Cannabis Concentration and Health Risks

A report for the Washington State Prevention Research Subcommittee (PRSC)

November 2020

In this report:

Joint University of Washington and Washington State University Workgroup:

Beatriz Carlini (Chair)
Celestina Barbosa-Leiker
Carrie Cuttler
Julia Dilley
Caislin Firth
Kevin Haggerty
Jason Kilmer
Michael McDonell
Nephi Stella
Denise Walker
Dale Willits

With:

Sara Broschart, *WA State Liquor and Cannabis Board*
Trecia Ehrlich, *WA State Liquor and Cannabis Board*
Kristen Haley, *WA State Department of Health*
Christine Steele, *WA State Health Care Authority, Division of Behavioral Health & Recovery*
Liz Wilhelm, *Prevention WINS*

Introduction and Consensus Statement

Across the State of Washington, individuals, families, communities, and health care systems are struggling to cope with substance use, misuse, and substance use disorders. Fortunately, we have made considerable progress in recent years. Decades of scientific research and technological advances have given us a better understanding of how we can effectively prevent harmful substance use. Yet, in a time of legalized retail cannabis sales, one question keeps getting raised….is high potency cannabis use safe for the citizens of Washington State? High potency cannabis typically includes products such as concentrated oils and butters that can contain up to 99% THC. The Division of Behavioral Health and Recovery at the Health Care Authority has a scientific advisory group, the Prevention Research Sub Committee. In March 2020, the sub-committee invited a work group of researchers to better understand the scientific evidence of the health and behavioral risks are of high potency cannabis use. The intent of the workgroup was to help inform policy and practice with the best science available.

The workgroup was organized and chaired by Dr. Bia Carlini at the UW Alcohol and Drug Abuse Institute. Dr. Carlini invited scientists in the field to present the evidence to each other in order to come to a consensus statement. The Prevention Research Sub Committee is grateful to the contributions from all these scientists.

Researchers from both Washington State University and University of Washington as well as others, worked together to address this important question. The charge of the workgroup was to provide policy makers with a summary of evidence on risk to health and behavior related to high potency cannabis. This report provides a consensus statement related to the health and behavior risk of high potency cannabis and offers a summary of research evidence supporting the consensus statement.

Kevin Haggerty, PhD, Social Development Research Group, University of Washington
Chair, Washington State Prevention Research Subcommittee (PRSC)

Why a consensus statement?

Once upon a time, cannabis use was mostly synonymous with consuming the cannabis plant. Anti-prohibition movements embraced the color green and the emblematic image of cannabis' pointy leaves to promote policy change. In the not so distant past, cannabis had 3-8% THC content. THC content of more than 10% was considered high-potency cannabis.

Fast forward to 2020 and cannabis cultivation, processing, and sales are run by for-profit enterprises in many US states. Cannabis lives in the world of business where product development and marketing are essential for survival. In WA State, product development has meant the disappearance of cannabis plants with less than 10% of THC. Twenty percent and over has become the new normal[1].

Meanwhile, cannabis as we knew it has changed. Processing, extraction, concentration, and the addition of new ingredients have become common. Highly potent manufactured cannabis products are available in retail stores, with THC content varying from 60-90%. They don't resemble the plant – they are as close to the cannabis plant as strawberries are to frosted strawberry pop tarts. Manufactured cannabis extracts now represent 35% of the WA cannabis market[2], up from 9% in 2014[3].

With such rapid change, science is lagging behind. Research funding takes time to obtain and federal policies prohibit studies that involve products consumed in the real world. This Consensus Statement and accompanying report represent a collective six-month effort of well-accomplished WA state scientists. Members of state agencies and community-based

organizations kindly volunteered to participate in workgroup meetings, serving as "real world" referees to this unprecedented effort in WA State.

We selected good quality cannabis studies that compare cannabis health risks utilizing a dose-response approach. Recent population data studies, collected after legalization, are also included, comparing risks of using cannabis flower with higher concentration manufactured products. While much more research is needed, this body of work has been an effort to have science to serve its purpose: guide informed policy debates and advance health and well-being.

References

1. Smart R, Caulkins JP, Kilmer B, Davenport S, Midgette G. Variation in cannabis potency and prices in a newly legal market: evidence from 30 million cannabis sales in Washington State. *Addiction*. 2017;112(12):2167-2177.
2. Kilmer, Beau, Steven Davenport, Rosanna Smart, Jonathan P. Caulkins, and Gregory Midgette, After the Grand Opening: Assessing Cannabis Supply and Demand in Washington State. Santa Monica, CA: RAND Corporation, 2019. https://www.rand.org/pubs/research_reports/RR3138.html.
3. *WA State House Commerce and Gaming Commission work session. Sep 15, 2020.* https://www.tvw.org/watch/?eventID=2020091004

Beatriz H Carlini, PhD, MPH,
Alcohol and Drug Abuse Institute and School of Public Health, University of Washington
Chair, PRSC Cannabis Concentration Workgroup

Consensus Statement

Members of this workgroup make up an interdisciplinary team which worked collaboratively to integrate current scientific knowledge about how THC concentration in cannabis affects the health and safety of consumers, and to produce this consensus statement. Our intent is to provide policy makers with a summary of evidence on topics of public health importance related to cannabis concentration.

Research Context

While more research is needed and research to date contains inherent limitations, evidence exists to make some well-supported assertions. It is helpful to first understand the range of studies examined, how they were conducted, and the challenges in drawing broad conclusions.

Unlike research on alcohol, which utilizes percent alcohol (proof) as a measure of potency, cannabis studies lack a consistent definition of what high potency cannabis products include. Potency of cannabis is typically defined by the amount of THC within cannabis products, with varying cut-offs; and more recently by mode of cannabis administration of high THC potency manufactured products such as cannabis concentrates (wax, shatter), and liquid extracts used in vaping devices and infused edibles (candy or cookies),

For these reasons, the workgroup synthesized the evidence on: a) the dose-response relationship between THC content and health outcomes and b) adverse events associated with consuming highly concentrated manufactured products. The gold standard of research is the Randomized Controlled Trial (RCT) in which study participants are randomized to receive an exposure or not, in this case to high potency cannabis. However, RCTs are not always possible or ethical to conduct in humans. Research on non-medical use of cannabis and opioids, and tobacco and alcohol consumption must rely on alternative study designs and use sophisticated statistical methods to mimic RCTs in order to draw conclusions.

- Evidence-based drug policy decisions have often been informed by proven methodologies in the form of observational studies where researchers do not intervene on study participants but observe them over time or animal studies, in which randomization can occur.
- In our review, we selected good quality animal studies and rigorously designed human studies that recruited people with a particular health outcome and compared their use of cannabis to usage among similar participants without that same health outcome. We also relied on surveys and secondary data analysis, where people report their cannabis use patterns, health behaviors, and health outcomes. These are the same designs and approaches that guide clinical and policy decisions for other substances, when used for non-medical purposes.

Why cannabis concentration matters

Cannabis concentrates are increasing in popularity in Washington state. Cannabis users are more likely to use concentrated forms of cannabis through dabbing, eating, or vaping than prior to legalization.

Who is affected?

In Washington state, dabbing - a method of consuming cannabis that results from a high dose of highly concentrated cannabis exposure in just one exposure is more common among adults who use more cannabis overall: men, younger adults, and low socio-economic populations (low income households, no health insurance). Current evidence suggests that adults who regularly consume cannabis may be able to self-titrate their use of cannabis products, adjusting their intake to compensate for potency. For adults, this may mitigate increased detrimental effects of high potency products in some areas. Dabbing is also more common among Latinx adults and people who report poor mental health.

Young people are particularly vulnerable to negative effects of high potency cannabis. Calls to Poison Centers about manufactured cannabis products (edibles, concentrates, and vaping liquids) are increasing nationally, while stable for use of cannabis flower. Negative effects from manufactured products are especially high among children, and exposure to vaping liquids is more likely to need medical intervention. There is strong evidence on the detrimental impact of THC use during adolescence (14-18 years of age), and negative impacts may be higher for adolescents who use cannabis with high THC concentration or use more frequently. Use of cannabis with high THC concentration increases the chances of developing cannabis use disorder or addiction to cannabis, particularly among adolescents.

High potency cannabis use can have lifelong mental health consequences, which often manifest in adolescence or early adulthood. Daily cannabis use, particularly of high potency products, increases the risk of developing a psychotic disorder, like schizophrenia, and is related to an earlier onset of symptoms compared to people who do not use cannabis. Among those with a psychotic disorder diagnosis, the use of high potency cannabis exacerbates disease symptoms. The role of which types of cannabis use are more likely to exacerbate pre-existing mental health conditions is an emerging area of research.

