Psychological and Developmental Impact of THC/Marijuana on Adolescents

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Disclosure:

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the speaker (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.

Objectives



Recognize evolving trends in youth substance abuse.



Discuss why adolescents are developmentally vulnerable to substance use and its effects.



Identify the developmental, psychiatric, and social sequelae that are occurring as a result.

Monitoring the Future Survey:

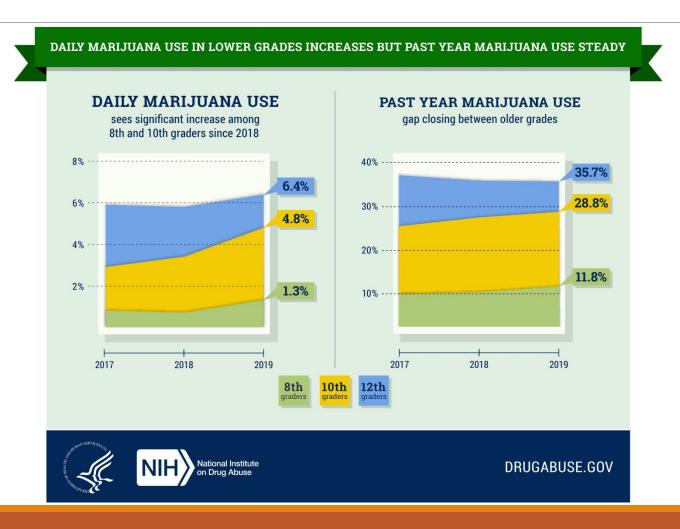
Widespread survey conducted on a large, varied population of youth, regarding their behaviors, attitudes, and values on substance abuse.

Pre-pandemic: More than 42,000 students from almost 400 schools participate

2023: 22,000 from 235 schools

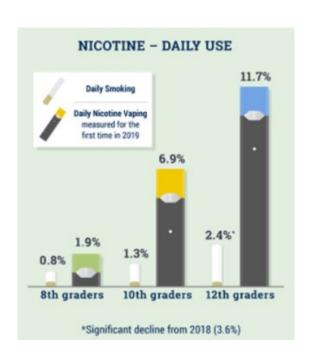
Values are reported from students in 8th, 10th, and 12th grades

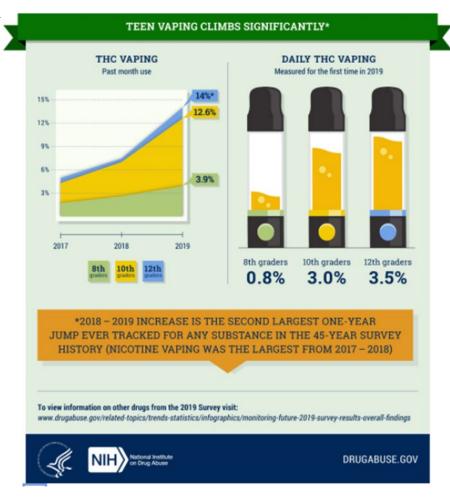
Monitoring the Future Survey, 2019:



Monitoring the Future Survey, 2019

- ➤ Teens are vaping both marijuana and nicotine in record numbers.
- ▶ Past-month marijuana vaping among 12th graders nearly doubled in a single year—the second largest one-year jump for any substance in the history of the survey.
- ➤ One in 4 students in 12th grade, 1 in 5 in 10th grade, and 1 in 11 in 8th grade reported vaping nicotine in the past month.





And then, the Pandemic: Monitoring the Future Survey, 2022-2024

Students who used cannabis (or marijuana) in the past 12 months:

12th grade: in 2021: 30.5%; 2022: 30.7%,: 2023: 29%

10th grade: in 2021: 17.3%; 2022: 19.5%,: 2023: 17.8%

8th grade: in 2021: 7.1%; 2022: 8.3%,: 2023: 8.3%

• lower than they were during the pre-pandemic years of 2020 and 2019, when prevalence levels were 35% and 36%, respectively. The decline from 35% in 2020 to 31% in 2021 is the largest one-year decline among 12th grade students ever recorded in the 48 years of the survey for this measure.

Students who alcohol in the past 12 months:

12th grade: in 2021: 46.5%; 2022: 51.9%,: 2023: 45.7%

10th grade: in 2021: 28.5%; 2022: 31.3%,: 2023: 30.6%

8th grade: in 2021: 7.1%; 2022: 8.3%,: 2023: 8.3%

Students with E-cigarette use in the past 12 months:

12th grade: in 2021: 26.6%; 2022: 27.3%,: 2023: 23.2%

Consider this was 35.3 percent in 2019!!!

10th grade: in 2021: 19.5%; 2022: 20.5%,: 2023: 30.6%

8th grade: in 2021: 7.1%; 2022: 8.3%,: 2023: 8.3%

Some Basic Concepts:

Typically, young adolescents tend to experiment with what is available around the home/ in the environment: tobacco, alcohol, inhalants, over- the counter substances.

Early use tends to occur in the context of experimenting with peers.

Perceived harm is a deterrent to use. A decrease in perceived harm, as is being experienced with legalization efforts on a national level, leads to increased use.

