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Cannabis 101

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Faculty Disclosure

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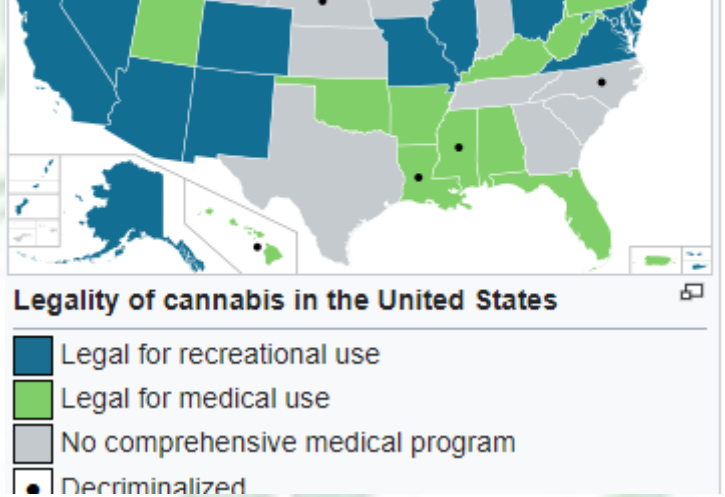
Timothy Wilens, MD has served as a consultant, or has received grant support from the following:

- Licensing agreements with 3D Therapeutics
- Clinical care: MGH, Bay Cove Human Services, Gavin, Major/Minor League Baseball
- (Co)Edited Update in ADHD Pharmacotherapy (Elsevier); *Straight Talk About Psychiatric Medications for Kids* (Guilford); *ADHD Across the Lifespan* (Cambridge), *MGH Comprehensive Clinical Psychiatry* (Elsevier), *MGH Psychopharmacology and Neurotherapeutics* (Elsevier); *Pharmacotherapy of ADHD*, Child Adolesc Psych Clin N Am (Elsevier)

Some of the medications discussed may not be FDA approved in the manner in which they are discussed including diagnosis(es), combinations, age groups, dosing, or in context to other disorders (e.g., substance use disorders)

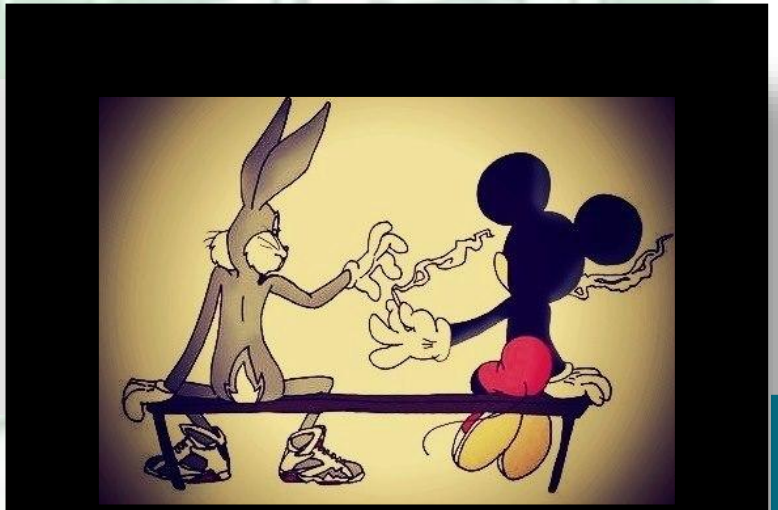


As of Decenber 2025

Medical: 41 States+ DC

Recreational: 24 States, 3 territories, DC

None: 4 States



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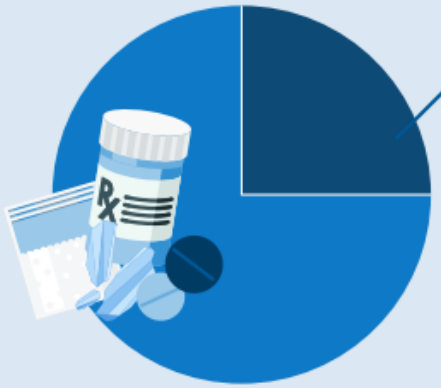
Weed Measurement	Gram Conversion	Average Costs	Average Cost Per Gram
Gram	1 gram	$9–$12	$10/gram
Eighth	3.5 grams	$30–$45	$10/gram
Quarter	7 grams	$50–70	$9/gram
Half-ounce	14 grams	$120–$140	$9/gram
Ounce	28 grams	$200–$300	$9/gram
Quarter Pound	114 grams	$600–$900	$6/gram
Half Pound	227 grams	$1200–$1400	$5/gram
Pound	454 grams	$2200–$2400	$5/gram

1 joint = 0.5 to 1.0 grams

The Average Cost of Marijuana by State; www.tripster.com/cannabis/cost/ 12/2025

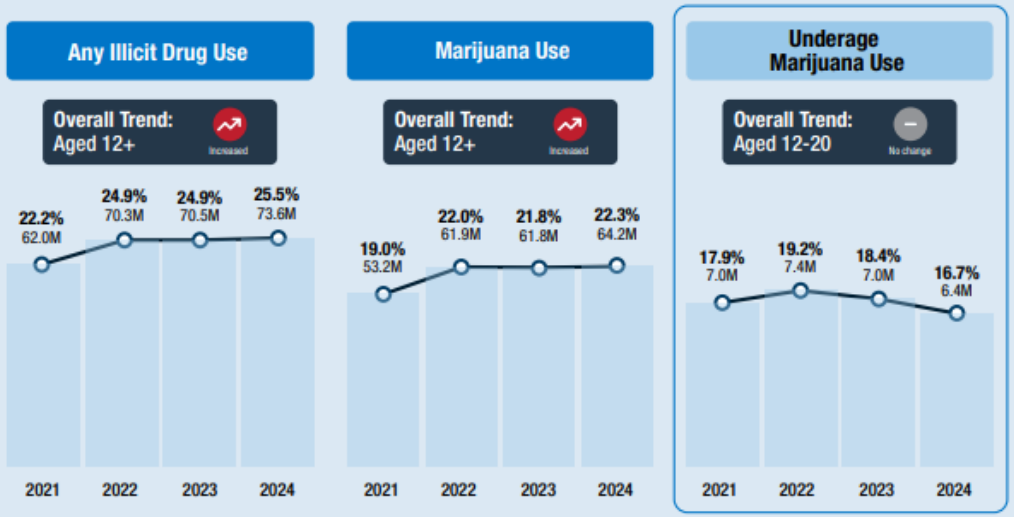
Illicit Drug Use in the Past Year

NSDUH asked respondents aged 12 or older about their use of drugs in the 12 months before the interview.



