

# Cannabis in Missouri in 2023

Kevin P. Hill, M.D., M.H.S.  
MPPA Spring Meeting  
6 May 2023

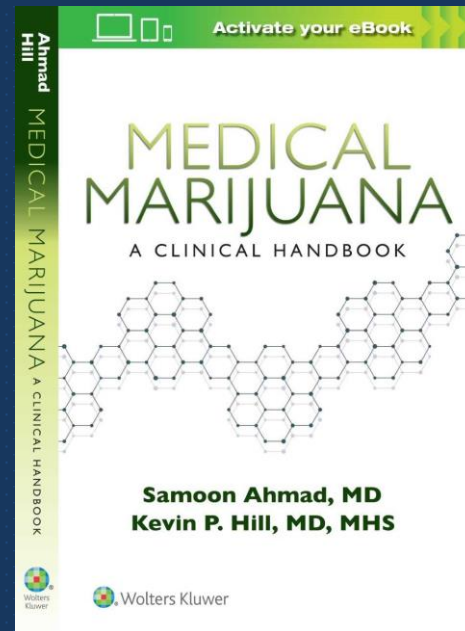
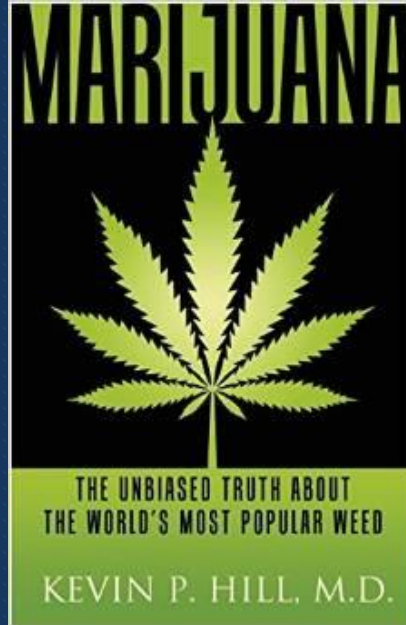


Beth Israel Deaconess  
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# Disclosures

- Books- Hazelden Publishing, Wolters-Kluwer.
- Consultant: NFL.



# Learning Objectives

- To discuss current epidemiology in context of changing cannabis policy.
- To review basic risks and benefits of cannabis.
- To describe potential side effects of CBD.

# Three Areas of Focus

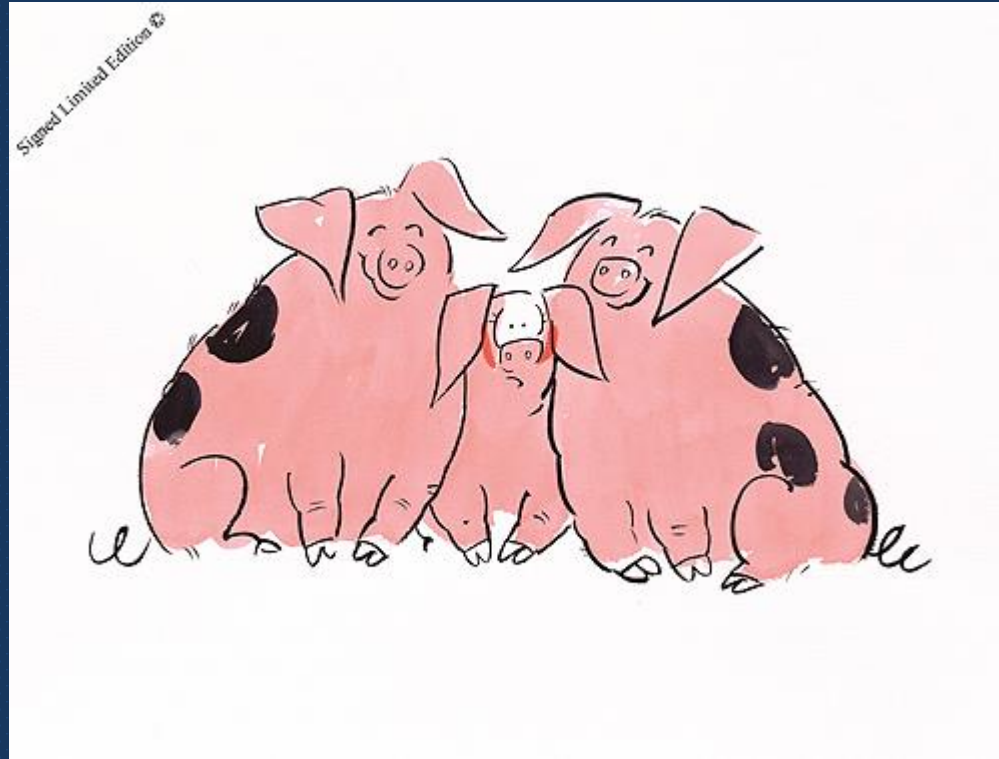
- Clinical work: Director of Addiction Psychiatry, private practice, pro sports teams and leagues.
- Clinical research: cannabis and cannabinoids for medical indications.
- Educational outreach: Science vs. public perception, schools, policymakers.

# Why Cannabis?

- Addiction treatment: 40% alcohol, 40% opioids, 20% everything else.
- Around 60%: time when smoked cannabis daily for years.
- How many of these folks would you see down the road if an effective cannabis intervention existed?