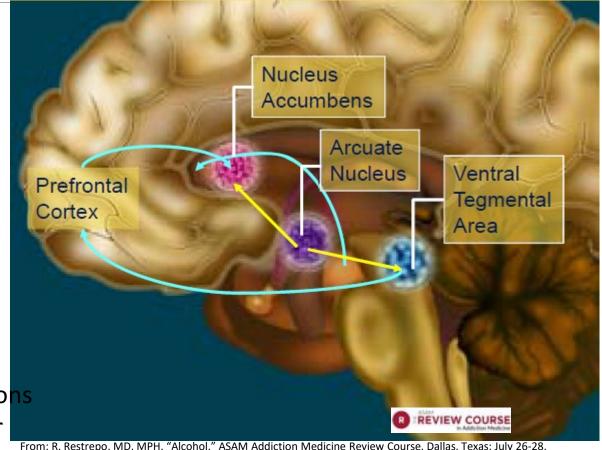
Early marketing of vaporized nicotine was geared specifically to youth, in both advertisements and the products themselves.

As adolescents age, their ability to procure substances increases, and use starts to be regular/daily for a subset that is now internally motivated to use, not just because of peer influence.

From 2002 to 2015, the prevalence of cannabis use by parents with children in the home increased from 4.9 to 6.8%

Adolescent Neurobiology and Vulnerability:

- The brain matures from back to front.
- Our emotional and pleasure- seeking centers and our memory centers are developed BEFORE the frontal lobes.
 - Middle Childhood/Early adolescence:
 - Nucleus Accumbens (reward/ pleasure circuit)
 - Amygdala (Pleasure vs pain and associated cues)
 - Late Adolescence (early to mid 20s)
 - Frontal lobes/ pre-frontal cortex.
- Teenagers:
 - Desire for pleasure and thrill-seeking
 - A weak "common sense" filter
 - The amygdala may solidify those pleasurable sensations and "cues" early on and prime the individual for later substance use disorders.



From: R. Restrepo, MD, MPH. "Alcohol." ASAM Addiction Medicine Review Course. Dallas, Texas; July 26-28, 2018.

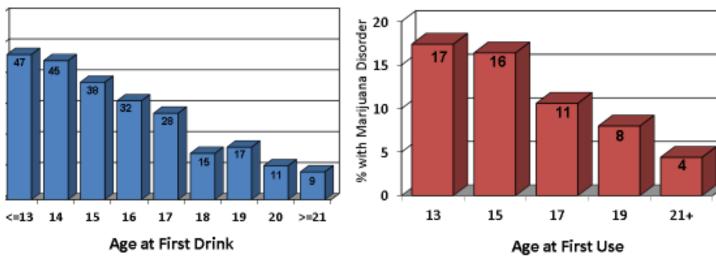
The Earlier the Use, the Greater the RISK:

- Age at first drink is inversely related to the risk of developing a alcohol use disorder.
 - nearly half of those who had their first drink at age 13 or younger developed an alcohol use disorder during their lifetime
 - less than 10% of those who had their first drink at age 21 or older did.
- The same was true with marijuana:
 - 1 in 5 youth who first used marijuana at age 13 or younger went on to develop a marijuana use disorder during their lifetime
 - 5% of those who did not use until at least age 21.
- Delaying use, even by a few years, greatly reduces the chances that someone will develop a substance use disorder.

Age at First Use and Later Risk

Alcohol

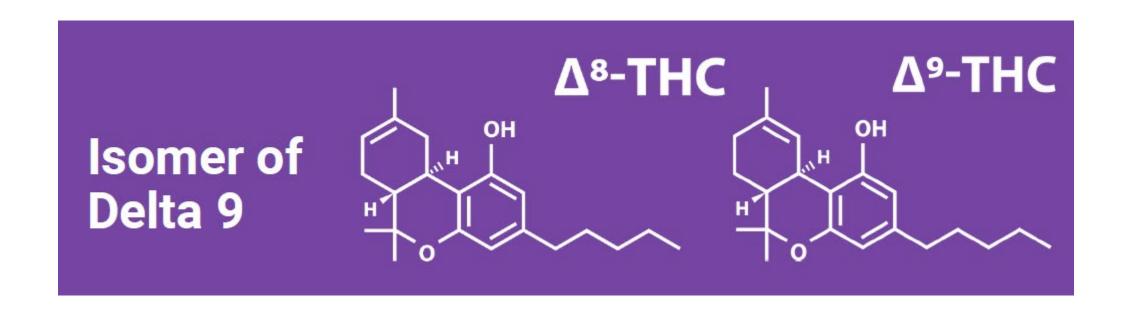
hol Marijuana



ingson RW, Heeren T, Winter MR. Age at drinking onset and alcohol dependence: Age at onset, duration, and severity. Arch Pediatr Adolesc Med. 2006;160(7): 759-746.

Lee C-YS. Likelihood of developing an alcohol and cannabis use disorder during youth; association with recent use and age. Drug Alcohol Depend. 2006;92(1-9):239-247.

What is Delta 8 THC?



What is Delta-8 THC?

Derived from hemp (any part of cannabis plant w/<0.3% delta-9THC) in very small amounts.

CBD (cannabidiol) is also legal to derive from hemp. Hemp can be engineered to contain as much as 20 percent CBD.

Hemp-derived CBD can be synthetically converted into delta-8 THC and produces much larger quantities than trying to extract from the plant, allowing for companies to more easily mass-produce this chemical.

- Extraction process involves ethanol or heptane and acid catalysts, like hydrochloric acid or p-toluenesulfonic acid. The solution is then neutralized and "purified."
- Significant concern, as with all currently vapor delivery systems, for toxic contaminants and solvents to be consumed. Quality is unregulated.

Federally legal in 2018 Farm Bill.

Illegal in several states- but not Ohio!

What is Delta 8 THC?

