from alcohol use (Thayer et al., 2017). In sum, while the issue is not closed, it seems far from clear that there is an impairment effect from cannabis use beyond the effects from tobacco use, and if there is an independent effect from cannabis, it appears to be smaller in magnitude than the effect from tobacco.

Traffic accident

A number of studies have found a significant increase in traffic accidents associated with cannabis use (Brubacher et al., 2019; Drummer et al., 2020; Hels et al., 2013; Kuypers et al., 2012; Li et al., 2017; Martin et al., 2017; reviews by Asbridge et al., 2012; Li et al., 2012; McCartney et al., 2021; Rogeberg and Elvik, 2016; Rogeberg, 2019), while some others have found no significant association (Longo et al., 2000; Lowenstein and Koziol-McLain, 2001; reviews by Elvik, 2013; White and Burns, 2021). A recent review by White and Burns (2021) provided interesting methodological perspectives on the risk of traffic accident related to cannabis use, observing that individual studies of this association tended to be biased in an inflationary direction. Their meta-analysis found an overall odds ratio of 1.37 for culpability studies, but after adjustment for bias this figure dropped to 0.68. The authors concluded that the "best estimate" bias-adjusted cannabis-crash odds ratio equals 1.0, indicating a null effect (White and Burns, 2021: 17).

At any rate, as with the issues of psychoses and cognitive impairments discussed above, the risk from legal drug use was at least as high as the risk from cannabis use. In this case, the risk from alcohol use was substantially larger than the risk from cannabis use in most of the studies that provided separate results for alcohol and cannabis. An overview of these results is presented in Table 2. Note that the figures from different studies cannot necessarily be directly compared because of varying methodologies. With the exception of the study by Kuypers et al. (2012), all studies found substantially lower odds ratios for cannabis than for alcohol, with median values indicating odds ratios of 1.74 for cannabis and 6.77 for alcohol. To understand Kuypers et al.'s divergent results, we should note that their analysis was based on a total of 5 cannabis cases and 9 controls, compared to 325 cannabis users in Martin et al. (2017), 34 in Lowenstein and Koziol-McLain (2001), 44 in Longo et al. (2000), 24 in Hels et al. (2013), and 98 in Drummer et al. (2020); thus, the study by Kuypers et al. is an outlier both in terms of the number of included cases and in the obtained odds ratios, and the inclusion of a few more individuals in their study might have changed the odds ratios substantially. By contrast, Kuypers et al.'s odds ratio for alcohol use was based on 99 cases and 176 controls, resulting in a more robust analysis. The relatively low increase in the risk for motor vehicle accident from cannabis use as compared to the more substantial risk from alcohol use has been confirmed in reviews (Biecheler et al., 2008; Rogeberg and Elvik, 2016; Sewell et al., 2009). In sum, the harmfulness of cannabis use in traffic appears to be substantially lower than the risk from alcohol use. According to Arkell et al. (2021a), "[t]he effects of THC on driving are generally modest and appear similar to the effects of low-dose alcohol" (361). This does not mean that we should neglect to warn against cannabis-intoxicated driving, but it seems clear that alcohol-intoxicated driving is a more important social problem, and there is no apparent scientific basis for punishing the former more severely than the latter.