# In The Middle



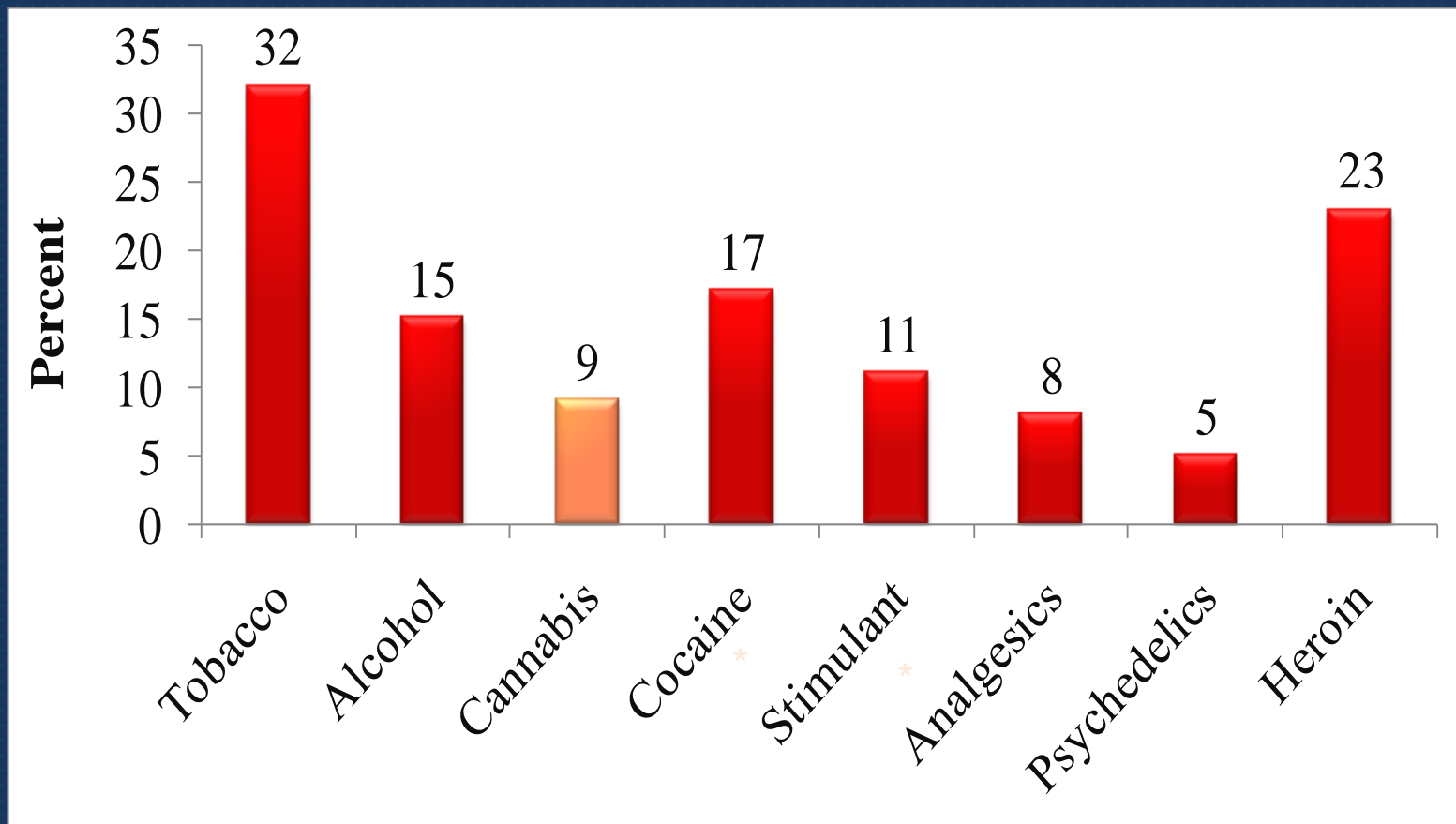
# National Statistics: Not Going Away

- About 22 million Americans used cannabis in the past year, use doubled in past 10 years (Hasin et al. 2015), 10% of users use for medical purposes. (Compton et al. 2017)
- Powerful messages— medical marijuana, legalization, celebrities.



**Development of Problems:  
About 9% of users may become dependent;  
17% (1 in 6) who start use in adolescence**

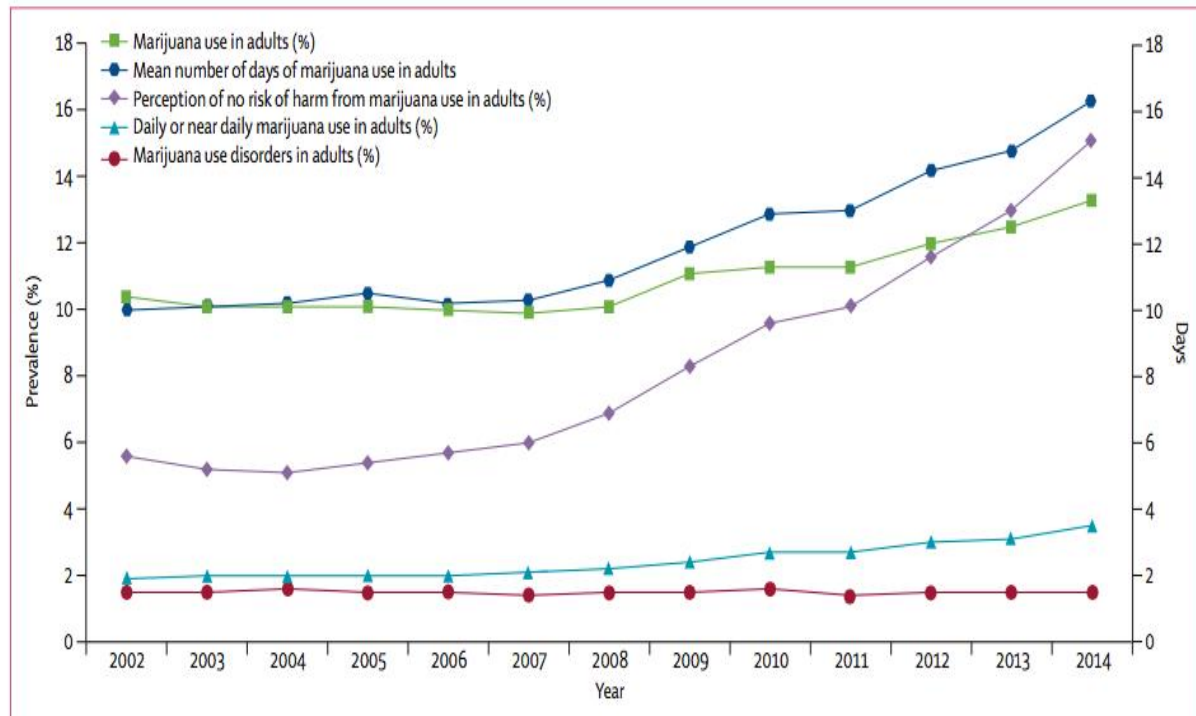
**Estimated Prevalence of Dependence Among Users**



