

Cannabis and Canada's children and youth

Christina N Grant, Richard E Bélanger; Canadian Paediatric Society Adolescent Health Committee

Posted: Nov 24 2016

Abstract

Cannabis is the most common illicit drug used worldwide and it is used frequently by Canadian teenagers. Cannabis use during adolescence can cause functional and structural changes to the developing brain, leading to damage. Marijuana use in this age group is strongly linked to: cannabis dependence and other substance use disorders; the initiation and maintenance of tobacco smoking; an increased presence of mental illness, including depression, anxiety and psychosis; impaired neurological development and cognitive decline; and diminished school performance and lifetime achievement. Rates of acute medical care and hospitalization for younger children who have ingested cannabis unintentionally are increasing. Ongoing debate concerning cannabis regulation in Canada makes paying close attention to the evidence for its health effects and ensuring that appropriate safeguards are in place, vital public health priorities.

Key Words: Adolescents; CUD; CWS; Neurodevelopment; THC; Youth

Cannabis refers to various psychoactive preparations of the plant Cannabis sativa, including marijuana (the dried and crushed leaves and flower buds), hashish (the resin of flower buds), and cannabis extracts (i.e., oils or wax). Common terms for marijuana include 'pot', 'grass' and 'weed'. Cannabis can be inhaled (as smoke or vapour) or ingested, depending on its form. When smoked, joints (cannabis cigarettes), blunts (cannabis cigars), and pipes (from personal devices to large, shared bongs) are commonly employed. A growing trend in e-cigarette use by youth has led to the more recent practice of 'vaping' cannabis.[1] 'Edibles' or marijuana-infused food products in various formats, including cookies and candies, may attract teens who wish to avoid smoking.[2]

Although some study participants claim that recreational cannabis use has positive effects,[3] most of the scientific literature has focused on its deleterious outcomes. In light of the current public debate on the decriminalization and legalization of cannabis in Canada, paediatricians and other health care providers need to be aware of the physical and mental health issues that are specific to cannabis use by youth as well as the risks to younger children of unintentional exposure. Cannabis use for medical purposes has been addressed in a recent position statement from the Canadian Paediatric Society.[4]

Incidence and prevalence

Cannabis is the world's most widely used illicit drug. In 2010. Canadian vouth ranked first for cannabis use among 43 countries and regions across Europe and North America, with one-third of youth (regardless of gender) having tried cannabis at least once by age 15. [5] Regional variations in the frequency of cannabis use exist, with Atlantic and Western provinces in Canada reporting higher use than other regions. [6] Indigenous youth are particularly at risk; nearly two-thirds of 15- to 19-year-old Inuit participants from an earlier study in Nunavik, Quebec, self-reported past-year use.[7] In Ontario, 13.8% of 7th to 12th graders reported pastmonth use for 2015, while 12th graders reported the highest daily use, at 5.6%.[8] Frequency of use increases as students progress through high school, yet global use among Canadian youth has declined since the turn of the century.

A concerning inverse relationship exists such that as the perceived harm related to cannabis use decreases. the frequency of cannabis use increases.[8] The effect of legalizing cannabis on rates of use in adolescents in some parts of the United States is under preliminary

study. Although early reports from Colorado and Washington do not appear to indicate a significant increasing prevalence among adolescents.[9][10] Colorado has recently reported one of the highest state prevalences for cannabis use in adolescents, while other states experienced a decline in use during the same period. Colorado has also reported increasing rates of use as students progress through high school,[10] while perceptions of risk declined among youth in both states.[9]