Cannabis use during pregnancy is associated with negative health impacts for infants (low birth weight, decreased IQ scores, attention problems) and can have social and legal repercussions for the pregnant woman. It is unclear to date whether use of cannabis with high THC concentration during pregnancy poses greater risk for poor health outcomes among infants. Similarly, while research supports a link between cannabis consumption and driving impairment, no consensus exists on THC concentration levels and ensuing impairment.

Conclusion

Workgroup members have reached consensus that research available to date documents that THC content of cannabis products contributes to adverse health effects in a dose-response manner. This increased risk imposed from using higher potency cannabis products is particularly concerning for young users and those with certain pre-existing mental health conditions. These harms are likely to disproportionately affect marginalized populations (low income, minorities) who choose high potency products because of their lower costs, ease and discrete nature of use, glamorization of its use through social media and advertising, and perception of safety.

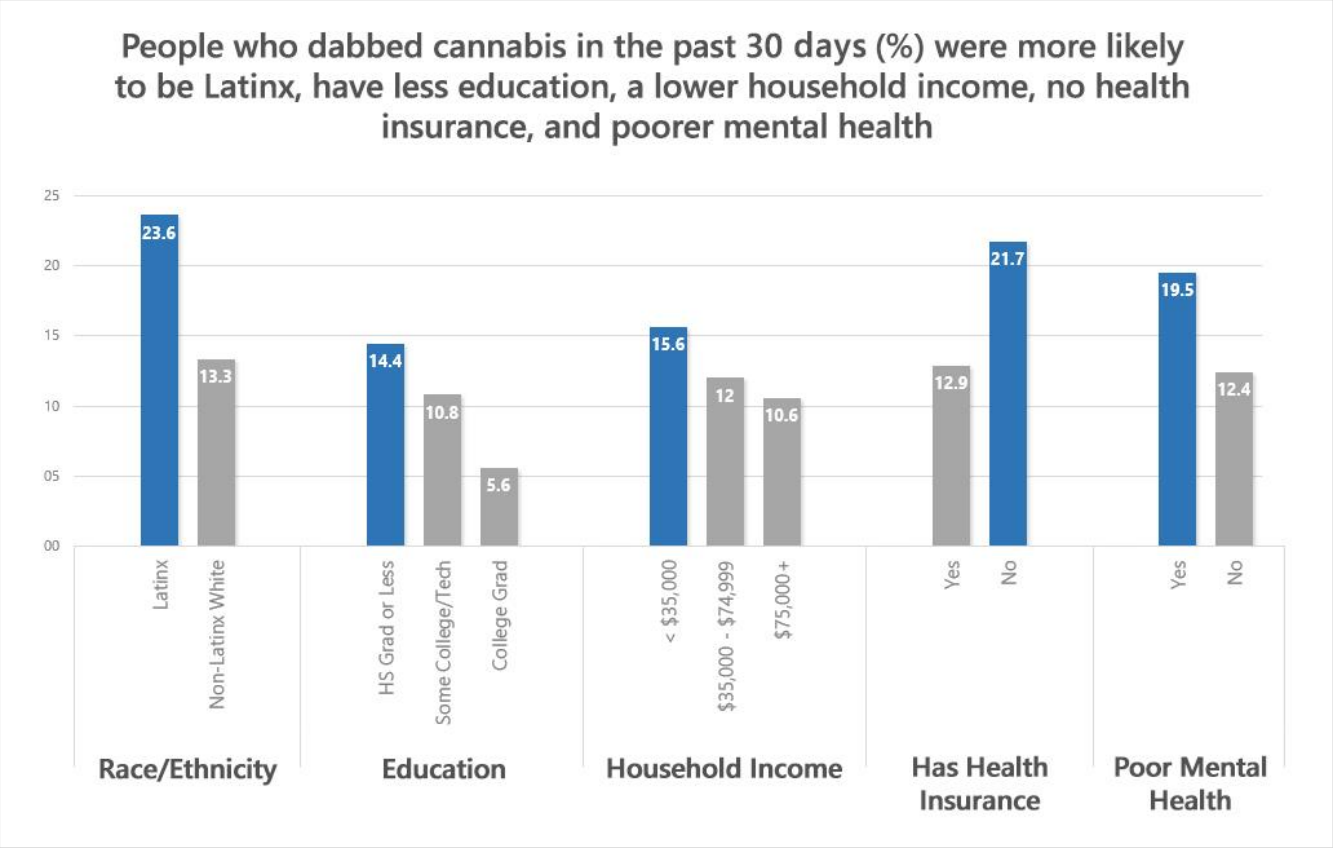
Epidemiology of Adult Cannabis Users in Washington State who Dab, Eat, or Vape Cannabis

Caislin Firth, PhD, MPH, Alcohol & Drug Abuse Institute, University of Washington

Using 2015-2017 Washington Behavioral Risk Factor Surveillance System (BRFSS)[1] data, we were able to identify populations of cannabis users who are more likely to use concentrated forms of cannabis by dabbing, eating, or vaping. We examined socio-demographic differences in specific modes of cannabis administration among adults who used cannabis in the past 30 days.

Because measuring THC content in cannabis products is not feasible for large population-based studies, a more common approach is to collect detailed information on the modes of cannabis administration that typically use concentrated cannabis products. Namely, dabbing, eating, or vaping cannabis. These modes of cannabis administration use solid or liquid concentrated products that have higher levels of THC content compared to cannabis flower,[2,3] and these modes of use have been associated with adverse health events like acute toxicity, emergency department visits, and poison center calls.[4,5] Unlike using a vaping device or consuming packaged edibles, dabbing is a riskier method of consuming cannabis because users are not able to effectively titrate their dose.[6] In addition, illicit cannabis cartridges made news headlines last year as contaminated cartridges caused an outbreak of lung injury.[7]

The purchase of concentrates from cannabis retailers is on the rise.[8] By October 2019, concentrates accounted for 35% of the cannabis market in Washington state, from 9% in 2014 and 27% in 2017[9], and the price for 10mg THC was cheaper when purchased as a solid concentrate instead of flower.[2] These findings are not unique to Washington. In Oregon, over half of the cannabis market share was for non-flower products by the end of 2018.[8]



*Poor mental health = >14 "poor mental health" days of past 30

People who report low socio-economic status, being of Latinx descent, and poor mental health are more likely do dab in Washington. Adults with a high school diploma or less and low income (below $35,000 annual household income) were more likely to use cannabis and report dabbing, a mode of consumption that implies a large intake of highly potent cannabis in one hit. Men and adults under the age of 35 also reported more cannabis use and were more likely to dab. In addition, adults without health insurance and those who suffered from poor mental health (as defined by at least 14 poor mental health days in the past month) were more likely to use cannabis and dab. Unlike previous population groups who used more cannabis and dabbed, Latinx adults used less cannabis compared to white adults but were more likely to report dabbing in the past month. Lesbian, Gay, and Bisexual adults were three times as likely to report using cannabis than heterosexual adults, but LGB adults were no more likely to dab than heterosexual adults.

In contrast, vaping is associated with high income households. The highest use of vaping was among 35 to 44 year old adults, adults with college degrees, and households that made over $75,000. Similarly, preferences for using edibles were highest among college graduates. There were no other population group differences in edible use.

Take Away: High potency cannabis extracts are increasing in popularity and segments of the population who are more likely to use cannabis tend to also report more dabbing. In Washington, marginalized communities and vulnerable individuals are more likely to use high-potency concentrates through dabbing. There are two notable exceptions: Lesbian, Gay, and Bisexual adults are 3 times as likely to use cannabis but do not prefer dabbing any more than heterosexual adults do, and Latinx adults are less likely to use cannabis but when they do, they prefer dabbing over non-Latinx, white adults.

Context: BRFSS surveys use well established methods of data collection from representative samples that enable individuals from diverse backgrounds to report their behaviors anonymously, allowing for fair public policy planning. While BRFSS data does not collected the exact concentration of cannabis products used, data on modes of consumption and types of products used are a valid – while not perfect – strategy to determine who is more likely to use cannabis in different ways.

