

Cannabinoids and the Adolescent Patient

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Disclosures

I have no relevant financial relationships to disclose.

All my investing seems to go to my kids.

Objectives

- Recognize the complexity of cannabinoid epidemiology and pharmacology in a rapidly evolving landscape
- Use current cannabinoid terminology to better care for adolescent patients
- Identify and treat cannabinoid-associated illnesses
- Improve our understanding of neurodevelopmental, cognitive, and psychological effects of adolescent cannabinoid use
- Understand the motivations behind legalization

Quick Definitions

Primary psychoactive
substance

Cannabinoid

Cannabis

delta-9-tetrahydrocannabinol (THC)

Cannabidiol (CBD)

Synthetic cannabinoids

Modulates effects of THC

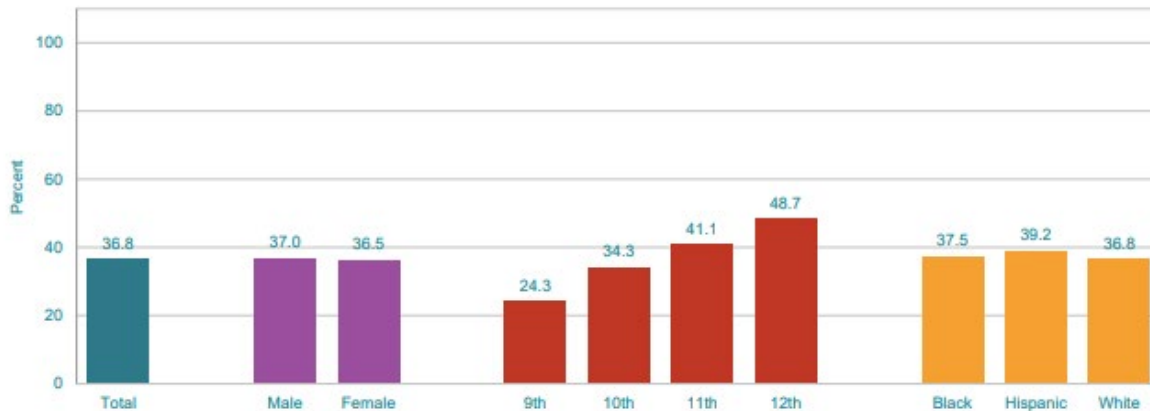
CB1, CB2 receptors

Can have far higher affinity for
receptor; varying effects

Miller SC, Fiellin DA, Rosenthal RN, Saitz R; American Society of
Addiction Medicine, eds. *The ASAM Principles of Addiction Medicine*.
6th ed. Wolters Kluwer; 2019.

Epidemiology

Percentage of High School Students Who Ever Used Marijuana,* by Sex, Grade,† and Race/Ethnicity, 2019



*One or more times during their life

†10th > 9th, 11th > 9th, 11th > 10th, 12th > 9th, 12th > 10th, 12th > 11th (Based on t-test analysis, p < 0.05.)

All Hispanic students are included in the Hispanic category. All other races are non-Hispanic.

This graph contains weighted results.

National Youth Risk Behavior Survey, 2019

Jones CM, Clayton HB, Deputy NP, et al. Prescription opioid misuse and use of alcohol and other substances among high school students - youth risk behavior survey, United States, 2019. *MMWR Suppl.* 2020;69(1):38- 46.