The effects of cannabinoids on the adolescent

Scientific research over the last 15 years has established that the human brain continues to develop into a person's early 20s. Concern is rising that exposure to cannabis during this important developmental period causes greater adverse effects in adolescents compared with older adults, whose brains are fully developed.[11][12] One of the main chemicals responsible for the perceptual and emotional changes associated with cannabis is delta-9-tetrahydrocannabinol (delta-9-THC), which stimulates the cannabinoid receptors. These receptors modulate the secretion of GABA (gamma-aminobutyric acid) and glutamate within the central nervous system, two neurotransmitters that have significant neurodevelopmental effects on the brain.[13] The frontal cortex, responsible for higher order cognitive processes such as judgment and decision-making, is undergoing rapid change and, as such, is more susceptible to THC.[14]-[16] The endocannabinoid system, which is involved in the maturation of cortical neuronal networks through the modulation of dopamine, is affected concurrently. When exogenous THC enters the system, it targets receptors in much higher quantities than endogenous cannabinoids and "floods" receptors, with two main results: a system that is no longer working as effectively and toxic changes to the neurons involved.[17]

Structural changes on MRI have also been documented in youth who use cannabis regularly. They show lower brain volumes, different folding patterns and thinning of the cortex. less neural connectivity and lower white matter integrity, all of which indicate damage by THC.[18] Finally, functional MRI studies in adolescents who use cannabis regularly have demonstrated increased neural activity, which means the brain is working harder to perform tasks. In other words, the brain must overcome or compensate for altered integrity caused by the effects of cannabis use.[19] Importantly, the THC content of marijuana available today is two to four times higher than from typical products used 40

years ago,[20] a factor likely to magnify impact on the adolescent brain.

Intoxication

The experience of being 'high' described by users encompasses a wide range of sensations, with euphoria, distorted perception and relaxation being the most common. Some users experience extreme anxiety and 'panic attack'-like symptoms.[21] Documented areas of impairment include short-term memory, performance of complex mental tasks, attention and judgment. Reaction times and motor skills are also compromised.[22] Many occasional users of cannabis only experience the intended effects of a high, but risks for an adverse experience still exist, especially for regular users.

Cannabis-impaired driving is now more prevalent among adolescents than alcohol-impaired driving.[8] In 2015, 9.8% of Ontario students in grades 10 to 12 with a driver's licence admitted to having driven after using cannabis at least once during the previous year.[8] One meta-analysis revealed that cannabis use more than doubled the risk of being in a motor vehicle accident. [23] Simulation studies have identified the deficits associated with driving under the influence of cannabis. with a lowered ability to stay within a lane being the driving skill most affected.[24][25] According to a recent survey, only 48% of Canadian teens 16 to 19 years of age recognized the danger of driving under the influence of cannabis, compared with 79% who recognized the risk of driving under the influence of alcohol.^[26] In fact, both cannabis and alcohol impair driving significantly, and it is likely that the effects are cumulative. [26] However, while blood ethanol levels are readily measurable and can establish recent use, reliable laboratory markers of acute cannabis use are still under investigation. Persistence of metabolites in urine for as long as 77 days after cessation of cannabis use has been described.[27]

Furthermore, consuming cannabis-infused edibles may inadvertently result in toxicity because absorption can take hours, compared with minutes when smoking.^[2] An individual who does not yet feel an effect may overconsume, and the unintended consumption of edibles manufactured to look like sweets by younger children is particularly concerning. In Colorado, rates of unintentional ingestion in children <9 years of age increased by 34% after legalization.[28] Thirty-five percent of these cases required hospitalization for overdose symptoms, including severe drowsiness and respiratory depression.[28]

Cannabis use disorder and cannabis withdrawal syndrome

It is estimated that one in six adolescents who use cannabis during their adolescence will meet criteria for dependence.[29][30] Cannabis use disorder (CUD), a new DSM 5 diagnosis, integrates cannabis abuse and dependence into a single entity.[31] CUD is defined as a problematic pattern of cannabis use leading to clinically significant impairment in areas of function or distress within a 12-month period.[31] Usually, adolescents experience the following functional impairments: reduced academic performance, truancy, reduced participation and interest in extracurricular activities, withdrawal from their usual peer groups, and conflict with family. The 12-month prevalence of CUD among North American adolescents is just above 3%, with males and older youth being disproportionately affected.[29]