A variant of delta-9-THC (delta-9 tetrahydrocannabinol), which is the main psychoactive compound of cannabis (marijuana).

Binds to same CB-1 receptors as delta-9 THC, causing similar intoxicating effects

Monitoring the Future Survey, 2024:

- First time surveyed, and only surveyed 12th graders
- Prevalence of 11.4% among 12th graders in 2023 for past 12-month use

Marijuana Use: Sequelae of Early Use

Cognitive and Memory Deficits

- "long-term marijuana use initiated in adolescence has negative effects on intellectual function and that the deficits in cognitive areas, such as executive function and processing speed, did not recover by adulthood, even when cannabis use was discontinued"*
- US Surgeon General's Advisory on Marijuana and the Developing Brain- 2019

Educational Failure/Increased School Drop-Out

Unemployment

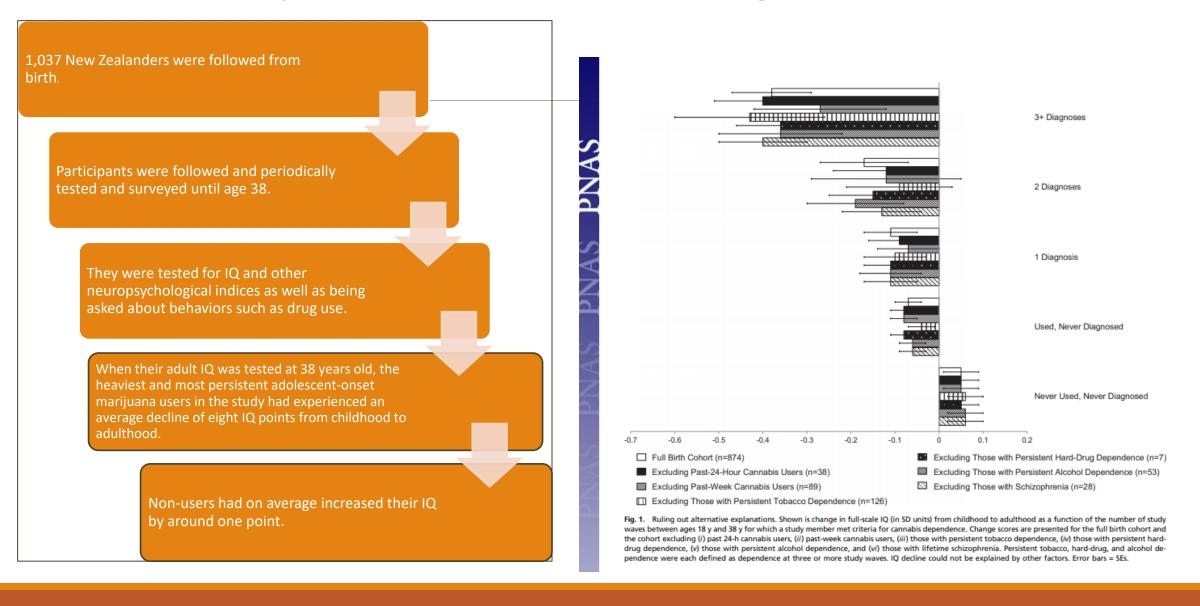
Relationship difficulties/ domestic violence

Increased prevalence of psychotic, mood, and other addictive disorders.

"Odds of negative developmental outcomes are increased in youth with early-onset, persistent, high frequency, and high-potency Δ -9-THC cannabis use, suggesting dose-dependent

relationships." Hammond CJ, Chaney A, Hendrickson B, Sharma P. Cannabis use among U.S. adolescents in the era of marijuana legalization: a review of changing use patterns, comorbidity, and health correlates. Int Rev Psychiatry. 2020 May;32(3):221-234. doi: 10.1080/09540261.2020.1713056. Epub 2020 Feb 6. PMID: 32026735.

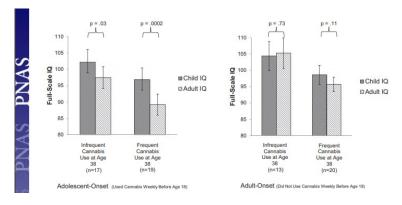
Dunedin Study- Cannabis Associated Cognitive Decline



Dunedin Study- Cannabis Associated Cognitive Decline

And even after setting aside the heaviest users, a decline of a few IQ points from their childhood value was still seen in less heavy users who had started in their teens.

What's more, the drop in mental function seemed irreversible even after persons had quit cannabis.





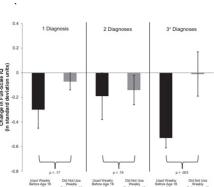


Fig. 51. Adolescent vulnerability. Shown is change in full-scale IO (in SD units) from bildhood to adulthood among study members with 1, 2, or 3+ Gagnoses of cannabis dependence as a function of age of onset of a teat veedly into the contract of the cont

Considerations:

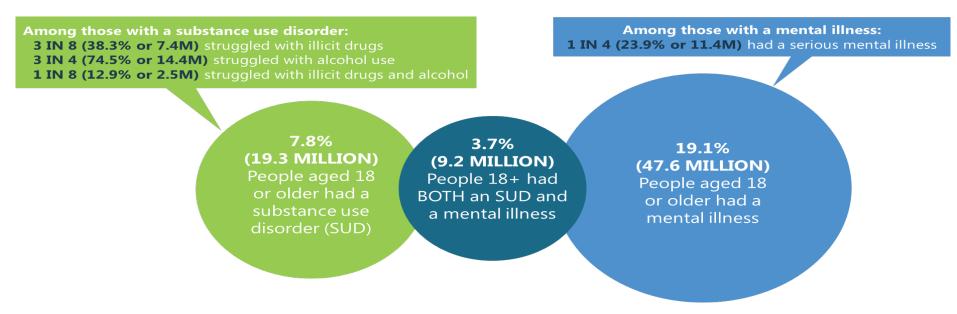
Studies point to a vulnerability of the adolescent brain, not only to functional loss, but to development of long-term disorders with early exposure to substance abuse.