Percentage of High School Students Who Ever Used Marijuana,* by Sexual Identity and Sex of Sexual Contacts, 2019

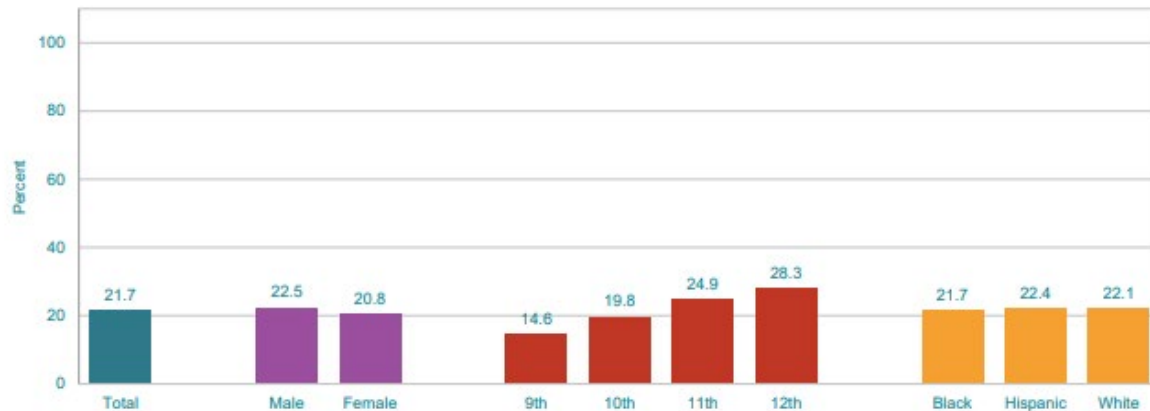


*One or more times during their life
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National Youth Risk Behavior Survey, 2019

Epidemiology

Percentage of High School Students Who Currently Used Marijuana,* by Sex, Grade,† and Race/Ethnicity, 2019



*One or more times during the 30 days before the survey

†10th > 9th, 11th > 9th, 11th > 10th, 12th > 9th, 12th > 10th, 12th > 11th (Based on t-test analysis, $p < 0.05$.)

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National Youth Risk Behavior Survey, 2019

Changes in Means of Delivery

No increase in overall cannabis use, **but**
there was a large increase in cannabis vaping in 2019

Johnston LD, Miech RA, O'Malley PM, Bachman JG, Schulenberg JE, Patrick ME. Monitoring the future national survey results on drug use 1975-2019: overview, key findings on adolescent drug use.

Early-onset (occasional and regular) use increases risk for nicotine dependence

Both early- and late-onset (occasional and regular) use increases risk for misuse of alcohol and illicit drugs

Taylor M, Collin SM, Munafò MR, MacLeod J, Hickman M, Heron J. Patterns of cannabis use during adolescence and their association with harmful substance use behaviour: findings from a UK birth cohort. *J Epidemiol Community Health*. 2017;71(8):764-770.

Changes in Concentration

From 1995 to 2014

- THC concentration increased from 4% to 12%
- THC : CBD ratio increased from 14 to 80

ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC. Changes in cannabis potency over the last 2 decades (1995-2014): analysis of current data in the United States. *Biol Psychiatry*. 2016;79(7):613-619.

Some dabs can have 90% THC concentration

- Increase in acute and chronic effects of cannabinoid use
- Psychosis
- Dependence liability

Miller SC, Fiellin DA, Rosenthal RN, Saitz R; American Society of Addiction Medicine, eds. *The ASAM Principles of Addiction Medicine*. 6th ed. Wolters Kluwer; 2019.

Freeman TP, Winstock AR. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. *Psychol Med*. 2015;45(15):3181-3189.



<https://www.getsmartaboutdrugs.gov/content/teens-and-vaping>

Common Methods and Paraphernalia

Joints

Bongs

Pipes

Blunts

Vape pens, dab pens, dab nails

Hash oil

Wax, budder

Shatter

Edibles

Sploof



Figure 7. (A) Cannabis concentrates, (B) resin with a dab tool, and (C) honey butane wax, one of the most concentrated forms of THC (delta-9-tetrahydrocannabinol). From the US Drug Enforcement Administration⁴³ (in the public domain; permission is not required).

Montalto GJ, Cius EG, Rahmandar MH. Cannabinoids and the Adolescent Patient: A Pragmatic Guide for Pediatric Practitioners. *Pediatr Ann.* 2021 Feb 1;50(2):e57-e64.

