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The Effects of Cannabis Use on the Development of Adolescents and Young Adults

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cannabis, adolescent cannabis use, cannabis dependence, cognitive impairment, psychosis, depression, educational outcomes, child development, mental disorders, cognition

Abstract

This review summarizes evidence on the effects of cannabis use on the development of adolescents and young adults. It draws on epidemiological studies, neuroimaging studies, case-control studies, and twin and Mendelian randomization studies. The acute risks include psychiatric symptoms associated with the use of high THC (tetrahydrocannabinol) products and motor vehicle accidents. Daily cannabis use during adolescence is associated with cannabis dependence and poor cognitive function, which may affect educational attainment and occupational choice. Daily use of highly potent cannabis is associated with more severe psychological symptoms, such as psychoses, mania, and suicidality. There are more mixed findings on depressive symptoms, anxiety, and violence and debates about the interpretation of these associations. Legalization of adult cannabis use may increase cannabis use and dependence among adolescents and young adults. The regulation of cannabis after legalization needs to minimize adolescent uptake and cannabis-related adverse developmental outcomes.

Contents

INTRODUCTION

Cannabis is an illicit drug widely used by youth in North America, Europe, and Oceania (AIHW 2017, EMCDDA 2018b, SAMHSA 2017a). In the past two decades in the United States, Canada, and other high-income countries, cannabis use by adults has been legalized, initially for medical use and more recently for adult recreational use (Hall et al. 2019). There are reasonable concerns that these changes in the legal status of adult cannabis use may increase use among adolescents in ways that increase the risks of a variety of adverse developmental outcomes in adulthood. This review highlights research on the adverse adult outcomes associated with adolescent cannabis use, discusses how these outcomes may be affected by the legalization of cannabis, and suggests ways in which cannabis may be regulated to reduce the adverse developmental effects of adolescent use.

THE EPIDEMIOLOGY OF CANNABIS USE IN ADOLESCENTS AND YOUNG ADULTS

In the United States in 2018, 12.5% of those aged 12–17 and 34.8% of those aged 18–25 reported using cannabis in the past year (CDC 2019). Among adolescents in grades 8–12, this proportion decreased from 26% in 2002 to 21% in 2007 before slightly increasing to 24–25% during the 2010s (Miech et al. 2019). First use of cannabis is most common during adolescence and is more common among males and those who are unemployed and have a lower income (Hasin 2018). Since 2008, more regular cannabis users have continued using into their 30s than in earlier birth cohorts (Terry-McElrath et al. 2018).

In Australia in 2016, 35% of adults aged 14 and older reported lifetime cannabis use and 10% reported use in the last year (AIHW 2017). Among 14–19-year-olds in 2016, the lifetime use of cannabis was 16% (12% in the last year). This increased to 43% (22% in the last year) among 20–29-year-olds. Males were more likely than females to have used cannabis in all age groups. The prevalence of cannabis use in the last year declined in 14–19-year-olds in both males (18% in 2004, 14% in 2016) and females (19% in 2004, 10% in 2016).

In the period 2015–2017, around a quarter (26%) of adults aged 15–64 in Europe reported lifetime cannabis use (EMCDDA 2018b). Over 20% of males and 15% of females aged 15–16 reported lifetime use of cannabis (ESPAD Group 2016). The highest lifetime prevalence of adolescent cannabis use in Europe was in the Czech Republic (37%) and France (31%). Use in the past year was 14% among those aged 15–34, with the lowest rate in Hungary (4%) and the highest in France (22%). Among European countries with trend data, past-year cannabis use among young adults decreased from the early 2000s to mid-2010s in England, Wales, and Spain and increased in Ireland, Finland, Bulgaria, Sweden, and Romania (EMCDDA 2018b).

The limited data suggest that the prevalence of cannabis use in adolescents in low- and middle-income countries (LMICs) is much lower than in high-income countries. In the Global School-based Student Health Survey (WHO 2019), only 2% of adolescents in LMICs reported using cannabis, with the highest prevalence in the Americas (7%).

WHY IS ADOLESCENT CANNABIS USE OF CONCERN?

Adolescence is a time in which major biological, neurobiological, social, and personal transitions are made. These include puberty, changes in capacities to reason and regulate emotions, and the negotiation of major social transitions, such as completing secondary schooling, making choices about future careers, undertaking further education and training, and entering the adult world of work. Young people also become more independent of their families of origin, develop personal relationships with peers, and find their life partners.

Adolescence is also a high risk period for initiating alcohol, tobacco, and cannabis use and for developing substance use disorders that may impair a young person's ability to complete the critical life transitions of adolescence (Hall et al. 2016a). Antisocial behavior may develop at this time and so may the first symptoms of anxiety and depressive disorders, psychotic disorders, and eating disorders, all of which make substantial contributions to the burden of disease in this age group (Patton et al. 2016). The brains of adolescents and young adults undergo substantial change, potentially increasing their vulnerability to the adverse effects of regular substance use on brain development (Lorenzetti et al. 2019).

The common mental disorders and substance use disorders often co-occur in adolescence and young adulthood (Hall et al. 2016a). This may be because they share risk factors, e.g., shared genetic risks and family environments, or the risk of developing one type of disorder may increase the risk of developing another. For example, conduct disorders increase the risks of substance use

disorders, and cannabis use may increase the risk of psychotic disorders and vice versa (Hall et al. 2016a).

Cannabis use is often initiated in adolescence, and cannabis use disorders are common among young people treated in addiction services in Australia (AIHW 2019), Europe (EMCDDA 2018b), and the United States (SAMHSA 2017b). In this article, we summarize evidence on the risks of adolescent cannabis use and describe the poor psychosocial outcomes associated with these cannabis use disorders. We focus on the following outcomes: cannabis dependence, cognitive impairment, educational underachievement, depression, psychoses, use of other illicit drugs, and other antisocial behaviors.

We follow the 2016 World Health Organization report on the health and social consequences of nonmedical cannabis use in placing the greatest weight on evidence from longitudinal studies of representative samples of young people who have been followed into adulthood when assessing whether these adverse outcomes are causally related to cannabis use (Hall et al. 2016b). We focus on studies that were best able to evaluate plausible alternative explanations of the associations, e.g., by statistically controlling for major confounders or using genetically informed designs (e.g., discordant twin studies and Mendelian randomization studies). We secondarily assess the biological plausibility of causal explanations by looking at evidence from animal studies on the effects of cannabinoids.

In the last section of the article, we discuss the potential effects that legalizing cannabis production and retail sale may have on harmful cannabis use by adolescents. We also briefly consider regulations that may minimize harmful cannabis use by adolescents and policies and interventions that may reduce the harm arising from adolescent cannabis use.

CORRELATES OF ADOLESCENT CANNABIS USE

Adverse Acute Effects

There is an extremely low risk that herbal cannabis use can produce a fatal overdose, and no reports of fatal overdoses are reported in the epidemiological literature up to 2009 (Calabria et al. 2010). More recently, there have been reports that require further investigation of cardiovascular deaths in healthy young men after smoking large amounts of cannabis (Hartung et al. 2014).

Cannabis users may experience acute adverse effects, such as anxiety, paranoia, psychotic-like experiences, and thoughts of self-harm or suicide (Dines et al. 2015, Hall et al. 2016b, NASEM 2017, Noble et al. 2019, Schmid et al. 2020, Tait et al. 2016, Zimmermann et al. 2019). These experiences may be severe enough for users to seek medical treatment. Cannabis use may also produce psychotic symptoms if cannabis products with high levels of THC (tetrahydrocannabinol) are used, such as extracts or edibles (Marconi et al. 2016).

Accidental Injury

In laboratory studies, THC produces dose-related impairments in reaction time, information processing, perceptual-motor coordination, motor performance, attention, and tracking behavior (Hall et al. 2016b, Kroon et al. 2019). These effects suggest that cannabis use could cause car crashes if users drive while intoxicated, but studies in driving simulators suggest that cannabis-impaired drivers are aware of their impairment and compensate by slowing down and taking fewer risks (NASEM 2017).

Systematic reviews and meta-analyses reported that drivers who test positive for THC have a modestly increased risk of serious and fatal injuries from motor vehicle accidents, a risk that increases when cannabis is used with alcohol (Elvik 2013, Hartman et al. 2016, Hels et al. 2011).

A meta-analysis of nine case-control and culpability studies by Asbridge et al. (2012) found that recent cannabis use (indicated by THC in blood or self-reported cannabis use) doubled the risk of a car crash {odds ratio (OR) = 1.92 [95% confidence interval (CI): 1.35, 2.73]}. The risk was marginally higher in better-designed studies (2.21 versus 1.78), in case-control studies rather than those that judged driver culpability (2.79 versus 1.65), and in studies of fatalities rather than studies of injuries (2.10 versus 1.74). Similar results (a pooled risk estimate of 2.66) were reported in a meta-analysis (Li et al. 2012), but a recent analysis reported a smaller pooled effect [OR = 1.36 (95% CI: 1.15, 1.61)] (Rogeberg & Elvik 2016). A major challenge in interpreting these studies is that THC metabolites indicate only that cannabis was used hours or days before the accident; they do not establish that the drivers were cannabis impaired at the time of the accident (NASEM 2017, Rogeberg & Elvik 2016).

Overall, the epidemiological and laboratory evidence on the acute effects of cannabis strongly suggests that cannabis users who drive while intoxicated have an increased risk of motor vehicle crashes of 1.5–3 times (NASEM 2017), which is lower than the risk for drivers impaired by intoxicating doses of alcohol of 6–15 times. These risks may be larger in younger, less experienced cannabis users and drivers.