**Anthony JC et al., 1994 (Confirmed by  
Lopez-Quintero et al. 2011)**



# Current Trends in Cannabis Use



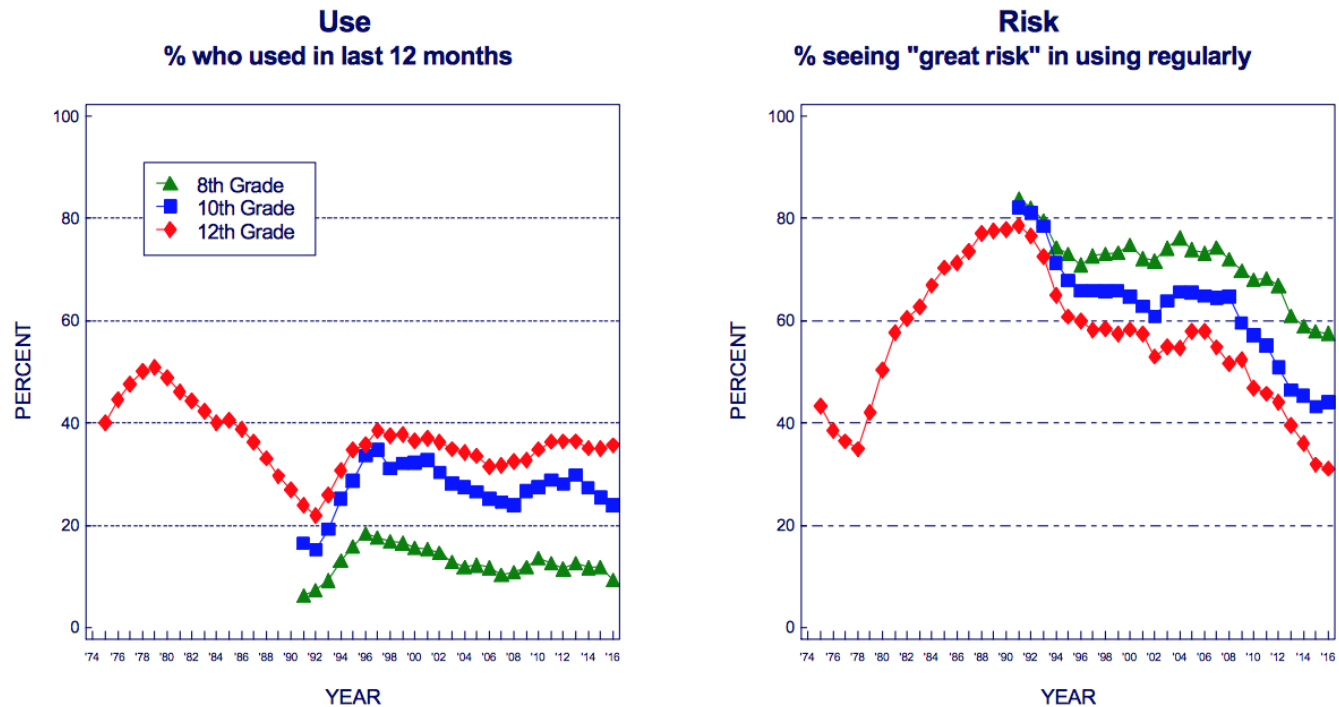
**Figure: Trends in marijuana use patterns, marijuana use disorders, and perceived risk of harm**

Annual prevalence and trends in any marijuana use, daily or near daily marijuana use, marijuana use disorders, mean number of days of marijuana use, and perception of no risk of harm from marijuana use in adults in the USA. \*Joinpoints indicate significant changes in non-linear trends.