Delaying exposure to substance exposure is key to the prevention of long-term substance abuse and is associated with less cognitive decline and better overall psychosocial functioning.

Early exposure to high-potency THC products, such as "Dab pens" or wax, is particularly concerning- and, unfortunately, that is what the trend is showing.

Mental Illness and Substance Use Disorders in America

PAST YEAR. 2018 NSDUH. 18+



In 2018, **57.8M** Americans had a mental and/or substance use disorder.

THC and Mental Health: Acute Toxicity in "Recreational Use"

Many cannabis products on the market- even herb, contain high concentrations of THC.

"Dabs"/ Wax/ Shatter is a highly concentrated forms of THC that are used via vaporization.

• Recall that the use of these products is escalating quickly in adolescents.

Use of these forms has been associated with the rapid onset of mood and psychotic symptoms in youth, even upon novel exposure.

With large exposure, THC has serotonergic activity, so higher concentration products increase risk of perceptual disturbances and affective destabilization.

The effects can be prolonged, and patients often require acute psychiatric hospitalization and antipsychotic medications to stabilize.

"Problem Cannabis Use"

Psychiatric Symptoms:

- Predict problematic cannabis use
- Predict perception of cannabis use as harmless.

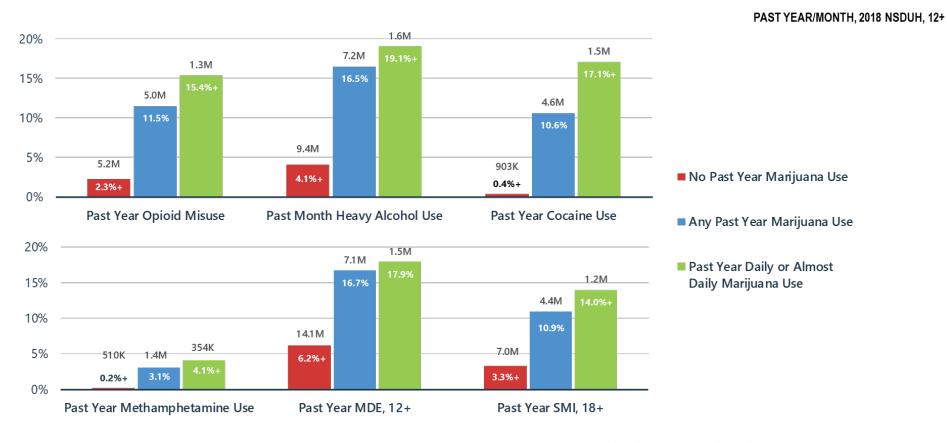
Much higher in individuals with mental illness including schizophrenia, mood and anxiety disorders, personality disorders and PTSD, compared to controls.

Repeated studies have shown synergistic effects:

- As cannabis use worsens, so does mental illness.
- As mental illness worsens, cannabis use escalates.

No evidence thus far has found any benefit for recommending marijuana for a mental health disorder that would outweigh the potential harms.

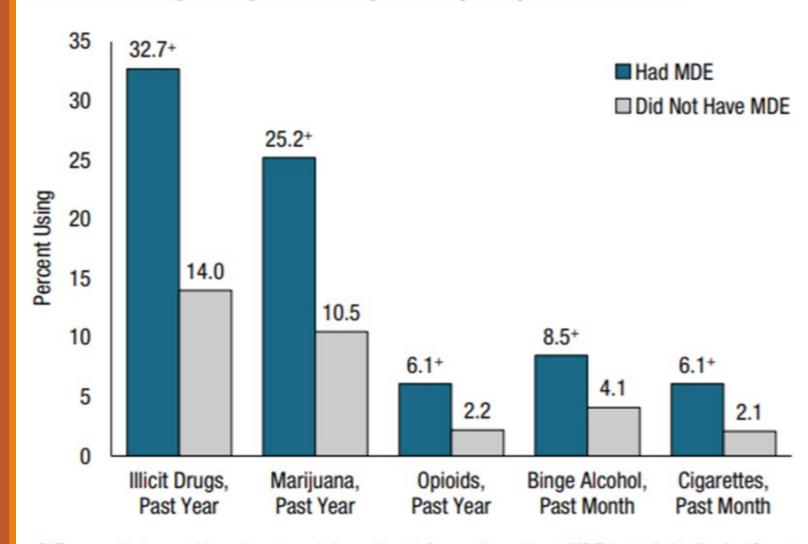
Marijuana: Association with other Substance Use and Depression



Difference between this estimate and the estimate for people with past year marijuana use is statistically significant at the .05 level.