Cannabis withdrawal syndrome (CWS) appears for the first time as a psychiatric diagnosis in the DSM 5.[31] CWS is defined by experiencing at least two of five psychological symptoms - irritability, anxiety, depressed mood, sleep disturbance, appetite changes and at least one of six physical symptoms – abdominal pain, shaking, fever, chills, headache, diaphoresis - after cessation of heavy cannabis use. Heavy cannabis use is defined as daily or near daily use for at least a few months. Withdrawal symptoms commonly occur 24 h to 72 h after last use^[32] and persist for one to two weeks. Sleep disturbance is often reported for up to one month. CWS may impede cannabis cessation and precipitate relapse.[32]

Cannabis use related to tobacco and other substances

Cannabis use is closely tied to the use of other substances, particularly alcohol and tobacco. Problem drinking among adolescents is strongly associated with cannabis use.[33] The use of marijuana and cigarettes at age 18 is predictive of heavy drinking at age 35.[34] Eighty percent of young cannabis users also smoke tobacco,[35][36] indicating a strong link between these two drugs. Cannabis use is also linked to tobacco via 'mulling': the addition of tobacco to cannabis cigarettes.[37] Mixing the two substances aids combustion and constitutes a significant exposure to nicotine.[38] Using both tobacco and cannabis concomitantly contributes significantly to symptoms of cannabis dependence because withdrawal symptoms following the simultaneous cessation from two substances are more severe than from one alone.[39]

Regarding other drugs, one prospective, longitudinal study demonstrated that cannabis use during adolescence is associated with a six-fold increase in future ecstasy consumption.^[40] A study from France of adults and adolescents reported past-year use of illicit drugs at 0.4% among cannabis non-users, compared with 25% among regular cannabis users.[41] A recent trend has been the consumption of synthetic cannabinoids. known colloquially as "K2" or "spice", which can be one hundred times more potent than THC[42] and have greater potential for toxic effects, including acute renal failure and death.[43]

Cannabis, depression and anxiety

Research suggests a strong association between daily cannabis use and depression in adolescents and young adults. However, a causal relationship has not been established. Epidemiological studies suggest that heavy cannabis use is associated with an increase in mood disorders, especially in individuals who may already be vulnerable to major depressive episodes (MDEs).[44][45] One study demonstrated a threefold higher risk for MDE.[46] Recent data suggest that cannabis use starting in adolescence and continuing into young adulthood is required for the association of cannabis with depression,[47] and the data confirming a specific association between cannabis use and anxiety disorders is weaker. However, one large cohort study found an association between frequent cannabis use and the incidence of anxiety symptoms in young adulthood. [48] It also appears that social anxiety disorder and post-traumatic stress disorder are risk factors for developing problematic patterns of cannabis use. [48][49]

Psychotic disorders and schizophrenia

Cannabis can produce an acute/transient psychosis in adolescents, even without a history of prior mental illness. Diverse psychotic symptoms have been reported, such as depersonalization, de-realization, dreamlike euphoria, disorientation, delusions, hallucinations and paranoid ideation.^[50] The strongest evidence of a direct effect of cannabis on perception and cognitive function comes from research involving healthy volunteers, who developed transient symptoms resembling schizophrenia after intravenous THC was administered.[51] In some adolescents, acute/transient psychotic symptoms persisted for days, prompting consultation for medical or psychiatric evaluation. Large longitudinal studies have demonstrated that more than 50% of youth who develop such symptoms will develop a future psychotic disorder.[52]

Although the absolute risk for developing psychosis is low, the risk for developing a psychotic outcome of any nature is increased by 40% in individuals who have used cannabis during their lifetime. [53] A strong association between heavy cannabis use and psychosis has been documented repeatedly in the literature. The association appears to be temporally related, demonstrates a dose-response relationship, and is biologically plausible. [54] One meta-analysis provided evidence of a relationship between cannabis use and onset of psychotic illness, thus supporting the hypothesis that cannabis use plays a causal role in the development of psychosis in some individuals, especially those who have a family or personal history of psychosis. [55]