73.6 million

1 in 4
(25.5%) used illicit drugs in the past year in 2024



Illicit drug use includes the use of marijuana, cocaine, heroin, hallucinogens, inhalants, and methamphetamine, as well as the misuse of prescription drugs (pain relievers, tranquilizers, stimulants, or sedatives).

Misuse of prescription drugs means use in any way not directed by a doctor, such as use without a prescription of one's own, or use in greater amounts, more often, or longer than told to take a drug.

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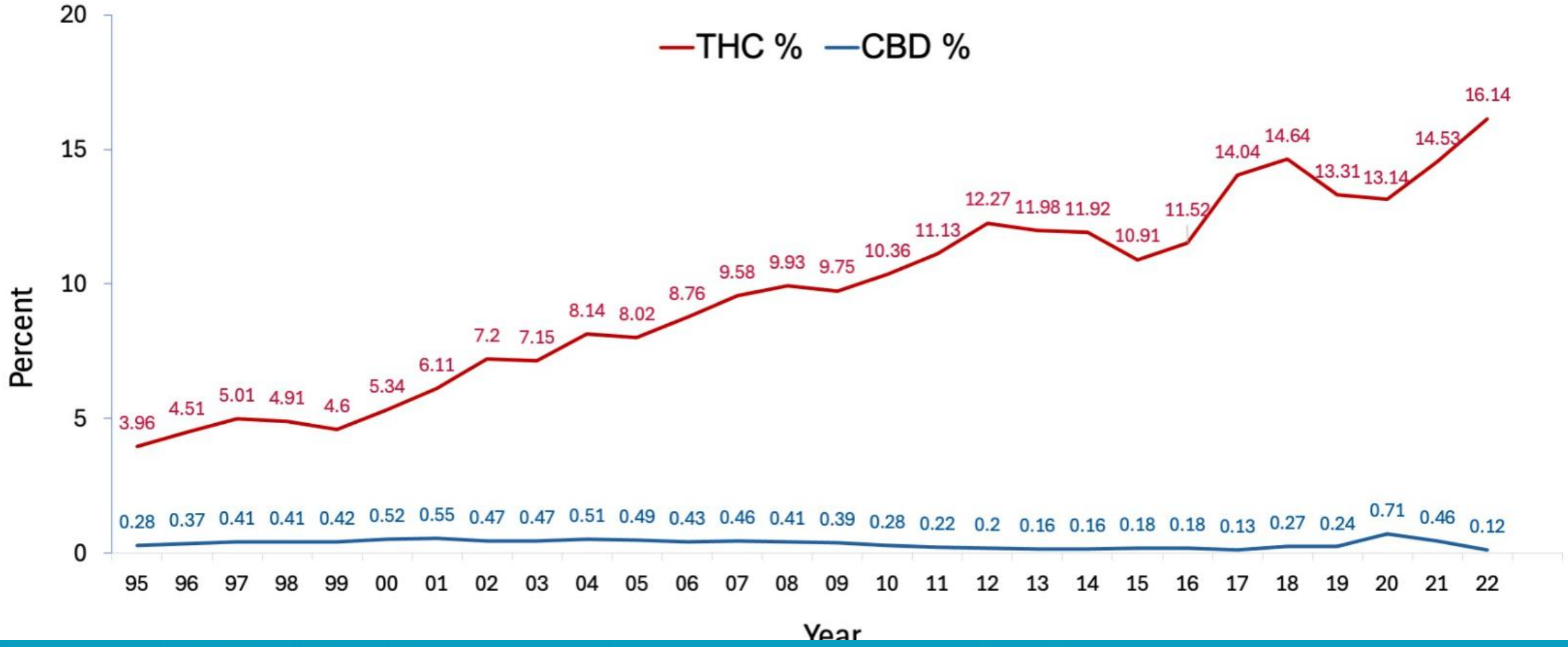
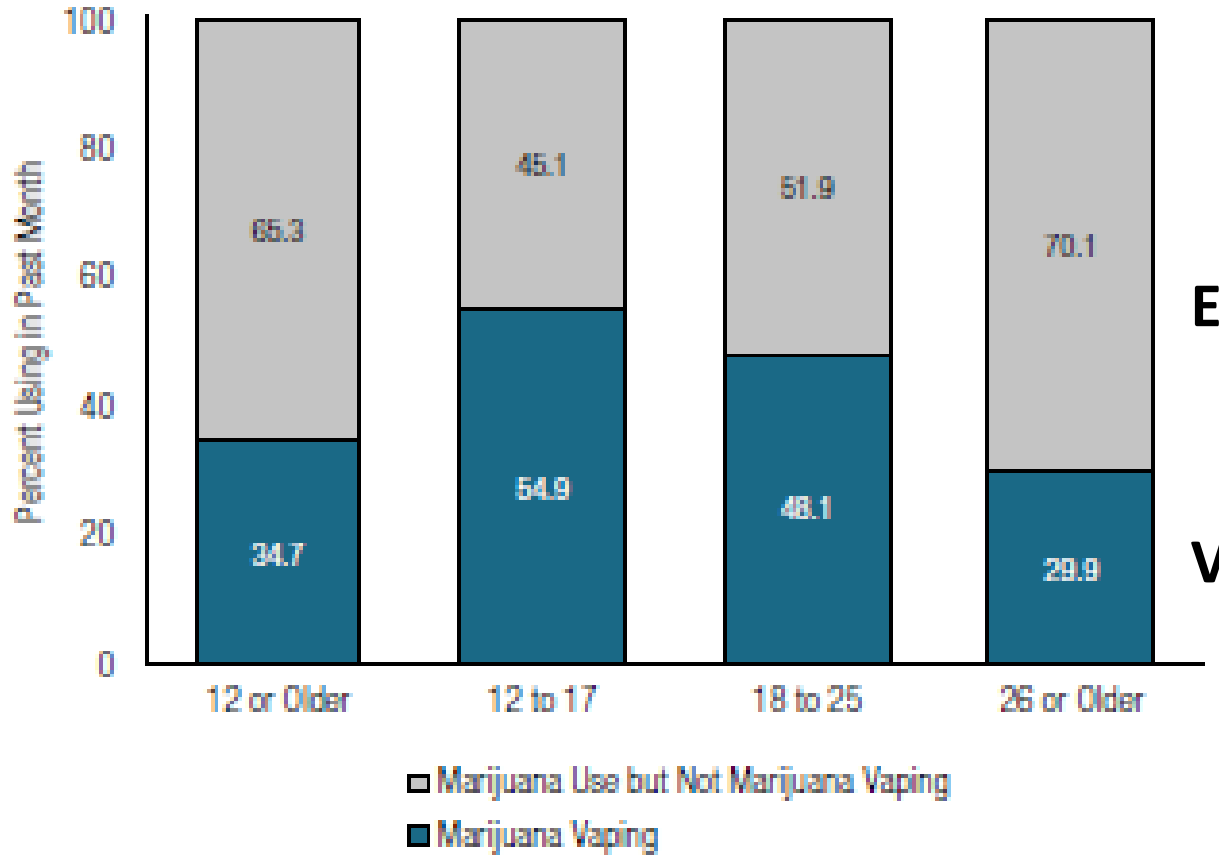
Marijuana Basics