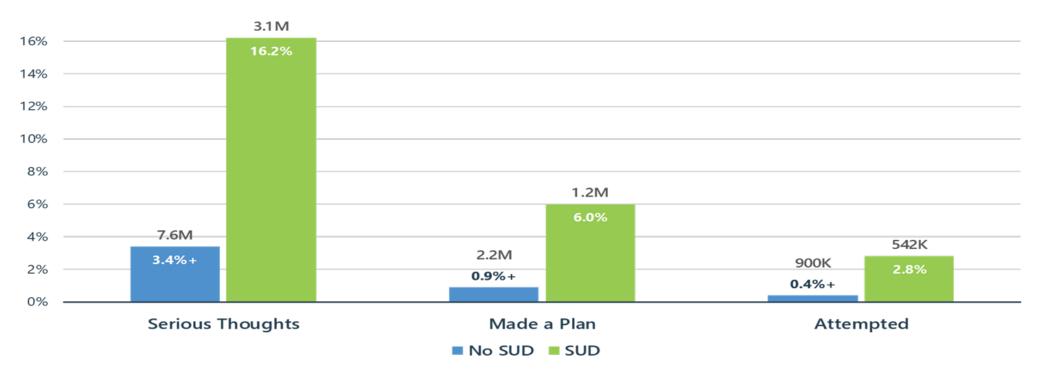
Mental Health Consequences of Substance Abuse:

Figure 52. Substance Use among Youths Aged 12 to 17, by Past Year Major Depressive Episode (MDE) Status: 2018



Difference between this estimate and the estimate for youths without MDE is statistically significant at the .05 level.

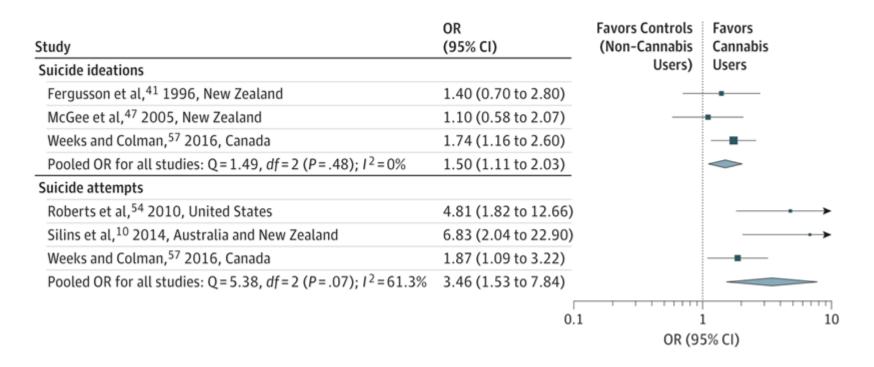
Note: Youth respondents with unknown MDE data were excluded.



+ Difference between this estimate and the estimate for adults with SUD is statistically significant at the .05 level

Substance Abuse and Suicide

Cannabis and Suicide Risk in Adolescents



Gobbi G, Atkin T, Zytynski T, et al. 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. doi:10.1001/jamapsychiatry.2018.4500

Legalization and Suicide Rates

Recent Study examined suicide rates in youth 12-15 years old and compared rates in states where there was no legalization of marijuana, legalized "medical marijuana" and states with legalized recreational marijuana using data from the National Vital Statistics System (2000-2019).

The unadjusted annual suicide rate (per 100,000) was:

No Legalization: 9.76

"Medical Marijuana": 12.77

Legalized "recreational" marijuana: 16.68

Legalization and Suicide Rates

Among female-identifying youth: Compared to states with no legalization, there was a 10 percent increased suicide rate in states with legalized medical marijuana and a 16 percent increase in states with legalized recreational marijuana.

Additionally, across female- and male-identifying youth aged 14-16 years, youth in recreational marijuana states were at 9% and 14% higher risk for suicide in contrast to youth is states with no legalization or "medical" marijuana, respectively.

The authors note that these data are consistent with existing data suggesting that onset of cannabis use before 16 years of age has a distinct impact on adolescent neurodevelopment and cognitive function.

Physical Heath Consequences:

(there are many, but only time to highlight some newer ones)

Cannabis Hyperemesis Syndrome:

- Syndrome of cyclic nausea and vomiting with abdominal pain in regular cannabis users.
- Has become far more frequent as the THC content and the THC/CBD ratio of marijuana products have increased
- Hallmark sign is hot showering/bathing to alleviate symptoms (somewhat controversial)
- Vicious cycle because of belief that smoking marijuana decreases nausea.
- Exact mechanism unknown but can cause repeated hospital stays and significant impairment.
 - BMJ July 2019;366:4336.
- Haloperidol is a promising treatment, but crux of long-term recovery is cessation of marijuana use.

Physical health Consequences: Vaping- Associated Lipoid Pneumonia

- Patients hospitalized for hypoxemic respiratory failure
- ➤ Many have required ICU care
- Some require intubation.
- > Anecdote: ECMO

➤ Diffuse basilar-predominant infiltrates with a range of "ground glass" opacities and nodular or "tree-in-bud" infiltrates.

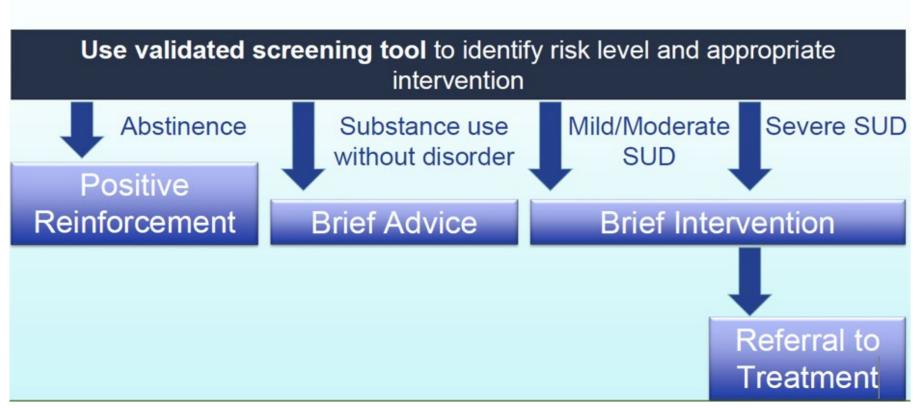


Davidson K, Brancato A, Heetderks P, et al. Outbreak of Electronic-Cigarette–Associated Acute Lipoid Pneumonia — North Carolina, July–August 2019. MMWR Morb Mortal Wkly Rep 2019;68:784–786.