Overall, individuals with a psychotic disorder show higher rates of cannabis use than those experiencing other mental disorders, with the exception of substance use disorder. More specifically, schizophrenia usually emerges toward the end of adolescence or in early adulthood, and accumulating evidence points to a causal relationship with heavy cannabis use. The prevalence of schizophrenia is about 1% in the adult population, and the risk of developing this illness is doubled in heavy cannabis users.^[55] Recent data indicates that using high-potency cannabis represents an even greater risk.^[56]

School performance, cognitive decline and lifetime achievement

The relationship between cannabis use and academic performance is complex. While direct causation between use and level of performance is uncertain, there are undeniable associations between cannabis use in youth and lower educational attainment.[57] This relationship could be due to the fact that students who do not do well in school are more likely to use cannabis. Alternatively, cannabis use and substandard educational attainment may have common risk factors.[57] However, the observation that cognitive function, particularly working memory, is impaired both acutely and in the days following cannabis use suggests a direct link between cannabis use and reduced educational achievement.[58] Short-term impairment in cognitive performance can lead students to fall behind, thus placing them at a disadvantage for future learning. Also, individuals who begin using cannabis in early adolescence or who chronically use cannabis are at risk for long-lasting cognitive impairments.[59] Specifically, deficits in decision-making skills, concept formation and planning have been reported, and studies suggest that cannabis users are less likely to complete high school.[57]

Scientific research is equivocal regarding the association between IQ and cannabis. Two recent longitudinal studies involving sets of twins indicated that the IQ scores of cannabis users declined significantly over time though not significantly more than in their noncannabis-using twin. [60] One large cohort study had previously found that IQ scores declined significantly among heavy cannabis users who were followed prospectively from adolescence to middle age. [61] A dose-response relationship was also found, such that the longer the duration of use, the greater the effect on IQ. If heavy cannabis use was sustained throughout follow-up, IQ scores dropped an average of 10 points. Also, when persistent users started heavy cannabis use during adolescence, their cognitive decline was greater than in individuals who started using after 18 years of age.

All the factors described above may contribute to higher unemployment levels, involvement in criminal activity, greater social assistance requirements as well as compound the lower levels of life satisfaction reported by heavy cannabis users. [62] While there are probably multiple explanations for the association between cannabis use and lower lifetime achievement, regular use can act as both cause and consequence. The point to bear in mind is that cognitive impairments have been linked to cannabis and some of these effects have a greater impact when cannabis is used in adolescence. [63] Among all trajectories of cannabis use, non-users consistently have the most favourable socio-economic and health outcomes at age 29, whereas early heavy users have the least. [13]

Conclusion

Youth should not use cannabis recreationally because its many potentially harmful effects are serious. These effects are present in the entire population; however, the developing brain is especially sensitive to the negative consequences of cannabis use. Canadian youth are at significant risk for developing CUD and, possibly, for doubling their risk of having a psychotic illness. Driving under the influence of cannabis increases the risk for motor vehicle accidents. Where cannabis has been legalized in the United States, children are requiring emergent medical care at greater rates due to unintentional ingestion.

The potential extension of the legal cannabis industry in Canada has raised a dilemma regarding the most appropriate age for its legal use, which should minimize harm to children and youth, the population most vulnerable to the product. On the one hand, prohibiting

cannabis use until the mid-twenties would protect adolescents during a period of critical brain development. On the other, adolescents and young adults are already experimenting frequently with marijuana. Aligning the legal age for cannabis use with that for other legally controlled substances, notably alcohol and tobacco, would help ensure that youth who have attained age of majority have access to a regulated product, with a known potency. Also, they would be less liable to engage in high-risk illegal activities to access cannabis.

Cannabis legislation will have a significant impact on the lives and health of children and youth, and safeguards are necessary. Based on the physical and mental health risks, and with many legal, financial and public safety issues at stake, policy makers - with support from physicians and the public at large - must continue to limit access to cannabis.