CHRONIC CANNABIS USE AND CANNABIS DEPENDENCE

Epidemiological studies of chronic cannabis use are rarely able to measure the doses of THC and other cannabinoids (e.g., cannabidiol) that cannabis users receive (Norberg et al. 2012). In the absence of dosage data, epidemiological studies have defined heavy or regular cannabis use as daily or near-daily use (Hall & Pacula 2010) because this is the pattern of use most consistently associated with adverse health and psychological outcomes (Hall 2015).

The major challenge in attributing adverse psychological outcomes to regular cannabis use is that regular cannabis users differ from nonusers and lighter users in a variety of ways that predict a higher risk of these adverse outcomes (Hall 2015, Hall et al. 2016b, NASEM 2017). They are, for example, more likely to use alcohol, tobacco, and other illicit drugs and to engage in risk-taking behavior than nonusers of cannabis (Coffey & Patton 2016, Hall & Fischer 2010). Statistical methods of control have been used to test the plausibility of confounding as an explanation of these relationships, but some epidemiologists have expressed doubts about whether this strategy can be wholly successful (Macleod et al. 2004).

Cannabis disorders have been the most common type of illicit drug dependence in epidemiological surveys in Australia, Canada, and the United States (Hall et al. 2016b), affecting 1–2% of adults in the past year and 4–8% of adults in their lifetime. Globally, approximately 18 million people were estimated to be cannabis dependent in 2017, and 4 million of these were between the ages of 15 and 19 (GBD 2017 Dis. Inj. Incid. Preval. Collab. 2018). Rates varied substantially by geographical location, with the highest prevalence in the United States, Canada, Australia, and New Zealand (**Figure 1**).

The risk of developing dependence was estimated to be 9% among those who ever used cannabis in the United States in the early 1990s (Anthony 2006). The equivalent risks at that time were 32% for nicotine, 23% for heroin, 17% for cocaine, 15% for alcohol, and 11% for stimulants (Anthony et al. 1994). In longitudinal studies, the risk of developing cannabis dependence is about one in six among adolescent users (Anthony 2006). It may be as high as 50% among persons who are daily cannabis users (van der Pol et al. 2013). A systematic review and meta-analysis (Leung et al. 2020) of data from six longitudinal studies in the United States, Australia, New Zealand, France, Germany, and the Netherlands that followed young people into adult life estimated the risk of dependence as 12% (95% CI: 7, 18) in young people who have ever used cannabis and a third [33% (95% CI: 22, 44)] in those who had used cannabis at least weekly.

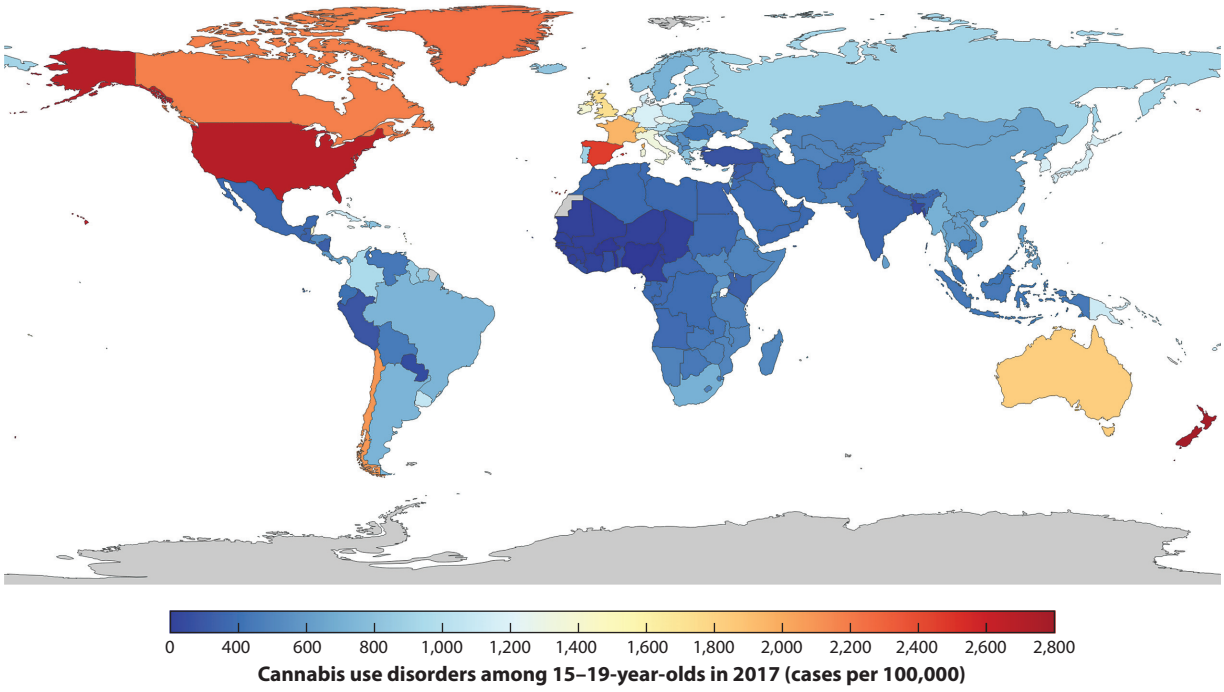

Figure 1

Estimated prevalence rates (cases per 100,000) of cannabis use disorders among 15–19-year-olds in 2017. Figure based on results from the Global Burden of Disease Study 2017 (GBD 2017 Dis. Inj. Incid. Preval. Collab. 2018) collected in the GBD Compare Visualization Hub, Institute for Health Metrics and Evaluation, University of Washington (IHME 2017) (CC BY-NC).

Cannabis users develop tolerance to THC (Ramaekers et al. 2020), and problem users who seek help often report withdrawal symptoms, such as anxiety, insomnia, appetite disturbance, and depression (Budney & Hughes 2006). These symptoms can impair everyday functioning and may present an obstacle to abstinence. They are markedly attenuated by THC (Werneck et al. 2018).

In 2019, more than 137,000 patients entering treatment in the past year in the European Union (including the United Kingdom), Norway, and Turkey named cannabis as their primary problem drug (EMCDDA 2019b); at the country level, it was the primary problem drug for just under half of all patients in the Netherlands (47%), Denmark (46%), France (49%), and Germany (43%). In Australia, cannabis was the main drug of concern in 22% of all alcohol and drug treatment episodes (AIHW 2019). In the United States, the proportion of admissions with cannabis as the primary substance of abuse increased from 16% of admissions in 2005 to 19% in 2010, then decreased to 14% in 2015, making it the third most common drug of concern after alcohol and opioids (SAMHSA 2017b).

The increase in the number of cannabis users seeking help to quit over the past two decades in Europe and Australia is not solely due to more users being legally coerced into treatment. There has been a similar increase in the Netherlands, where cannabis use was decriminalized over 40 years ago (EMCDDA 2019b).

Rates of recovery from cannabis dependence among those seeking treatment are very similar to those for alcohol (Florez-Salamanca et al. 2013). In clinical trials, cognitive behavior therapy, motivational enhancement, and contingency management reduce the severity of cannabis

problems and frequency of use, but only a minority of patients become and remain abstinent 6 and 12 months after treatment (Budney et al. 2019, Danovitch & Gorelick 2012, Gates et al. 2016). There are no effective pharmacological treatments for cannabis dependence (Nielsen et al. 2019).

CHRONIC CANNABIS USE AND COGNITIVE AND BRAIN FUNCTION

Neuroimaging Studies

Structural neuroimaging studies have compared adolescents who are regular cannabis users with nonusers on volumes and thickness of specific brain regions. A meta-analysis of these studies (Lorenzetti et al. 2019) found smaller volumes in adolescents who were regular cannabis users than controls in brain regions implicated in learning, memory and stress (e.g., hippocampus), and inhibitory control (e.g., orbitofrontal cortex), though different studies report volume differences in different regions.

Systematic reviews of functional magnetic resonance imaging studies have found differences in brain activity between adolescent cannabis users and controls (Batalla et al. 2013, Blest-Hopley et al. 2018, Bloomfield et al. 2019, Chye et al. 2019). In a meta-analysis of these studies (Blest-Hopley et al. 2018), adolescent cannabis users had larger functional alterations in brain pathways involved in inhibitory control and habitual/compulsive substance use than nonusers. Lorenzetti et al. (2016) found differences in the activity of frontal-parietal regions between heavier and occasional cannabis users. As with structural imaging studies, larger studies are needed to resolve differences between studies in the location of these differences.

Overall, the structural and functional neuroimaging case-control studies have found that adolescent cannabis use is associated with some differences in the structure of prefrontal and temporal brain regions and with functional differences in the parietal cortex and putamen. These results need to be replicated and longitudinal studies done to assess the extent to which observed differences are causes or consequences of cannabis use because in some studies some differences have predated and predicted regular cannabis use (Chye et al. 2019, Jacobus et al. 2019).

Case-Control Studies of Cognitive Performance

Systematic reviews and meta-analyses of studies have compared cognitive performance in adolescent cannabis users and controls (Broyd et al. 2016, Scott et al. 2018). Scott et al. (2018) found impaired performance in adolescent cannabis users in the same functions found to be impaired in adult cannabis users, namely, learning, (delayed) memory, attention, and several executive functions (abstraction/shifting, inhibition, updating/working memory, and speed of information processing). These alterations are more marked in adolescents who have sought treatment for cannabis use disorders (Scott et al. 2018). In young cannabis users up to 26 years of age, performance was intact in the verbal, visuospatial, and motor performance domains, all of which consistently differ between older adult cannabis users and controls (Broyd et al. 2016). There was cognitive recovery with abstinence in some of these studies (Scott et al. 2018).