References

1. Washington State Department of Health. Behavioral Risk Factor Surveillance System (BRFSS). https://www.doh.wa.gov/DataandStatisticalReports/DataSystems/BehavioralRiskFactorSurveillanceSystemBRFSS. Accessed August 4, 2020
2. Davenport S. Price and product variation in Washington's recreational cannabis market. *Int J Drug Policy*. 2019; 102547. doi:10.1016/j.drugpo.2019.08.004
3. Cinnamon Bidwelll L, YorkWilliams SL, Mueller R, Bryan AD, Hutchison KE. Exploring cannabis concentrates on the legal market: User profiles, product strength, and health-related outcomes. *Addict Behav Reports.* August 2018;102-106. doi:10.1016/j.abrep.2018.08.004
4. Fischer B, Russell C, Sabioni P, et al. Lower-Risk Cannabis Use Guidelines: A Comprehensive Update of Evidence and Recommendations. 2017; doi:10.2105/AJPH.2017.303818
5. Pierre JM, Gandal M, Son M. Cannabis-induced psychosis associated with high potency "wax dabs." *Schizophr Res.* 2016;172(1-3):211-212. doi:10.1016/j.schres.2016.01.056
6. Sagar KA, Lambros AM, Dahlgren MK, Smith RT, Gruber SA. Made from concentrate? A national web survey assessing dab use in the United States. *Drug Alcohol Depend.* 2018;190:133-142. doi:10.1016/j.drugalcdep.2018.05.022
7. Centers for Disease Control and Prevention. Outbreak of Lung Injury Associated with the Use of E-Cigarette, or Vaping, Products. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html#epi-chart. Accessed August 4, 2020.
8. Firth CL, Davenport S, Smart R, Dilley JA. How high: Differences in the developments of cannabis markets in two legalized states. *Int J Drug Policy*. 2020;75:102611. doi:10.1016/j.drugpo.2019.102611
9. Washington Liquor and Cannabis Board. Cannabis potency policy considerations. Commerce & Gaming Committee, Washing State House of Representatives. September 2020. https://www.tvw.org/watch/?eventID=2020091004

High Potency Cannabis, Residues and Contaminants

Beatriz Carlini, PhD MPH, Alcohol & Drug Abuse Institute, University of Washington

Contamination of cannabis products in the Washington legal market has been an issue for all cannabis products. Pesticides, heavy metals, mold and fungi have been identified and documented in cannabis sold in WA and other legal markets. High potency cannabis concentrates need extra production steps to be manufactured, adding the potential for more contaminants like solvents and additives. Solvents are used in the manufacturing of concentrates (with the exception of hash). In the case of concentrates in cartridges, sold for vaping, **additives** are needed to make vaporization possible. There are several different additives that companies use including propylene glycol, polyethylene glycol, vegetable glycerin, medium-chain triglycerides, vitamin E acetate, and even terpenes.[1]

A study of 57 samples of concentrates sold for dabbing in California found that 71.9% of them had residual solvents.[2] Isopentane was the most frequently detected residual solvent, followed by butane, heptane, hexane, isobutene, isopropyl alcohol, neopentane, pentane, and propane. A third of the samples analyzed had pesticide residues. The most frequently found pesticide was paclobutrazol, a plant growth regulator. Other pesticides found were bifenthrin and myclobutanil.[3]

Edible cannabis products are manufactured with food ingredients. As such, they are subject to the same types of contamination as any conventional food production[4] and need to be closely regulated. Due to federal prohibition, this regulation is still far from ideal.

Health effects due to contaminants and residues. The most known negative effect due to residues and contamination of cannabis products is EVALI, an acute lung injury outbreak during the Summer of 2019 that resulted in 2,807 hospitalizations and 68 deaths nationwide.[5] The additive Vitamin E acetate, present in both illegal and legal cartridges sold nationwide, has been identified as the agent for EVALI. This crisis could have been avoided with proper regulation of these products.

A growing but still small number of studies have reported negative effects of other high potency cannabis. Examples are a case of neuro-and cardiotoxicity presented in emergency departments attributed to dabbing[6] and an analysis of health insurance claims found that cannabis users were 3.5 times more likely than persons who did not use cannabis to have a fungal infection in 2016.[7]

Take Away: Manufactured cannabis products such as high potency concentrates are more likely to contain residues and contaminants due to the extra steps needed for their production, including solvent-base extraction and additives. The health effects of exposing human lungs to possible residues are still not fully known.

Context: Sales of manufactured cannabis products are increasing faster than flower in the US legal cannabis market, increasing the chances of new outbreaks such as EVALI. State agency task forces to advance testing and regulations on these products are urgently needed and are currently being put in place in Washington.

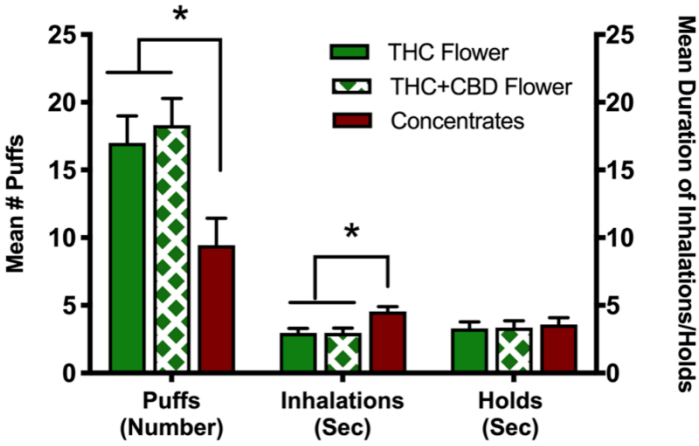
References

1. Russo EB. Current Therapeutic Cannabis Controversies and Clinical Trial Design Issues. *Front Pharmacol*. 2016;7:309. Published 2016 Sep 14. doi:10.3389/fphar.2016.00309.
2. Cannabis Daily. https://cannabisdaily.today/growing-concerns-about-cannabis-vape-cartridge-additives/. Accessed August 19, 2020.
3. Raber JC, Elzinga S, Kaplan C. Understanding dabs: contamination concerns of cannabis concentrates and cannabinoid transfer during the act of dabbing. *J Toxicol Sci*. 2015;40(6):797-803. doi:10.2131/jts.40.797.
4. Soroosh AJ, Henderson R, Dodson L, Mitchell CS, Fahey JW. Mitigating potential public health problems associated with edible cannabis products through adequate regulation: A landscape analysis [published online ahead of print, 2020 Aug 14]. *Crit Rev Food Sci Nutr*. 2020;1-9.
5. Centers for Disease Control and Prevention. Outbreak of Lung Injury Associated with the Use of E-Cigarette, or Vaping, Products. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html#epi-chart. Accessed August 19, 2020.
6. Rickner SS, Cao D, Kleinschmidt K, Fleming S. A little "dab" will do ya' in: a case report of neuro-and cardiotoxicity following use of cannabis concentrates. *Clin Toxicol (Phila)*. 2017;55(9):1011-1013. doi:10.1080/15563650.2017.1334914.
7. Benedict K, Thompson GR 3rd, Jackson BR. Cannabis Use and Fungal Infections in a Commercially Insured Population, United States, 2016. *Emerg Infect Dis*. 2020;26(6):1308-1310. doi:10.3201/eid2606.191570.

High Potency Cannabis Flower and Concentrates: Self-administration Patterns in the Real World

Carrie Cuttler, PhD, Health and Cognition Lab., Washington State University

The Health and Cognition lab at Washington State University (WSU) conducts observational research to examine the acute effects of high-potency cannabis products sold in Washington state retail stores. The results from this research indicate that regular cannabis users self-titrate their use of extremely high-potency cannabis concentrates. Specifically, Cuttler et al.[1] found that the average number of puffs/hits inhaled by participants smoking cannabis flower (with a mean THC concentration of 22.8%) was 17.65, while the average number of puffs/hits taken by participants vaping a cannabis concentrate (with a mean THC concentration of 71.4%) was 9.45. Further, participants who vaped cannabis concentrates self-reported comparable levels of intoxication to those who smoked cannabis flower immediately after use, 25 minutes after use, and 50 minutes after use of their products. Finally, we failed to detect any evidence that cannabis concentrates were more cognitively impairing than cannabis flower despite our use of 8 different cognitive tests, each with multiple sub-scores. The findings that cannabis users report similar levels of intoxication following the use of cannabis concentrates or cannabis flower, and that cannabis concentrates are no more cognitively impairing than cannabis flower, converge with recent findings of an independent research group in Colorado conducting similar observational research.[2]



Also consistent with these findings, in collaboration with the McLaughlin Lab at WSU, we recently found that female rats self-administered less of a higher potency cannabis extract than lower potency cannabis extracts.[3] Additionally, while the rates of self-responding for cannabis extract increased significantly over time in the lower potency groups the group that was self-administering the highest concentration of cannabis did not escalate their dose over time. Consistent with this, plasma THC concentrations were significantly lower in the group self-administering the highest concentration of cannabis. Finally, Cooper and Haney[4] and Ramesh, Haney, & Cooper[5] also found that regular cannabis users adjust their inhalation patterns as a function of THC content such that people using higher potency products inhaled less deeply, although it should be noted that their studies relied on cannabis from the NIDA drug supply which is far lower potency (2-6% THC).

Take Away: Collectively, these findings demonstrate that humans and animals can self-titrate their use of cannabis products, adjusting their intake to compensate for potency. This may mitigate some of the increased detrimental effects of high potency products.

Context: The human study reported above was conducted with adult regular cannabis users and cannot be generalized for people under 21 and non-regular users.

