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How to Talk to Patients about Cannabis Use

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December 10th 2021

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Cooper University Health Care

State of New Jersey DHS Department of Human Services

Cooper Medical School of Rowan University

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Disclosures

Lynda Bascelli – none

Carley Schaffer – none

Clement Chen – none

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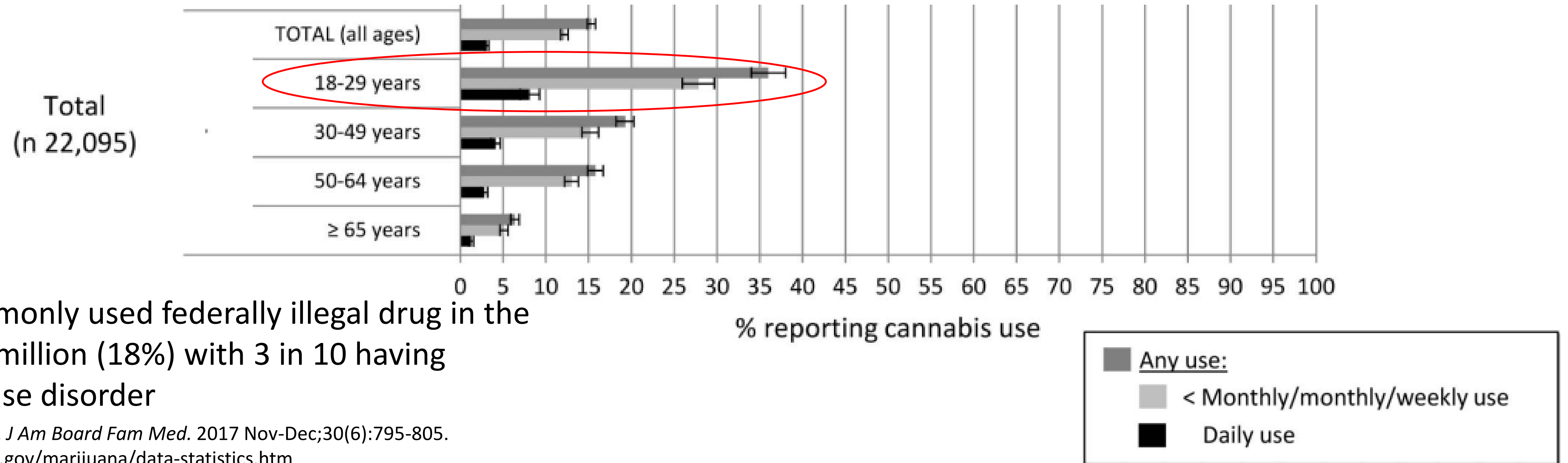
Objectives

- Identify the prevalence of cannabis use in the U.S.
- Distinguish the components of cannabis and their expected effects
- Discuss the risks of THC and the growing potency of cannabis
- Summarize available literature on cannabis use on other medical conditions and the implications of legalization
- Apply principles of harm reduction in talking to patients about cannabis use
- Explain the role of the general practitioner in assessing for and reducing the risk of cannabis use

The "What" of Cannabis Use

Cannabis Use in the U.S.

- Observational cohort study of adults who made a visit to primary care clinics with annual behavioral health screening



Most commonly used federally illegal drug in the U.S.; 48.2 million (18%) with 3 in 10 having cannabis use disorder

Lapham GT, et al. *J Am Board Fam Med.* 2017 Nov-Dec;30(6):795-805.
https://www.cdc.gov/marijuana/data-statistics.htm