# 12<sup>th</sup> Graders' Past Year Cannabis Use vs. Perceived Risk of Occasional Cannabis Use

FIGURE 3

**Marijuana: Trends in Annual Use, Risk, Disapproval, and Availability**  
Grades 8, 10, and 12

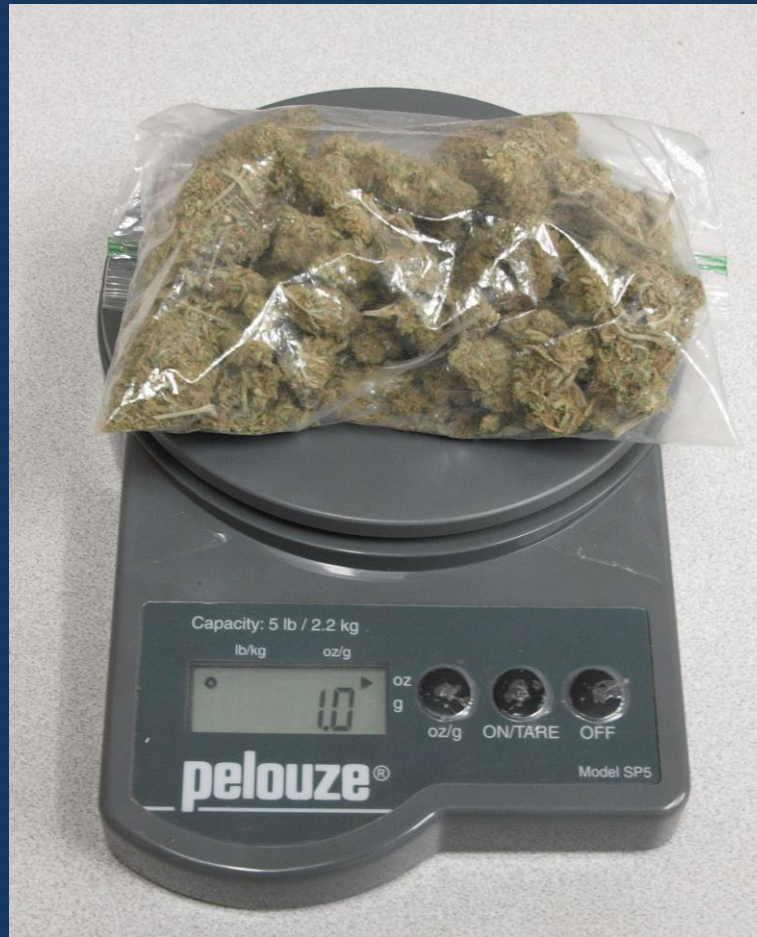


SOURCE: The Monitoring the Future study, the University of Michigan.

# Amendment 3, passed 11/22

- Legalized recreational cannabis and strengthened medical cannabis in Missouri.
- Expunges non-violent marijuana convictions by June 8, 2023.
- Establishes possession limits for recreational and increases them for medical.





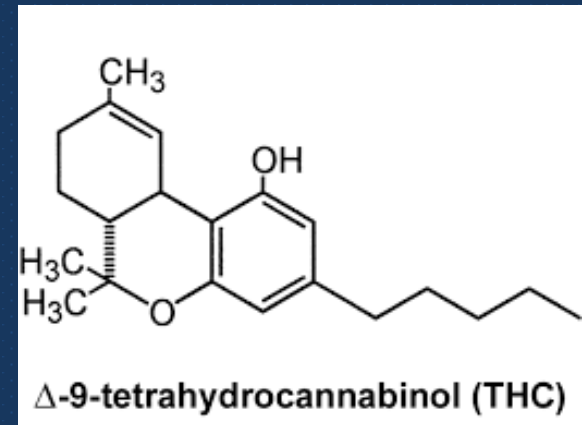
One Ounce of Cannabis

# Some Basic Math and Amendment 3

- Typical joint is 0.5-1 grams.
- 27 grams in an ounce, so that's 54 joints/ounce.
- Amendment 3: recreational users may possess up to 3 ounces at a time, so over 150 joints.
- It also increased limit for medical cannabis patients from 4 ounces per month to 6!

# Pharmacology of Cannabis

- 140+ pharmacologically-active cannabinoids.
- THC: euphoria, anti-inflammatory, psychosis.
- CBD: non-intoxicating, anti-anxiety, antipsychotic?



**RISKS**

# Drug Effects: Acute and Chronic





# Acute Adverse Effects of THC

- Impaired judgement.
- Impaired coordination and motor skills (driving).
- Memory loss and learning difficulties.
- Psychosis.



# Driving



- When you're drunk you run red lights
- When you're stoned you stop at green lights

# Driving

- No .08 BAC equivalent for marijuana.
- Technology does not exist to test for marijuana in the field in a way comparable to alcohol testing.
- Blood level plus field sobriety tests may be best we can do right now.

OPINION

## Clardy Law would keep roads safe

Next to alcohol, marijuana is the second-most commonly found substance in the bodies of drivers involved in fatal crashes.

By Kevin P. Hill and John F. Carmichael Jr. Updated January 18, 2022, 3:00 a.m.