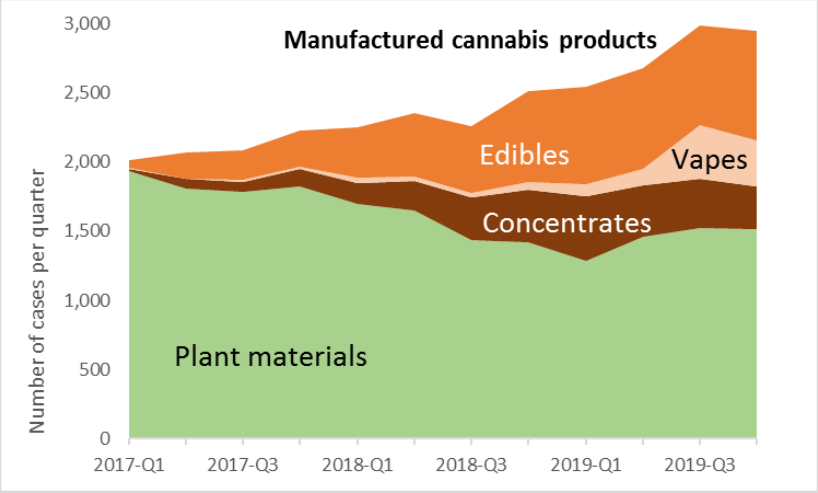
References

1. Cuttler C, LaFrance EM, & Stueber A. Acute effects of high potency cannabis flower and cannabis concentrates on everyday life memory and decision making. *Drug and Alcohol Dependence*. (under review).
2. Bidwell CL, Ellingson JM, Karoly HC, YorkWilliams SL, Hitchcock LN, et al. Association of naturalistic administration of cannabis flower and concentrates with intoxication and impairment. *JAMA Psychiatry*. Published online June 2020; doi:10.1001/jamapsychiatry.2020.0927.
3. Glodosky NC, Cuttler C, Freels TG, Wright HR, Rojas MJ, Baglot SL, Hill MN, & McLaughlin RJ. Cannabis vapor self-administration elicits sex- and dose-specific alterations in stress reactivity in rats. Neurobiology of Stress. 2020; 13(100260). https://doi.org/10.1016/j.ynstr.2020.100260.
4. Cooper ZD & Haney M. Comparison of subjective, pharmacokinetic, and physiological effects of marijuana smoked as joints and blunts. *Drug and Alcohol Dependence*. 2009;103(3):107–113. https://doi.org/10.1016/j.drugalcdep.2009.01.023.
5. Ramesh D, Haney M, & Cooper ZD. Marijuana's dose- dependent effects in daily marijuana smokers. *Experimental and Clinical Psychopharmacology*. 2013;21(4):287–293. https://doi.org/10.1037/a0033661.

Exposure to Cannabis Products reported to US Poison Control Centers, 2017-2019

Julia Dilley, Ph.D., M.E.S., Program Design and Evaluation Services, Multnomah County Health Department and Oregon Department of Human Services Division of Public Health

We accessed information from the National Poison Data System about cannabis exposures reported to U.S. poison centers from January 2017-December 2019. We compared trends and characteristics of two groups of cannabis products: plant materials (flower, joints), and relatively higher THC potency manufactured products such as edibles (infused candy or cookies), cannabis concentrates (wax, shatter), and liquid extracts used in vaping devices.



A total of 29,471 cannabis-related exposures were reported during the three-year period. The greatest share was for cannabis plant materials (65.6%) followed by edibles (19.1%), concentrates (9.7%), and vape liquids (3.8%.) As seen in the Figure below, case reports over time were relatively stable for plant material exposures. However, manufactured product exposures increased substantially between October-December 2017 and the same quarter in 2019: for edibles (259 to 789), concentrates (from 128 to 307), and vape liquids (15 to 333).

Individuals exposed to manufactured products were more likely to be children ages 11 or younger (29.7% vs. 9.8% of plant materials cases). The majority of plant material cases (61.0%) involved co-use of other substances, (e.g., alcohol), but only 17.9% of manufactured cannabis product cases involved additional substances. Among adults exposed only to cannabis in Oct-Dec 2019, vape liquid exposure cases were more likely to require healthcare treatment (43.6%) than plant material (30.8%), edible (30.1%), and concentrate (27.7%) exposures.

Take Away: Poison Centers nationally are receiving more calls about manufactured cannabis products including edibles, concentrates, and vaping liquids. Manufactured products are more likely than plant products to be the only substance involved in the case. Children may be at greater risk for exposure. More serious health outcomes were observed for vape liquid exposures during late 2019, possibly associated with the vape-related EVALI outbreak during this time.

Context: Poison center utilization has been decreasing over the years, as people turn more often to online resources when experiencing minor health effects of an exposure. Given this, the increase in calls related to manufactured cannabis products such as concentrates, vapes, and edibles is especially troubling.

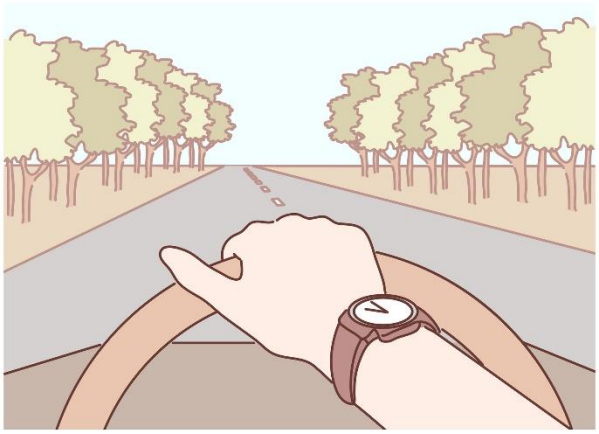
Reference

Julia Dilley, PhD, MES [(1)], Ashley Brooks-Russell, PhD, MPH [(2)], Jennifer M. Whitehill, PhD [(3)], Lucia Terpak, MA[(2)], Janessa M. Graves, PhD, MPH [(4)]. Manuscript in preparation. September 4, 2020. (1) Program Design and Evaluation Services, Multnomah County Health Department and Oregon Public Health Division, Portland, OR; (2) Department of Community and Behavioral Health, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO; (3) Department of Health Promotion and Policy, University of Massachusetts Amherst, Amherst, MA; (4) Washington State University College of Nursing, Spokane, WA

Traffic Safety and Cannabis Potency

Dale Willits, PhD, Department of Criminal Justice & Criminology, Washington State University

While research supports a link between cannabis consumption and driving impairment, no consensus exists on THC concentration levels and impairment. This lack of consensus is likely advanced by study designs that focus on a single area or single class of driver, as well as the broad lack of data in this area. Research in this area is also limited by the degradation of blood evidence between driving and blood test results.[1] The research that exists typically focuses on apprehended drivers, which is problematic in terms of potential selection effects. Additionally, while research indicates considerable variation in THC doses and cognitive impairment,[2] driving impairment and THC concentration studies have failed to account for individual level differences in tolerance. Lastly, research on apprehended suspects and THC concentration levels has produced mixed results. For example, research conducted in Norway demonstrates that of drivers suspected of driving impaired, those with higher THC blood concentrations were more likely to be judged as impaired than those with lower levels of THC blood concentrations.[3] Yet other research from Norway found no relationship between THC blood concentration levels and clinical judgments of impairment.[4]



Despite this uncertainty, legislative actions are often based on the assumption that greater levels of THC blood concentration levels indicate greater levels of impairment. Per se laws are based on the notion that testing above a certain blood concentration level are reflective of impairment. As of August 2020, 6 states have adopted per se limits ranging from 2 ng/ML to 5 ng/ML and an additional 12 states have adopted "zero-tolerance" laws (effectively, 0 ng/ML per se laws). Both the AAA Foundation[5] and the National Highway Transportation Safety Administration[6] note that the weak correlation between THC levels and impairment suggests that threshold-based limits are not meaningful for determining legal provisions.

Take Away: No consensus has been achieved on the relationship between THC blood levels and levels of impairment. As such, there is a great need for additional research on THC concentration and driving performance. Future research in this area would benefit from more representative samples (those who use cannabis but who are not arrested) and from well-designed samples including regular and occasional cannabis users.

Context: Legislative actions are often based on the assumption that greater levels of THC blood concentration levels indicate greater levels of impairment.