Screening for Cannabis Use (Disorder)

S2BI

National Institute on Drug Abuse. Screening tools for adolescent substance use.

BSTAD

“Do you use to get high with your friends, or do you use to get through the day?”

Montalto GJ, Cius EG, Rahmandar MH. Cannabinoids and the Adolescent Patient: A Pragmatic Guide for Pediatric Practitioners. *Pediatr Ann.* 2021 Feb 1;50(2):e57-e64.

Physical Effects of Cannabinoids

Cannabinoid hyperemesis syndrome

Cannabis withdrawal

Acute toxicity from synthetic cannabinoids

Cannabinoid Hyperemesis Syndrome

- Current cannabinoid use, uncontrolled vomiting, abdominal pain
- Pathophysiology (theories)
 - Downregulated CB1 receptors in brain due to chronic use
 - CB1 receptors in GI tract slow gut motility
 - Increased splanchnic flow
- Diagnosis of exclusion; differential includes infectious and inflammatory processes, biliary disease, pregnancy, increased ICP
- Three-quarters weekly daily cannabis use, 95% weekly

Richards JR, Gordon BK, Danielson AR, Moulin AK. Pharmacologic treatment of cannabinoid hyperemesis syndrome: a systematic review. *Pharmacotherapy*. 2017;37(6):725- 734.

Sorensen CJ, DeSanto K, Borgelt L, Phillips KT, Monte AA. Cannabinoid hyperemesis syndrome: diagnosis, pathophysiology, and treatment--a systematic review. *J Med Toxicol*. 2017;13(1):71-87.

Bhatt S, Queen J. Cannabinoid hyperemesis syndrome. *Curr Emerg Hosp Med Rep*. 2019;7(1):14-18.

Cannabinoid Hyperemesis Syndrome Treatment

- Correct GI, electrolyte, renal abnormalities (look at K^+)
- Stop cannabinoid use (may take a couple of days)*
- Ondansetron does nothing
- **Benzodiazepines** have the best supporting evidence
- Haloperidol with varying success
- Capsaicin

*more on this later

Richards JR, Gordon BK, Danielson AR, Moulin AK. Pharmacologic treatment of cannabinoid hyperemesis syndrome: a systematic review. *Pharmacotherapy*. 2017;37(6):725- 734.

Galli JA, Sawaya RA, FriedenberG FK. Cannabinoid hyperemesis syndrome. *Curr Drug Abuse Rev*. 2011;4(4):241-249.

Bhatt S, Queen J. Cannabinoid hyperemesis syndrome. *Curr Emerg Hosp Med Rep*. 2019;7(1):14-18.

Cannabis Use Disorder

- Affects 2.1% of 12 – 17-year-olds, 5.9% of 18 – 25-year-olds
 - Using more than intended; inability to cut back; impaired social, work, relationship interactions; risky use; can lead to dependence and withdrawal (DSM-V)
 - More than 1/3 of adolescents may exhibit withdrawal symptoms
- Cannabinoid withdrawal
 - Irritability
 - Anger
 - Anxiety
 - Depression
 - Insomnia
 - Anorexia, weight loss
 - Restlessness
 - Abdominal pain
 - Headaches
 - Tremors

Depression
Anxiety
PTSD

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders. 5th ed.* Arlington, VA: American Psychiatric Publishing; 2013.

Cooper ZD, Haney M. Cannabis reinforcement and dependence: role of the cannabinoid CB1 receptor. *Addict Biol.* 2008;13(2):188-195.

Simpson AK, Magid V. Cannabis use disorder in adolescence. *Child Adolesc Psychiatr Clin N Am.* 2016;25(3):431-443.