In the Office:

SBIRT framework



Akron Children's Addiction Services:



Don't go it alone. Help is a phone call away.

Akron Children's Hospital is collaborating with the Northeast Ohio community to address the overwhelming addiction concerns we are facing. Our Addiction Services Program focuses on education, prevention, care coordination, community outreach and referral to community resources.

To make an appointment with our Addiction Services, please call 330-543-5015. You can also speak with your child's primary care physician.

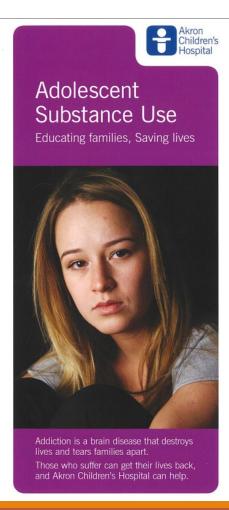
For immediate assistance, contact the United Way Help Center: 2-1-1



This brochure is not intended as a substitute for your health professional's opinion or care. It was created in part by a donation from Fighting for Alyssa, a non-

profit that raises awareness about substance use disorder, and advocates for education and treatment.





Addiction Services Program at Akron Children's Hospital

The Addiction Services Program at Akron Children's Hospital provides evidence-based treatment services for adolescents with substance use disorders up to age 18.

Akron Children's Hospital is in a unique position to work with youth of all ages. Our primary care and school health programs offer us unique access and opportunities to educate children about the risks associated with substance misuse and substance use disorders. At the same time, we recognize that education of parents to protect children from prescriptions in the home is equally important. As health care providers, we also have the responsibility to have guidelines in place to prevent overprescribing.

As a leader in pediatric care, Akron Children's Hospital has the goal of preventing today's children and teens from becoming the next generation struggling with addiction.

Treatment Options

Outpatient Program

The outpatient program provides evidence-based treatment services for adolescents with substance use and co-occurring mental health disorders up to age 18. This includes:

- Medication-assisted treatment for withdrawal management
- Urine drug screening
- Weekly individual counseling and family therapy as needed

The initial intake consists of a diagnostic assessment with a licensed clinical counselor that specializes in substance use disorder treatment and typically lasts up to 90 minutes. A patient may be referred to our addiction medicine physician for a medical evaluation, if needed. After school appointments and telehealth options are available.

Intensive Outpatient treatment (IOP)

IOP offers intensive outpatient services for adolescents with moderate to significant difficulty achieving and maintaining their sobriety. A licensed clinician completes a comprehensive mental health and substance use evaluation to ensure the patient and family meet criteria for this level of care according to the American Society of Addiction Medicine.

If an adolescent meets the criteria for IOP, the program provides:

- Structured group therapy experience for 9 hours per week
- · Ongoing individual and family counseling
- Urine drug screening
- · Case management
- Evaluation from an addiction medicine physician

Adolescents attend three sessions per week and the average length of treatment is 4-6 weeks, in which new skills are taught to aid the patient with establishing and maintaining sobriety, developing relapse prevention skills, and improving their sober support network.

Marketing

.... AND A CALL TO ACTION







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1:35







Craftbox V-Play 20K Disposable Vape with Built in Gaming System 25mL

CRAFTBOX/V-PLAY

\$14.95 \$30.00 SALE





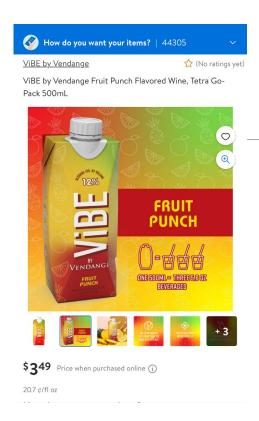
THC Marketing:

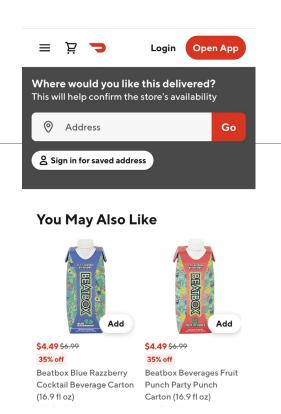








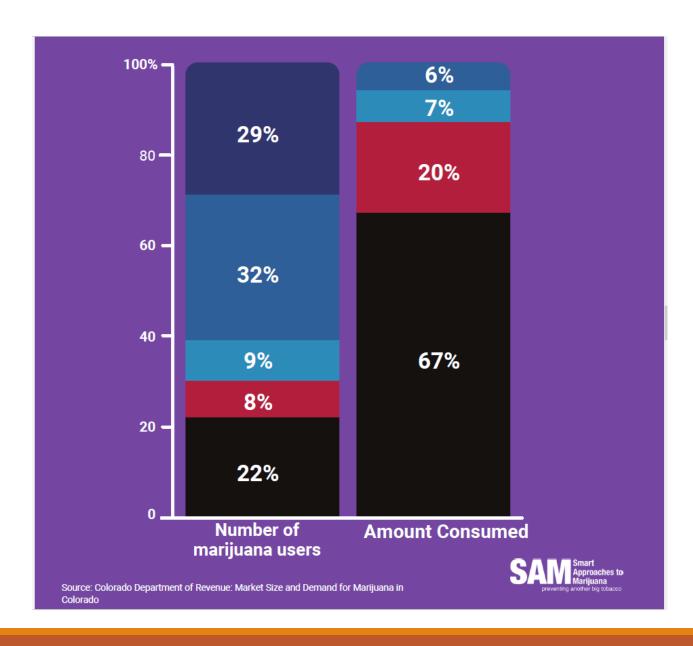








Alcohol Marketing:

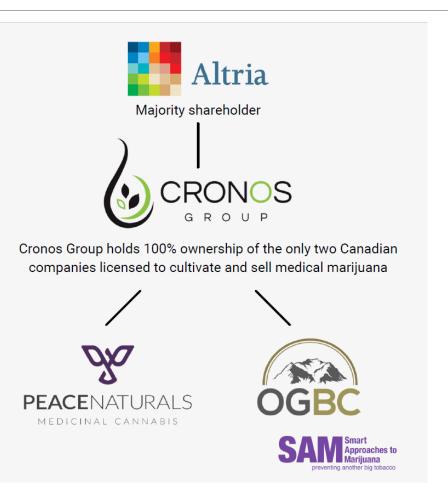


Aiming at Kids is Profitable!!!

And Now This....

Altria Makes \$1.8 Billion Investment in Big Marijuana





In Conclusion:

Early exposure to substances leads to an increased risk for developmental stagnation/decline, substance use disorders, and acute and chronic psychological and physiological illness.

Unfortunately, decreased risk awareness and increased accessibility to high-potency cannabis and THC concentrates is on the rise.

Public health initiatives should focus on educating the community about these risks, and we should be confronting and correcting the public notion that substances like marijuana are a "natural" option for treating mental illness, especially in youth.

References:

- Blohm, Eike^a; Sell, Peter^b; Neavyn, Mark^c Cannabinoid toxicity in pediatrics, Current Opinion in Pediatrics: April 2019 Volume 31 Issue 2 p 256-261 doi: 10.1097/MOP.0000000000000739
- Broussard, Camille. "Vaping and Emerging Substances." 2024 ACMT Symposium: Substance Use in Adolescents & Young Adults: Unique Challenges. Washington, D.C. April 11, 2024.
- Broussard, Camille. "Assessment and Treatment of SUD in Youth: Beyond SBIRT." 2024 ACMT Symposium: Substance Use in Adolescents & Young Adults: Unique Challenges. Washington, D.C. April 11, 2024.
- Chocron Y, Zuber JP, Vaucher J. Cannabinoid hyperemesis syndrome. BMJ 2019;366:14336.
- Davidson, J. "Marijuana." 2024 ACMT Symposium: Substance Use in Adolescents & Young Adults: Unique Challenges. Washington, D.C. April 11, 2024.
- Davidson K, Brancato A, Heetderks P, et al. Outbreak of Electronic-Cigarette-Associated Acute Lipoid Pneumonia North Carolina, July-August 2019. MMWR Morb Mortal Wkly Rep 2019;68:784-786. DOI: http://dx.doi.org/10.15585/mmwr.mm6836e1external icon.
- De Gregorio D, Dean Conway J, Canul ML, Posa L, Bambico FR, Gobbi G. Effects of chronic exposure to low doses of Δ9- tetrahydrocannabinol in adolescence and adulthood on serotonin/norepinephrine neurotransmission and emotional behaviors. Int J Neuropsychopharmacol. 2020 Jul 29:pyaa058. doi: 10.1093/ijnp/pyaa058. Epub ahead of print. PMID: 32725198.
- Gobbi G, Atkin T, Zytynski T, et al. 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. doi:10.1001/jamapsychiatry.2018.4500
- Goldman, W. "Neurobiology of Addiction." Grand Rounds, Akron Children's Hospital. May 1, 2020.
- Gorelick D (2018). "Cannabis use and disorder: Epidemiology, Comorbidity, health consequences, and medico-legal status." In R Hermann (Ed.), *UpToDate*. Retrieved Sept 20, 2019.
- Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clinical Pharmacokinetics [Internet]. 2003 [cited 2019Aug28];42(4):327-60. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12648025
- Hammond CJ, Chaney A, Hendrickson B, Sharma P. Cannabis use among U.S. adolescents in the era of marijuana legalization: a review of changing use patterns, comorbidity, and health correlates. Int Rev Psychiatry. 2020 May;32(3):221-234. doi: 10.1080/09540261.2020.1713056. Epub 2020 Feb 6. PMID: 32026735.
- Hingson RW, Heeren T, Winter MR. Age at Drinking Onset and Alcohol Dependence: Age at Onset, Duration, and Severity. Arch Pediatr Adolesc Med. 2006;160(7):739-746. doi:10.1001/archpedi.160.7.739
- Huestis M. Pharmacokinetics of THC in Inhaled and Oral Preparations. Marihuana and Medicine [Internet]. [cited 2019Aug28]; Available from: https://page-one.springer.com/pdf/preview/10.1007/978-1-59259-710-9_11
- Inayat, F., Virk, H. U., Ullah, W., & Hussain, Q. (2017). Is haloperidol the wonder drug for cannabinoid hyperemesis syndrome?. BMJ case reports, 2017, bcr2016218239. https://doi.org/10.1136/bcr-2016-218239
- Lauckner JE, Jensen JB, Chen HY, Lu HC, Hille B, Mackie K. GPR55 is a cannabinoid receptor that increases intracellular calcium and inhibits M current. Proc Natl Acad Sci USA. 2008 Feb 19;105(7):2699-2704.
- Lautieri A, Thomas S, Stein S. What Is a Dab and How Is It Abused? Laguna Treatment Hospital [Internet]. [cited 2019Aug28]; Available from: https://lagunatreatment.com/marijuana-abuse/what-is-a-dab/
- Lowe DJE, et al. "Cannabis and Mental illness, A Review." Eur Arch Psychiatry Clin Neurosci. 2019 Feb;269(1):107-120. doi: 10.1007/s00406-018-0970-7. Epub 2018 Dec 19.
- Meier, et al. "Cannabis use and neuropsychological decline." Proceedings of the National Academy of Sciences Oct 2012, 109 (40) E2657-E2664; DOI: 10.1073/pnas.1206820109
- Miech, R. A., Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2020). Monitoring the Future national survey results on drug use, 1975-2019: Volume I, Secondary school students. Ann Arbor: Institute for Social Research, The University of Michigan.
- Miech, R. A., Johnston, L. D., Patrick, M.E., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E., (2023). Monitoring the Future national survey results on drug use, 1975-2022: Secondary school students. Monitoring the Future Monograph Series. Ann Arbor, MI: Institute for Social Research, University of Michigan.
- Miech, R. A., Johnston, L. D., Patrick, M.E., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E., (2024). Monitoring the Future national survey results on drug use, 1975-2022: Secondary school students. Monitoring the Future Monograph Series. Ann Arbor, MI: Institute for Social Research, University of Michigan.