Recommendations

To protect children and adolescents from the harms associated with recreational cannabis use and cannabis dependence, the Canadian Paediatric Society recommends the following:

Governments should:

- Prohibit sales of all cannabis products to children and youth under the legal age for buying tobacco products and alcohol (18 or 19 years, depending on location).
- Consider limiting the concentration of THC in cannabis that 18- to 25-year-olds can purchase legally.
- · Enact and rigorously enforce regulations on the cannabis industry to limit the availability and marketing of cannabis to minors. These regulations must:
 - prohibit dispensaries from being located close to elementary, middle and high schools, licensed child care centres, community centres, residential neighbourhoods and youth facilities.
 - prohibit the sale of cannabis products by means of self-service displays or dispensing devices.
 - mandate strict labelling standards for all cannabis products, including a complete and accurate list of ingredients and an exact measure of cannabis concentration.

- mandate package warnings for all cannabis products, including known and potential harmful effects of exposure (e.g., to young children and the fetus during pregnancy), similar to messaging on cigarette packaging.
- mandate and enforce strict marketing and promotional standards, including a ban on all cannabis industry-related advertising and on the sponsorship of events, activities or permanent facilities by the cannabis industry.
- mandate and enforce a ban on the marketing of cannabis-related products using strategies or venues that attract children and youth, including (but not limited to) 'candy-like' edibles, 'giveaways' and promotion through social media.
- restrict the online sales of all cannabis and related products only to individuals identified as being older than the legal drinking age in the province or territory where they reside.
- Extend and align existing anti-tobacco legislation at all government levels to include cannabis (i.e., prohibiting smoking in public venues, smoking in cars where a child is present).
- · Fund public education campaigns to reinforce that cannabis is not safe for children and youth by raising awareness of the harms associated with cannabis use and dependence. These campaigns should be developed in collaboration with youth leaders and should include messages from young opinion-leaders.
- · Invest in the development and implementation of programs for routine roadside detection of cannabinoids and determine suitable consequences for vouth who are found to be under the influence.
- · Increase funding for the research, prevention and treatment of substance use in adolescents and young adults.
- · Increase funding for mental health promotion and for treating mental illness in this age group.
- Consult with Indigenous communities on adapting legislation, preventative measures and/or interventions to meet local conditions and cultural requirements.
- · Actively monitor the impacts on youth of changes to cannabis legislation.

Health care providers should:

- · Be aware of and communicate the health risks related to cannabis use.
- Screen all children and youth for cannabis exposure and/or use and educate adolescents and families on the health risks and harms associated with cannabis.
- Provide anticipatory guidance to parents and older children on the potential health risks of cannabis use.

Acknowledgements

This statement has been reviewed by the Bioethics. Community Paediatrics, Drug Therapy and Hazardous Substances and Mental Health and Developmental Disabilities Committees of the Canadian Paediatric Society. The authors wish to acknowledge Dr. Heather VanderMeulen's contribution to the manuscript sections on cannabis-impaired driving and school performance, cognitive decline and lifetime achievement.

References

- 1. Morean ME, Kong G, Camenga DR, Cavallo Da, Krishnan-Sarin S. High school students' use of electronic cigarettes to vaporize cannabis. Pediatrics 2015;136(4): 611-6.
- 2. Friese B, Slater MD, Annechino R, Battle RS. Teen use of marijuana edibles: A focus group study of an emerging issue. J Prim Prev 2016;37(3):303-9.
- 3. Morgan CJ, Noronha LA, Muetzelfeldt M, Feilding A, Curran HV. Harms and benefits associated with psychoactive drugs: Findings of an international survey of active drug users. J Pyschopharmacol 2013;27(6): 497-506.
- 4. Rieder MJ, Canadian Paediatric Society, Drug Therapy and Hazardous Substances Committee. Is the medical use of cannabis a therapeutic option for children? Paediatr Child Health 2016;21(1):31-8.
- 5. WHO. Social determinants of health and well-being among young people. Health behaviour in school-aged children (HBSC) study: International report from the 2009/2010 survey. Copenhagen: WHO Regional Office for Europe, 2012.
- Health Canada, Canadian alcohol and drug use monitoring survey (CADUMS): Canadians aged 15 years and older 2012: http://www.hc-sc.gc.ca/hc-ps/drugs-drogues/ stat/ 2012/summary-sommaire-eng.php September 19, 2016).
- 7. Brunelle N, Plourde C,, Landry M, et al. Patterns of psychoactive substance use among youths in Nunavik. Indittera 2010;2:1-12.
- 8. Boak A, Hamilton HA, Adlaf EM, Mann RE. Drug use among Ontario students, 1977-2015: Detailed OSDUHS