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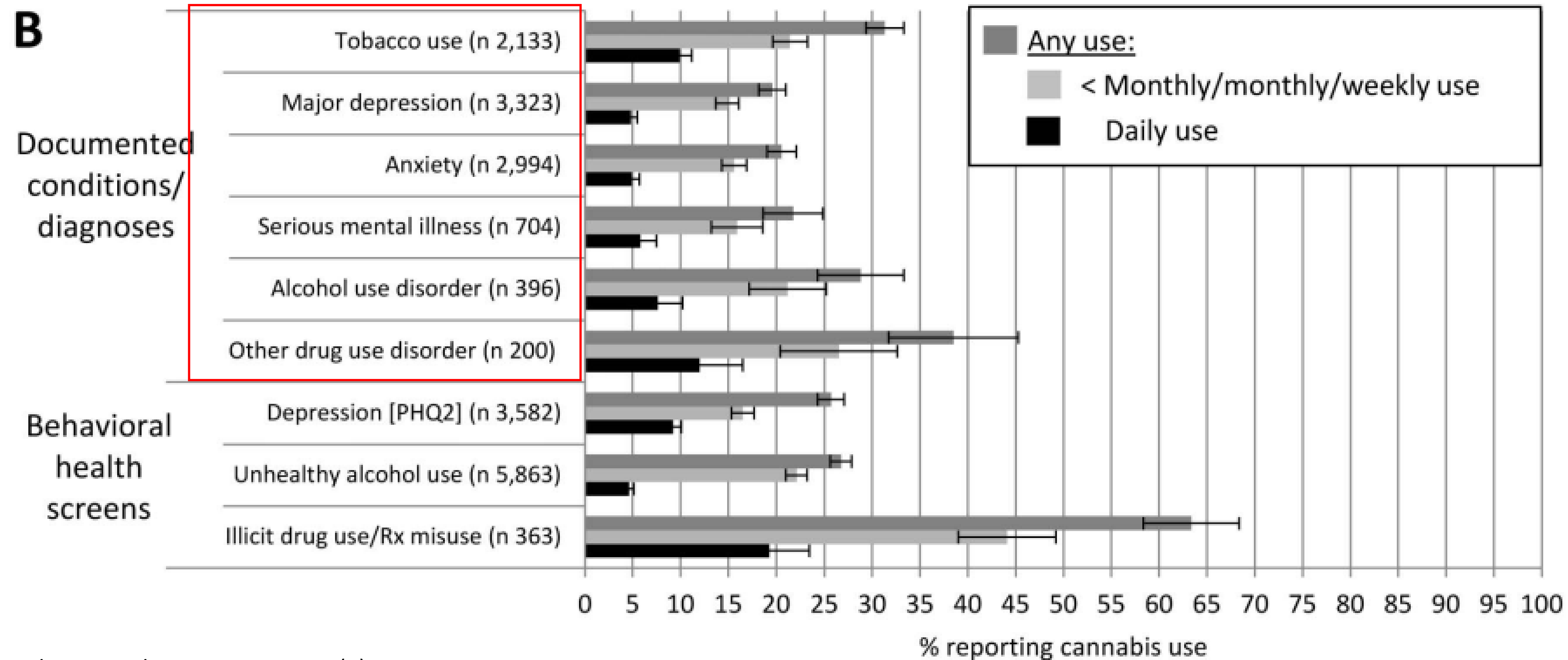
Cannabis Use in the U.S.



Lapham GT, et al. *J Am Board Fam Med.* 2017 Nov-Dec;30(6):795-805.

Cannabis Benefits

Known	Possible	Inconclusive
• Pain • Neuropathic, fibromyalgia • Cachexia • Nausea and vomiting • Spasticity from Multiple Sclerosis • Resistant Epilepsy	• Reduction in long-term use of opioids and opioid withdrawal • Dystonia • Glaucoma	• Alzheimer disease • Parkinson's Disease • Anxiety and depression • Antitumor • Inflammatory bowel diseases • Heart failure • Hepatitis C • Ischemia/Reperfusion injury • Sleep

Page RL, et al. *Circulation.* 2020 Sep 8;142(10):e131-e152.

Cannabis Components

Delta-9-Tetrahydrocannabinol (THC)

- Pros
  - Analgesic (refractory chronic pain)
  - Antiemetic (FDA-approved formulation)
  - Muscle relaxant
  - Appetite stimulant (FDA-approved formulation)
- Cons
  - Euphoria
  - Cannabinoid Hyperemesis Syndrome
  - Psychosis
  - Risk of worsened co-morbid OUD and associated consequences
  - Risk of dependence → addiction

Cannabidiol (CBD)

- Pros
  - Analgesic?
  - Anti-seizure (FDA-approved formulation)
  - Anxiolytic and antipsychotic???
  - Neuroprotective
- Cons
  - Decreased appetite
  - Diarrhea
  - Liver impairment