# Marijuana Myths

- Not Harmful
- Not Addictive
- No Withdrawal



# Implications on Youth Health

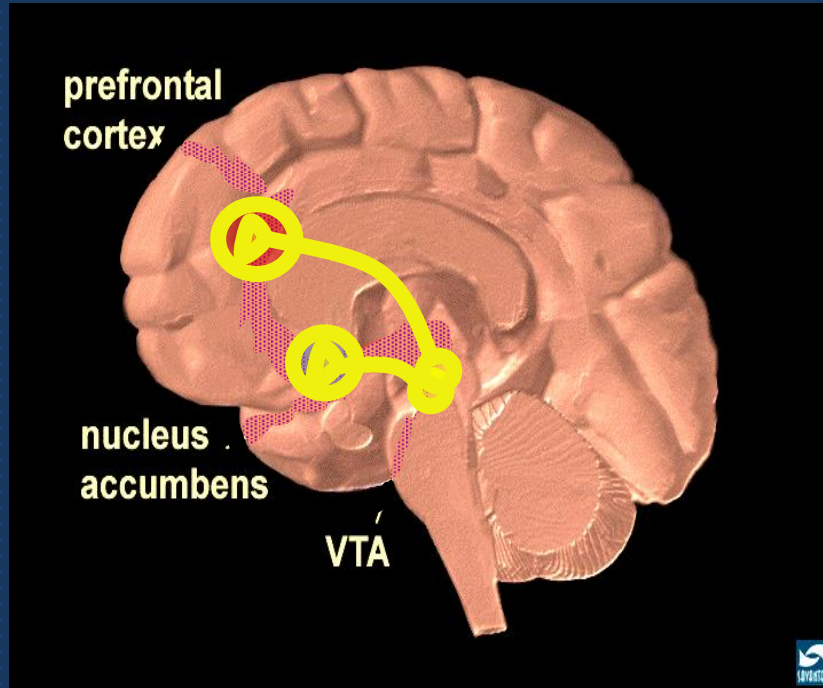


# Marijuana's Effects on the Brain

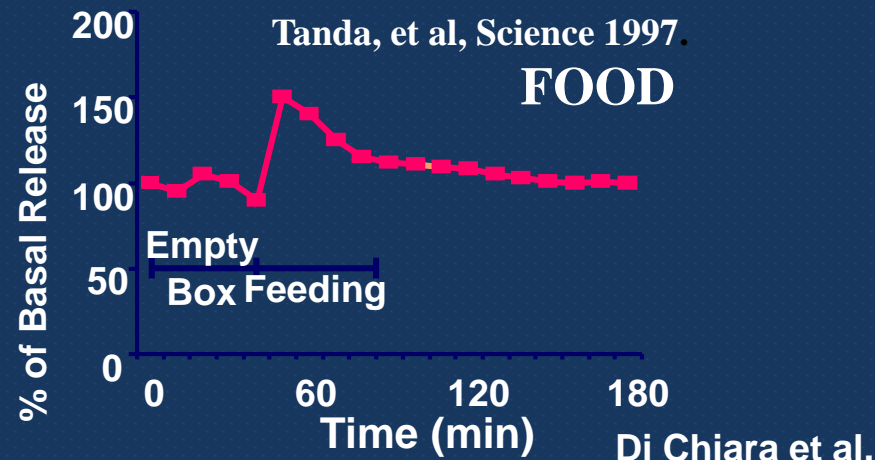
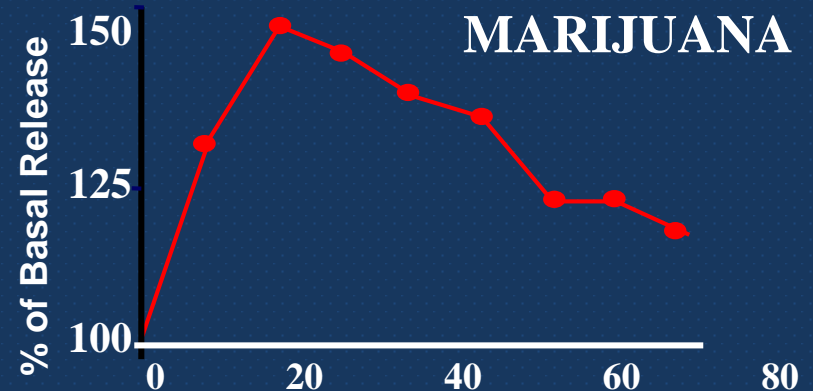
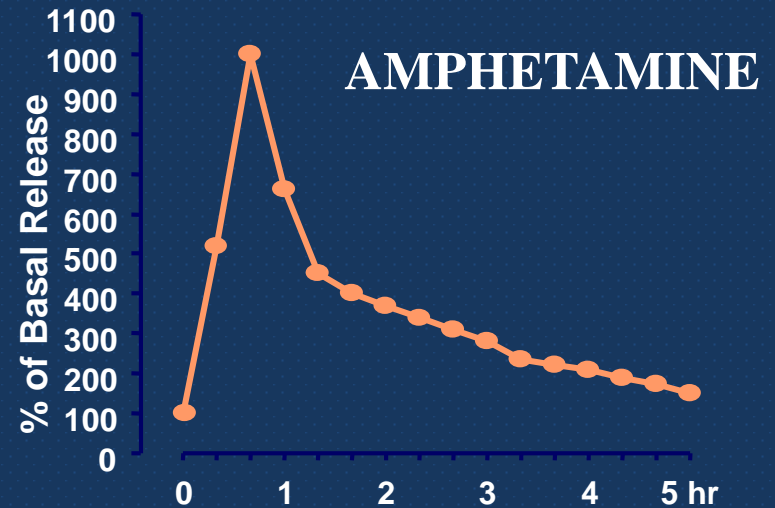
Marijuana affects several different parts of the brain, including those responsible for memory, learning, coordination and sensory and time perception.