Furthermore, research into the association between tobacco use and risk for traffic accident have found significant increases in risk. This line of research extends back at least to Liddell (1982), who found that people who often smoke while driving have a risk ratio of 1.73 for motor vehicle accident, and an early review concluded that "smokers appear 1.5 times more likely to have a motor vehicle crash" (Sacks and Nelson, 1994: 515). Similar figures have been obtained in more recent research. Wen et al. (2005) adjusted for age and alcohol use to find that tobacco users had a risk ratio of 1.88 for motor vehicle accidents, while the fully adjusted model by Lonczak et al. (2007) indicated a significant odds ratio of 1.55 for traffic-related injuries. In the fully adjusted model by Hutchens et al. (2008), being a current smoker incurred an odds ratio of 2.08 for crash involvement, while Vingilis et al. (2018) found that after adjusting for demographics, driving exposure, and risky alcohol use, current smokers faced a significant odds ratio of 1.27 for collision involvement. With a significant odds ratio of 2.45, tobacco use was the variable with the highest impact in Luht et al.'s (2018) fully adjusted model for high-risk traffic behavior, while Igarashi et al. (2019) adjusted for age and alcohol use to find a non-significant hazard ratio of 1.54 for traffic accident death among current (male) smokers of more than 20 cigarettes per day. Finally, Obadeji et al. (2020) found a non-significant unadjusted odds ratio of 1.45 for accident among motorcyclists with a history of tobacco use, and Talukder et al.'s (2021) study of heavy vehicle drivers found a significant unadjusted odds ratio of 2.09 for accident among people who smoke during driving. While the outcome variables in these studies are somewhat divergent, the median odds ratio of 1.64 may seem to indicate that tobacco use is almost as strongly associated with risk of traffic accident as is cannabis use. Some of the effect seems to be related to being distracted because of smoking while driving, however, although this may be true for cannabis as well. In the study by Hutchens et al. (2008), both current tobacco users and current alcohol users had higher odds ratios than current cannabis users for collision involvement, whereas the opposite was true in the study by Obadeji et al. (2020). Unfortunately, most studies have not analyzed the risk from tobacco use and cannabis use in the same participant samples.

Researchers have expressed concern over the relatively high and increasing numbers of drivers involved in accidents who test positive for cannabis, however (Brubacher et al., 2019; Pearlson et al., 2021). In the study by Brubacher et al. (2019) of non-fatally injured drivers in Canada, for instance, alcohol was detected in 14.4% of

drivers and THC in 8.3% (it is also noteworthy that sedating medications were detected in 19.8%). While the figure for THC was well below that for alcohol, it might seem to indicate that cannabis use is becoming a major factor in road traffic incidents. However, this interpretation is complicated by the fact that THC and its metabolites are detectable in blood samples for as much as 30 days after the last use occasion in chronic users (Bergamaschi et al., 2013; Peng et al., 2020). Thus, detection of THC in blood samples is not a reliable indicator for recent cannabis use, and the substantial figures for THC detection in relation to traffic accidents may reflect a large number of frequent users who were not driving under the effect of acute intoxication (Bergamaschi et al., 2013; Brubacher et al., 2019; Grotenhermen et al., 2007; Karschner et al., 2016; Peng et al., 2020). Furthermore, there has also been a considerable increase in roadside drug testing in recent years (e.g. Mills et al., 2021), and some of the observed increase in THC-positive drivers involved in accidents may be attributable to more stringent testing regimes.

Nevertheless, there remains a persistent concern among some researchers that cannabis use may impair driving even in the absence of acute intoxication (Dahlgren et al., 2020). This concern is related to the identification of cognitive impairment in chronic cannabis users reviewed above, as such impairment may translate into increased risk for traffic accidents. As discussed previously, however, the long-term impairment from cannabis use appears to be smaller in magnitude than a similar impairment from tobacco use, and the effect from cannabis was often strongly attenuated when controlled for tobacco use (McCaffrey et al., 2010; Mokrysz et al., 2016; Stiby et al., 2015). This indicates that the impairment may be due to a selection effect related to the demographic characteristics of both cannabis and tobacco users; at any rate, the long-term impairment from cannabis use does not appear to be a greater concern than the impairment from tobacco use.

Finally, it has been argued that there is scant evidence to support *per se* limits of THC for drivers, and particularly for limits below 5 ng/mL, which may not indicate any impairment at all (Arkell et al., 2021b; Brubacher et al., 2019; Grotenhermen et al., 2007; Pearlson et al., 2021; Peng et al., 2020). Unlike the more straightforward pharmacokinetics of ethanol, the diffusion of fat-soluble THC in biological material is complex and non-linear, so that THC concentration in blood samples is not linearly correlated with concentrations in the brain (Hartman et al., 2016). Thus, "[t]here appears to be a poor and inconsistent relationship between magnitude of impairment and THC concentrations in biological samples" (Arkell et al., 2021b: 102), and especially so for frequent users, for whom there is evidence of tolerance to psychomotor impairment (Desrosiers et al., 2015). *Per se* limits for THC are therefore likely to produce a number of false positive cases, "resulting in conviction for driving under the influence of drugs (DUID) based on cannabis that the subject may have consumed days to weeks ago, when they are now completely unimpaired" (Pearlson et al., 2021: 10). In addition, *per se* limits are likely to result in many false negative cases among moderate cannabis users, because the time period between driving under cannabis intoxication and the acquisition of the driver's blood sample is often sufficient to let the THC drop below the legal limit, and extrapolation backwards in time is not possible (Hartman et al., 2016). Thus, the reliance on *per se* limits very likely punishes chronic cannabis users for driving while sober at the same time as it fails to punish occasional cannabis users for driving while intoxicated.