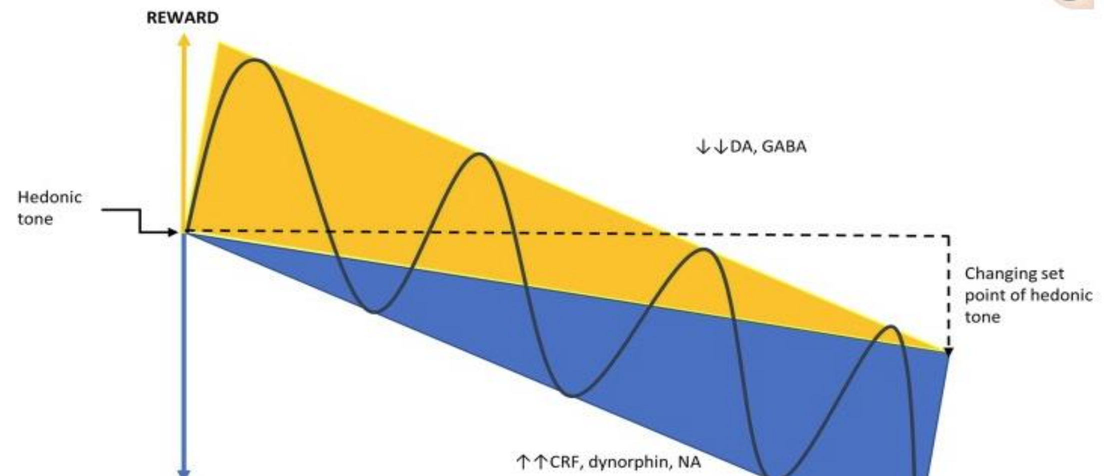
Many drug interactions and additive effects

Clinical Resource, *Comparison of Cannabinoids. Pharmacist's Letter/Prescriber's Letter.* September 2018.

Cannabis Withdrawal

- Anger
- Anxiety
- Restlessness
- Depressed mood
- Disturbed sleep
- Strange dreams
- Decreased appetite
- Weight loss
- Headache
- Night sweats

- Not as:
  - Painful as heroin withdrawal
  - Dangerous as alcohol withdrawal
  - Long-lasting as cocaine withdrawal