# IT IS ADDICTIVE!



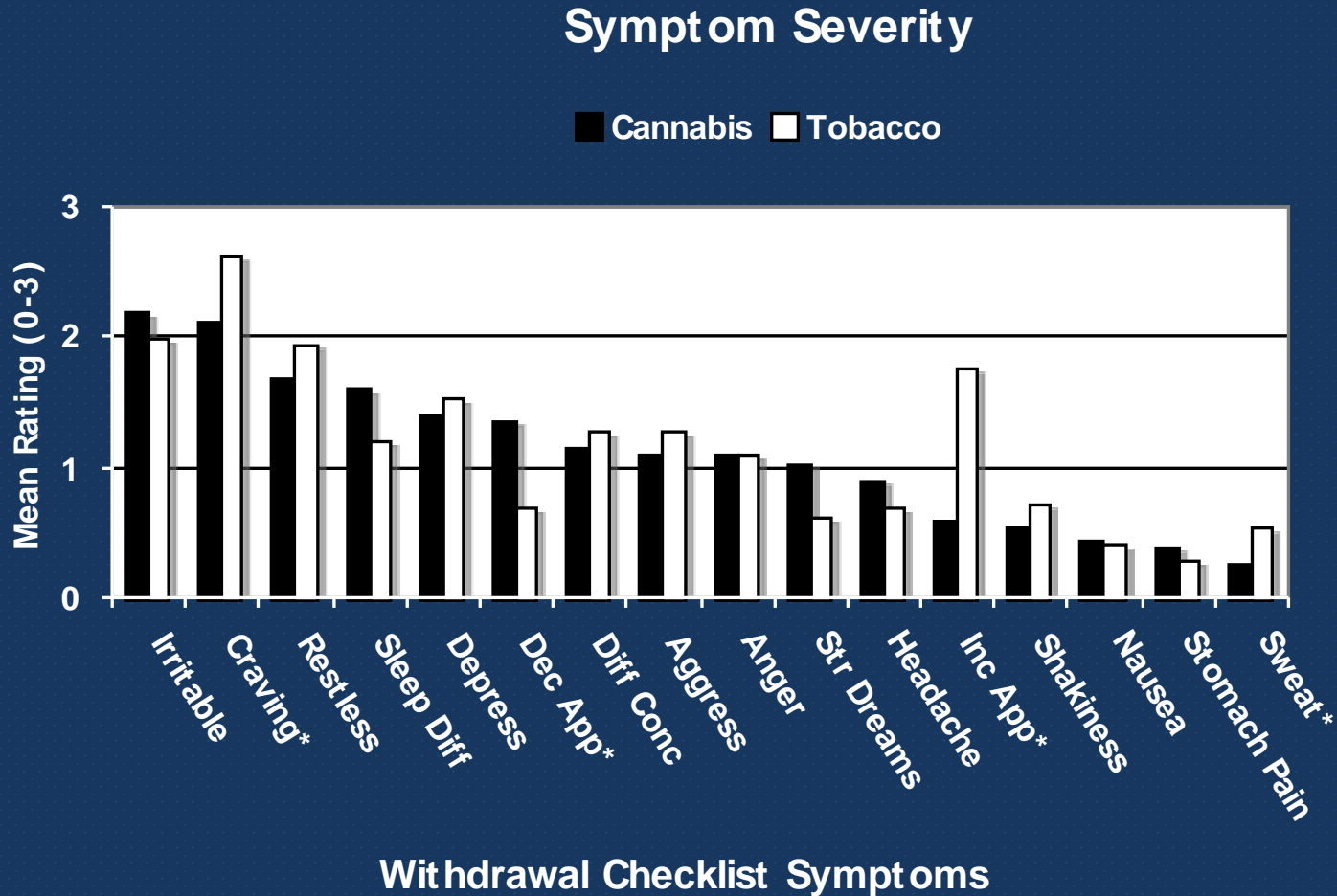
Drugs of abuse increase DA in the Nucleus Accumbens....triggers the neuroadaptions that result in addiction?





# There is Withdrawal!

(Vandrey et al., 2005; Vandrey et al. 2008, Budney et al., 2009)





# Gateway Drug?

- Does use of cannabis lead to other drug use? Is this a causal relationship?
- Most cannabis users don't go on to using other drugs.
- But use of cannabis/nicotine/alcohol at a young age is worrisome.



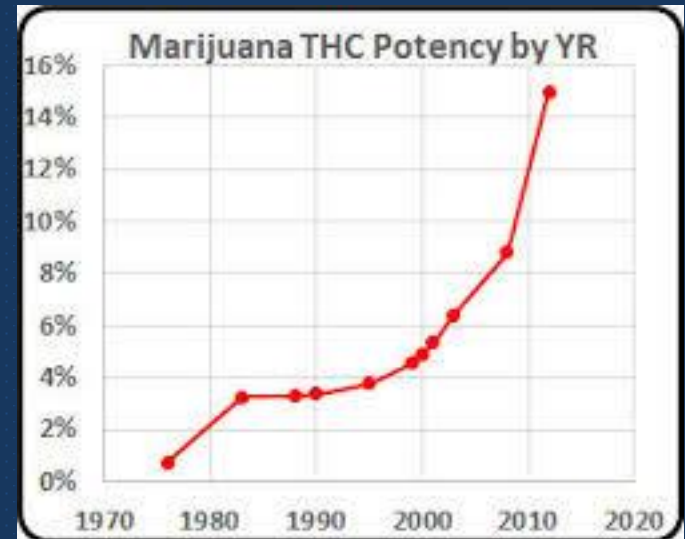
# CHRONIC: DOSE MATTERS

- Early onset  poor cognitive function, IQ decline (Pope 2003, Gruber 2011, Meier 2012, Scott 2018)
-  Anxiety (Crippa 2009)
-  Depression (Degenhardt 2003, Gobbi 2019 meta-analysis)
-  Suicidal ideation (Gobbi 2019)
-  Risk of psychosis (Kuepper 2011, Di Forti 2015)

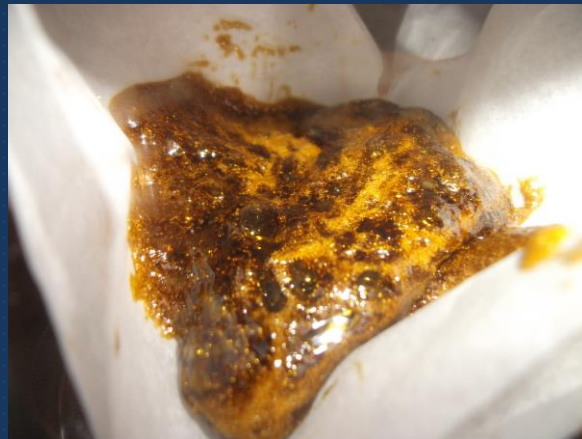
Review of Cannabis and Psychiatric Disorders: Halah et al. Curr Addict Rep 2016

# Potency Rising

- 60s, 70s, 80s: avg THC content 3-4%.
- Now: avg THC content 19% (EISohly 2021).
- BUT – you can get cannabis (plant not oil) in the 20s and low 30s.



# Other Forms of Cannabis



# Edibles

- Excellent example of poor education and policy— 1375% increase in ED poisonings from 2017-2021. (Tweet et al. 2023)
- Typical THC brownie=100 mg THC, serving size is 10 mg, so...
- Overdose due to packaging, storage, poor understanding of pharmacokinetics.