Comparative harms assessments

The discussion so far allows for the tentative conclusion that while cannabis use may be associated with increased risk for psychosis-related disorders, cognitive impairments, and traffic accidents, these effects from cannabis do not appear to be larger than the corresponding effects from tobacco or alcohol. This identification of low relative harm is supported by assessments in other areas. For the issue of acute lethal toxicity, Gable (2004) found that alcohol had a safety ratio of 10, comparing unfavorably to the safety ratios for instance of cocaine (15), MDMA (16), LSD (1000), psilocybin (1000), and cannabis (>1000). As summarized in Table 3, this tendency toward relative low harm extends also to the tendency for dependence formation, both in the classic assessment by Anthony et al. (1994) and in a more recent assessment by Lopez-Quintero et al. (2011). Similarly, Schlag (2020) recently found that the United States' Substance Abuse and Mental Health Services Administration survey from 2016 obtained results that broadly mirrored those by Anthony et al. Nevertheless, it might be noted that some assessments diverge substantially from these figures, with Hasin et al. (2015) finding that as many as 31% of cannabis users fulfilled criteria for use disorder. However, this study was based on DSM-IV ("Diagnostic and Statistical Manual of Mental Disorders, 4th edition"; American Psychiatric Association, 1994) criteria that counted "legal problems" as a sufficient indicator for abuse. This inclusion of legal problems entails that localities with a higher police presence will tend to see higher prevalence of cannabis use disorder, which seems problematic from a mental health perspective that is concerned with health harms irrespective of varying law enforcement regimes. This indicator for legal problems is also problematic for a number of other reasons (Hasin et al., 2013), and was dropped from the 5th edition of the DSM (American Psychiatric Association, 2013). It should also be noted that the assessment by Hasin et al. (2015) did not comparatively assess the prevalence of use disorders for other drugs with the same methodology.

Table 3. Overview of drug harms and dependence formation.

	Dependence formation		Harm to users[a]		
	Anthony et al. (1994)	Lopez-Quintero et al. (2011)	Nutt et al. (2010)	van Amsterdam et al. (2015)	Bonomo et al. (2019)
Alcohol (ethanol)	15.4	22.7	26	22	36
Cannabis	9.1	8.9	11	17	11
Tobacco (nicotine)	31.9	67.5	16	19	18

Note: [a]Some numbers based on visual inspection of graphically presented information.

Furthermore, overall assessments of the harmfulness of these drugs both in the UK (Nutt et al., 2010), in Europe (van Amsterdam et al., 2015), and in Australia (Bonomo et al., 2019) uniformly found alcohol and tobacco to be more harmful to users than cannabis (Table 3), as did Sellman's (2020) analysis. The assessments by Nutt et al. (2010), van Amsterdam et al. (2015), and Bonomo et al. (2019) also agreed that both alcohol and tobacco were more harmful to others than cannabis was (not shown). With regard to violent behavior, there is broad agreement in research literature that although some forms of illicit drug use may be associated with violence, the association is much stronger for alcohol use. A review by Parker and Auerhahn (1998) found no significant evidence for an association between drug use and violence, but strong evidence for an association between alcohol use and violence: "when violent behavior is associated with a substance, that substance is, overwhelmingly, alcohol" (306–307). Sacks et al. (2009) found a stronger effect on violence from alcohol (odds ratio: 1.33) than from illicit drugs (odds ratio: 1.10) in a sample of people in substance abuse treatment programs, and a study of violence at ambulance attendances in Australia found that "[a]lcohol intoxication was involved in more than half of attendances where aggression/violence was recorded, and was almost twice as prevalent as those involving illicit drug use where aggression/violence was recorded" (Coomber et al., 2019: 1). A recent review by White et al. (2019) found clear evidence of an association between alcohol use and violence, but no clear evidence from illicit drugs. Most of these studies and reviews did not investigate the effect specifically from cannabis, but a few that did found that acute cannabis intoxication tended not to increase, and might reduce, violent behavior (Boles and Miotto, 2003; Hoaken and Stewart, 2003).