References

1. Jones AW, Holmgren A, & Kugelberg FC. Driving under the influence of cannabis: a 10-year study of age and gender differences in the concentrations of tetrahydrocannabinol in blood. *Addiction*. 2008;*103*(3):452-461.
2. Ramaekers, JG, Kauert, G, Theunissen, EL, Toennes, SW, & Moeller, MR. Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. *Journal of psychopharmacology*. 2009;*23*(3):266-277.
3. Khiabani HZ, Bramness JRG., Bjørneboe, A, & Mørland JR. Relationship between THC concentration in blood and impairment in apprehended drivers. *Traffic injury prevention*. 2006;*7*(2):111-116.
4. Bramness JG, Khiabani HZ, & Mørland, J. Impairment due to cannabis and ethanol: clinical signs and additive effects. *Addiction*. 2010;*105*(6):1080-1087.
5. Logan B, Kacinko SL, & Beirness DJ. An Evaluation of Data from Drivers Arrested for Driving Under the Influence in Relation to Per se Limits for Cannabis. *AAA Foundation for Traffic Safety*. 2016.
6. Compton R. Marijuana-Impaired Driving - A Report to Congress. (DOT HS 812 440). Washington, DC: *National Highway Traffic Safety Administration*. July 2017.

Cannabis Use Disorder and High Potency Cannabis

Denise Walker, PhD, School of Social Work, University of Washington
Jason Kilmer, PhD, Psychiatry and Behavioral Sciences, University of Washington

Cannabis addiction, technically known as Cannabis Use Disorder (CUD), is a condition that impairs social functioning, memory, decision-making, and school/work performance. A small but growing literature suggests that frequent cannabis use and high potency cannabis increase the chances of experiencing CUD,[1-4] especially in young people who report a "better high" and a more frequent experience of paranoia and memory impairment.[4]

For youth experimenting with cannabis, cannabis concentrate use was most strongly associated with progression and persistence of use during a 12-month period than for other cannabis products.[5] Although this study did not evaluate CUD symptoms specifically, it does suggest potency can be a contributing factor to youth experimental use transitioning to more regular use.

A study in the U.S. tracked THC potency and CUD symptom onset[6] and found that "higher potency cannabis, on average in the U.S., used at cannabis initiation was associated with over four times the risk of CUD symptom onset within the first year of initiation, as compared to those not endorsing symptom onset." With college students, those who frequently used high potency products reported a higher risk of cannabis dependence, measured by a scientifically validated instrument, CUDIT-R.[7]

Take Away: Use of cannabis with high THC concentration (or high potency) increases the chances of developing CUD or addiction to cannabis, particularly among young people.

Context: These studies have been conducted by observing people over time (prospectively or retrospectively). It is not ethical to conduct studies that randomize people to different concentrations of cannabis to ascertain risk of addiction overtime. The scientific knowledge related to the higher potential of addiction of crack (vs. cocaine) or fentanyl (vs. heroin) are also observational in nature.

References

1. Bidwell LC, YorkWilliams SL, Mueller RL, Bryan AD, Hutchison KE. Exploring cannabis concentrates on the legal market: User profiles, product strength, and health-related outcomes. *Addictive Behaviors Reports*. 2018;8:102-106.
2. Curran HV, Hindocha C, Morgan CJA, Shaban N, Das RK, & Freeman TP. Which biological and self-report measure of cannabis use predict cannabis dependency and acute psychotic-like effects? *Psychological Medicine*. 2019;49:1574-1580.
3. Hines LA, Freeman TP, Gage SH, Zammit S, Hickman M, Cannon M, Munafo M, MacLeod J, & Heron J. Association of high-potency cannabis use with mental health and substance use in adolescence. *JAMA Psychiatry*. 2020;epub ahead of print E1-#8.
4. Freeman TP, & Winstock AR. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. *Psychological Medicine*. 2015;45:3181-3189.
5. Barrington-Trimis JL, Cho J, Ewusi-Boisvert E, Hasin D, Unger JB, Miech RA, & Leventhal AM. Risk of persistence and progression of use of five cannabis products after experimentation among adolescents. *JAMA Network Open*. 2020;3(1):e1919792. Doi:10.1001/jamanetworkopen.2019.19792.
6. Atterberry BJ, Treloar Padovano H, Foster KT, Zucker RA, & Hicks BM. Higher average potency across the United States is associated with progression to first cannabis use disorder symptom. *Drug and Alcohol Dependence*. 2019;195:186-192.
7. Gunn RL, Aston ER, Sokolovsky AW, White HR, & Jackson KM. Complex cannabis use patterns: Associations with cannabis consequences and cannabis use disorder symptomatology. *Addictive Behaviors*. 2020;*105*:epub ahead of print.

THC Potency and Onset of Psychotic Disorders

Michael McDonell, PhD, Elson S. Floyd College of Medicine
Chair, Collaborative for Cannabis Policy, Research, and Outreach, Washington State University

Psychotic disorders are mental disorders that cause abnormal thinking and perceptions. Two of the main symptoms are delusions and hallucinations.[1] A 2020 review of 56 good quality studies on cannabis and psychosis concluded that frequent cannabis use, especially daily use, and the consumption of high-potency cannabis increase the risk of developing psychosis.[2] It also shows that cannabis use is associated with an earlier onset of psychosis and increased risk of transition in individuals at a clinical high risk of psychosis. Daily high-potency cannabis use during adolescence is also associated with an earlier onset of psychotic symptoms (6 years earlier) than non-cannabis users.[3]

One of the best studies conducted on cannabis and psychosis included 901 patients aged 18–64 years in 11 sites across Europe and Brazil who had recently experienced their first episode of psychosis.[4] These patients were matched with 1237 similar people (that is, matched by age, race, and socio-economic-status) who did not have psychosis. This is known as case-control study and is a rigorous way to assess whether two things are associated. The study divided the types of cannabis used by participants into two categories: low potency (THC <10%) and high potency (THC ≥10%). They found that daily cannabis users had three-fold increase in the risk of having a psychotic disorder compared with never users. Those who used high potency cannabis daily were about five-times more likely to have a psychotic disorder than never users (*Figure 1*).

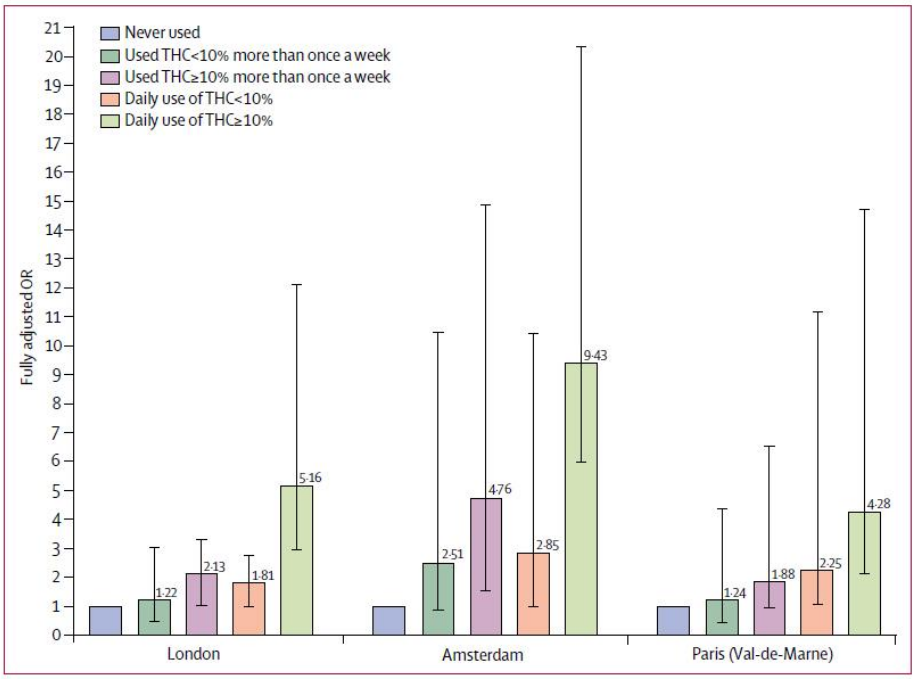


Figure 1: **Fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in three sites.** Data are shown for the three sites with the greatest consumption of cannabis: London (201 cases, 230 controls), Amsterdam (96 cases, 101 controls), and Paris (52 cases, 100 controls). Error bars represent 95% CIs. OR=odds ratio.

Use of high potency cannabis was a strong predictor of psychotic disorder in cities where high potency cannabis was widely available. They concluded that "differences in frequency of daily cannabis use and in use of high-potency cannabis contributed to the striking variation in the incidence of psychotic disorder across the 11 studied sites."

Take Away: Daily cannabis use, particularly of high potency products, increases the risk of developing a psychotic disorder, like schizophrenia, AND earlier onset of symptoms compared to cannabis abstention. Daily use of cannabis, particularly high potency cannabis, is associated with increased symptoms of psychosis in people who have a psychotic disorder.

Context: Studies on this topic define high potency cannabis as products with 10% or more THC. There are no published studies investigating the association between products available in US legal market (60%-90% THC) and the onset of first episode psychosis or on increases of symptoms of in those who have a psychotic disorder.