References:

- National Academies of Sciences, Engineering, and Medicine. 2017. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press. https://doi.org/10.17226/24625.
- NIDA. 2020, August 13. Stats & Trends in Teen Drug Use with Interactive Chart. Retrieved from https://teens.drugabuse.gov/teachers/stats-trends-teen-drug-use on 2020, September 21
- Noel, C. "Evidence for the use of "medical marijuana" in psychiatric and neurological disorders." *Ment Health Clin* [Internet]. 2017; 7(1):29-38. DOI:10.9740/mhc.2017.01.029
- Olsavsky AK, Hinckley JD, Vidal C. Editorial: Marijuana Legalization and Suicide in Adolescents and Transitional-Age Youth: Important Future Directions for This Line of Research. J Am Acad Child Adolesc Psychiatry. 2024 Mar;63(3):307-309. doi: 10.1016/j.jaac.2023.10.007. Epub 2023 Oct 25.
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- Bottom of Form
- Pacher P, Bátkai S, Kunos G. The endocannabinoid system as an emerging target of pharmacotherapy. Pharmacol Rev. 2006 Sep;58(3):389-462.
- Patrick, M. E., Miech, R. A., Johnston, L. D., & O'Malley, P. M. (2023). Monitoring the Future Panel Study annual report: National
 data on substance use among adults ages 19 to 60, 1976-2022. Monitoring the Future Monograph Series. Ann Arbor, MI: Institute
 for Social Research, University of Michigan
- Richter, L. What is vaping? Center on Addiction [Internet]. [cited 28 Aug 2019]. Available from: https://www.centeronaddiction.org/e-cigarettes/recreational-vaping/what-vaping
- Ryan SA, Ammerman SD, COMMITTEE ON SUBSTANCE USE AND PREVENTION "Counseling Parents and Teens About Marijuana Use in the Era of Legalization of Marijuana." Pediatrics. 2017 Mar;139(3). pii: e20164069. doi: 10.1542/peds.2016-4069.
- R. G. Poulton, M. Brooke, T. E. Moffitt, W. R. Stanton, P. A. Silva "Prevalence and correlates of cannabis use and dependence in young New Zealanders." N Z Med J. 1997 Mar 14; 110(1039): 68-70.
- R. Restrepo, MD, MPH. "Alcohol." ASAM Addiction Medicine Review Course. Dallas, Texas; July 26-28, 2018.
- Russo EB. The cas for the entourage effect and conventional breeding of clinical cannabis: no "strain," no gain. Front Plant Sci. 2019;9:1969.
- Stuyt E. The Problem with the Current High Potency THC Marijuana from the Perspective of an Addiction Psychiatrist. Mo Med. 2018 Nov-Dec;115(6):482-486.
- US Food and Drug Administration. "What You Need to Know (And What We're Working to Find Out) About Products Containing Cannabis or Cannabis-derived Compounds, Including CBD." FDA Consumer Update. July 17, 2019.
- What is Marijuana? National Institute on Drug Abuse [Internet]. 2019 Jul [cited 2019Aug28]; Available from: https://www.drugabuse.gov/publications/research-reports/marijuana/what-marijuana
- Winters, K. C., & Lee, C. Y. (2008). Likelihood of developing an alcohol and cannabis use disorder during youth: association with recent use and age. Drug and alcohol dependence, 92(1-3), 239-247. https://doi.org/10.1016/j.drugalcdep.2007.08.005
- Wilkenson, et al. "A systematic Review of the Evidence for Medical Marijuana in Psychiatric Indications." *J Clin Psychiatry*. 2016 Aug;77(8):1050-64. doi: 10.4088/JCP.15r10036. Review.