In conclusion, these literature reviews indicate that the health risks associated with the use of cannabis are generally modest. While cannabis users appear to be susceptible to psychosis-related disorder, cognitive impairment, and traffic accidents, the risks involved seem to be lower than the corresponding risks from alcohol and tobacco use. In terms of mental health problems, addictiveness, acute lethal toxicity, violent behavior, traffic-related injury, and overall harm, cannabis appears to be at least as safe as the legal drugs alcohol and tobacco. Researchers wishing to study the health consequences of illegal drug use are advised to assess the corresponding health consequences of alcohol and tobacco use in the same participant samples, thus providing readers with an opportunity to contextualize the relative health risks of different legal and illegal drugs. It would be interesting to include tobacco use alongside alcohol and various illicit drugs in studies of risk for traffic accidents, for instance, as this might allow us to approach an understanding of how much of the identified risk from drug use for traffic accidents is due to actual (acute, subacute, or long-term) cognitive debilitation, and how much is a selection effect related to demographics or to personality structure and the propensity for risk taking. One study of the personality structure of psychedelics users found that their risk taking score was substantially higher than the scores obtained in a sample of the general population (Johnstad, 2021), and it would not be surprising if such propensity for risk taking impacts upon one's style and manner of driving, resulting in an increased risk for traffic accidents that is unrelated to any debilitating effect (acute or otherwise) from drug use itself. Tobacco use, which is related to a number of serious medical conditions, may also be indicative of an increased propensity for risk taking, and more generally seems to be associated with many of the same demographic and socioeconomic factors as illicit drug use. It is therefore likely that the inclusion of tobacco as an independent risk factor in studies of traffic accidents would allow researchers to identify the use of this licit and non-intoxicating drug as being associated with an increased risk for accidents.

Methodological critique

The above review suggested that selection effects might explain some of the effect in the associations identified between cannabis use and psychopathology. This part of the article explicates two points of methodological critique against studies into drug harms related to the effects from general escapism and from criminalization. The first point of critique suggests that chronic heavy cannabis use should be understood as a form of high escapist behavior,

and that such escapism is generally associated with underlying problems and life issues that are, in and of themselves, associated with psychopathology. Research into the harms from heavy cannabis use therefore tends to conflate two separate effects, one being the effect from the drug use itself and the other being the selection effect from belonging to the population segment who chooses high escapist lifestyles. The second point of critique argues that drug criminalization changes the composition of the population of drug users in the direction of people with a higher extent of underlying problems and life issues, and that this dynamic makes illicit drug use appear more harmful than what would be the case if the drugs in question were legally available. In sum, the first point of critique explains how the correlation between cannabis and tobacco use and negative health outcomes may be spurious, while the second point of critique emphasizes that the extent of such spuriousness will be stronger for criminalized substances.

High escapism

In the above discussion of cognitive impairment, a study by Becker et al. (2014) found evidence of numerous cognitive deficits among people who smoked an average of 10 cannabis hits per day 333 days per year. While it is possible that some of this impairment effect is caused by cannabis use, a selection effect also seems to be in play. If we divide the general population into two groups, with the first group being the people who has the time to smoke ten cannabis hits (almost) every day of the year and the other group being the people who do not have time for that, it does not seem difficult to estimate which group is likely to be better educated and have the most successful careers. I would make the same point about the group of people who watch television for 10 h every day: while it is possible that constant bingeing on light entertainment has negative health consequences in and of itself, it is also obvious that the population of heavy TV users who have the time for daily 10-h binges does not contain many hard-working professionals or people deeply invested in their families and friends. Conversely, this population clearly contains many people with chronic health conditions and people who are otherwise socially marginalized for various reasons. Evidence of a decline in cognitive capacity associated with television bingeing (e.g. Fancourt and Steptoe, 2019; Lindstrom et al., 2005) is therefore unsurprising, because heavy TV use, like heavy drug use, is effectively an indicator of life not going well. The reason why life is not going well may have as strong an association with cognitive impairment as bingeing on TV does. Controlling for demographic, socioeconomic, and health-related confounders will remove some of the effect from such underlying reasons, but unemployment, poverty, and health conditions are just a few of many reasons why people feel miserable and see their lives as failures. Statistical control removes the effect from these specific sources of misery and will thereby generally attenuate results, but leaves the corresponding effects from childhood trauma, loneliness, abusive relationships, undiagnosed depression, and a whole range of other issues to masquerade as effects from the high-escapist behavior.