Epidemiological Studies of Cognitive Functioning

Several longitudinal studies have found a larger decline in IQ among cannabis users than in their nonusing peers (Meier et al. 2012, Mokrysz et al. 2016), and studies of twins discordant for cannabis use have generally found that the twin who used cannabis had a lower IQ than the twin who did not (Jackson et al. 2016). It is unclear, however, if these IQ differences can be attributed to cannabis

use. They have not persisted after controlling for confounders (e.g., socioeconomic status, tobacco use) in some studies (Mokrysz et al. 2016), whereas they have in other studies (e.g., Meier et al. 2012). The twin studies also suggest that the IQ differences could be explained by shared genetic and environmental risk factors (Jackson et al. 2016, Meier et al. 2018). Several longitudinal studies have reported improvements in IQ and specific cognitive abilities if regular cannabis users become abstinent (Meier et al. 2018, Tait et al. 2011).

A major limitation of many of these studies is that they have included only a small proportion of daily cannabis users and regular users were more likely to be lost at follow-up. Both of these factors may bias studies against finding cognitive effects of regular cannabis use (Lorenzetti et al. 2020). Furthermore, the twin studies have included relatively small numbers of twins who were discordant for cannabis use. They have also used limited assessments of cognitive performance, and self-reported cannabis use has often been retrospective, so twins classified as regular cannabis users may have ceased using cannabis before the assessment (Lorenzetti et al. 2020).

Consistent Findings on Cognitive Effects

There have been two consistent findings on cognitive effects in these different types of studies (Lorenzetti et al. 2020). The first is that differences in brain structure and poorer cognitive performance may precede cannabis use and increase the risk of early and regular cannabis use. In both longitudinal and twin studies, young people with poorer executive function, less inhibitory control, and poorer memory were more likely to become regular cannabis users than their peers or their cotwins who did not use cannabis (Morin et al. 2019, Tait et al. 2011). This finding suggests that young people with poorer cognitive ability are more likely to start using cannabis at an early age, to become regular users, and to continue to use into adulthood. A plausible hypothesis is that regular adolescent cannabis use may also worsen the performance of these less cognitively able young people (Lorenzetti et al. 2020). This hypothesis is supported by the finding in some longitudinal studies that the relationship between cannabis and poor cognitive performance persists after adjustment for differences in baseline cognitive performance (Meier et al. 2012).

The cognitive impairments in daily cannabis users can impair their everyday performance in terms of attention and memory. Meier et al. (2012) reported that family and friends noticed deficits in the functional daily life performance of regular cannabis users. In the Avon cohort, there were significant differences in secondary school examinations between regular and nonregular users (Mokrysz et al. 2016). Marie & Zölitz (2017) found that University of Maastricht course grades, especially in mathematics and statistics, improved more in students who were no longer able to purchase cannabis in coffee shops after restrictions by nationality were introduced in 2011 to discourage drug tourism.

A second finding is that the cognitive performance of regular cannabis users on IQ and specific cognitive tests often improves after abstinence (Lorenzetti et al. 2020). This suggests that regular cannabis users are cognitively impaired when they are using cannabis regularly. There are too few studies with enough statistical power to assess whether smaller, longer-term residual cognitive effects remain after abstinence. The fact that the cognitive effects of regular cannabis use in adolescence recover after abstinence is encouraging (Scott et al. 2018), but many adolescents who are regular cannabis users find it difficult to quit in adulthood (Volkow et al. 2016, Zehra et al. 2018). Moreover, even if they do quit as young adults and show cognitive recovery after abstinence, their daily cannabis use during adolescence may have reduced their educational attainment, limiting their choice of an occupation and reducing their income in adult life (Fergusson & Boden 2008).

THE PSYCHOSOCIAL CONSEQUENCES OF ADOLESCENT CANNABIS USE

Educational Outcomes

Regular cannabis users have poorer educational outcomes than their peers who do not use cannabis regularly (Pacheco-Colón et al. 2019), but there has been some debate about how this association is best explained. Is cannabis use a contributory cause of poor school performance? Are young people at high risk of poor educational attainment more likely to become regular cannabis users? Are regular cannabis use and poor educational attainment the results of common causes (Lynskey & Hall 2000)? These possibilities need not be mutually exclusive: Poor school performance may make young people more likely to become regular users, and regular cannabis use may further impair their already poor school performance.

Macleod et al.'s (2004) systematic review of longitudinal studies of adolescent cannabis use found that cannabis use was associated with poorer educational attainment. The authors argued, however, that the association was unlikely to be causal because it was attenuated after controlling for confounders. By contrast, Townsend et al.'s (2007) review of evidence from longitudinal studies of associations between cannabis use and dropping out of school found only one study (Ellickson et al. 1998) in which cannabis use no longer predicted school dropout after controlling for confounding variables. Friemel's (2019) review of systematic reviews of studies of cannabis and educational outcomes found a consistent association between cannabis use and early school dropout and so did a review by Pacheco-Colón et al. (2019).

Horwood et al. (2010) assessed the association between age of onset of cannabis use (<15, 15–17, and never before age 18) and high school completion, university enrollment, and degree completion in three Australasian cohort studies with over 6,000 participants. This study adjusted for a wide range of confounders, e.g., family sociodemographic background, child cognitive ability and educational achievement before the onset of cannabis use, family functioning, and child and early adolescent behavioral adjustment. Horwood et al. (2010) found that the later the age of first cannabis use, the greater an adolescent's educational achievement. Those who had not used by age 18 were 2.4 to 4.1 times more likely to complete high school than adolescents who used cannabis before age 15. The odds of university enrollment were 1.8 to 2.9 times greater, and the odds of obtaining a university degree were 3.0 to 4.4 times greater. After controlling for confounders, adolescents who had not used cannabis by age 18 were 1.9 to 2.9 times more likely to have higher educational achievement than those who began using cannabis before age 15. The authors estimated that early cannabis use explained up to 17% of the variance in failure to complete high school, enroll in university, and attain a university degree.

An Australian discordant twin study has raised questions about whether the association is causal (Verweij et al. 2013). Verweij et al. argued that the association was better explained by shared genetic and environmental risk factors for early cannabis use and early school leaving because they found no difference in risk of early school leaving between twins who did and did not use cannabis. These findings are supported by two earlier analyses of US twin study data (Bergen et al. 2008, Grant et al. 2012). As with the cognitive effects of regular cannabis use, a plausible hypothesis is that poorer educational performance increases the risk of cannabis use, which in turn further impairs educational outcomes.

Other Illicit Drug Use

In epidemiological studies in the United States, Australia, and New Zealand in the 1970s and 1980s, (*a*) regular cannabis users were more likely to use heroin and cocaine and (*b*) the younger a person was when they first used cannabis, the more likely they were to use other illicit drugs

(Kandel 2002). Three broad explanations were provided for these patterns of drug involvement: (*a*) cannabis users had more opportunities to obtain other illicit drugs from the same black market that provided their cannabis; (*b*) early cannabis users were more likely to use other illicit drugs for reasons that were unrelated to their cannabis use (e.g., their higher risk-taking or sensation-seeking); and (*c*) the pharmacological effects of cannabis increased a young person's propensity to use other illicit drugs (Hall & Pacula 2010).

More recent international data suggest that the order in which cannabis and other drugs are used varies with the prevalence of different types of illicit drug use in the population (Degenhardt et al. 2010). There is also support for the first two hypotheses in that young people in the United States who use cannabis report more opportunities to use cocaine at an earlier age (Wagner & Anthony 2002). Socially deviant young people (who are also more likely to use cocaine and heroin) start using cannabis at an earlier age than their peers (Fergusson et al. 2008). A modeling study (Morral et al. 2002) also suggested that these shared risk factors could wholly explain the relationships between cannabis and other illicit drug use in the United States.

The shared risk factor hypothesis has been tested in longitudinal studies by assessing whether cannabis users are more likely to report heroin and cocaine use after statistically controlling for confounding factors. Adjustment for confounders (including unmeasured ones using fixed effects regression) (Fergusson et al. 2006) does not eliminate the relationship between regular cannabis use and the use of other illicit drugs (Hall & Lynskey 2005).

Richmond-Rakerd and colleagues (2015) used discrete-time multiple event process survival mixture analyses to examine patterns of substance use in the US National Longitudinal Study of Adolescent to Adult Health. The most common sequence—tobacco and alcohol, then cannabis—was aligned with the earlier gateway pattern. The study also found that there were common risk factors for these use patterns, with delinquent behavior predicting multiple substance use, regardless of which substance was used first.

Twins who are discordant for cannabis use (i.e., one has and the other has not used cannabis) have been studied to test whether the relationship between cannabis use and the use of other illicit drugs is due to a shared genetic vulnerability to use drugs. Lynskey et al. (2003) suggested that the association was not wholly due to shared genetic vulnerability because the twin who had used cannabis was more likely to use other illicit drugs than the cotwin who had not. This relationship persisted after controlling for nonshared environmental factors. Similar results have been reported in a large discordant twin study in the United States (Grant et al. 2010) and in a smaller twin sample from the Netherlands (Lynskey et al. 2006).