References

1. U.S. National Library of Medicine. Psychotic Disorders. *National Institute on Health*. https://medlineplus.gov/psychoticdisorders.html. Retrieved September 3, 2020.
2. Van der Steur SJ, Batalla A, Bossong MG. Factors Moderating the Association Between Cannabis Use and Psychosis Risk: A Systematic Review. *Brain Sci*. 2020;10(2):97. Published 2020 Feb 12. doi:10.3390/brainsci10020097.
3. Di Forti, M. *et al.* Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. *Schizophr Bull.* 2014;40:1509–1517.
4. Di Forti M, *et al.* The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *The Lancet Psychiatry*. 2019;6:427–436.

Impact of Cannabis Use and Potency during Adolescence

Nephi Stella, PhD, Pharmacology, University of Washington

Adolescence is a critical developmental stage when the functional connectivity of the brain and its role in higher cognitive functions are both defined and delineated. This "critical period" of brain development exhibits increased vulnerability to drug exposure, including THC exposure.

A review of the literature on the impact of THC exposure and potency on adolescent brain development identified 25 publications that addressed this question and were published in academic peer-reviewed journals from 2010 and later, 11 which are cited here. Studies on the impact of cannabis use on human adolescent brain development can be summarize in three topic areas **1)** cognitive aptitude and behavior, **2)** disruption of brain anatomy and connectivity, **3)** disruption in motivated behavior and dopamine function.

1) Disruption of cognitive aptitude and behavior. Adolescents were 16 to18 years of age in the 3 studies examined.[1-3] Reported cannabis use was mainly based on frequency: for example, once in the last year, once the last 6 months, weekly, and daily.[1] The studies found increase in the likelihood of developing depression and suicidal ideation for adolescent cannabis users compared to nonusers.[1] Use of high-potency cannabis was associated with increased frequency of cannabis use disorder (CUD) and increased likelihood of anxiety disorder.[2,3]

2) Disruption of brain anatomy and connectivity. In the three studies examined,[4-6] adolescents were 14-18 years of age. Changes in brain anatomy were determined by magnetic resonance imaging (MRI). Reported cannabis use was broad and

yet impact on brain anatomy was consistent. Specifically, just one or two instances of cannabis use resulted in anatomical disruptions in brain cortical subareas, decrease in perceptual reasoning, and an increase in the likelihood of generalized anxiety symptoms.[4] Heavy cannabis use during adolescence (4 days/week for an average of 11 joints/week and for an average of 6 years) disrupts brain anatomy and connectivity in brain cortex and nucleus accumbens, a brain area involved in motivated behavior, and the amygdala, a brain area involved in emotional behavior.[6] Lifetime cannabis use (i.e. 1000-1200 days of use) correlated with a decrease in functional connectivity between brain cortices across time, and slower cognitive function.[5]

3) Disruption in motivated behavior and dopamine function. Subjects were 21-55 years of age in this final study.[7] Dopamine function was measured by photon emission tomography (PET) scans. The cohort was defined as having CUD with a mean of 11 years of use, age of onset dependence 21 years, days used in the month preceding the measurement was 29 days, and an average 79 grams of cannabis used per month. They showed lower dopamine release (30-50%) in striatum that correlated with inattention and greater negative symptoms (such as blunted affect and emotional withdrawal), and had poorer working memory.[7]

There is also a strong body of research using animal models, exploring **THC impacts on adolescent rodent brain development**. We selected 4 studies that either used an oral route of THC administration that better reflect the human condition or measured disruption in motivated behavior and dopamine function in adulthood. These studies found significant impact of THC consumption during adolescence in adult behavior including impaired motivated/reward behaviors[8] and increased repetitive and compulsive-like behaviors.[9] THC injections during adolescence impairs sub-cortical dopamine function in adulthood.[10-11]

Take Away: Strong evidence exists on the detrimental impact of THC use during adolescence. This impact can be modeled in adolescent rodents, providing an opportunity to study the response of the developing brain and explore treatment approaches. Available evidence suggests a dose-response relationship, where negative impacts are higher with highly potent THC and/or more frequent use.

Context: Human studies suggest that limiting the availability of high-potency cannabis may reduce the number of individuals who develop CUD and the risk of mental health disorders.

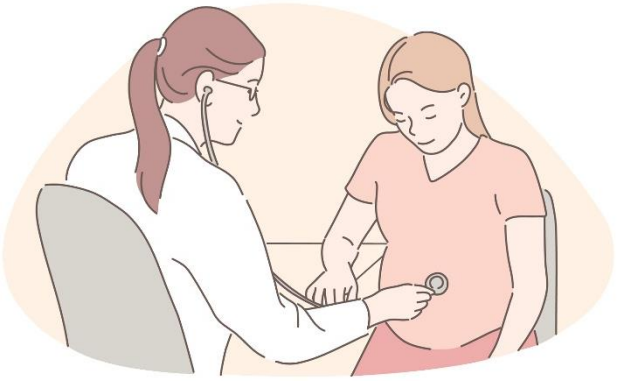
References

1. Gobbi G, Atkin T, Zytynski T, Wang S, Askari S, Boruff J, . . . Mayo . Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: a systematic review and meta-analysis. *JAMA psychiatry*. 2019;76(4):426-434.
2. Hines LA, Freeman TP, Gage SH, Zammit S, Hickman M, Cannon M, . . . Heron J. Association of high-potency cannabis use with mental health and substance use in adolescence. *JAMA psychiatry*. 2020.
3. Kelly BC & Vuolo M. Cognitive aptitude, peers, and trajectories of marijuana use from adolescence through young adulthood. *PloS one*. 2019;14(10):e0223152.
4. Orr C, Spechler P, Cao Z, Albaugh M, Chaarani B, Mackey S, . . . Garavan H. Grey matter volume differences associated with extremely low levels of cannabis use in adolescence. *Journal of Neuroscience*. 2019;39(10):1817-1827.
5. Camchong J, Lim KO, & Kumra S. Adverse effects of cannabis on adolescent brain development: a longitudinal study. *Cerebral cortex*. 2017;27(3):1922-1930.
6. Gilman JM, Kuster J.K, Lee S, Lee MJ, Kim BW, Makris N, . . . Breiter HC. Cannabis use is quantitatively associated with nucleus accumbens and amygdala abnormalities in young adult recreational users. *Journal of Neuroscience*. 2014;34(16):5529-5538.
7. Van de Giessen E, Weinstein JJ, Cassidy CM, Haney M, Dong Z, Ghazzaoui R, . . . Abi-Dargham A. Deficits in striatal dopamine release in cannabis dependence. *Molecular psychiatry*. 2017;22(1):68-75.
8. Kruse LC, Cao JK, Viray K, Stella N, & Clark JJ. Voluntary oral consumption of Δ9-tetrahydrocannabinol by adolescent rats impairs reward-predictive cue behaviors in adulthood. *Neuropsychopharmacology*. 2019;44(8):1406-1414.
9. Murphy M, Mills S, Winstone J, Leishman E, Wager-Miller J, Bradshaw H, & Mackie K. Chronic adolescent Δ9-tetrahydrocannabinol treatment of male mice leads to long-term cognitive and behavioral dysfunction, which are prevented by concurrent cannabidiol treatment. *Cannabis and cannabinoid research*. 2017;2(1):235-246.
10. Renard J, Rosen LG, Loureiro M, De Oliveira C, Schmid S, Rushlow WJ, & Laviolette SR. Adolescent cannabinoid exposure induces a persistent sub-cortical hyper-dopaminergic state and associated molecular adaptations in the prefrontal cortex. *Cerebral Cortex*. 2016;27(2):1297.
11. Renard J, Szkudlarek HJ, Kramar CP, Jobson CEL, Moura K, Rushlow WJ, & Laviolette SR. Adolescent THC exposure causes enduring prefrontal cortical disruption of GABAergic inhibition and dysregulation of sub-cortical dopamine function. *Scientific reports*. 2017;7(1):11420-14.

Cannabis Use during Pregnancy

Celestina Barbosa-Leiker, PhD, College of Nursing, Washington State University

Cannabis use during pregnancy has significantly increased in the last two decades[1] along with cannabis use for nonpregnant women aged 12 to 44 years. Past-month cannabis use among pregnant women increased from 3.4% to 7.0% from 2002 to 2017, and daily/nearly daily use in pregnant women has more than tripled, increasing from 0.9% to 3.4% over the same time frame.[2] The perception that there is no risk associated with regular cannabis use increased 3-fold among reproductive-age women from 2005 to 2015,[3] and 70% of pregnant and non-pregnant women believe there are no risk or a slight risk associated with using cannabis once or twice per week while pregnant.[4]



Cannabis use during pregnancy has been associated with health outcomes. Self-reported cannabis use during pregnancy has been associated with low birth weight,[5-7] stillbirth,[8] and decreased IQ scores, attention problems, decreased cognitive function, and decreased academic ability.[9] Δ^9 tetrahydrocannabinol (THC) can cross the placenta during gestation[10] and is also passed to the baby during breastfeeding.[11-13] While there is an absence of research on THC dose as it relates to outcomes in pregnant women or their infants, animal models have demonstrated various deleterious outcomes related to a THC dose response, including low birth weight,[14] reductions in brain and liver growth,[15] and deficits in learning and memory.[16-17]

Many states have legalized medicinal or adult cannabis use without fully decriminalizing possession or use of cannabis, which results in social and legal repercussions for perinatal women who use cannabis. For example, there may be a burden on child protection agencies,[18] strained patient-provider interactions,[19] and disciplinary or legal interventions that may have adverse psychosocial effects on a new family.[20-21]

Take Away: Cannabis use during pregnancy is associated with negative health impacts for infants and can have social and legal repercussions for the pregnant woman. To date, there is no evidence from human studies to determine whether increases in THC potency result in greater risk for poor health outcome among infants.