- findings. CAMH Research Document Series, no. 41. Toronto, Ont.: Centre for Addiction and Mental Health,
- 9. Colorado Department of Public Safety. Marijuana legalization in Colorado: Early findings; A report pursuant to March senate bill 13-283. 2016: cdpsdocs.state.co.us/ors/docs/reports/2016-SB13-283-Rpt.pdf (Accessed September 19, 2016).
- 10. Roffman R. Legalization of cannabis in Washington State: How is it going? Addiction 2016; 111(7):1139-40.
- 11. Giedd JN, Blumenthal J, Jeffries NO, et al. Brain development during childhood and adolescence: A longitudinal MRI study. Nat Neurosci 1999;2(10):861-3.
- 12. Lenroot RK. Giedd JN. Brain development in children and adolescents: Insights from anatomical magnetic resonance imaging. Neurosci Biobehav Rev 2006;30(6): 718-29.
- 13. Hurd YL, Michaelides M, Miller ML, Jutras-Aswad D. Trajectory of adolescent cannabis use on addiction vulnerability. Neuropharmacology 2014;76 Pt B:416-24.
- 14. George T, Vaccarino F, eds. Substance abuse in Canada: The effects of cannabis use during adolescence. Ottawa. Ont.: Canadian Centre on Substance Abuse. 2015.
- 15. Blakemore SJ. Teenage kicks: Cannabis and the adolescent brain. Lancet 2013;381(9870):888-9.
- 16. Anderson VA, Anderson P, Northam E, Jacobs R, Catroppa C. Development of executive functions through late childhood through late adolescence in an Australian sample. Dev Neuropsychol 2001;20(1):385-406.
- 17. Bossong MG, Niesink RJ. Adolescent brain maturation, the endogenous cannaboid system and the neurobiology of cannabis-induced schizophrenia. Prog Neurobiol 2010;92(3):370-85.
- 18. Lisdahl KM, Wright NE, Kirchner-Medina C, Maple KE, Shollenbarger S. Considering cannabis: The effects of regular cannabis use on neurocognition in adolescents and young adults. Curt Addict Rep 2014;1(2):144-56.
- 19. Jager G, Block RI, Luijten M, Ramsay NF. Cannabis use and memory brain function in adolescent boys: A crosssectional multicenter functional magnetic resonance imaging study. J Am Acad Child Adolesc Psychiatry 2010;49(6):561-72.
- 20. Cascini F, Aiello C, Di Tanna G. Increasing delta-9tetrahydrocannabinol (?-9-THC) content in herbal cannabis over time: Systematic review and meta-analysis. Curr Drug Abuse Rev 2012;5(1):32-40.
- 21. Karila L, Roux P, Rolland B, et al. Acute and long-term effects of cannabis use: A review. Curr Pharm Des 2014;20(25):4112-8.
- 22. Li MC, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, Li G. Marijuana use and motor vehicle crashes. Epidemiol Rev 2012:34:65-72.
- 23. Papafotiou K, Carter JD, Stough C. The relationship between performance on the standardised field sobriety tests, driving performance and the level of Delta-9tetrahydrocannabinol (THC) in blood. Forensic Sci Int 2005;155(2-3):172-8.