CANNABIS USE AND MENTAL DISORDERS

Cannabis Use and Psychosis

A large prospective study in Sweden in 1987 suggested that cannabis was a contributory cause of schizophrenia. In this 15-year follow-up of 50,465 Swedish male conscripts, those who had tried cannabis by age 18 were 2.4 times more likely to receive a diagnosis of schizophrenia over the next 15 years than those who had not (Andreasson et al. 1987). After statistical adjustment for a personal history of psychiatric disorders and parental divorce, those who had used cannabis 10 or more times by age 18 were 2.3 times more likely to be diagnosed with schizophrenia than those who had not used cannabis.

It is unclear how well the study ruled out confounding or the possibility that persons who were developing schizophrenia used cannabis to self-medicate. Later studies have addressed these

problems. Zammit et al.'s (2002) 27-year follow-up of the Swedish cohort found a dose-response relationship between frequency of cannabis use at age 18 and risk of schizophrenia over the 27-year follow-up. This effect persisted after statistically controlling for confounding. They estimated that 13% of cases of schizophrenia could have been averted if all cannabis use had been prevented in the cohort.

The Swedish cohort findings have been supported by longitudinal studies in the Netherlands (van Os et al. 2002), Germany (Henquet et al. 2005), and New Zealand (Arseneault et al. 2002, Fergusson et al. 2003). All studies found a relationship between cannabis use and the risks of either psychotic disorders or psychotic symptoms that persisted after adjustment for confounders. A meta-analysis of these studies found that psychotic symptoms or psychotic disorders were marginally more common among those who had ever used cannabis [OR of 1.4 (95% CI: 1.20, 1.65)] (Moore et al. 2007) and more common still among regular cannabis users [OR of 2.09 (95% CI: 1.54, 2.84)]. Reverse causation was addressed in some of these studies by excluding cases that reported psychotic symptoms at baseline and by statistically adjusting for preexisting psychotic symptoms. The common cause hypothesis was harder to exclude because the association between cannabis use and psychosis was attenuated after statistical adjustment and no study assessed all confounders.

A meta-analysis of studies conducted since Moore et al.'s (2007) meta-analysis found an even stronger association between cannabis use and psychosis (OR of nearly 4) in persons who used more potent forms of cannabis (Marconi et al. 2016). Young persons with psychoses or psychotic symptoms who use cannabis have an average earlier age of first episode psychosis (Large et al. 2011), and young persons with a first episode of psychosis who stop using cannabis have better clinical outcomes than those who persist in using it, i.e., fewer psychotic symptoms and better social functioning (Schoeler et al. 2016).

A number of genetic studies have assessed whether the association between cannabis use and psychosis is explained by a shared genetic liability to use cannabis and develop a psychosis. These have included Mendelian randomization studies (e.g., Gage et al. 2017) and studies that have adjusted the association for a polygenetic risk of psychosis score (e.g., Verweij et al. 2017). The value of the former studies has been limited by (*a*) the failure of genome-wide association studies to identify genes that influence the liability to use cannabis and (*b*) the fact that most genetic studies have assessed only lifetime cannabis use (rather than daily use). The studies using polygenetic risk scores have found that these scores only weakly predict cannabis use and psychosis risk and that the statistical adjustment for genetic risk does not eliminate the association between the two.

Those who are skeptical of a causal role for cannabis argue that it is inconsistent with the absence of an increase in the incidence of schizophrenia over the period when cannabis use has increased among young adults. The evidence is mixed. An Australian study did not find any increase in the incidence of psychosis while cannabis use increased during the 1980s and 1990s (Degenhardt et al. 2003). A similar British modeling study (Hickman et al. 2007) concluded it was too early to detect any increase in incidence in Britain. Two case register studies in Britain (Boydell et al. 2006) and Switzerland (Ajdacic-Gross et al. 2007) reported an increased incidence of psychoses in recent birth cohorts, while another British study of patients in general practice failed to do so (ACMD 2008). It is difficult to decide whether cannabis use has had any effects on psychosis incidence because it produces a very modest increase in risk even if the relationship is causal. The interpretation of incidence trends in psychoses is complicated by changes in diagnostic criteria, psychiatric services for psychosis, and the quality of administrative data on the treated incidence of psychosis.

Cannabis Use and Depression

There are high rates of comorbidity between cannabis use disorders and depressive disorders in epidemiologic surveys (Macleod et al. 2004, Mammen et al. 2018). In longitudinal studies, the relationship between regular cannabis use and depression has been weaker than that for cannabis and psychosis (Degenhardt et al. 2012). A meta-analysis (Moore et al. 2007) found only a modest increase in risk of depressive disorders [OR = 1.49 (95% CI: 1.15, 1.94)]. The authors argued that most of these studies had not controlled for confounders or excluded the possibility that depressed young people were self-medicating. Similar conclusions were drawn from a meta-analysis of data from four Australasian cohort studies (Horwood et al. 2012) and systematic reviews and meta-analyses of longitudinal studies (Gobbi et al. 2019, Lev-Ran et al. 2014).

A systematic review of prospective studies of people with mood disorders found that cannabis use, or a comorbid cannabis use disorder, was associated with more severe symptoms of depression (Mammen et al. 2018). Esmaeelzadeh et al. (2018) reported a systematic review and meta-analysis of longitudinal studies of mental disorders and substance use in young people. They found a consistent association between cannabis use at baseline and depression at follow-up after adjusting for potential confounders, including a prior history of mental disorders. They also found a stronger association between cannabis use in adolescence and depression at follow-up [OR = 1.33 (1.19, 1.49)] than between depression at baseline and later cannabis use [OR = 1.03 (1.01, 1.05)].

Cannabis Use and Anxiety Disorders

Epidemiological evidence is also mixed on whether cannabis use can increase the risk of anxiety disorders (Esmaeelzadeh et al. 2018, Moore et al. 2007). The systematic review and meta-analysis of Moore et al. (2007) found that cannabis exposure was not significantly associated with anxiety disorders after adjusting for potential confounders [OR = 1.40 (0.96, 2.04)]. Gobbi and colleagues (2019) drew the same conclusion from a meta-analysis of three longitudinal studies of anxiety in young adults in the United States [OR = 1.18 (0.84, 1.67)]. A systematic review found an association between cannabis use and social anxiety disorders and acute anxiety, but mixed results for generalized anxiety disorders (Zimmermann et al. 2019). Another systematic review found that cannabis use was associated with more symptoms of anxiety and posttraumatic stress disorder, but not with panic disorders (Mammen et al. 2018). Kedzior & Laeber's (2014) systematic review and meta-analysis of general population studies found a modestly increased risk of anxiety disorders from cannabis use [OR = 1.24 (1.06, 1.45); adjusted OR = 1.28 (1.06, 1.54)]. Cannabis use at baseline was associated with anxiety at follow-up in five studies that adjusted for confounders, but the authors suggested that cannabis use may have a bidirectional effect in that some people use cannabis to cope with anxiety, while regular cannabis use worsens anxiety.

Cannabis Use and Bipolar Disorders

Persons with bipolar disorders have higher rates of cannabis use disorders than the general population (e.g., Agrawal et al. 2011, Lai & Sitharthan 2012, Lev-Ran et al. 2013, Silberberg et al. 2012). In longitudinal studies, cannabis use at baseline predicts more manic symptoms at follow-up (Henquet et al. 2006), and persons with bipolar disorders who continue to use cannabis have more manic episodes than those who do not (Silberberg et al. 2012). Systematic reviews of these studies consistently find an association between cannabis use and poor outcomes in bipolar disorder (Bally et al. 2014, Gibbs et al. 2015, Mammen et al. 2018, Marangoni et al. 2016, Messer et al. 2017). Cannabis use is also associated with a younger age of onset of manic symptoms, more

frequent depressive or manic episodes, more severe bipolar symptoms, rapid cycling or mixed episodes, and less improvement with treatment.

Marangoni and colleagues (2016) systematically reviewed longitudinal studies on the risks of substance use in bipolar disorder. In three studies, cannabis users had a two- to ninefold higher risk of bipolar disorders later in life. One study found a higher risk if cannabis was used weekly. These findings suggest that regular cannabis use may play a contributory causal role in precipitating bipolar disorders, but many of these studies have not adequately controlled for confounding variables or ruled out reverse causation (Silberberg et al. 2012).

Cannabis Use and Suicidality

Some case-control studies have found associations between cannabis use and suicide in adolescents and young adults (e.g., Beautrais et al. 1999), but prospective epidemiological studies have produced more mixed results. Fergusson & Horwood (1997) found a dose-response relationship between frequency of cannabis use by age 16 and self-reported suicide attempts, but this did not persist after controlling for confounders. A reanalysis of their data (van Ours et al. 2013) found that using cannabis more than weekly increased suicidal ideation in males. Patton et al. (1997), by contrast, found that cannabis was only associated with self-harm in females. Rasic et al. (2013) reported that heavy cannabis use increased the risk of depression but did not affect suicide risk. A meta-analysis of earlier studies (Moore et al. 2007) concluded that the study designs and measures were too varied to quantify risk and that most studies had not excluded reverse causation or controlled for confounding.

A study of mortality among 6,445 persons treated for a cannabis use disorder in Norway found an elevated risk of suicide [OR = 5.3 (95% CI: 3.3, 7.79)] (Arendt et al. 2013). The sample comprised heavier, more problematic cannabis users than other studies, and a substantial proportion had injected drugs, a behavior associated with an increased suicide risk (Degenhardt et al. 2012). Exclusion of cannabis users who were known to be injectors marginally reduced the suicide risk [OR = 4.8 (95% CI: 2.4, 8.9)]. Because the study used case registers it had a limited ability to control for possible confounders, but the results suggest that suicide risk may be elevated in very heavy cannabis users who seek treatment.