Percentage of THC and CBD in Cannabis Samples Seized by the DEA, 1995-2022



Source: Univ Mississippi Potency Monitoring Program; NIDA.gov

Figure 12. Type of Past Month Marijuana Use: Among Past Month Marijuana Users Aged 12 or Older; 2022



Edible, smoking

Vaping

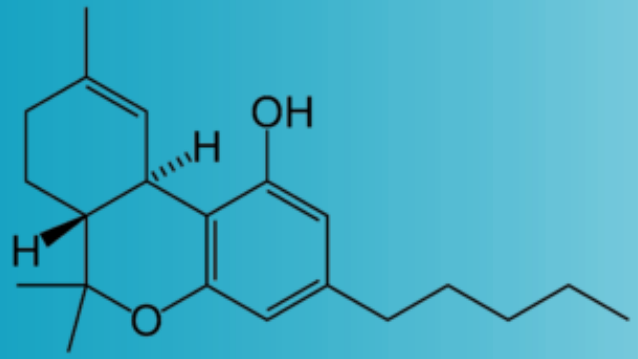
NSDUH 2022; SAMSHA Report 2023

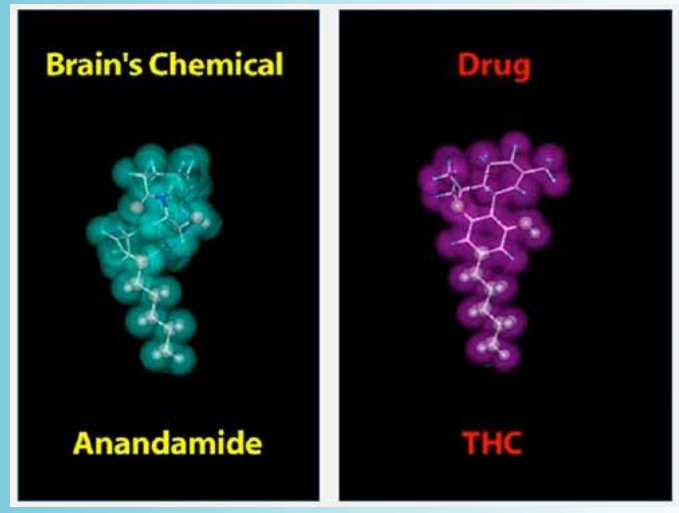
Marijuana Preparations

- **Smoked**
  - Leaves of *Cannabis indiva (sedative)* vs *sativa (thoughts & feelings)* (much overlap genetically)
  - 10-16% THC (vs 3-4% in the 70's and 80's)
- **Hash**
  - Resin of *cannabis indiva or sativa*
  - 5-40% THC
  - Powder referred to as "*Kief*" (trichome resin buds)
- **Hash "Oil" (Wax)**
  - Very potent distillate of hash
  - 30-90% THC
- **Edibles**
  - Cannabis leaves, hash, hash oil
  - Delayed onset of euphoria, higher overdose rate
- **Synthetic (K2, Spice)**
  - Synthetic THC-like compounds
  - Very long duration of action, psychotogenic, seizures
  - Not picked up on routine toxicology testing

Biochemistry of Marijuana

- Active Ingredients
  - Delta-9 Tetrahydrocannabinol (THC)
  - Cannabidiol (CBD)
- Binds to the cannabinoid receptors (brain, body)
- Similar to naturally occurring Anandamide
  - Sanskrit for “awe inspiring”





Pertwee, R (1997). “Pharmacology of cannabinoid CB1 and CB2 receptors”. *Pharmacology & Therapeutics*. 74(2):129–80; Tanda and Goldberg, *Psychopharm. (Berl).* 2003;169:115-34.