Besides ignoring the impact from a range of underlying problems, statistical models generally also ignore the likely interaction effects between such problems. Being poor and having a debilitating health issue are both examples of underlying problems that might lead to high-escapist activities, but the misery-inducing effect of both in combination is likely higher than the separate effect from each added together. The same probably goes for every pair of such underlying risk factors for high escapism. You cannot control for the fact that practically everybody who watches television for 10 h every day, smokes cannabis ten times a day, or is otherwise near-constantly occupied by escapist activities over long periods of time is perpetually dissatisfied with their lives and, for the most part, with themselves. High escapism is always related to living a life one feels a need to escape from.

Thus, one basic point of methodological critique against the type of studies that associate heavy drug use with cognitive impairment or psychosis is that they measure not only the effect from cannabis use, but also the selection effect from being the type of person who settles into a life of near-constant intoxication. There is a reason why people end up in high-escapism lifestyles, and this reason is also generally associated with relative cognitive impairment and negative health outcomes. These are the people who feel that they did not succeed in life, and more often than not, their lack of success reflects underlying problems and incapacities. Fancourt and Steptoe (2019) sought to establish a threshold for recommended levels of television viewing below what might pose risks for cognitive decline, and identified 3.5 h per day as a limit. However, while it may be true that people put themselves at risk by viewing television for more than 3.5 h per day, I believe it is also true that only people with high escapist tendencies, reflecting a high level of underlying problems and life dissatisfaction, would choose to watch so much television. The same point holds for drug use: for the most part, only very miserable people choose to get intoxicated several times every day over long periods of time. These people are, to borrow a phrase from Frantz Fanon, the wretched of the earth, and when you study the health ramifications of a given behavior whose prevalence is practically confined to this group of wretched people, you will measure first of all their wretchedness. High escapism is, for practical purposes, an indicator of life dissatisfaction and misery.

In the study of the negative consequences of one specific high-escapist activity, therefore, we will end up measuring the effect from this activity itself (if any) combined with the effect from high escapism in general, which always reflects

underlying life issues. As such, negative consequences of specific high-escapist activities will be tangled up in selection effects related to membership in the population of people with major life issues, and such membership is generally associated with a range of negative outcomes. To avoid being entangled in the effects from general escapism, research on putative negative consequences from drug use should preferably focus on moderate patterns of drug use. Moderate drug use is not associated with a constant need to escape from one's miserable life, and if such drug use incurs negative consequences for health or functionality, these consequences are more likely related to the drug use itself.

Drug criminalization

While the above assessments indicate that the harms associated with the use of cannabis are lower than corresponding harms associated with alcohol and tobacco use, there is also reason to believe that harms related to illicit drug use may be exaggerated as a consequence of the fact that these drugs have generally been criminalized for decades. This section will discuss the possibility that some of the health risk identified for illicit drug use may be a consequence of criminalization and its complex impact on usage patterns in different population segments. In effect, empirical research into the health consequences of illicit drug use may have been blindsided by the fact that such drug use is criminalized and stigmatized in our societies.

The basis for this methodological critique is the underlying hypothesis that any criminalized behavior will appear to be associated with more health problems than a corresponding non-criminalized behavior, because the fact of criminalization impacts the diffusion of this behavior in society. Specifically, I think there is reason to believe that the criminalization of cannabis has served to shift the center of gravity in the group of cannabis users towards segments of the overall population that have less than average concern about getting in trouble with the law, and these population segments are probably at higher risk for non-moderate drug use and, therefore, for worse health outcomes than cannabis users from other segments of the overall population.