# Four students at Dorchester school sent to hospital after ingesting cannabis-infused chocolate

By [Emily Sweeney](#) and [Naomi Martin](#) Globe Staff. Updated May 2, 2023, 6:15 p.m.



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# Concentrates

- Wax, shatter, butter– dabbing.
- Plant matter distilled into 80-90% THC.
- Worst effects of THC more likely to occur at high concentrations- psychosis, hyperemesis.



# Alcohol vs. Marijuana

## “The Athlete Special”

	Alcohol	Marijuana
Addictive?	YES	YES
Performance Enhancer?	NO	NO
Impacts Performance Next Day?	YES	YES
Helps with Sleep?	NO	NO



# State of the Science: Medical Cannabis



# FDA-Approved Cannabinoids

- Dronabinol (Marinol)- oral THC.
- Nabilone (Cesamet)- CB<sub>1</sub> agonist.
- FDA-Approved for 1) Nausea and vomiting associated with chemotherapy 2) Appetite stimulation in wasting illnesses like AIDs.
- CBD (Epidiolex)- FDA-approved for 3 epilepsy syndromes.

# Policy Ahead of the Science

## Medical Cannabis Laws Versus Scientific Evidence



Gregory Malik Burnett, MD, MBA, MPH<sup>a,b</sup>,  
David A. Gorelick, MD, PhD, DLFAPA, FASAM<sup>c</sup>, Kevin P. Hill, MD, MHS<sup>d,e,\*</sup>

Psychiatr Clin N Am (2022) 347-373

# Medical Indications According to Laws

- 37 states, DC, 3 territories have medical cannabis laws.
- Many of the same conditions, but 42 conditions overall.
- # varies from 5-29 conditions.

(Burnett, Gorelick, Hill, Psychiatric Clinics of North America, 2022)



## **Level of Evidence (graded per NASEM: Conclusive, substantial, moderate, limited or no evidence)**

- 5 (12%) of 42 QCs have conclusive or substantial evidence of efficacy and are listed in more than half of all jurisdictions.
- 50% of QCs have no or insufficient evidence of benefit from medical cannabis.
- 9% have limited evidence of harm for medical cannabis.

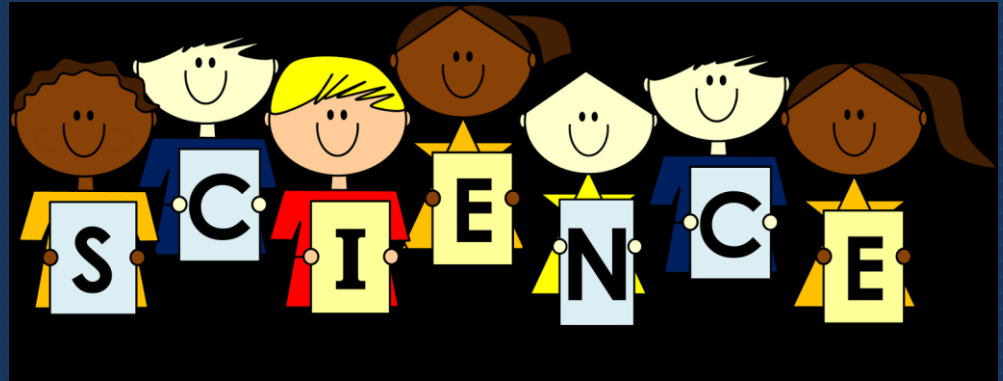
(Burnett, Gorelick, Hill, Psychiatric Clinics of North America  
2022)

# Overall

- Mean number of QCs per jurisdiction and proportion of QCs with and without evidence of benefit has not varied meaningfully since 1996.
- Many possible reasons for this: rate and scale of the science has not kept pace with interest, easier for states just to copy what other states have done.

# Medical Indications Based on Good Quality Evidence

- High quality evidence (approx. half of studies positive) for
- chronic pain
- neuropathic pain
- spasticity associated with Multiple Sclerosis. (Hill JAMA 2015)
- CBD is FDA-approved for 2 pediatric epilepsies and seizures associated with tuberous sclerosis. (Devinsky 2017, Thiele 2018)





Public Release

# *Health Effects of Cannabis and Cannabinoids*

*Current State of  
Evidence and  
Recommendations for  
Research*

This report will be available to  
download as a free pdf:  
[Nationalacademies.org/CannabisHealthEffects](https://www.nationalacademies.org/CannabisHealthEffects)

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# Other reviews

- Conclusive or substantial evidence that cannabis or cannabinoids are effective:
- chronic pain in adults,
- chemotherapy-induced nausea and vomiting (FDA-approval- dronabinol),
- patient-reported multiple sclerosis spasticity symptoms. (NASEM 2017).
- Moderate quality: chronic pain and spasticity (Whiting JAMA 2015).

# Risks and Benefits of Cannabis and Cannabinoids in Psychiatry

Kevin P. Hill, M.D., M.H.S., Mark S. Gold, M.D., Charles B. Nemeroff, M.D., Ph.D., William McDonald, M.D.,  
Adrienne Grzenda, M.D., Ph.D., Alik S. Widge, M.D., Ph.D., Carolyn Rodriguez, M.D., Ph.D., Nina V. Kraguljac, M.D.,  
John H. Krystal, M.D., Linda L. Carpenter, M.D.