Marijuana Distribution after Smoking

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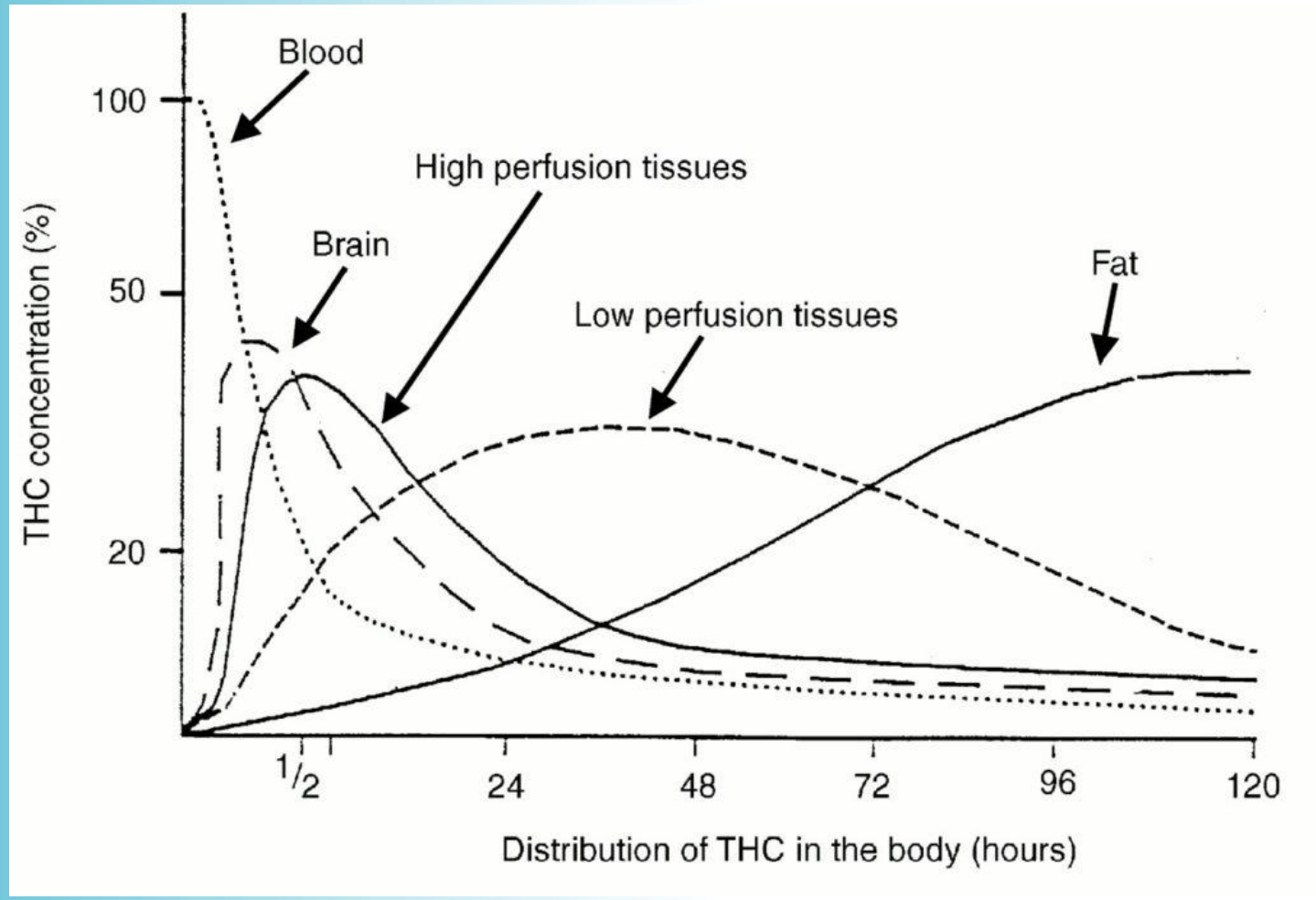
Marijuana rapidly redistributes from blood to brain and other tissues. Distribution to fat is delayed.



Wadieh E et al. Neuropsychiatric Effects of Marijuana, Addiction Medicine and Therapy. 2017. Vol 3(2): 61-64

Euphoria, Performance, and THC Levels

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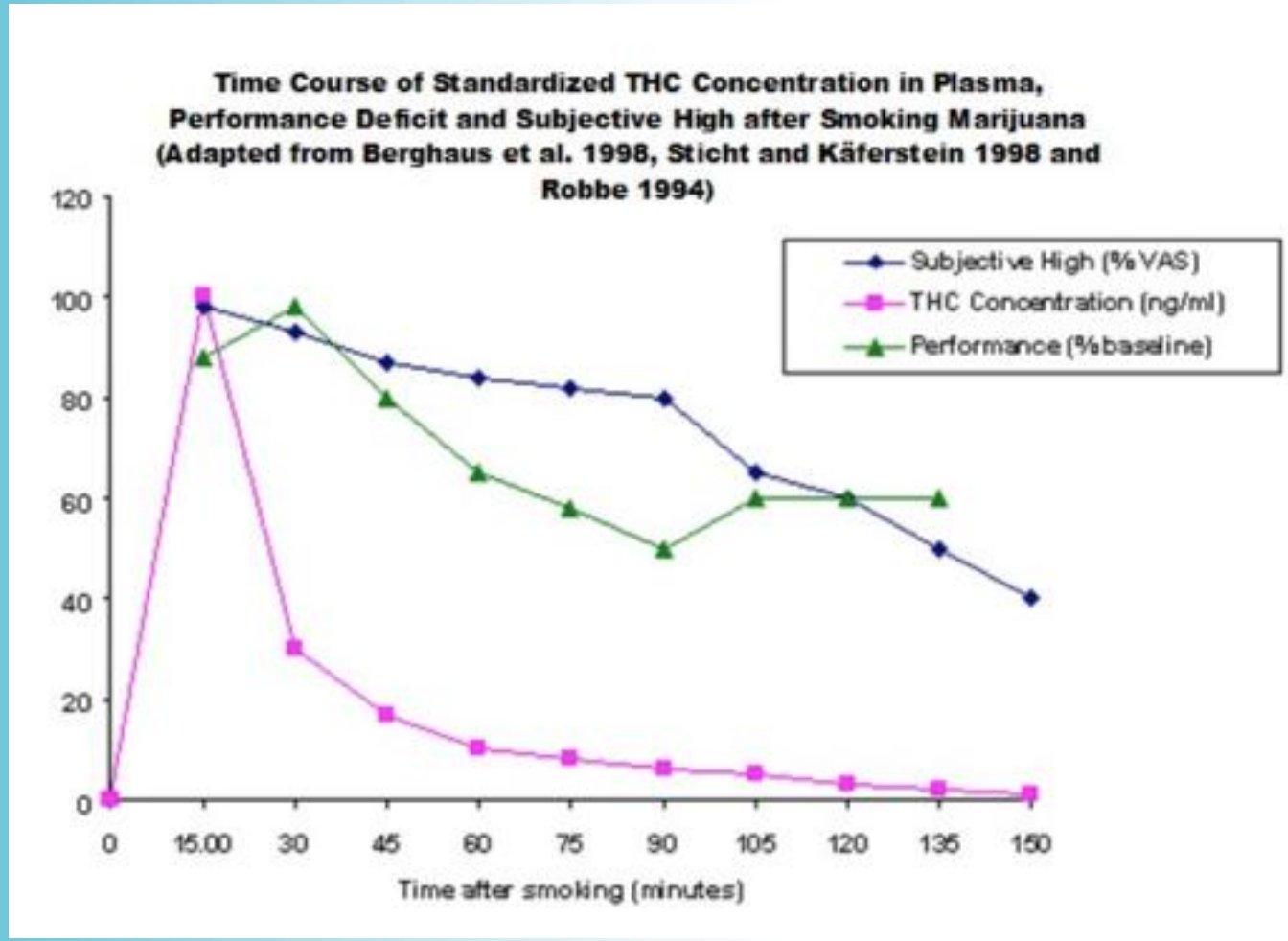
Time course of smoked marijuana compared to performance difficulties and euphoria (VAS)