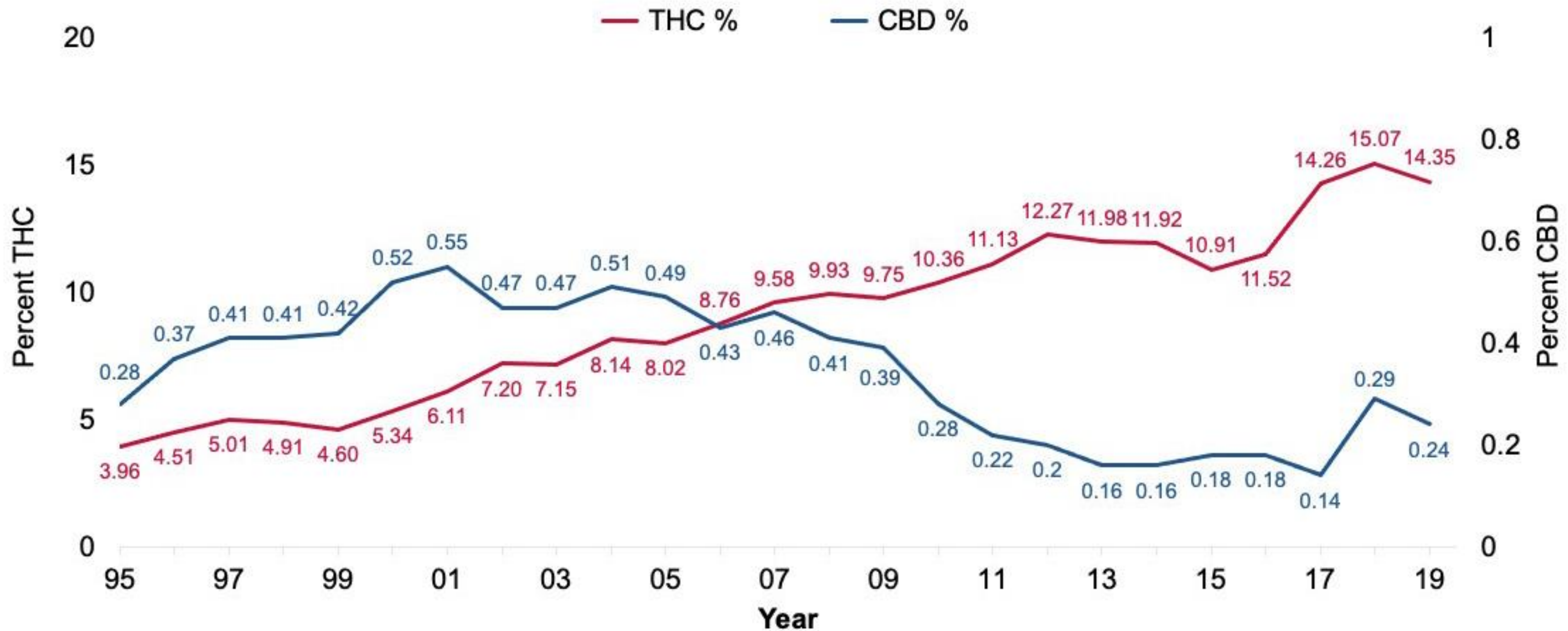


Kakko J, et al. *Front Psychiatry.* 2019 Aug 30:10:592.
Page RL, et al. *Circulation.* 2020 Sep 8;142(10):e131-e152.

Credit: Dr. Petros Levounis

Risk of THC

Historical Timeline of THC vs. CBD Content



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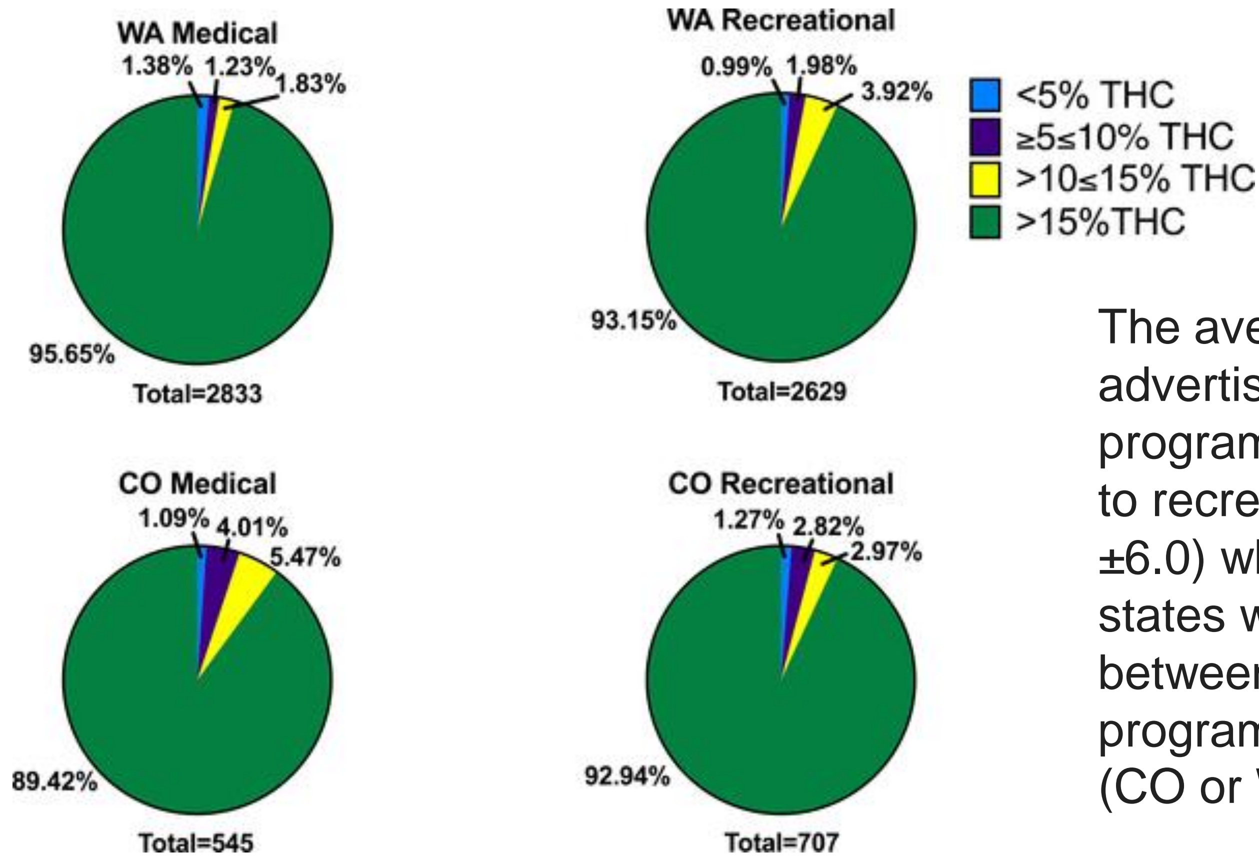
Proportion of Products of Different Levels of THC



The average THC concentration advertised online in medicinal programs was similar (19.2% ±6.2) to recreational programs (21.5% ±6.0) when compared between states with different programs, or between medicinal and recreational programs within the same states (CO or WA).