Gobbi and colleagues' (2019) systematic review and meta-analysis of longitudinal studies of adolescent cannabis use and suicidal behavior found that cannabis use during adolescence was associated with a modest increase in the risk of suicidal ideation [OR = 1.50 (1.11, 2.03)] and a larger increase in the risk of suicidal attempts [OR = 3.46 (1.53, 7.84)] in young adults. Similar findings were reported in another review that compared the effects of any cannabis use with those of heavy cannabis use (Borges et al. 2016). The associations between cannabis use and suicidal ideation [OR = 2.53 (1.00, 6.39)] and suicide attempts [OR = 3.20 (1.72, 5.94)] were strongest in young people who engaged in heavy cannabis use.

Cannabis Use and Antisocial Behavior

The illegality of cannabis use under prohibition can lead to a criminal record, a risk that is eliminated in adults by decriminalization or the legalization of cannabis use. Cannabis use, however, is not regarded as criminogenic in the same way that heavy heroin use can be (e.g., users committing criminal offences to fund their drug use) or that the pharmacological effects of heavy cocaine use may prompt users to engage in acts of violence. Drug dealing and property offences are also less often committed by cannabis users because cannabis is easier to obtain and much less expensive than heroin. Unemployed daily cannabis users may fund their use by low-level dealing, that is,

buying cannabis in larger amounts than they need at a discount and then selling the surplus to peers.

Cannabis also does not have a reputation as a drug that can cause violence. Indeed, cannabis is more often perceived as relaxing and reducing users' motivation to engage in violent acts. Recent epidemiological evidence has challenged this view by suggesting that regular cannabis use can increase the risk of violence in persons with psychoses. A meta-analysis of predictors of violence in persons with psychoses (Witt et al. 2013) found that polysubstance abuse [OR = 10.3 (95% CI: 2.5, 41.4)] and comorbid substance use disorder [OR = 3.1 (95% CI: 1.9, 5.0)] were associated with an increased risk of violence. It was uncertain, however, whether cannabis misuse did so because only four studies assessed this possibility [OR = 1.3 (95% CI: 0.7, 2.4)]. A more recent meta-analysis of 12 studies of cannabis and violence in persons with psychoses (Dellazizzo et al. 2019) found an increased risk of violence among persons with psychoses who were regular cannabis users [OR = 3.02 (95% CI: 2.01, 4.54)] and a higher risk among those who misused cannabis [OR = 5.8 (95% CI: 3.27, 10.28)]. The authors cautioned against drawing a causal conclusion from the association between cannabis use and violence because these studies did not control for a large number of potential confounders, and it was not possible to exclude the possibility that persons with psychoses who were prone to violence were more likely to become regular cannabis users. This issue warrants further study.

THE POTENTIAL EFFECTS OF CANNABIS LEGALIZATION ON ADOLESCENT CANNABIS USE

The regulation of cannabis has changed dramatically in the past two decades in North America and, to a lesser extent, in other high-income countries (EMCDDA 2018a, Hall et al. 2019). Adult cannabis use has been illegal in most of these countries since the middle of the twentieth century, but an increasing number of countries have decriminalized personal use or legalized cannabis use for medicinal purposes (Hall et al. 2019, Room et al. 2010). More recently, Canada, Uruguay, and 11 states in the United States have legalized cannabis use by adults for recreational purposes (Hall et al. 2019).

Most North American jurisdictions that have legalized adult use have decided to regulate cannabis like alcohol, i.e., to license commercial cannabis growers, processors, and sellers to supply cannabis to users for a profit (Hall et al. 2019). This model has increased adults' access to more potent cannabis products and substantially reduced the price of cannabis (Hall et al. 2019, Smart & Pacula 2019). There is a reasonable concern that cannabis legalization will also increase the prevalence and frequency of cannabis use among adolescents and young adults (Hall et al. 2019). This section reviews evidence on the effects of cannabis legalization on adolescents and young adults. It also includes some provisional predictions about how these outcomes may change after the legalization of a commercial cannabis industry.

The Impacts of Cannabis Legalization So Far

Cannabis legalization is still at an early stage in implementation, even in the early adopter states in the United States, making it difficult to evaluate its impacts. Some things are clear, however. Legalization has reduced cannabis prices and increased the potency of cannabis flower in the US states that have legalized it (Smart et al. 2017). The sales of more potent cannabis products, such as edibles, oils for vaporization, and extracts and waxes that contain more than 60% THC, have also increased (Smart et al. 2017). These products comprised 21% of sales in Washington state by 2016 (Smart et al. 2017), and this proportion has since increased (EMCDDA 2019a).

In household surveys, adult cannabis users in US states that have legalized medical cannabis use report using cannabis more often (Caulkins 2017). There have not been consistent increases in cannabis use among adolescents and young adults so far (Dilley et al. 2019), despite declines in the perceived risks of cannabis use in this age group (Hasin 2018).

Road crash fatalities in which THC has been detected have increased since legalization in US states, but it is uncertain to what extent these reflect increased cannabis-impaired driving or increased testing for THC. Accident fatality rates have not differed between states that have and have not legalized cannabis (Aydelotte et al. 2017), apart from a short-lived increase immediately after legalization (Hall & Lane 2020).

The potential adverse health effects of the increased use of more potent cannabis products are of concern. In some surveys, persons who use cannabis extracts with very high THC content report more symptoms of dependence and mental distress (Chan et al. 2017). In the Netherlands, the number of persons seeking help to quit cannabis increased as potency increased and later fell when cannabis potency was reduced (Freeman et al. 2018). Some argue that the effects of increased THC content will be minimal because users titrate their doses of THC to achieve the desired level of intoxication. However, it is unclear how well users can titrate their doses and, if they can do so, whether they in fact do adjust their doses (van der Pol et al. 2014).

The following are plausible hypotheses about the future adverse effects of increased cannabis potency. A higher THC content may increase anxiety, depression, and psychotic symptoms in naive users, an effect that may deter continued use. More potent cannabis products may also increase the risks of dependence and psychotic symptoms in regular users if they do not titrate their doses. Adverse effects on the respiratory and cardiovascular systems may be reduced if regular users smoke smaller amounts of more potent cannabis products.

The Future Impacts of Legal Recreational Cannabis Markets

Experience with alcohol regulation (Babor et al. 2010) suggests that in the longer term the commercialization of cannabis will increase the frequency of use among current users. There are some indications that this is already happening (Caulkins 2017, Hasin 2018). In the longer term, the population prevalence and the intensity of cannabis use will probably increase as the use of cannabis becomes more socially acceptable, prices fall further, cannabis access increases, and more attractive cannabis products are developed and marketed. Greater promotion and use of more potent cannabis products may increase the prevalence of dependence and other harms to regular cannabis users. The cannabis industry is already following the examples of the alcohol, tobacco, and gambling industries in opposing policies that promote public health over corporate profits, e.g., by lobbying for reduced cannabis taxes, opposing the regulation of the THC content of cannabis products, and campaigning for the legalization of cannabis consumption lounges and the home delivery of cannabis products (Hall et al. 2019). The cannabis industry may also lobby for politically appealing but ineffective policies that promote responsible use and allocate a token amount of cannabis tax revenue to treating problem cannabis users, as the gambling industry has done.

Strategies for Reducing Cannabis-Related Harm After Legalization

When cannabis is a legal commodity, governments can use taxes and regulations like those for alcohol to reduce its adverse public health impact (Babor et al. 2010). These include increasing taxes to discourage heavy use, limiting the number and location of retail outlets, restricting advertising and promotions, educating users about safer patterns of use, discouraging adolescents from

initiating use, improving access to treatment for problem cannabis users, and deterring cannabis users from driving while impaired.

After legalization, cannabis users need accurate information about cannabis products, e.g., their THC content, the risks and benefits of using more potent cannabis, and ways to minimize the harms (Fischer et al. 2017). They need to be informed about the lack of evidence for many of the putative medical uses of cannabis and cannabinoids, including cannabidiol, which is increasingly promoted as a wellness product. They also need to be better informed about the risks of developing cannabis dependence, using cannabis during pregnancy, driving while impaired, and exacerbating psychoses and other mental disorders. The design of effective educational programs requires research on the product labels and health warnings that are the most credible to cannabis users.

CONCLUSION

The daily use of cannabis by adolescents and young adults poses risks to the successful completion of psychosocial development. The major acute risk of cannabis use is a car crash if a young person drives while intoxicated. Serious injuries can impair a young person's chances of living a full and productive life. The major risk of regular cannabis use in adolescence is cannabis dependence. This can be a problem if a young person spends much of their waking time in an intoxicated state and finds it difficult to cease using despite wishing to do so.

Cannabis dependence is associated with increased risks of other poor psychosocial outcomes in young adulthood. These include psychoses, depression and anxiety disorders, cognitive impairment, early school leaving, other illicit drug use, and in the case of persons with psychoses, violence. Debate continues on which of these outcomes are causally related to cannabis use. The evidence is strongest for cannabis dependence and psychosis, cognitive impairment in daily cannabis users, and poor educational outcomes if cannabis is used daily in adolescence. In the case of anxiety and depression, it is unclear to what extent the association reflects self-medication or uncontrolled confounding and to what extent cannabis use worsens the course of these disorders.

A number of potential effects of cannabis legalization on adolescent cannabis use are of concern. The major concern is that young people will have greater access to more potent and cheaper cannabis products in a social setting in which adult cannabis use is condoned and modeled. The risk is that these developments will increase the prevalence of cannabis dependence and the harms associated with cannabis dependence in young people.