Robbe HWJ (1994). Influence of Marijuana on Driving. Institute for Human Psychopharmacology, University of Maastricht, Sticht, G. & Käferstein, H. (1998). Pharmacokinetic evaluation of published studies on controlled smoking of marijuana. In N. Kloeden & A. J. McLean (eds.), Alcohol, drugs and traffic safety (Vol.1, pp. 397-402). Adelaide: University of Adelaide, NHMRC Road Accident Research Unit

THC Generally Lacks Pharmacokinetic Drug Interactions: Summary of In Vitro Predictions of Oral THC vs Clinical Results

In Vitro Activity	Examples of Theoretical Substrates	Clinical Confirmation?
Inhibits CYP1A2	Caffeine, olanzapine, clozapine	No Inhibition
Inhibits CYP2B6	bupropion, efavirenz	*Not assessed to date*
Inhibits CYP2D6	dextromethorphan, codeine, tamoxifen	No Inhibition
Inhibits CYP2C9	fluoxetine, losartan, phenytoin, tolbutamide	No Inhibition
Inhibits CYP2C19	clopidogrel, diazepam, phenytoin, omeprazole	No Inhibition
Inhibits CYP3A4	midazolam, simvastatin, tacrolimus	No Inhibition
Inhibits CES1	methylphenidate, oseltamivir, clopidogrel	*Not assessed to date*

Qian. Clin Psychopharmacol. 2019;39:462. Bansal. Clin Pharmacol Ther. 2023;114:693.
Slide courtesy of J Markowitz.

CBD Has Multiple Pharmacokinetic Drug Interactions: Summary of In Vitro Predictions vs Clinical Results

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In vitro Activity	Examples of Theoretical Substrates	Clinical Confirmation?
Inhibits CYP1A2	olanzapine, clozapine, **caffeine**	Yes **(AUC ↑ 39%)**
Inhibits CYP2B6	bupropion, efavirenz	*Not assessed to date*
Inhibits CYP2C8	montelukast, paclitaxel, pioglitazone	*Not assessed to date*
Inhibits CYP2C9	fluoxetine, phenytoin, tolbutamide, **losartan**	Yes **(AUC ↑ 77%)**
Inhibits CYP2C19	diazepam, phenytoin, **omeprazole**	Yes **(AUC ↑ 207%)**
Inhibits CYP2D6	codeine, tamoxifen, **dextromethorphan**	No inhibition
Inhibits CYP3A4/5	simvastatin, tacrolimus, paxlovid, **midazolam**	Yes **(AUC ↑ 56%)**
Inhibits UGT1A9	propofol, fenofibrate	*Not assessed to date*
Inhibits UGT2B7	lamotrigine, morphine, lorazepam	*Not assessed to date*
Inhibits CES1	oseltamivir, clopidogrel, methylphenidate	No inhibition

Qian. Clin Psychopharmacol. 2019;39:462. Markowitz. Med Cannabis Cannabinoids. 2022;5:199.
Bansal. Clin Pharmacol Ther. 2023;114:693. Slide courtesy of J Markowitz

frontiers in Psychiatry

CLINICAL TRIAL
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Effects of Cannabidiol and Delta-9-Tetrahydrocannabinol on Emotion, Cognition, and Attention: A Double-Blind, Placebo-Controlled, Randomized Experimental Trial in Healthy Volunteers

*Timo Woelfl[1], Cathrin Rohleder[1,2], Juliane K. Mueller[1,3], Bettina Lange[1], Anne Reuter[1], Anna Maria Schmidt[1], Dagmar Koethe[2,4], Martin Hellmich[5] and F. Markus Leweke[1,2]**

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The two main phytocannabinoids—delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)—have been extensively studied, and it has been shown that THC can induce transient psychosis. At the same time, CBD appears to have no psychotomimetic potential. On the contrary, emerging evidence for CBD's antipsychotic properties suggests that it may attenuate effects induced by THC. Thus, we investigated and compared the effects of THC and CBD administration on emotion, cognition, and attention as well as the impact of CBD pre-treatment on THC effects in healthy volunteers. We performed a placebo-controlled, double-blind, experimental trial (GEI-TCP II; ClinicalTrials.gov identifier: NCT02487381) with 60 healthy volunteers randomly allocated to four parallel intervention groups, receiving either placebo, 800 mg CBD, 20 mg THC, or both cannabinoids. Subjects underwent neuropsychological tests assessing working memory (Letter Number Sequencing test), cognitive processing speed (Digit Symbol Coding task), attention (d2 Test of Attention), and emotional state (adjective mood rating scale [EWL]). Administration of CBD alone did not influence the emotional state, cognitive performance, and attention. At the same time, THC affected two of six emotional categories—more precisely, the performance-related activity and extraversion—, reduced the cognitive processing speed and impaired the performance on the d2 Test of Attention. Interestingly, pre-treatment with CBD did not attenuate the effects induced by THC. These findings show that the acute intake of CBD itself has no effect *per se* in healthy volunteers and that a single dose of CBD prior to THC administration was insufficient to mitigate the detrimental impact of THC in the given setting. This is in support of a complex interaction between CBD and THC whose effects are not counterbalanced by CBD under all circumstances.