Cash MC, Cunnane K, Fan C, Romero-Sandoval EA (2020) Mapping cannabis potency in medical and recreational programs in the United States. PLOS ONE 15(3): e0230167. https://doi.org/10.1371/journal.pone.0230167

High-Potency Cannabis and Risk for Psychotic Disorder

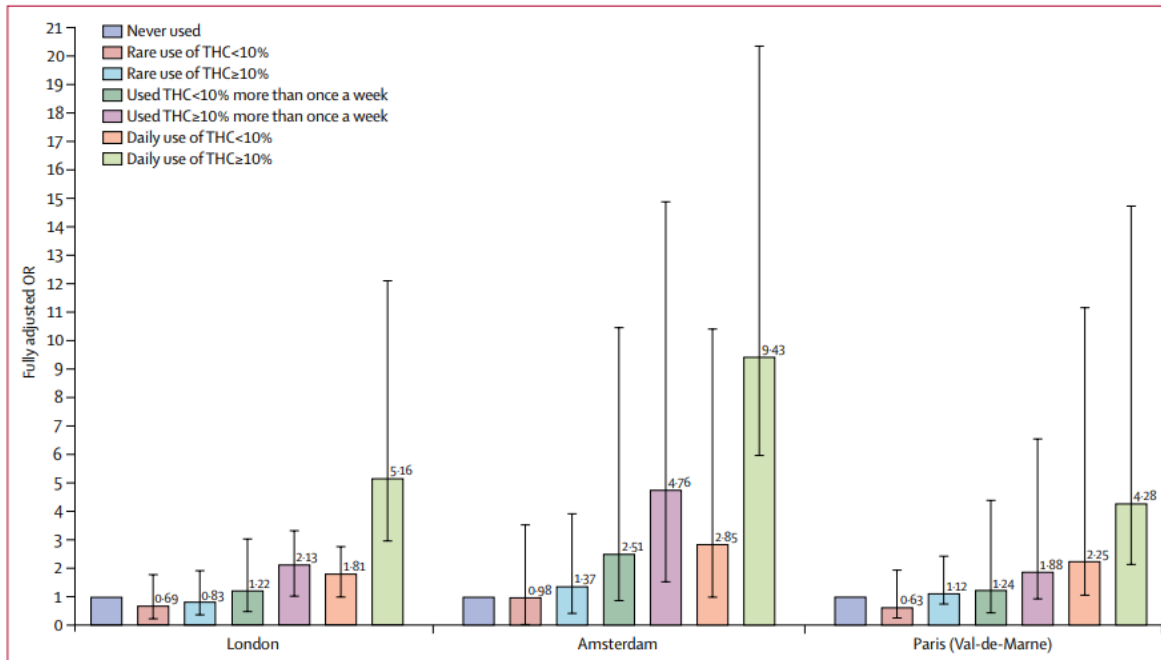


***Figure 2:* Fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in three sites**
Data are shown for the three sites with the greatest consumption of cannabis: London (201 cases, 230 controls), Amsterdam (96 cases, 101 controls), and Paris (54 cases, 100 controls). Error bars represent 95% CIs. OR=odds ratio.

- 4x greater in Paris
- 5x greater in London
- >9x in Amsterdam

- High correlation between amount of drug used, age at first use, and genetic vulnerability

Di Forti, et al. *Lancet Psychiatry.* 2019 May;6(5):427-36.
https://www.drugabuse.gov/publications/research-reports/marijuana/there-link-between-marijuana-use-psychiatric-disorders#:~:text=Recent%20research%20suggests%20that%20smoking,who%20have%20never%20used%20marijuana.&text=The%20amount%20of%20drug%20used,shown%20to%20influence%20this%20relationship.