In jurisdictions where cannabis is legal, mitigation policies are available that do not exist under prohibition. These include the use of taxation to discourage adolescent initiation and heavy cannabis use and restrictions on retail outlets and advertising. These approaches could be useful additions to more traditional ways of preventing regular cannabis use in adolescence and treating dependent cannabis users. It remains to be seen if governments will use public health regulations to reduce the harms of adolescent cannabis use after legalization.

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LITERATURE CITED

ACMD (Advis. Counc. Misuse Drugs). 2008. *Cannabis: classification and public health*. Corp. Rep., Home Office, London

Agrawal A, Nurnberger JI Jr., Lynskey MT. 2011. Cannabis involvement in individuals with bipolar disorder. *Psychiatry Res.* 185:459–61

AIHW (Aust. Inst. Health Welfare). 2017. Data tables: Chapter 5 Illicit use of drugs. In *National Drug Strategy Household Survey 2016: Detailed Findings*. Rep., AIHW, Canberra, Aust. **https://www.aihw.gov.au/reports/illicit-use-of-drugs/ndshs-2016-detailed/data**

AIHW (Aust. Inst. Health Welfare). 2019. *Alcohol and other drug treatment services in Australia 2017–18: key findings*. Rep., AIHW, Canberra, Aust.

Ajdacic-Gross V, Lauber C, Warnke I, Haker H, Murray RM, Rossler W. 2007. Changing incidence of psychotic disorders among the young in Zurich. *Schizophr. Res.* 95:9–18

Andreasson S, Allebeck P, Engstrom A, Rydberg U. 1987. Cannabis and schizophrenia: a longitudinal study of Swedish conscripts. *Lancet* 2:1483–86

Anthony J. 2006. The epidemiology of cannabis dependence. In *Cannabis Dependence: Its Nature, Consequences and Treatment*, ed. RA Roffman, RS Stephens, pp. 58–105. Cambridge, UK: Cambridge Univ. Press

Anthony JC, Warner LA, Kessler RC. 1994. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: basic findings from the National Comorbidity Survey. *Exp. Clin. Psychopharmacol.* 2:244–68

Arendt M, Munk-Jorgensen P, Sher L, Jensen SO. 2013. Mortality following treatment for cannabis use disorders: predictors and causes. *J. Subst. Abuse Treat.* 44:400–6

Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. 2002. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ* 325:1212–13

Asbridge M, Hayden JA, Cartwright JL. 2012. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. *BMJ* 344:e536

Aydelotte JD, Brown LH, Luftman KM, Mardock AL, Teixeira PGR, et al. 2017. Crash fatality rates after recreational marijuana legalization in Washington and Colorado. *Am. J. Public Health* 107:1329–31

Babor T, Caetano R, Casswell S, Edwards G, Giesbrecht N, et al. 2010. *Alcohol: No Ordinary Commodity: Research and Public Policy*. Oxford, UK: Oxford Univ. Press

Bally N, Zullino D, Aubry J-M. 2014. Cannabis use and first manic episode. *J. Affect. Disord.* 165:103–8

Batalla A, Bhattacharyya S, Yucel M, Fusar-Poli P, Crippa JA, et al. 2013. Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings. *PLOS ONE* 8:e55821

Beautrais AL, Joyce PR, Mulder RT. 1999. Cannabis abuse and serious suicide attempts. *Addiction* 94:1155–64

Bergen SE, Gardner CO, Aggen SH, Kendler KS. 2008. Socioeconomic status and social support following illicit drug use: causal pathways or common liability? *Twin Res. Hum. Genet.* 11:266–74

Blest-Hopley G, Giampietro V, Bhattacharyya S. 2018. Residual effects of cannabis use in adolescent and adult brains—a meta-analysis of fMRI studies. *Neurosci. Biobehav. Rev.* 88:26–41

Bloomfield MAP, Hindocha C, Green SF, Wall MB, Lees R, et al. 2019. The neuropsychopharmacology of cannabis: a review of human imaging studies. *Pharmacol. Ther.* 195:132–61

Borges G, Bagge CL, Orozco R. 2016. A literature review and meta-analyses of cannabis use and suicidality. *J. Affect. Disord.* 195:63–74

Boydell J, van Os J, Caspi A, Kennedy N, Giouroukou E, et al. 2006. Trends in cannabis use prior to first presentation with schizophrenia, in South-East London between 1965 and 1999. *Psychol. Med.* 36:1441–46

Broyd SJ, van Hell HH, Beale C, Yücel M, Solowij N. 2016. Acute and chronic effects of cannabinoids on human cognition—a systematic review. *Biol. Psychiatry* 79:557–67

Budney AJ, Hughes JR. 2006. The cannabis withdrawal syndrome. *Curr. Opin. Psychiatry* 19:233–38
Budney AJ, Sofis MJ, Borodovsky JT. 2019. An update on cannabis use disorder with comment on the impact of policy related to therapeutic and recreational cannabis use. *Eur. Arch. Psychiatry Clin. Neurosci.* 269:73–86
Calabria B, Degenhardt L, Hall W, Lynskey M. 2010. Does cannabis use increase the risk of death? Systematic review of epidemiological evidence on adverse effects of cannabis use. *Drug Alcohol Rev.* 29:318–30
Caulkins JP. 2017. Recognizing and regulating cannabis as a temptation good. *Int. J. Drug Policy* 42:50–56
CDC (Cent. Dis. Control Prev.). 2019. *Annual surveillance report of drug-related risks and outcomes—United States, 2019*. US Surveill. Spec. Rep. CDC, Atlanta, GA
Chan GCK, Hall W, Freeman TP, Ferris J, Kelly AB, Winstock A. 2017. User characteristics and effect profile of Butane Hash Oil: an extremely high-potency cannabis concentrate. *Drug Alcohol Depend.* 178:32–38
Chye Y, Christensen E, Yucel M. 2019. Cannabis use in adolescence: a review of neuroimaging findings. *J. Dual Diagn.* 16:83–105
Coffey C, Patton GC. 2016. Cannabis use in adolescence and young adulthood: a review of findings from the Victorian Adolescent Health Cohort Study. *Can. J. Psychiatry* 61:318–27
Danovitch I, Gorelick DA. 2012. State of the art treatments for cannabis dependence. *Psychiatr. Clin. North Am.* 35:309–26
Degenhardt L, Dierker L, Chiu WT, Medina-Mora ME, Neumark Y, et al. 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 Alcohol Depend.* 108:84–97
Degenhardt L, Hall WD, Lynskey M. 2003. Testing hypotheses about the relationship between cannabis use and psychosis. *Drug Alcohol Depend.* 71:37–48
Degenhardt L, Hall WD, Lynskey M, Coffey C, Patton G. 2012. The association between cannabis use and depression: a review of the evidence. In *Marijuana and Madness*, ed. D Castle, R Murray, D D'Souza, pp. 114–28. New York: Cambridge Univ. Press
Dellazizzo L, Potvin S, Beaudoin M, Luigi M, Dou BY, et al. 2019. Cannabis use and violence in patients with severe mental illnesses: a meta-analytical investigation. *Psychiatry Res.* 274:42–48
Dilley JA, Richardson SM, Kilmer B, Pacula RL, Segawa MB, Cerda M. 2019. Prevalence of cannabis use in youths after legalization in Washington State. *JAMA Pediatr.* 173:192–93
Dines AM, Wood DM, Galicia M, Yates CM, Heyerdahl F, et al. 2015. Presentations to the emergency department following cannabis use—a multi-centre case series from ten European countries. *J. Med. Toxicol.* 11:415–21
Ellickson P, Bui K, Bell R, McGuigan KA. 1998. Does early drug use increase the risk of dropping out of high school? *J. Drug Issues* 28:357–80
Elvik R. 2013. Risk of road accident associated with the use of drugs: a systematic review and meta-analysis of evidence from epidemiological studies. *Accid. Anal. Prev.* 60:254–67
EMCDDA (Eur. Monit. Cent. Drugs Drug Addict.). 2018a. *Cannabis legislation in Europe: an overview*. Rep., Publ. Off. Eur. Union, Luxembourg
EMCDDA (Eur. Monit. Cent. Drugs Drug Addict.). 2018b. *European Drug Report 2018: trends and developments*. Rep., Publ. Off. Eur. Union, Luxembourg
EMCDDA (Eur. Monit. Cent. Drugs Drug Addict.). 2019a. *Developments in the European cannabis market*. Rep., Publ. Off. Eur. Union, Luxembourg
EMCDDA (Eur. Monit. Cent. Drugs Drug Addict.). 2019b. *Statistical Bulletin 2019—treatment demand*. Rep., Publ. Off. Eur. Union, Luxembourg
Esmaeelzadeh S, Moraros J, Thorpe L, Bird Y. 2018. Examining the association and directionality between mental health disorders and substance use among adolescents and young adults in the U.S. and Canada—a systematic review and meta-analysis. *J. Clin. Med.* 7:543
ESPAD Group (Eur. Sch. Surv. Proj. Alcohol Other Drugs Group). 2016. *ESPAD report 2015: results from the European School Survey Project on Alcohol and Other Drugs*. Rep., Publ. Off. Eur. Union, Luxembourg
Fergusson D, Boden J. 2008. Cannabis use and later life outcomes. *Addiction* 103:969–76
Fergusson D, Boden J, Horwood L. 2006. Cannabis use and other illicit drug use: testing the cannabis gateway hypothesis. *Addiction* 101:556–69
Fergusson D, Boden J, Horwood L. 2008. The developmental antecedents of illicit drug use: evidence from a 25-year longitudinal study. *Drug Alcohol Depend.* 96:165–77