Before we continue into the discussion of how criminalization may affect the user population, I wish to note that there is also a second reason to suspect that drug criminalization may affect the perception of health outcomes for drug users. This second reason is that criminalization may serve to increase the harms from drug use because it leads to a situation of poor quality control. Unscrupulous drug dealers may add harmful adulterants in order to increase bulk or may sell illicit substances under false labels. This has been a problem for 3,4-methylenedioxymethamphetamine (MDMA), where we have seen paramethoxymethamphetamine (PMMA) being sold as MDMA (Saleemi et al., 2017; Vevelstad et al., 2012). If the resulting health harms are identified as MDMA-related in subsequent research, MDMA will thereby appear to be more harmful than it would have been under a policy regime allowing for better quality control.

The dynamic I will focus on in the rest of this discussion is more methodologically complex, and is related to the possibility that the criminalization policy serves to alter the composition of the user population. While the intention behind the criminalization regime is to reduce drug use overall, it is not obvious that this is what the policy actually achieves (Hughes et al., 2018; Kotlaja and Carson, 2019; Scheim et al., 2020; Stevens, 2019). What may seem likely, however, is that criminalization serves to reduce drug use among certain population segments, while possibly increasing use among other segments (or at least not reducing it to the same extent). To take two obvious points, there will be little post-criminalization drug use among people who work in occupations with frequent mandatory drug tests or among people who are strictly law-abiding. More generally, criminalization means that drug users are at risk of getting in legal trouble, and the prospect of legal trouble is more worrisome to some people than to others. It would be reasonable to assume that people who are happy with their lives and optimistic about the future may feel that they have a lot to lose from getting in legal trouble, while unhappy and pessimistic people may feel they do not have as much to lose and may, therefore, not be deterred to the same extent by the criminalization regime. In addition, it seems reasonable to believe that generally unhappy people may value drug effects more highly than happy people, because unhappy people presumably have fewer sources of happiness in their lives. If drug use offers such people a temporary escape into a state of chemically induced happiness, they may therefore be inclined to value it more highly, which probably also means that they are willing to take greater risks to keep it as a source of happiness in their lives. I would connect this point with my earlier discussion of heavy drug use as a product of the desire for escape from one's miserable life, and observe that people who are driven by such escapist desires are probably less averse to the legal risks associated with illicit drug use. The prospect of legal problems—or of health problems relating to drug use disorder—may not deter such people to the same extent as these factors would deter generally happy (or non-miserable) people.

Arguably, therefore, drug criminalization shifts drug use towards population segments who are less than averagely concerned about getting into legal trouble. While there may be any number of rationales underlying such sentiments, it seems likely that feeling one has little to lose is associated with what I earlier called wretchedness, which is in turn related to factors such as poverty, unemployment, childhood trauma, low education, etc. If we have very good

data, we can control for some of these factors, but not for all of them, and not for the interaction effects between such factors. Unemployment is probably misery-inducing for most people, but for people who lived in poverty even when they had a job, losing that job may be a disaster. And even if it is possible to control for all the main sources of wretchedness in principle, the research into drug harms does not do so in practice.

In the argument so far, drug criminalization serves to shift drug use towards population segments at increased risk for drug use disorder and related health problems by removing moderate users from the group, because these moderate users are deterred to a greater extent by the prospect of legal trouble and have less need for drug use as a source of temporary happiness. In addition to this effect, however, it is possible to argue that drug criminalization increases drug abuse in underprivileged communities. The basis for such an argument is that criminalization causes the growth of a lucrative illicit drug market where criminal gangs will fight for market access and thereby cause violence to many communities. Children growing up in communities marred by gang violence are at risk for being traumatized by seeing friends and family members get hurt or killed, or from being hurt themselves, and people with childhood trauma are at risk for drug use disorder. Furthermore, when criminal groups gain wealth from controlling the profitable illicit drug trade, they also gain power to affect communities beyond serving as drug suppliers. A community under mafia dominion will probably see increased unemployment and social misery, and unhappy people are at increased risk for drug use disorder. There may also be an effect on the extent of drug use caused by criminal entrepreneurship: adolescents in mafia-controlled communities may have few career prospects outside the mafia organization, and whatever entrepreneurial talents they possess are more likely to be channeled into criminal activity. By finding clever new ways to market and distribute illicit drugs, such entrepreneurs probably contribute to increased drug use. From the perspective of drug-supplying criminal gangs, furthermore, drug use disorder is more profitable than moderate drug use, since people characterized by the former are more frequent customers.