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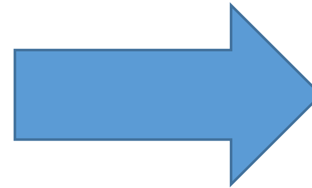
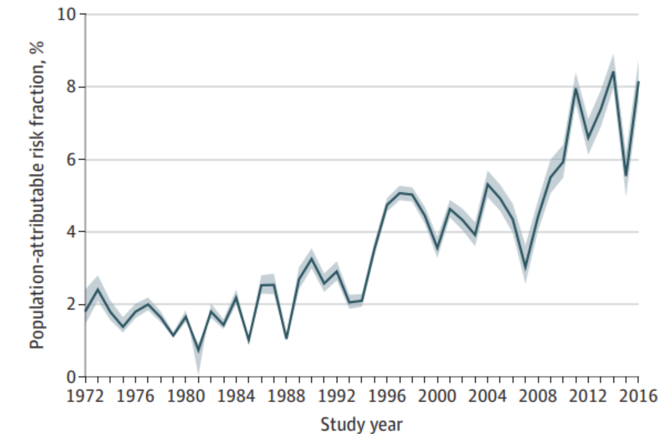
Link Between Cannabis and Psychosis?

- Meta-analysis of 18 studies showed that there is a positive dose-dependent relationship of cannabis use to psychosis
  - OR of 3.90 (95% CI 2.84 to 5.34) for the risk of schizophrenia amongst heaviest cannabis users
- Population-Attributable Risk Fraction (PARF) for Cannabis Use Disorder in Schizophrenia
  - Large longitudinal population-based study of over 7 million in Denmark from 2001 to 2017
    - Increased from 2% → 6-8% since 2019
    - 3-4-fold increase in PARF score
- Daily cannabis use associated ↑ up to 5-fold amongst high-potency cannabis across Europe in a multicenter case-control study
  - 3-5 fold increase
  - 20.4% PARF for daily cannabis use





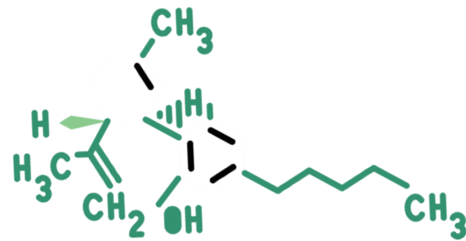
Marconi A, et al. *Schizophr Bull.* 2016 Sep;42(5):1262-9.
Hjorthoj C, et al. *JAMA Psychiatry.* 2021;78(9):1013-19.
Di Forti M, et al. *Lancet Psychiatry. 2019 May6(5):427-36.*

Cannabinoid Hyperemesis Syndrome

- **Chronic cannabis use** leading to cyclic, recurrent episodes of severe nausea/vomiting and abdominal pain
- 3 phases: Prodromal, hyperemetic, and recovery
- Relief can be achieved by "hot bathing"
- True resolution of the problem: Stopping cannabis use
- Cause???
- Misdiagnosis is high

Galli JA, et al. *Curr Drug Abuse Rev.* 2011 Dec;4(4):241-49.

The Impact of Cannabis Use on Pain Management, Opioid Use Disorder and other Comorbid Conditions



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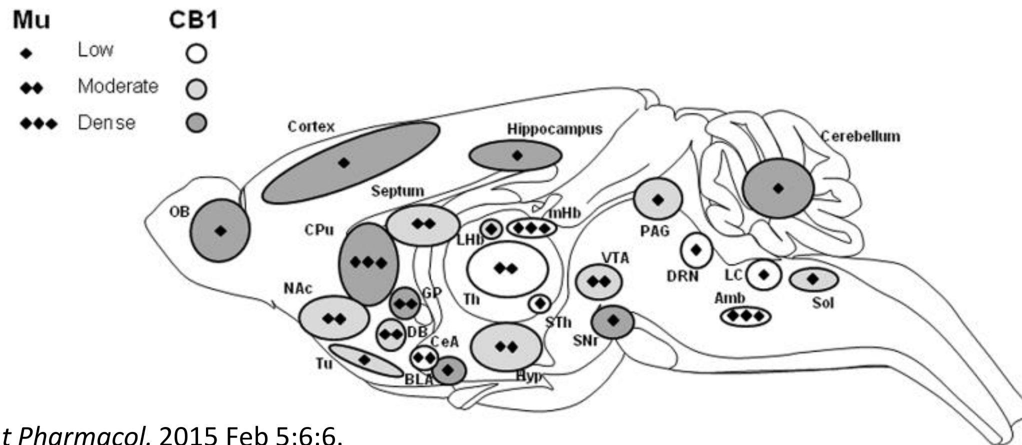
Cannabinoid and Opioid Receptors Distributed in Same Regions of CNS