Fergusson D, Horwood L. 1997. Early onset cannabis use and psychosocial adjustment in young adults. *Addiction* 92:279–96
Fergusson D, Horwood L, Swain-Campbell N. 2003. Cannabis dependence and psychotic symptoms in young people. *Psychol. Med.* 33:15–21
Fischer B, Russell C, Sabioni P, van den Brink W, Le Foll B, et al. 2017. Lower-risk cannabis use guidelines: a comprehensive update of evidence and recommendations. *Am. J. Public Health* 107:e1–12
Florez-Salamanca L, Secades-Villa R, Budney AJ, Garcia-Rodriguez O, Wang S, Blanco C. 2013. Probability and predictors of cannabis use disorders relapse: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend.* 132:127–33
Freeman TP, van der Pol P, Kuijpers W, Wisselink J, Das RK, et al. 2018. Changes in cannabis potency and first-time admissions to drug treatment: a 16-year study in the Netherlands. *Psychol. Med.* 48:2346–52
Friemel CM. 2019. Psychosocial consequences. In *Cannabis: Potential and Risks*, ed. E Hoch, CM Friemel, M Schneider, pp. 129–48. Heidelberg, Ger.: Springer Nature
Gage SH, Jones HJ, Burgess S, Bowden J, Davey Smith G, et al. 2017. Assessing causality in associations between cannabis use and schizophrenia risk: a two-sample Mendelian randomization study. *Psychol. Med.* 47:971–80
Gates PJ, Sabioni P, Copeland J, Le Foll B, Gowing L. 2016. Psychosocial interventions for cannabis use disorder. *Cochrane Database Syst. Rev.* 5:CD005336
GBD 2017 Dis. Inj. Incid. Preval. Collab. 2018. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 392:1789–858. Erratum. 2019. *Lancet* 393:e44
Gibbs M, Winsper C, Marwaha S, Gilbert E, Broome M, Singh SP. 2015. Cannabis use and mania symptoms: a systematic review and meta-analysis. *J. Affect. Disord.* 171:39–47
Gobbi G, Atkin T, Zytynski T, Wang S, Askari S, et al. 2019. Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: a systematic review and meta-analysis. *JAMA Psychiatry* 76:426–34
Grant JD, Lynskey MT, Scherrer JF, Agrawal A, Heath AC, Bucholz KK. 2010. A cotwin-control analysis of drug use and abuse/dependence risk associated with early-onset cannabis use. *Addict. Behav.* 35:35–41
Grant JD, Scherrer JF, Lynskey MT, Agrawal A, Duncan AE, et al. 2012. Associations of alcohol, nicotine, cannabis, and drug use/dependence with educational attainment: evidence from cotwin-control analyses. *Alcohol Clin. Exp. Res.* 36:1412–20
Hall WD. 2015. What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? *Addiction* 110:19–35
Hall WD, Fischer B. 2010. Harm reduction policies for cannabis. In *Harm Reduction: Evidence, Impacts and Challenges*, ed. T Rhodes, D Hedrich, pp. 235–51. Lisbon, Port.: Eur. Monit. Cent. Drugs Drug Addict.
Hall WD, Lane T. 2020. Road safety risks of cannabis use: sales need to fund research. *Am. J. Public Health* 110:265–66
Hall WD, Lynskey M. 2005. Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. *Drug Alcohol Rev.* 24:39–48
Hall WD, Pacula RL. 2010. *Cannabis Use and Dependence: Public Health and Public Policy*. Cambridge, UK: Cambridge Univ. Press
Hall WD, Patton G, Stockings E, Weier M, Lynskey M, et al. 2016a. Why young people's substance use matters for global health. *Lancet Psychiatry* 3:265–79
Hall WD, Renström M, Poznyak V. 2016b. *The Health and Social Effects of Nonmedical Cannabis Use*. Geneva: World Health Organ.
Hall WD, Stjepanovic D, Caulkins J, Lynskey M, Leung J, et al. 2019. Public health implications of legalising the production and sale of cannabis for medicinal and recreational use. *Lancet* 394:1580–90
Hartman RL, Brown TL, Milavetz G, Spurgin A, Pierce RS, et al. 2016. Cannabis effects on driving longitudinal control with and without alcohol. *J. Appl. Toxicol.* 36:1418–29
Hartung B, Kauferstein S, Ritz-Timme S, Daldrup T. 2014. Sudden unexpected death under acute influence of cannabis. *Forensic Sci. Int.* 237:e11–13

Hasin DS. 2018. US epidemiology of cannabis use and associated problems. *Neuropsychopharmacology* 43:195–212

Hels T, Bernhoft IM, Lyckegaard A, Houwing S, Hagenzieker M, et al. 2011. *Risk of injury by driving with alcohol and other drugs, DRUID (Driving under the Influence of Drugs, Alcohol and Medicines)*. Rep., Ghent Univ., Ghent, Belg.

Henquet C, Krabbendam L, de Graaf R, ten Have M, van Os J. 2006. Cannabis use and expression of mania in the general population. *J. Affect. Disord.* 95:103–10

Henquet C, Krabbendam L, Spauwen J, Kaplan C, Lieb R, et al. 2005. Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ* 330:11

Hickman M, Vickerman P, Macleod J, Kirkbride J, Jones P. 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

Horwood LJ, Fergusson DM, Coffey C, Patton GC, Tait R, et al. 2012. Cannabis and depression: an integrative data analysis of four Australasian cohorts. *Drug Alcohol Depend.* 126:369–78

Horwood LJ, Fergusson DM, Hayatbakhsh MR, Najman JM, Coffey C, et al. 2010. Cannabis use and educational achievement: findings from three Australasian cohort studies. *Drug Alcohol Depend.* 110:247–53

IHME (Inst. Health Metrics Eval.). 2017. GBD compare data visualization. *Institute of Health Metrics and Evaluation*. **https://vizhub.healthdata.org/gbd-compare/#**

Jackson NJ, Isen JD, Khoddam R, Irons D, Tuvblad C, et al. 2016. Impact of adolescent marijuana use on intelligence: results from two longitudinal twin studies. *PNAS* 113:E500–8

Jacobus J, Courtney KE, Hodgdon EA, Baca R. 2019. Cannabis and the developing brain: what does the evidence say? *Birth Defects Res.* 111:1302–7

Kandel D. 2002. *Stages and Pathways of Drug Involvement: Examining the Gateway Hypothesis*. New York: Cambridge Univ. Press

Kedzior KK, Laeber LT. 2014. A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population—a meta-analysis of 31 studies. *BMC Psychiatry* 14:136

Kroon E, Kuhns L, Hoch E, Cousijn J. 2019. Heavy cannabis use, dependence and the brain: a clinical perspective. *Addiction* 115:559–72

Lai H, Sitharthan T. 2012. Exploration of the comorbidity of cannabis use disorders and mental health disorders among inpatients presenting to all hospitals in New South Wales, Australia. *Am. J. Drug Alcohol Abuse* 38:567–74

Large M, Sharma S, Compton MT, Slade T, Nielssen O. 2011. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Arch. Gen. Psychiatry* 68:555–61

Leung J, Chan GC, Hides L, Hall WD. 2020. What is the prevalence and risk of cannabis use disorders among people who use cannabis? A systematic review and meta-analysis. *Addict. Behav.* 109:106479

Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. 2013. Bipolar disorder and co-occurring cannabis use disorders: characteristics, co-morbidities and clinical correlates. *Psychiatry Res.* 209:459–65

Lev-Ran S, Roerecke M, Le Foll B, George TP, McKenzie K, Rehm J. 2014. The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. *Psychol. Med.* 44:797–810

Li M-C, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, Li G. 2012. Marijuana use and motor vehicle crashes. *Epidemiol. Rev.* 34:65–72

Lorenzetti V, Alonso-Lana S, Youssef GJ, Verdejo-Garcia A, Suo C, et al. 2016. Adolescent cannabis use: What is the evidence for functional brain alteration? *Curr. Pharm. Des.* 22:6353–65

Lorenzetti V, Chye Y, Silva P, Solowij N, Roberts CA. 2019. Does regular cannabis use affect neuroanatomy? An updated systematic review and meta-analysis of structural neuroimaging studies. *Eur. Arch. Psychiatry Clin. Neurosci.* 269:59–71

Lorenzetti V, Hoch E, Hall W. 2020. Adolescent cannabis use, cognition, brain health and educational outcomes: a review of the evidence. *Eur. Neuropsychopharmacol.* 36:169–80

Lynskey M, Hall W. 2000. The effects of adolescent cannabis use on educational attainment: a review. *Addiction* 95:1621–30

Lynskey M, Heath AC, Bucholz KK, Slutske WS, Madden PA, et al. 2003. Escalation of drug use in early-onset cannabis users versus co-twin controls. *JAMA* 289:427–33