- 24. Ramaekers JG, Robbe HW, O'Hanlon JF. Marijuana, alcohol and actual driving performance. Hum Psychopharmacol 2000;15(7):551-8.
- 25. Hartman RL, Brown TL, Milavetz G, et al. Cannabis effects on driving lateral control with and without alcohol. Drug Alcohol Depend 2015;154:25-37.
- 26. Canadian Council of Motor Transport Administrators. Public Opinion Survey on Drugs and Driving – Summary http://ccmta.ca/images/publications/pdf// CCMTA_Public_Opinion_Survey_of_Drugs_and_Driving_ir (Accessed September 26, 2016).
- 27. Smith-Kielland A, Skuterud B, Mørland J. Urinary excretion of 11-nor-9-corboxy-delta9- tetrahydrocannabinol and cannabinoids in frequent and infrequent drug users. J Anal Toxicol 1999:23(9):323-32.
- 28. Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional pediatric exposures to marijuana in Colorado, 2009-2015. JAMA Pediatr 2016;170(9):e160971.
- 29. Turner SD, Spithoff S, Kahan M. Approach to cannabis use disorder in primary care: Focus on youth and other high-risk users. Can Fam Physician 2014;60(9):801-8, e423-32.
- 30. Volkow ND. Baler RD. Compton WM. Weiss SR. Adverse effects of marijuana use. N Engl J Med 2014;370(23):2219-27.
- 31. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Arlington, VA: APA, 2013.
- 32. Budney AJ, Hughes JR. The cannabis withdrawal syndrome. Curr Opin Psychiatry 2006;19(3):233-8.
- 33. Georgiades K, Boyle MH. Adolescent tobacco and cannabis use: Young adult outcomes from the Ontario child health study. J Child Psychol Psychiatry 2007;48(7):724-31.
- 34. Merline A, Jager J, Schulenberg JE. Adolescent risk factors for adult alcohol use and abuse: Stability and change of predictive value across early and middle adulthood. Addiction 2008;103(Suppl 1):84-99.
- 35. Suris JC, Akre C, Berchtold A, Jeannin A, Michaud PA. Some go without a cigarette: Characteristics of cannabis users who have never smoked tobacco. Arch Pediatr Adolesc Med 2007;161(11):1042-7.
- 36. Degenhardt L, Coffey C, Carlin JB, Swift W, Moore E, Patton GC. Outcomes of occasional cannabis use in adolescence: 10-year follow-up study in Victoria, Australia. Br J Psychiatry 2010;196(4):290-5.
- 37. Bélanger RE, Akre C, Kuntsche E, Gmel G, Suris JC. Adding tobacco to cannabis-- its frequency and likely implications. Nicotine Tob Res 2011;13(8):746-50.
- 38. Bélanger RE, Marclay F, Berchtold A, Saugy M, Cornuz J. Suris JC. To what extent does adding tobacco to cannabis expose young users to nicotine? Nicotine Tob Res 2013;15(11): 1832-8.
- 39. Vandrey RG, Budney AJ, Hughes JR, Liquori A. A within-subject comparison of withdrawal symptoms during abstinence from cannabis, tobacco, and both substances. Drug Alcohol Depend 2009;92(1-3):48-54.