Keywords: cannabinoids, cannabis, tetrahydrocannabinol, cannabidiol, healthy subjects, model psychosis, rct

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CBD -> No Effects

THC -> reduced cognitive processing speed and impaired performance on the d2 Test of Attention

Psychiatry Research 308 (2022) 114347

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Review article

A scoping review of the use of cannabidiol in psychiatric disorders

Anna E. Kirkland [a,*], Matthew C. Fadus [b], Staci A. Gruber [c,d], Kevin M. Gray [a], Timothy E. Wilens [b,e], Lindsay M. Squeglia [a]

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CBD
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ABSTRACT

Cannabidiol (CBD) has become a fast-growing avenue for research in psychiatry, and clinicians are challenged with understanding the implications of CBD for treating mental health disorders. The goal of this review is to serve as a guide for mental health professionals by providing an overview of CBD and a synthesis the current evidence within major psychiatric disorders. PubMed and PsycINFO were searched for articles containing the terms "cannabidiol" in addition to major psychiatric disorders and symptoms, yielding 2952 articles. Only randomized controlled trials or within-subject studies investigating CBD as a treatment option for psychiatric disorders ($N = 16$) were included in the review. Studies were reviewed for psychotic disorders ($n = 6$), anxiety disorders ($n = 3$), substance use disorders (tobacco $n = 3$, cannabis $n = 2$, opioid $n = 1$), and insomnia ($n = 1$). There were no published studies that met inclusion criteria for alcohol or stimulant use disorder, PTSD, ADHD, autism spectrum disorder, or mood disorders. Synthesis of the CBD literature indicates it is generally safe and well tolerated. The most promising preliminary findings are related to the use of CBD in psychotic symptoms and anxiety. There is currently not enough high-quality evidence to suggest the clinical use of CBD for any psychiatric disorder.

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The most promising preliminary findings are related to the use of CBD in psychotic symptoms and anxiety

Putative Medical Uses of Major Constituents of Marijuana: THC & CBD

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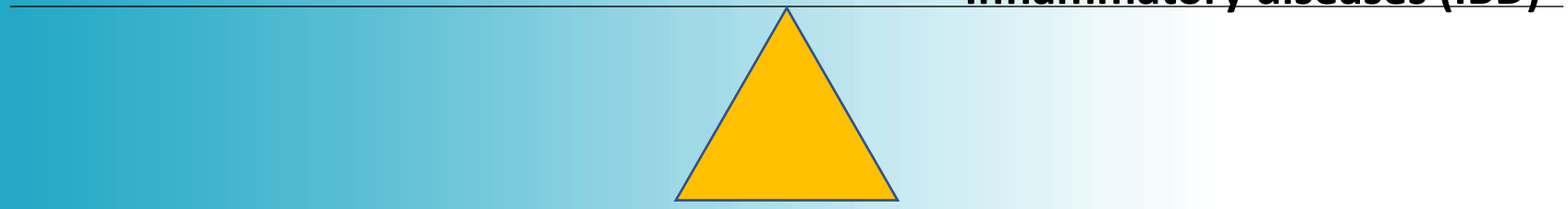
THC

Pain
Nausea/Vomiting
Spasticity
Glaucoma
Insomnia
Appetite

CBD

Seizures
Pain
Migraines
Anxiety
Pre-psychotic sxs
Depression
Inflammatory diseases (IBD)



META-ANALYSIS SUBSTANCE USE

Systematic Review and Meta-Analysis: Medical and Recreational Cannabis Legalization and Cannabis Use Among Youth in the United States

Aditya K.S. Pawar, MD, Elizabeth S. Firmin, BA, Timothy E. Wilens, MD, Christopher J. Hammond, MD, PhD

Objective: Dramatic changes in state-level cannabis laws (CL) over the past 25 years have shifted societal beliefs throughout the United States, with unknown implications for youth. In the present study, we conducted an updated systematic review and meta-analysis examining estimated effects of medical cannabis legalization (MCL) and recreational cannabis legalization (RCL) on past-month cannabis use among US youth.

Method: A systematic review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, followed by a subsequent meta-analysis investigating the associations between state-level cannabis laws (ie, MCL vs non-MCL, and RCL vs non-RCL) and past-month cannabis use prevalence among US adolescents and young adults. Supplemental analyses examined age-group effects and design-related factors.

Results: Our search identified 4,604 citations, 34 and 30 of which were included in qualitative and quantitative analyses, respectively. Meta-analysis of MCL studies identified no significant association between MCL and change in past-month youth cannabis use (odds ratio [OR] = 0.981, 95% CI = 0.960, 1.003). Meta-analysis of RCL studies showed significantly increased odds of past-month cannabis use (OR = 1.134, 95% CI = 1.116-1.153). Meta-analysis of more recent studies, however, showed a significantly increased odds of past-month cannabis use among both adolescents and young adults (OR = 1.089, 95% CI = 1.015,1.169, and OR = 1.221, 95% CI = 1.188,1.255, respectively).

Conclusion: Cannabis legalization has complex and heterogenous effects on youth use that may differ across law types. Our meta-analytic results showed modest positive effects of RCL on past-month cannabis use (more so in young adults than in adolescents) and minimal effects of MCL on these outcomes in US youth. Given the shift toward recreational legalization, additional focus on RCL effects is warranted.

Key words: recreational cannabis laws; medical cannabis laws; adolescents; cannabis use; meta-analysis

J Am Acad Child Adolesc Psychiatry 2024;■(■):■-■.

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- Study of influence of Medical or Recreational Cannabis Laws on Use in Teens
- N=34 studies (med legal) and 30 (recreational legal)

Findings:

- No impact of medically legal on use
- Recreationally legal increased odds of past month cannabis in young adults > adolescents

Marijuana Risks

- **Lung-based (adults)**
  - Wheezing
  - Exacerbation in COPD/Asthma
  - Less irritation compared to cigarettes
- **Cancer risk (adults)**
  - No increased risk of lung or other cancers
  - Trend to decreased prostate cancer
- **Motor vehicle accidents (adolescents/adults)->**
  - About two-fold increased risk while intoxicated
  - Increased in fatal accidents in states with legalization