Context: Longitudinal human studies largely rely on pregnant women to self-report their cannabis use to enter the study. Because of the potential legal consequences associated with cannabis and other substance use during pregnancy, pregnant women may be less likely to report their cannabis use or seek prenatal care.

References

1. Brown QL, Sarvet AL, Shmulewitz D, Martins SS, Wall MM, & Hasin DS Trends in Marijuana Use Among Pregnant and Nonpregnant Reproductive-Aged Women, 2002-2014. *JAMA*. 2017;*317*(2):207-209. doi:10.1001/jama.2016.17383
2. Volkow ND, Han B, Compton WM, & McCance-Katz EF. Self-reported Medical and Nonmedical Cannabis Use Among Pregnant Women in the United States. *JAMA*. 2019;322(2):167-169. doi:10.1001/jama.2019.7982.
3. Jarlenski M, Koma JW, Zank J, Bodnar LM, Bogen DL, & Chang JC. Trends in perception of risk of regular marijuana use among US pregnant and nonpregnant reproductive-aged women. *American Journal of Obstetrics and Gynecolog.* 2017;*217*(6):705-707. doi: https://doi.org/10.1016/j.ajog.2017.08.015.
4. Ko JY, Farr SL, Tong VT, Creanga AA, & Callaghan WM. Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. *Am J Obstet Gynecol.* 2015;*213*(2):201 doi:10.1016/j.ajog.2015.03.021.
5. Gunn JK, Rosales CB, Center KE, Nunez A, Gibson SJ, Christ C, & Ehiri JE. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. *BMJ Open*. 2016;*6*(4):e009986. doi:10.1136/bmjopen-2015-009986
6. Hayatbakhsh MR, Flenady VJ, Gibbons KS, Kingsbury AM, Hurrion E, Mamun AA, & Najman JM. Birth outcomes associated with cannabis use before and during pregnancy. *Pediatr Res.* 2012;*71*(2):215-219. doi:10.1038/pr.2011.25.

7. Howard DS, Dhanraj DN, Devaiah CG, & Lambers DS. Cannabis Use Based on Urine Drug Screens in Pregnancy and Its Association With Infant Birth Weight. *J Addict Med*. 2018;*13*(6):436-441. doi:10.1097/ADM.0000000000000516.
8. American College of Obstretricians and Gynocologists Committee on Obstretic Practice. Committee Opinion No. 722 Summary: Marijuana Use During Pregnancy and Lactation. *Obstetrics & Gynecology*. 2017;*130*(4) ;931-932. doi:10.1097/aog.0000000000002349.
9. Colorado Department of Public Health & Environment. *Monitoring Health Concerns Related to Marijuana in Colorado: 2014*. Retrieved from https://drive.google.com/file/d/0B0tmPQ67k3NVVUhScGZUSWpGQ1k/view
10. Hutchings DE, Gamagaris Z, Miller N, & Fico TA. The effects of prenatal exposure to delta-9-tetrahydrocannabinol on the rest-activity cycle of the preweanling rat. *Neurotoxicol Teratol*. 1989;*11*(4):353-356. doi:10.1016/0892-0362(89)90006-8.
11. Metz TD, & Borgelt LM. Marijuana Use in Pregnancy and While Breastfeeding. *Obstet Gynecol*. 2018;*132*(5):1198-1210. doi:10.1097/AOG.0000000000002878.
12. Reece-Stremtan S & Marinelli KA. ABM clinical protocol #21: guidelines for breastfeeding and substance use or substance use disorder, revised 2015. *Breastfeed Med*. 2015;*10*(3) ;135-141. doi:10.1089/bfm.2015.9992.
13. Ryan SA, Ammerma, SD, & O'Connor ME. Marijuana Use During Pregnancy and Breastfeeding: Implications for Neonatal and Childhood Outcomes. *Pediatrics*. 2018;*142*(3) ;e20181889. doi:10.1542/peds.2018-1889.
14. Benevenuto SG, Domenico MD, Martin, MA, Costa NS, de Souza AR, Costa JL, . . . Veras MM Recreational use of marijuana during pregnancy and negative gestational and fetal outcomes: An experimental study in mice. *Toxicology*. 2017;*376*:94-101. doi:10.1016/j.tox.2016.05.020.
15. Natale BV, Gustin KN, Lee K, Hollowa, AC, Laviolette SR, Natale DRC, & Hardy DB. Δ9-tetrahydrocannabinol exposure during rat pregnancy leads to symmetrical fetal growth restriction and labyrinth-specific vascular defects in the placenta. *Scientific Reports*. 2020;*10*(1):544. doi:10.1038/s41598-019-57318-6.
16. Campolongo P, Trezza V, Cassano T, Gaetani S, Morgese MG, Ubaldi M, . . . Cuomo, V. Perinatal exposure to delta-9-tetrahydrocannabinol causes enduring cognitive deficits associated with alteration of cortical gene expression and neurotransmission in rats. *Addict Biol*. 2007;*12*(3-4):485-495. doi:10.1111/j.1369-1600.2007.00074.x.
17. Silva L, Zhao N, Popp S, & Dow-Edwards D. Prenatal tetrahydrocannabinol (THC) alters cognitive function and amphetamine response from weaning to adulthood in the rat. *Neurotoxicology and Teratology*. 2012;*34*(1):63-71. doi: https://doi.org/10.1016/j.ntt.2011.10.006.
18. Jarlenski M, Zank J, Tarr J, & Chang JC. Public health messages about perinatal marijuana use in an evolving policy context. *Subst Abus*. 2017;*38*(1):48-54. doi:10.1080/08897077.2016.1268240.
19. American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. AGOG Committee Opinion No. 473: substance abuse reporting and pregnancy: the role of the obstetrician-gynecologist. *Obstet Gynecol*. 2011;*117*(1):200-201. doi:10.1097/AOG.0b013e31820a6216.
20. Roberts SC, & Nuru-Jeter A. Women's perspectives on screening for alcohol and drug use in prenatal care. *Womens Health Issues*. 2010;*20*(3):193-200. doi:10.1016/j.whi.2010.02.003.
21. Roberts SC, & Pies C. Complex calculations: how drug use during pregnancy becomes a barrier to prenatal care. *Matern Child Health J*. 2011;*15*(3):333-341. doi:10.1007/s10995-010-0594-7.

Moving Forward – A brief research agenda

Research available to date documents that THC content in cannabis products contributes to adverse health effects in a dose-response manner. This increased risk imposed from using higher potency cannabis products is particularly concerning for young users and those with certain pre-existing mental health conditions. To further our understanding on the impact of high-THC content cannabis products, more research is needed.

A non-exhaustive agenda of research topics are listed below.

Epidemiology and consumers' motives

- Understand motivations and factors involved in the choice of using high potency concentrated cannabis products over lower potency products.
- Understand how advertisement and marketing influence product use, and identify solutions to educate users and reduce unintended harms associated with using concentrated cannabis products.

Measurement

- Establish standardized units of THC potency and of THC use frequency that will enable thorough comparison of results.
- Establish good measures for "dose" of cannabis products, including so that eventually caps might be established for potency
- Better understanding of what "potency" means (THC, CBD, a ratio of the two, something else)
- Define thresholds for problem use (similar to alcohol thresholds for "heavy" or "binge" drinking that are risk factors for acute effects and dependence, but which are different than dependence - maybe these would vary by population group such as by age, gender, and by THC level and/or product type)
- More precise laboratory measurements of THC (and other content) in manufactured products, and better protocols for standardizing and certifying/monitoring lab performance to measures potency

Driving

- Further understanding on THC concentration impact on driving performance. Driving simulator and closed-course options present safe pathways for this research, including both regular and occasional cannabis users to better document any variation in concentration effects.
- Observational research must expand beyond the analysis of officer initiated DUI arrests and fatal crashes to include non-fatal crashes, to provide a broader representation of cannabis-involved incidents.