CUD Treatment

- Multidisciplinary
 - Psychotherapy
 - Address comorbidities
 - Break cycle of cannabinoid hyperemesis – cannabinoid withdrawal
- N-acetylcysteine
 - Gabapentin
 - Mirtazapine
 - Antidepressants
 - Atypical antipsychotics
 - Mood stabilizers

Simpson AK, Magid V. Cannabis use disorder in adolescence. *Child Adolesc Psychiatr Clin N Am.* 2016;25(3):431-443.

Bonnet U, Preuss UW. The cannabis withdrawal syndrome: current insights. *Subst Abuse Rehabil.* 2017;8:9-37.

Synthetic Cannabinoids

- Structurally similar to THC
- Full agonists at CB1, CB2
- High affinity for receptor
- Wide chemical diversity, wide range of symptoms
- Altered mental status
- Agitation
- Psychosis
- Sympathomimetic response
- Rhabdo, hyperthermia, AKI have all been reported



www.drugabuse.gov/drug-topics/synthetic-cannabinoids-k2spice

Cooper ZD. Adverse effects of synthetic cannabinoids: management of acute toxicity and withdrawal. *Curr Psychiatry Rep.* 2016;18(5):52.

Deng H, Verrico CD, Kosten TR, Nielsen DA. Psychosis and synthetic cannabinoids. *Psychiatry Res.* 2018;268:400-412.

Synthetic Cannabinoids



- High index of suspicion
- Not on routine drug screen assays
- Supportive care
- Renal protection
- Benzodiazepines for agitation, anxiety, psychosis, seizures
- Neuroleptics for psychosis, agitation

Cooper ZD. Adverse effects of synthetic cannabinoids: management of acute toxicity and withdrawal. *Curr Psychiatry Rep.* 2016;18(5):52.

Brief Word on EVALI

- Cough, shortness of breath, chest pain
- Nausea, emesis, diarrhea
- Fever, chills

- May be related to vitamin E acetate (additive)
- High percentage of patients with EVALI have vaped THC
- Peaked in late 2019

Krishnasamy VP, Hallowell BD, Ko JY, et al. Update: Characteristics of a Nationwide Outbreak of E-cigarette, or Vaping, Product Use–Associated Lung Injury — United States, August 2019–January 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:90–94.

Mental Health and Cannabinoids

Effects were not seen with
adult-onset cannabis use

- Persistent cannabis use starting between ages 13 and 15 years:
 - Lower IQ scores
 - Lower processing speed
 - Executive functioning deficits
- Younger age of onset, more persistent use, more profound decline
- Daily use of cannabis prior to age 17 years decreased likelihood of completing high school

Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci USA*. 2012;109(40):E2657-E2664.

Silins E, Horwood LJ, Patton GC, et al; Cannabis Cohorts Research Consortium. Young adult sequelae of adolescent cannabis use: an integrative analysis. *Lancet Psychiatry*. 2014;1(4):286-293.

Mental Health and Cannabinoids

Hines LA, Freeman TP, Gage SH, et al. Association of high-potency cannabis use with mental health and substance use in adolescence. *JAMA Psychiatry*. 2020;77(10):1044-1051.

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.

Anxiety disorder
Depression, SI, SA
Psychosis

Higher potency THC

Cannabis use starting in adolescence

Frequent use prior to age 15 years
Higher potency THC

Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ*. 2002;325(7374):1212-1213.

Di Forti M, Quattrone D, Freeman TP, et al; EUGEI WP2 Group. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *Lancet Psychiatry*. 2019;6(5):427-436.