Likelihood to Develop CUD Based on Frequency of Use

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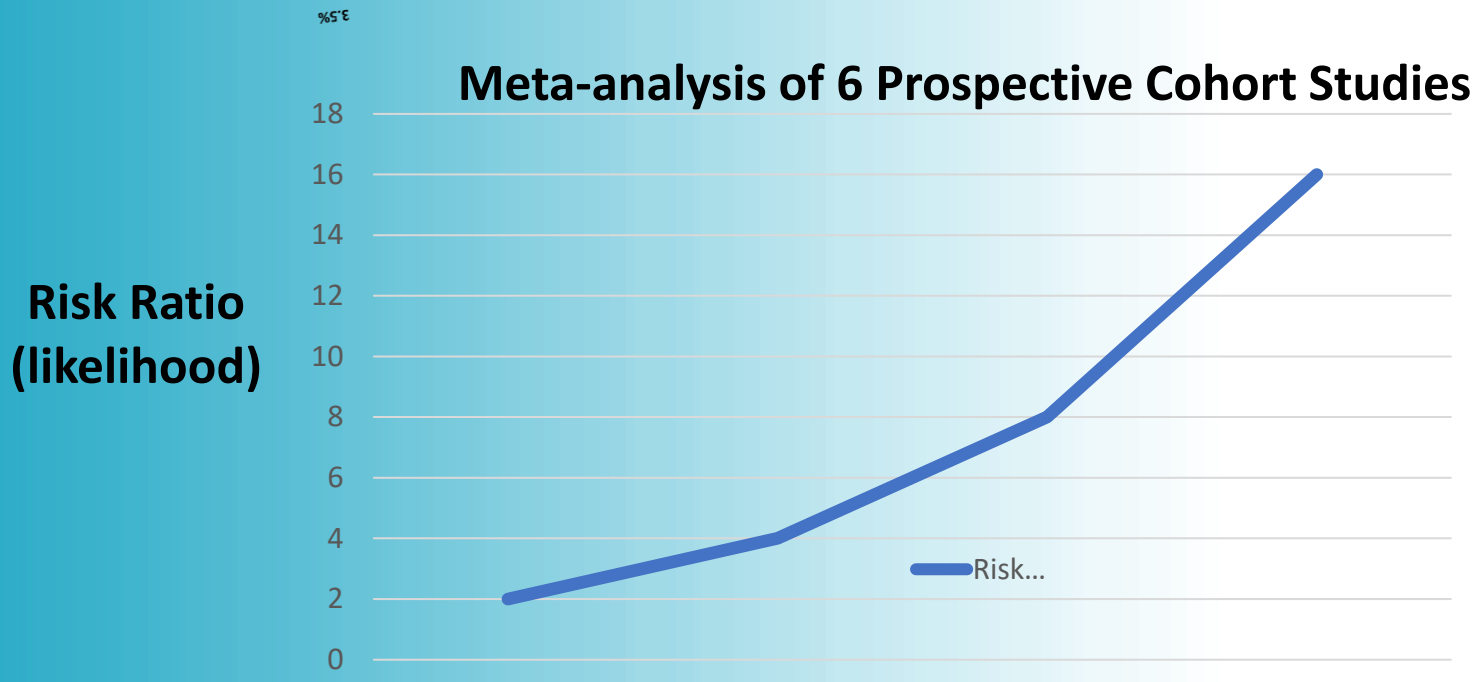


	Yearly	Monthly	Weekly	Daily
Absolute Risk Increase	**3.5%**	**8%**	**17%**	**36%**

Robinson T, et al. *Drug Alc Dep*. 2022. https://doi.org/10.1016/j.drugalcdep.2022.109582

JAMA Psychiatry | Original Investigation

Association of Cannabis Use During Adolescence With Neurodevelopment

Matthew D. Albaugh, PhD; Jonatan Ottino-Gonzalez, PhD; Amanda Sidwell, BS; Claude Lepage, PhD; Anthony Juliano, PsyD; Max M. Owens, PhD; Bader Chaarani, PhD; Philip Spechler, PhD; Nicholas Fontaine, BS; Pierre Rioux, MSc; Lindsay Lewis, PhD; Seun Jeon, PhD; Alan Evans, PhD; Deepak D'Souza, MD; Rajiv Radhakrishnan, MD; Tobias Banaschewski, MD, PhD; Arun L. W. Bokde, PhD; Erin Burke Quinlan, PhD; Patricia Conrod, PhD; Sylvane Desrivières, PhD; Herta Flor, PhD; Antoine Grigis, PhD; Penny Gowland, PhD; Andreas Heinz, MD, PhD; Bernd Ittermann, PhD; Jean-Luc Martinot, MD, PhD; Marie-Laure Paillère Martinot, MD, PhD; Frauke Nees, PhD; Dimitri Papadopoulos Orfanos, PhD; Tomáš Paus, MD, PhD; Luise Poustka, MD; Sabina Millenet, PhD; Juliane H. Fröhner, MSc; Michael N. Smolka, MD; Henrik Walter, MD, PhD; Robert Whelan, PhD; Gunter Schumann, MD; Alexandra Potter, PhD; Hugh Garavan, PhD; for the IMAGEN Consortium

MGH MASSACHUSETTS GENERAL HOSPITAL

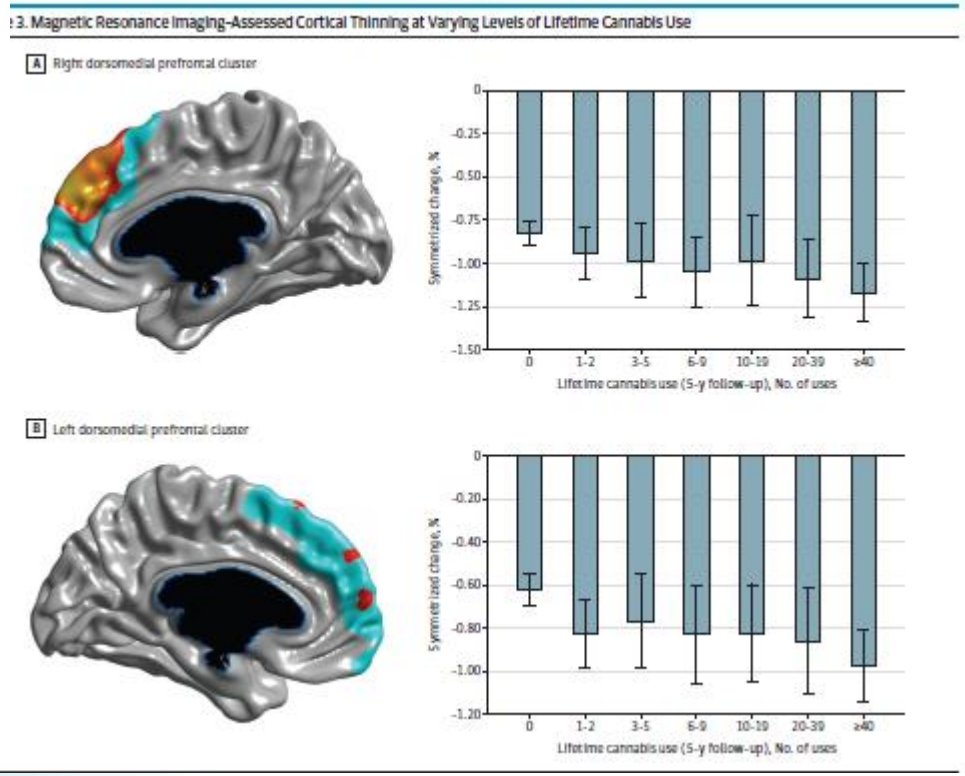
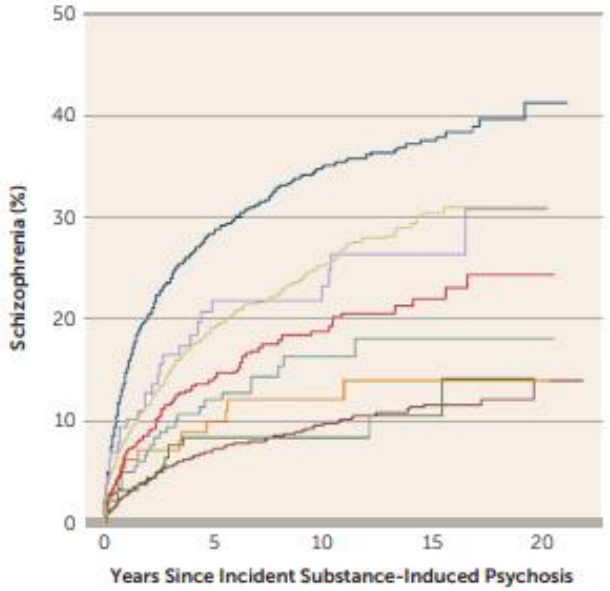