Adolescents

- Study the impact of the dose-dependent use of THC by common modes of delivery (e.g. smoking, vaping and edibles) and common regimens (e.g. weekly, daily, multiple time per day) on adolescent brain development and in both human and preclinical model systems (e.g. rodents and primates) in both sexes.
- Implement harm reduction strategies to limit the availability of high-potency cannabis and study if and how these strategies reduce the number of individuals who develop CUD and the risk of mental health disorders.

Reduce research constraints imposed by federal policies: We urgently need research on market products. Reducing restrictions imposed by the DEA would allow us to do higher quality research on market products.

Workgroup Members

Celestina Barbosa-Leiker, PhD is an Associate Professor in the College of Nursing and Vice Chancellor for Research at Washington State University Health Sciences Spokane. Dr. Barbosa-Leiker's primary research investigates the transition from pregnancy to parenthood in women with substance use disorders. She is currently leading an interdisciplinary research team to assess mothers, infants, and healthcare providers in order to better care for women with opioid use disorders, as well as for women using cannabis during pregnancy. The results of these studies will help better educate healthcare providers and pregnant women, inform maternal and infant health policy, and improve standards of care.

Beatriz H Carlini, PhD, MPH is a Research Scientist at the University of Washington's Alcohol & Drug Abuse Institute (ADAI) and Affiliate Associate Professor at the School of Public Health, Health Services Department. Her research career has been dedicated to understanding the public health impact of legal psychoactive substances such as alcohol, inhalants, tobacco, and more recently, cannabis. Since 2016, Dr. Carlini leads ADAI Cannabis Research and Education, including coordinating collaboration with other marijuana researchers at the UW, acting as the Program Chair of UW Marijuana Research Symposium and serving as a liaison with policy makers within the state and researchers at other universities. In 2019 she was named Director of the Tobacco Studies Program in the UW School of Public Health, where she also teaches Tobacco-related Health Disparities and Social Justice. As a first generation immigrant and a foreign-born American citizen, Dr. Carlini is especially interested in the impact of cannabis and tobacco use on perpetuating health and social disparities. Dr. Carlini has a passion for fostering social inclusion, challenging stereotypes, and fighting stigma. She applies an equity lens to her work as a researcher and educator.

Carrie Cuttler, PhD is an Assistant Professor in the Department of Psychology at Washington State University. Her research focuses on the chronic and acute effects of cannabis on cognition and mental health (e.g., depression, anxiety, obsessive-compulsive disorder). Her current research projects focus on examining i) the acute effects of cannabis on various psychological and medical symptoms and on trying to identify the doses and chemotypes that most effectively reduce these symptoms, ii) the link between stress and cannabis use, with a particular emphasis on the stress response of cannabis users, and iii) the influence of cannabis use (early vs. late onset, concentrate vs. flower) on memory and executive functioning. Dr. Cuttler also created and validated the Daily Sessions, Frequency, Age of Onset of Cannabis Use Inventory (DFAQ-CU) which measures a variety of aspects of cannabis consumption.

Julia Dilley, PhD, MES is a Senior Research Scientist and Epidemiologist with Multnomah County Health Department and State of Oregon Public Health Division. For more than 20 years Julia has supported public health systems in Washington, Oregon, Alaska and New Mexico. Much of her research focuses on public health effects of cannabis, alcohol and tobacco policies, and improving public health data quality for surveillance and evaluation. She is currently the principal investigator for a federally funded research study of cannabis legalization impacts in Washington and Oregon, focused on the role of city and county policies and local-area cannabis market variation. She also co-chairs a national subcommittee of the Council of State and Territorial Epidemiologists (CSTE) that is developing cannabis surveillance best practices.

Caislin Firth, PhD, MPH is a Research Scientist at the Alcohol and Drug Abuse Institute (ADAI) at the University of Washington (UW). Outside of ADAI, Caislin is a postdoctoral fellow in the Faculty of Health Sciences at Simon Fraser University where she works as a social epidemiologist focused on designing equitable healthy cities and mitigating negative health effects of gentrification. She also holds an adjunct position with the RAND Corporation to examine population health effects of cannabis legalization. With a background working in local government in the Pacific Northwest, Caislin uses an interdisciplinary approach, in partnership with cities and advocacy groups, to identify solutions that address poor health outcomes experienced among marginalized populations. Caislin's research spans criminal justice, cannabis, and healthy city research. Caislin is a Horowitz Foundation Social Policy Fellow and received a PhD in Epidemiology from the UW where her dissertation focused on the impacts of socio-spatial inequities of cannabis legalization on youth.

Kevin Haggerty, PhD, MSW is the Director of the Social Development Research Group in the UW School of Social Work. He is a principal investigator on a variety of projects, including Utah Communities That Care Training program, Staying Connected with Your Teen, Families Facing the Future (formerly Focus on Families) and a National Institute on Drug Abuse-funded study on Family Connections. He is an investigator of the Community Youth Development Study, which tests the effectiveness of the Communities That Care (CTC) program. Dr. Haggerty specializes in prevention programs at the community, school and family level. For more than 30 years, he has focused on developing innovative ways to organize the scientific knowledge base for prevention so that parents, communities and schools can better identify, assess and prioritize customized approaches that meet their needs. An expert on substance abuse and delinquency prevention, Dr. Haggerty speaks, conducts trainings, and writes extensively on this field.

Jason R. Kilmer, PhD is an Associate Professor in Psychiatry and Behavioral Sciences at the University of Washington (UW), and serves as an investigator on several studies evaluating prevention and intervention efforts for alcohol, cannabis, and other drug use by college students. In addition to research and teaching, he has worked extensively with college students and student groups around alcohol and other drug prevention programming and presentations throughout his career. Jason also serves as the chairperson of Washington state's College Coalition for Substance Abuse Prevention.

Mike McDonell, PhD, MS is a Professor in the Elson S. Floyd College of Medicine at Washington State University and the Director of Behavioral Health Innovations. He is a clinical psychologist with over 20 years of experience developing, testing, and implementing strength-based interventions for people with addiction and mental illness in community settings. He leads multiple National Institutes of Health funded studies demonstrating that incentives can be used to reduce alcohol and drug use in individuals living with co-occurring serious mental illness. He also leads efforts to test incentive interventions in collaboration with American Indian and Alaska Native communities. Trained as a child psychologist specializing in early onset serious mental illness and treatments of foster care-involved youth, Dr. McDonell also leads evaluations of Washington state's first episode psychosis program and a program designed to provide housing and substance use treatment for parents at risk for losing custody of their children. Dr. McDonell is also involved in Washington State University's cannabis related research efforts, as the Chair of the Collaborative on Cannabis Policy, Research, and Outreach.

Nephi Stella, PhD is a professor in Pharmacology and Psychiatry and Behavioral Sciences at the University of Washington. His studies focus on the therapeutic value of phytocannabinoids and molecules that target the cannabinoid signaling system. The goal of this research is to develop novel therapeutics for the safe treatment of devastating brain diseases, including brain cancer, and to better understand the toxicity associated with cannabis use on brain development and function. This body of work led to the optimization of several medicinal properties of phytocannabinoids, synthetic cannabinoids and endocannabinoids for the treatment and possible cure of devastating untreatable diseases, including Dravet Syndrome and glioblastoma.

Denise Walker is a Research Professor at the University of Washington, Director of the Innovative Programs Research Group and is a licensed clinical psychologist. A main area of her research expertise is on the development and evaluation of interventions for marijuana disorders for both adults and adolescents, utilizing brief interventions, longer courses of treatment, and aftercare. She has been involved in the development and evaluation of the Teen Marijuana Check-Up (TMCU), a school-based intervention to elicit self-referral by heavy using adolescents. The TMCU has been the focus of five clinical trials and is identified as an "Evidence Based" intervention by SAMHSA. Another focus of her work is on the development of interventions that motivate change for other high risk populations including active duty military with an alcohol disorder, active duty military with untreated PTSD, and domestic violence perpetrators. Dr. Walker has published over 60 peer-reviewed publications, book chapters and books and has received numerous NIH and DoD grants.

Dave Willits, PhD is an Assistant Professor of Criminal Justice and Criminology at Washington State University. Dr. Willits earned his Ph.D. from the University of New Mexico in 2012 and previously held a tenure-track position in the California State University system. His research interests explore issues related to drug policy, policing, violence, and public health. He is the Co-Principal Investigator on a National Institute of Justice funded project examining the effects of I-502 on crime and law enforcement in Washington. His research on marijuana examines the effects of legalization on crime, police performance, jail populations, and traffic safety.

Beatriz Carlini, Caislin Firth, and Sharon Garrett (editors)
Erinn McGraw and Meg Brunner (graphic design)

University of Washington, Alcohol & Drug Abuse Institute

ADAI | ALCOHOL & DRUG ABUSE INSTITUTE