While this is not the place for an in-depth analysis of the costs and benefits of drug criminalization, the above sketch has at least pointed to a range of social mechanisms whereby drug criminalization can contribute to increased drug abuse. In sum, the hypothesis here being presented is that drug criminalization alters the composition of the group of drug users by removing users at low risk for drug use disorder and adding users at high risk for such disorder. After criminalization, therefore, a society will tend to see a higher proportion of non-moderate drug use among its drug users, because people at low risk for drug abuse are more likely to be deterred by criminalization than people at high risk for drug abuse.

If this argument is correct, the health risks associated with illicit drug use are probably overstated since these analyzes have generally been based on societies that criminalize the relevant drugs. This would imply that harms associated with drug use should decrease after decriminalization, for which there is some support in recent research. After cannabis decriminalization in the United States, Williams et al. (2017) and Mauro et al. (2019) found a significant increase in past-month cannabis use, but not a significant increase in cannabis use disorder. Similarly, Compton et al. (2016) found no increase in cannabis use disorder between 2002 and 2014, and the United Nations Office on Drugs and Crime (2019) reported that while cannabis use increased in the United States in the period 2002–2017, the number of cannabis use disorders remained stable or declined (among those aged 12–17, cannabis use disorder was nearly halved). A study on the impact of state-level policy liberalism on cannabis use and use disorder found that liberal states had higher use, but lower prevalence of use disorder among users (Philbin et al., 2019).

We can understand the effect from criminalization as a selection effect, but at the societal level rather than the level of the individual study. Under a criminalization regime, the group of people who use drugs will include a higher proportion of individuals who live troubled lives, and since troubled people are at risk for drug use disorder, the harms associated with drug use will therefore appear to be greater. While it is not presently possible to estimate the magnitude of this putative effect, it seems likely that some of the health risk identified for drug use is actually a consequence of the drug criminalization regime itself.

It may be objected to the discussion in this section that several points have been made on a basis of conjecture. There is not much empirical research into the issue of how criminalization affects different patterns of drug use, and my suggestion that a drug criminalization policy changes the composition of the drug user population by removing light and moderate users while adding heavy users is not in any meaningful sense a proven fact. I would contend, however, that since this point is intended to serve as a methodological objection to other studies indicating harms from drug use, it is not my responsibility to prove the point so much as these other researchers' responsibility to disprove it. As the case stands at present, I have presented grounds for the reasonable suspicion that findings about health harms from illicit drug use have been unduly affected by the fact that these drugs are criminalized, which seems likely to change the composition of the drug-using population in the direction of the types of people who are at risk for ending up in patterns of drug abuse.

Conclusion

Cannabis and tobacco use appear to be associated with similar magnitudes of risk for psychosis, cognitive

impairment, and traffic accident. With regard to the risk for traffic accident, alcohol intoxication is substantially more problematic than cannabis intoxication. Furthermore, the large shift especially in tobacco prevalence over the past decades seems not to have resulted in corresponding changes in the occurrence of psychosis, indicating that the association between tobacco and psychosis is probably non-causal. This would seem to imply that the association between cannabis and psychosis, which appears to be somewhat weaker than the corresponding association for tobacco, is probably non-causal as well.

The methodological critiques in the second part of the article offer explanatory perspectives on the conclusions from the literature review. The first point of critique suggests that the research into harms from cannabis use has mistaken negative health outcomes associated with high escapist behavior for negative health outcomes caused by cannabis use. According to this line of critique, the correlation between cannabis use and negative outcomes such as psychosis is largely spurious: people get entangled in high escapist behavior because their lives are miserable, and the misery of their existence is associated with (or constituted by, in the case of underlying health issues) negative health outcomes. In other words, their underlying misery or wretchedness explains their high risk for both negative health outcomes and substance use disorder. The second point of critique suggests that criminalization serves to shift the user population in the direction of people at higher risk for non-moderate use because wretched people, having little to lose, are less risk-averse and therefore less likely to be deterred by a criminalization policy. The association between misery and substance use disorder is therefore stronger for criminalized substances.

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