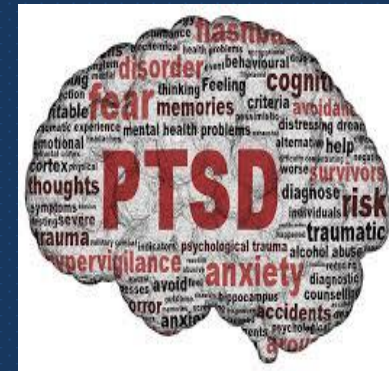
American Journal of Psychiatry, Dec 2021

# Anxiety

- Limited evidence of efficacy based upon 31 published studies (including 17 RCTs). (Black et al. 2019)
- Efficacy for anxiety accompanying other disorders and social anxiety.
- No study evaluated medical cannabis specifically as pharmacotherapy for specific anxiety disorders.



# PTSD



- Moderate level of evidence, although only 13 studies and 2 RCTs.
- RCT of nabilone showed that nabilone increased overall well-being and reduced disturbed dreaming (Jetly 2015).
- Crossover trial of 3 weeks X 2 of 3 smoked cannabis preparations and PLA was negative (Bonn-Miller et al. 2021).
- Results from other small studies mixed at best and observational study of 2276 veterans showed cannabis use to be associated with worse outcomes in PTSD symptom severity, violent behavior, and alcohol/drug use (Wilkinson 2015).

# Depression

- Limited evidence of harm based upon 40 studies (22 RCTs).
- None evaluated primary depression.
- None showed benefit; some with THC-predominant products showed worse mood at higher doses.



# Cannabis Use Disorder

- No medical cannabis trials.
- Dronabinol: better treatment retention and less withdrawal than PLA but no separation in 2-week abstinence from cannabis over 12 weeks (Levin et al. 2011).
- CBD 400 mg and 800 mg safe and more efficacious than PLA over 4 weeks in reducing cannabis use (Freeman et al. 2020).

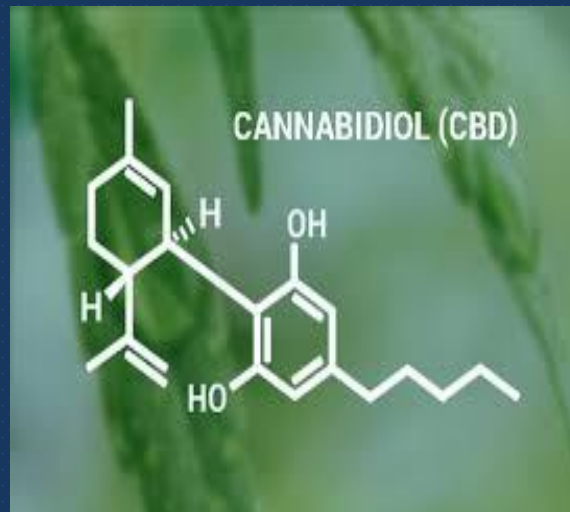
# Opioid Use Disorder

- CBD 400 mg or 800 mg daily for 3 days significant reduction in opioid craving and withdrawal symptoms in pts with OUD (Hurd et al. 2019).
- No interventional studies evaluated opioid use.
- Especially dangerous to use cannabinoids in lieu of evidence-based treatments for OUD. (Hill et al. 2021)



# Cannabidiol (CBD)

- Incredibly popular, but lots we don't know.
- Multiple mechanisms of action, each with different dosing requirements.
- Patients are either interested in taking it or they are already taking it.





# Cannabidiol (CBD)

- Only Epidiolex is FDA-approved.
- Promising, but most evidence pre-clinical. (Pisanti et al. 2017)
- Not regulated, often mislabeled. (Spindle et al. 2022, Bonn-Miller et al. 2017, Poklis 2018)



**Research Letter**

April 25, 2023

# Quantity of Melatonin and CBD in Melatonin Gummies Sold in the US

Pieter A. Cohen, MD<sup>1</sup>; Bharathi Avula, PhD<sup>2</sup>; Yan-Hong Wang, PhD<sup>2</sup>; [et al](#)

» [Author Affiliations](#) | [Article Information](#)

*JAMA*. 2023;329(16):1401-1402. doi:10.1001/jama.2023.2296

# Progress, But Caution Needed

- FDA-approval for Dravet syndrome, Lennox-Gastaut syndrome, Tuberous Sclerosis based upon strong RCTs.
- Promising results for anxiety, schizophrenia.
- Reduction in opioid-related anxiety and cue-reactivity. (Hurd 2019)

# CBD: The Truth

- Limited evidence for sleep.
- Topical CBD cream not absorbed into bloodstream, making it an expensive version of OTC creams.
- Companies make often outrageous claims.
- CBD cannot convert to THC.


# CBD Problems

- Liver toxicity (Watkins et al. 2020)
- When used in lieu of evidence-based treatments.
- When purchased online, still very expensive!



# Cannabidiol Interactions with Medications, Illicit Substances, and Alcohol: a Comprehensive Review



*Premalatha Balachandran, PhD<sup>1</sup>, Mahmoud Elsohly, PhD<sup>1,2</sup>, Kevin P. Hill, MD, MHS<sup>3,4</sup>* 

<sup>1</sup>National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, University, MS, USA; <sup>2</sup>Department of Pharmaceutics and Drug Delivery, School of Pharmacy, University of Mississippi, University, MS, USA;

<sup>3</sup>Department of Psychiatry, Harvard Medical School, Boston, MA, USA; <sup>4</sup>Division of Addiction Psychiatry, Beth Israel Deaconess Medical Center, Boston, MA, USA.

Drug-drug interactions (including benzodiazepines, anti-epileptics, morphine). JGIM 2021

# Policy Ahead of the Science



# Critical Period

- Train has left the station, so how do we give people what they want while mitigating risk?
- We need research on medical cannabis efficacy so that physicians and patients can make informed choices about whether medical cannabis should be a part of their treatment plans.





# Acknowledgments

Addiction Psychiatry Team

Verona White

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Joanne Devine

Matt Day

**Questions?**