Legalization in Illinois

CHICAGO SUN*TIMES

THE WATCHDOGS NEWS POLITICS

'Epic failure' of Illinois' legal weed backers in Springfield to keep promises on diversity

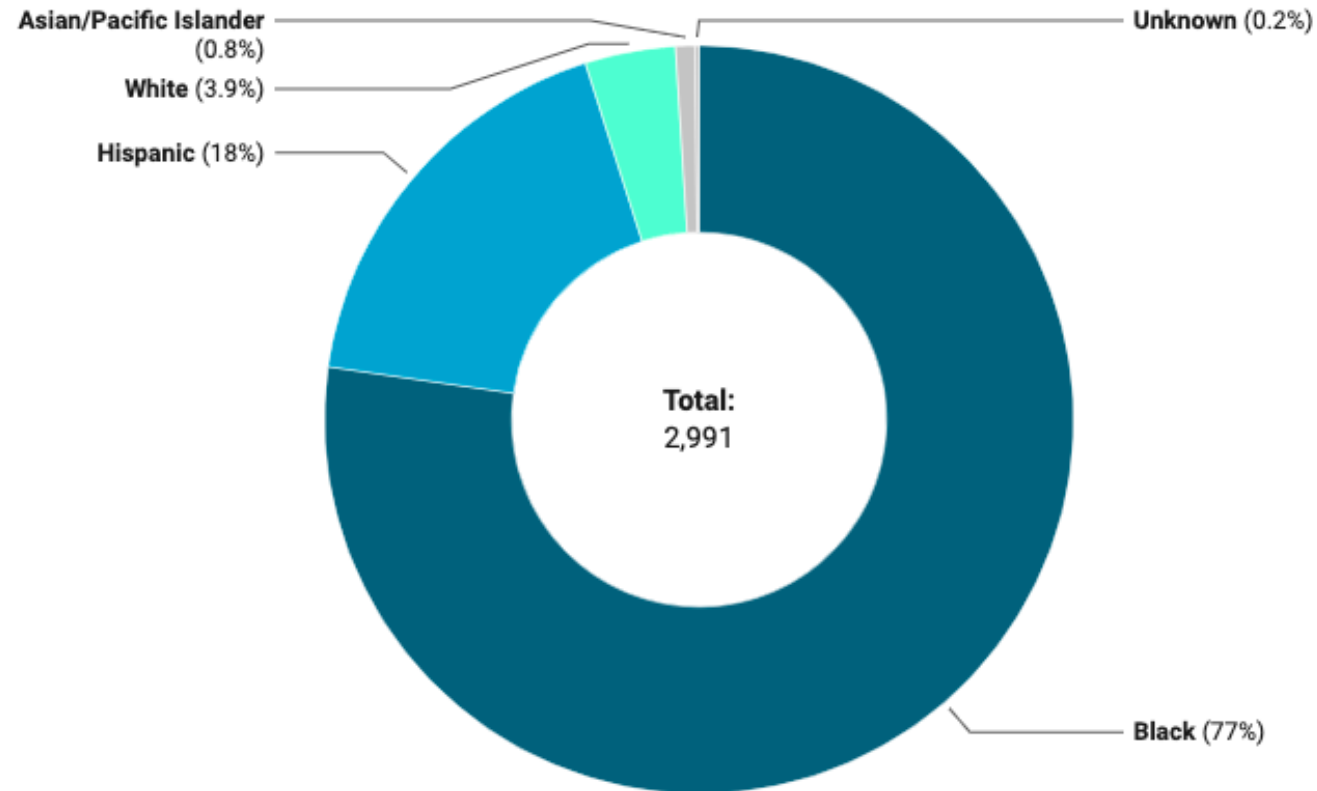
Nearly a year after recreational marijuana's legalization took effect, there's not a single licensed marijuana business in the state with a majority owner who's a person of color.

By Tom Schuba | Updated Dec 11, 2020, 3:40pm CST

Legalization in Illinois

2020 marijuana arrests by race

Black people accounted for more than three-quarters of the arrests for Chicago marijuana-related offenses in 2020.



- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders. 5th ed.* Arlington, VA: American Psychiatric Publishing; 2013.
- Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ.* 2002;325(7374):1212-1213.
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- Richards JR, Gordon BK, Danielson AR, Moulin AK. Pharmacologic treatment of cannabinoid hyperemesis syndrome: a systematic review. *Pharmacotherapy.* 2017;37(6):725-734.
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