IMAGEN Multisite Study (8 sites)
N=799 children with scans and 5 year f/u
Mean age 14.4 yo (base) and 19 yo at f/u
MRI imaging for cortical thickness development
Main findings
-No differences at baseline between cannabis users
-Age related thinning in cannabis use –dose response relationship
-Overlay in cortical thinning linked to CB1 receptor density (from other PET study)

JAMA Psychiatry. 2021;78(9):1031-1040. doi:10.1001/jamapsychiatry.2021.1258
Published online June 16, 2021.

Marijuana Use & Psychotic Symptoms

- Marijuana use during adolescence is related to subclinical or full acute psychotic episodes and future psychotic disorders
  Casadio et al. 2011. Semple et al. 2005; Wilkinson et al. 2014; Moore et al. 2007; Kuepper et al. 2011 Starzer *Am J Psych*. 2018.
- Synthetic marijuana (K2/Spice) bidirectionally linked with serious mental illness/psychosis, prolonged psychosis
- Almost one-half of individuals who experience psychosis with marijuana develop schizophrenia
  Starzer et al. 2018.



Bechtold J, et al. *Am J Psychiatry.* Aug 01 2016;173(8):781-789. Starzer, et al. *Am J Psychiatry* 175:4, April 2018.

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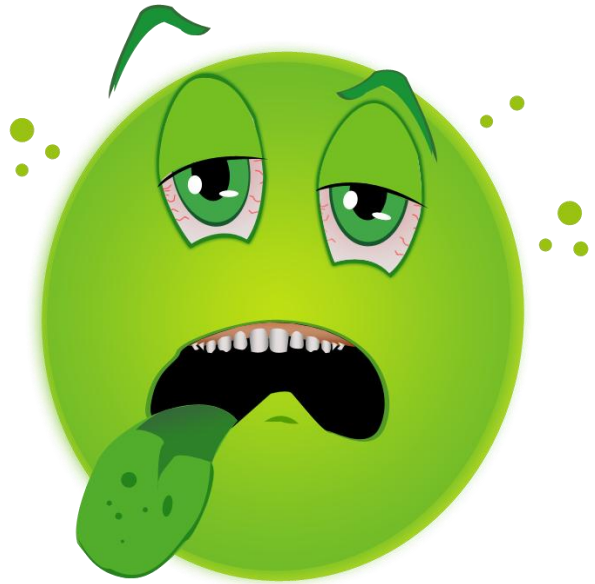
Cannabis Withdrawal

- **3 or more symptoms that develop within one week of stopping heavy cannabis use**
  - **Irritability, anger, or aggression**
  - **Nervousness or anxiety**
  - **Sleep difficulty (insomnia, disturbing dreams)**
  - **Decreased appetite or weight loss**
  - **Restlessness**
  - **Depressed mood**
  - **One or more physical symptoms causing significant discomfort: abdominal pain, shakiness/tremor, sweating, fever, chills, or headaches**



Budney AJ[1], Hughes JR.; Curr Opin Psychiatry. 2006 May;19(3):233-8.

Substance Use Disorder: Treatment

- **Motivational Interviewing**
- **Cognitive Behavioral Therapy**
- **Contingency management**
  - **e.g., pay for improvement; use of "items" such as cell phones, car use to 'trade' for negative use**
- **Groups: for youth and parents (support, coaching)**
- **Address behavioral health issues**
  - **e.g., ADHD, mood disorders**

Wilens, McKowen & Kane. Contemp Peds 2013.

Pharmacotherapy for Cannabis Use Disorders

- **N-Acetyl Cysteine (NAC)-nutraceutical-dosing 1200 mg BID**
  RCT; Grey et al. Am J Psych 2012; 2017 (in young adults only)
- **Topirimate**
  (RCTs: Roten et al., Add Beh 38(3) 2013; Miranda et al. Addiction Biol, 2016; Emery et al., Psychopharm, 2021 V 238)
- **Buspirone**
  Pilot RCT; McRae-Clark et al., 2009
- **Gabapentin**
  Pilot RCT; Mason et al., 2012
- **Nabilone –** Synthetic analogue of THC (Pharm of CUD, 2020)
- **Rimonabant-** experimental (CB-1 receptor blocker; EU approval and withdrawal: mood/SI)
  Huestis MA, et al. Psychopharm 2007

Cannabis Use Disorders: Summary

MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

- **Cannabis is the most common non-alcohol substance of use, misuse, and addiction**
- **Cannabis has substantial addiction potential**
- **Cannabis use (and disorders) onset typically in adolescence**
- **Use in adolescents ≤16 years of age particularly problematic for potential structural brain changes and lasting neurocognitive dysfunction**
- **Treatment is multimodal-pharmacotherapy may help reduce use**