Lynskey M, Vink JM, Boomsma DI. 2006. Early onset cannabis use and progression to other drug use in a sample of Dutch twins. *Behav. Genet.* 36:195–200
Macleod J, Oakes R, Copello A, Crome I, Egger M, et al. 2004. Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. *Lancet* 363:1579–88
Mammen G, Rueda S, Roerecke M, Bonato S, Lev-Ran S, Rehm J. 2018. Association of cannabis with long-term clinical symptoms in anxiety and mood disorders: a systematic review of prospective studies. *J. Clin. Psychiatry* 79:17r11839
Marangoni C, Hernandez M, Faedda GL. 2016. The role of environmental exposures as risk factors for bipolar disorder: a systematic review of longitudinal studies. *J. Affect. Disord.* 193:165–74
Marconi A, Di Forti M, Murray RM, Lewis CM, Vassos E. 2016. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr. Bull.* 42:1262–69
Marie O, Zölitz U. 2017. "High" achievers? Cannabis access and academic performance. *Rev. Econ. Stud.* 84:1210–37
Meier M, Caspi A, Ambler A, Harrington H, Houts R, et al. 2012. Persistent cannabis users show neuropsychological decline from childhood to midlife. *PNAS* 109:E2657–64
Meier M, Caspi A, Danese A, Fisher HL, Houts R, et al. 2018. Associations between adolescent cannabis use and neuropsychological decline: a longitudinal co-twin control study. *Addiction* 113:257–65
Messer T, Lammers G, Müller-Siecheneder F, Schmidt R-F, Latifi S. 2017. Substance abuse in patients with bipolar disorder: a systematic review and meta-analysis. *Psychiatry Res.* 253:338–50
Miech RA, Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE, Patrick ME. 2019. *Monitoring the Future national survey results on drug use, 1975–2018: Volume I, secondary school students*. Rep., Inst. Soc. Res., Univ. Michigan, Ann Arbor, MI
Mokrysz C, Landy R, Gage SH, Munafo MR, Roiser JP, Curran HV. 2016. Are IQ and educational outcomes in teenagers related to their cannabis use? A prospective cohort study. *J. Psychopharmacol.* 30:159–68
Moore TH, Zammit S, Lingford-Hughes A, Barnes TR, Jones PB, et al. 2007. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet* 370:319–28
Morin JG, Afzali MH, Bourque J, Stewart SH, Seguin JR, et al. 2019. A population-based analysis of the relationship between substance use and adolescent cognitive development. *Am. J. Psychiatry* 176:98–106
Morral A, McCaffrey D, Paddock S. 2002. Reassessing the marijuana gateway effect. *Addiction* 97:1493–504
NASEM (Natl. Acad. Sci. Eng. Med.). 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: NASEM
Nielsen S, Gowing L, Sabioni P, Le Foll B. 2019. Pharmacotherapies for cannabis dependence. *Cochrane Database Syst. Rev.* 1:CD008940
Noble MJ, Hedberg K, Hendrickson RG. 2019. Acute cannabis toxicity. *Clin. Toxicol.* 57:735–42
Norberg M, Mackenzie J, Copeland J. 2012. Quantifying cannabis use with the timeline followback approach: a psychometric evaluation. *Drug Alcohol Depend.* 121:247–52
Pacheco-Colón I, Ramirez AR, Gonzalez R. 2019. Effects of adolescent cannabis use on motivation and depression: a systematic review. *Curr. Addict. Rep.* 6:532–46
Patton G, Harris J, Schwartz M, Bowes G. 1997. Adolescent suicidal behaviors: a population-based study of risk. *Psychol. Med.* 27:715–24
Patton G, Sawyer SM, Santelli JS, Ross DA, Afifi R, et al. 2016. Our future: a *Lancet* commission on adolescent health and wellbeing. *Lancet* 387:2423–78
Ramaekers JG, Mason NL, Theunissen EL. 2020. Blunted highs: pharmacodynamic and behavioral models of cannabis tolerance. *Eur. Neuropsychopharmacol.* 36:191–205
Rasic D, Weerasinghe S, Asbridge M, Langille D. 2013. Longitudinal associations of cannabis and illicit drug use with depression, suicidal ideation and suicidal attempts among Nova Scotia high school students. *Drug Alcohol Depend.* 129:49–53
Richmond-Rakerd LS, Fleming KA, Slutske WS. 2015. Investigating progression in substance use initiation using a discrete-time multiple event process survival mixture (MEPSUM) approach. *Clin. Psychol. Sci.* 4:167–82
Rogeberg O, Elvik R. 2016. The effects of cannabis intoxication on motor vehicle collision revisited and revised. *Addiction* 111:1348–59

Room R, Fischer B, Hall WD, Lenton S, Reuter P. 2010. *Cannabis Policy: Moving Beyond Stalemate*. Oxford, UK: Oxford Univ. Press

SAMHSA (Subst. Abuse Ment. Health Serv. Adm.) 2017a. *Results from the 2016 National Survey on Drug Use and Health: detailed tables*. Rep., SAMHSA, Rockville, MD

SAMHSA (Subst. Abuse Ment. Health Serv. Adm.). 2017b. *Treatment Episode Data Set (TEDS) 2005–2015. National admissions to substance abuse treatment services.* Rep., SAMHSA, Rockville, MD

Schmid Y, Scholz I, Mueller L, Exadaktylos AK, Ceschi A, et al. 2020. Emergency department presentations related to acute toxicity following recreational use of cannabis products in Switzerland. *Drug Alcohol Depend*. 206:107726

Schoeler T, Monk A, Sami MB, Klamerus E, Foglia E, et al. 2016. Continued versus discontinued cannabis use in patients with psychosis: a systematic review and meta-analysis. *Lancet Psychiatry* 3:215–25

Scott JC, Slomiak ST, Jones JD, Rosen AFG, Moore TM, Gur RC. 2018. Association of cannabis with cognitive functioning in adolescents and young adults: a systematic review and meta-analysis. *JAMA Psychiatry* 75:585–95

Silberberg C, Castle D, Koethe D. 2012. Cannabis, cannabinoids, and bipolar disorder. In *Marijuana and Madness*, ed. D Castle, R Murray, D D'Souza, pp. 129–36. New York: Cambridge Univ. Press

Smart R, Caulkins JP, Kilmer B, Davenport S, Midgette G. 2017. Variation in cannabis potency and prices in a newly legal market: evidence from 30 million cannabis sales in Washington state. *Addiction* 112:2167–77

Smart R, Pacula RL. 2019. Early evidence of the impact of cannabis legalization on cannabis use, cannabis use disorder, and the use of other substances: findings from state policy evaluations. *Am. J. Drug Alcohol Abuse* 45:644–63

Tait RJ, Caldicott D, Mountain D, Hill SL, Lenton S. 2016. A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment. *Clin. Toxicol.* 54:1–13

Tait RJ, Mackinnon A, Christensen H. 2011. Cannabis use and cognitive function: 8-year trajectory in a young adult cohort. *Addiction* 106:2195–203

Terry-McElrath YM, Patrick ME, O'Malley PM, Johnston LD. 2018. The end of convergence in developmental patterns of frequent marijuana use from ages 18 to 30: an analysis of cohort change from 1976–2016. *Drug Alcohol Depend*. 191:203–9

Townsend L, Flisher AJ, King G. 2007. A systematic review of the relationship between high school dropout and substance use. *Clin. Child Fam. Psychol. Rev.* 10:295–317

van der Pol P, Liebregts N, Brunt T, van Amsterdam J, de Graaf R, et al. 2014. Cross-sectional and prospective relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: an ecological study. *Addiction* 109:1101–9

van der Pol P, Liebregts N, de Graaf R, Korf DJ, van den Brink W, van Laar M. 2013. Predicting the transition from frequent cannabis use to cannabis dependence: a three-year prospective study. *Drug Alcohol Depend*. 133:352–59

van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, Verdoux H. 2002. Cannabis use and psychosis: a longitudinal population-based study. *Am. J. Epidemiol.* 156:319–27

van Ours JC, Williams J, Fergusson D, Horwood LJ. 2013. Cannabis use and suicidal ideation. *J. Health Econ.* 32:524–37

Verweij KJ, Abdellaoui A, Nivard MG, Cort AS, Ligthart L, et al. 2017. Genetic association between schizophrenia and cannabis use. *Drug Alcohol Depend*. 171:117–21

Verweij KJ, Huizink AC, Agrawal A, Martin NG, Lynskey MT. 2013. Is the relationship between early-onset cannabis use and educational attainment causal or due to common liability? *Drug Alcohol Depend*. 133:580–86

Volkow N, Swanson JM, Evins AE, DeLisi LE, Meier MH, et al. 2016. Effects of cannabis use on human behavior, including cognition, motivation, and psychosis: a review. *JAMA Psychiatry* 73:292–97

Wagner FA, Anthony JC. 2002. Into the world of illegal drug use: exposure opportunity and other mechanisms linking the use of alcohol, tobacco, marijuana, and cocaine. *Am. J. Epidemiol.* 155:918–25

Werneck MA, Kortas GT, de Andrade AG, Castaldelli-Maia JM. 2018. A systematic review of the efficacy of cannabinoid agonist replacement therapy for cannabis withdrawal symptoms. *CNS Drugs* 32:1113–29

WHO (World Health Organ.). 2019. *Global school-based student health survey (GSHS)*. Dataset, WHO, Geneva. **https://www.who.int/ncds/surveillance/gshs/datasets/en/**

Witt K, van Dorn R, Fazel S. 2013. Risk factors for violence in psychosis: systematic review and meta-regression analysis of 110 studies. *PLOS ONE* 8:e55942

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. *BMJ* 325:1199

Zehra A, Burns J, Liu CK, Manza P, Wiers CE, et al. 2018. Cannabis addiction and the brain: a review. *J. Neuroimmune Pharmacol.* 13:438–52

Zimmermann M, Chong AK, Vechiu C, Papa A. 2019. Modifiable risk and protective factors for anxiety disorders among adults: a systematic review. *Psychiatry Res.* 285:112705

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Errata

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