- 40. Zimmerman P, Wittchen HU, Waszak R, Nocon A, Höfler M, Lieb R. Pathways into ecstasy use: The role of prior cannabis use and ecstasy availability. Drug Alcohol Depend 2005;79(3):331-41.
- 41. Beck F, Legelye S, Spilka S. Multiple psychoactive substance use (alcohol, tobacco and cannabis) in the French general population in 2005. Presse Med 2008;37(2 Pt 1):207-15.
- 42. Bebarta VS, Ramirez S, Varney SM. Spice: A new "legal" herbal mixture abused by young active duty military personnel. Subst Abus 2012:33(2):191-4.
- 43. National Conference of State Legislatures. Synthetic cannabinoids (aka "K2"/"Spice") enactments. Washington, DC. 2012: http://www.ncsl.org/issues-research/justice/synthetic-cannabinoids-enactments.aspx (Accessed September 19, 2016).
- Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. Cannabis use and mental health in young people: Cohort study. BMJ 2002;325(7374):1195-8.
- 45. Rubino T, Zamberletti E, Parolaro D. Adolescent exposure to cannabis: A risk for psychiatric disorders. J Psychopharmacol 2012;26(1):177-88.
- 46. Rey JM, Sawyer MG, Raphael B, Patton GC, Lynskey M. Mental health of teenagers who use cannabis: Results from an Australian study. Br J Psychiatry 2002;180:216-21.
- 47. Meier MH, Hall W, Caspi A, et al. Which adolescents develop persistent substance dependence in adulthood? Using population-representative longitudinal data to inform universal risk assessment. Psychol Med 2016;46(4):877-89.
- 48. Buckner JD, Schmidt NB, Lang AR, Small JW, Schlauch RC, Lewinson PM. Specificity of social anxiety disorder as a risk factor for alcohol and cannabis dependence. J Psychiatr Res 2008;42(3):230-39.
- 49. Cornelius JR, Kirisci L, Reynolds M, Clark DB, Hayes J, Tarter R. PTSD contributes to teen and young adult cannabis use disorders. Addict Behav 2010;35(2):91-4.
- 50. Johns A. Psychiatric effects of cannabis. Br J Psychiatry 2001:178:116-22.
- 51. D'Souza DC, Perry E, MacDougall, et al. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: Implications for psychosis. Neuropsychopharmacology 2004;29(8):1558-72.
- 52. Arendt M, Rosenberg R, Foldager L, Perto G, Munk-Jørgensen P. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: Follow-up study of 535 incident cases. Br J Psychiatry 2005;187(6):510-5.
- 53. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review. Lancet 2007;370(9584):319-28.
- 54. Radhakishnan R, Wilkinson ST, D'Souza DC. Gone to pot-- A review of the association between cannabis and psychosis. Front Psychiatry 2014;5:54.
- Large M, Sharma S, Compton MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: A systematic meta-analysis. Arch Gen Psychiatry 2011;68(6): 555-61.

- Di Forti M, Sallis H, Allegri F, et al. Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. Schizophr Bull 2014;40(6): 1499-508.
- 57. Lynskey M, Coffey C, Degenhardt L, Carlin JB, Patton G. A longitudinal study of the effects of adolescent cannabis use on high school completion. Addiction 2003;98(5):685-92.
- Brook JS, Stimmel MA, Zhang C, Brook DW. The association between earlier marijuana use and subsequent academic achievement and health problems: A longitudinal study. Am J Addict 2008;17(2):155-60.
- Fergusson DM, Horwood LJ, Beautrais AL. Cannabis and educational achievement. Addiction 2003;98(12): 1681-92.
- Jackson NJ, Isen JD, Khoddam R, et al. Impact of adolescent marijuana use on intelligence: Results from two longitudinal twin studies. Proc Natl Acad Sci USA 2016;113(5):E500-8.

- Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci USA 2012;109(40):E2657-64.
- Fergusson DM, Biden JM. Cannabis use and later life outcomes. Addiction 2008;103(6):969-76.
- 63. Schweinsburg AD, Brown SA, Tapert SF. The influence of marijuana use on neurocognitive functioning in adolescents. Curr Drug Abuse Rev 2008;1(1):99-111.

CPS ADOLESCENT HEALTH COMMITTEE

Members: Giuseppina Di Meglio MD, Natasha Johnson MD, Margo Lane MD (Chair), Karen Leis MD (Board Representative), Mark Norris MD, Gillian Thompson NP-Paediatrics (past member), Ellie Vyver MD

Liaison: Christina N Grant MD, CPS Adolescent Health Section

Principal authors: Christina N Grant MD, Richard E Bélanger MD