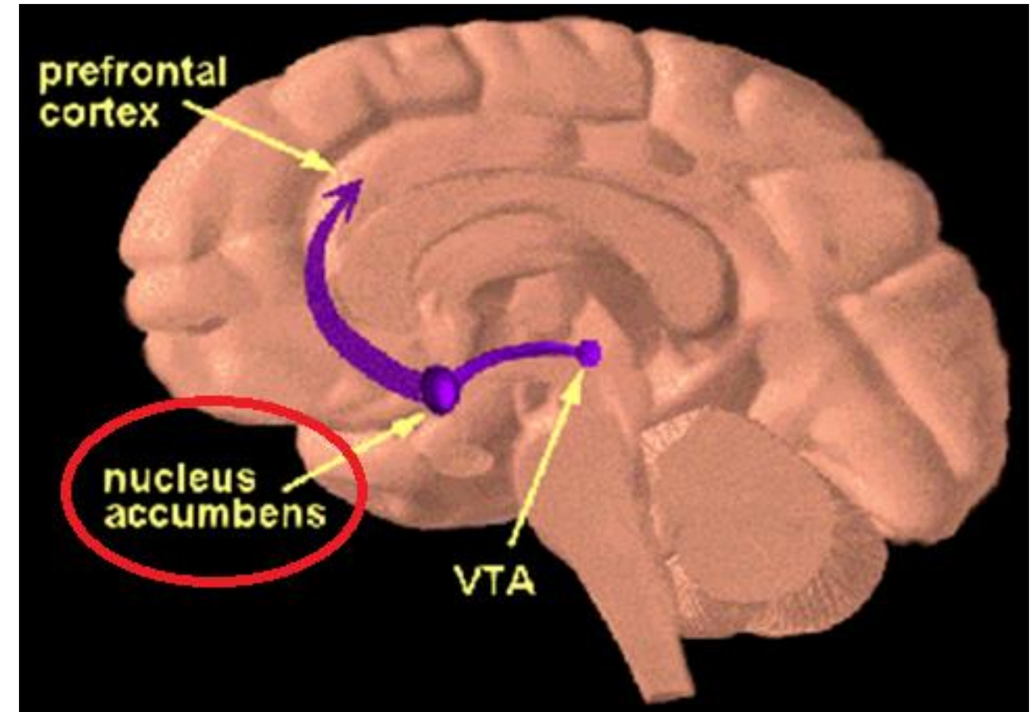
Analgesic synergy?

Use of cannabis to spare-opioid consumption has had conflicting results

Use of CBD?



Befort K. *Front Pharmacol.* 2015 Feb 5;6:6.



Effect of Cannabis Use in People with Chronic Non-Cancer Pain

- Prospective, national, observational cohort study in Australia of over 1500 people interviewed and who were prescribed opioids
- Participants followed yearly for 4 years, starting from 2012-2014
- 24% of participants had used cannabis for pain
- At 4-year follow-up, participants who used cannabis had **greater pain severity score** (RR 1.14, 95% CI 1.01-1.29 for less frequent used; RR 1.17, 1.03-1.32 for daily cannabis use), **lower pain self-efficacy scores**, and **greater generalized anxiety disorder severity score**.

- SUMMARY: No evidence that cannabis use improved patient outcomes such as reducing pain severity or exerting an opioid-sparing effect

Campbell G, et al. *Lancet Public Health.* 2019 Jul;3(7):e341-e350.

18

Effect of Cannabis and Patient Outcomes in those on MOUD

- Systematic review of 41 studies
- Primary outcome relationship
  - Opioid use, treatment adherence, treatment retention
- Majority showed no statistical significance
- Called for more studies looking at adjunctive effects of cannabis use on opioid craving and withdrawal

- Prospective cohort study of 211 participants found that the odds of same-day opioid use with cannabis was nearly 2 (aOR 1.86 95% CI 1.44-2.41) relative to opioid use on days without cannabis use
  - Cannabis not used as a substitute

Lake S, et al. *Clin Psychol Rev.* 2020 Dec;82:101939.
Gorfinkel LR, et al. *Addiction.* 2021 May;116(5):1113-1121.

Opioid and Cannabis Co-Use and Association with Substance Misuse, Mental Health, and Pain

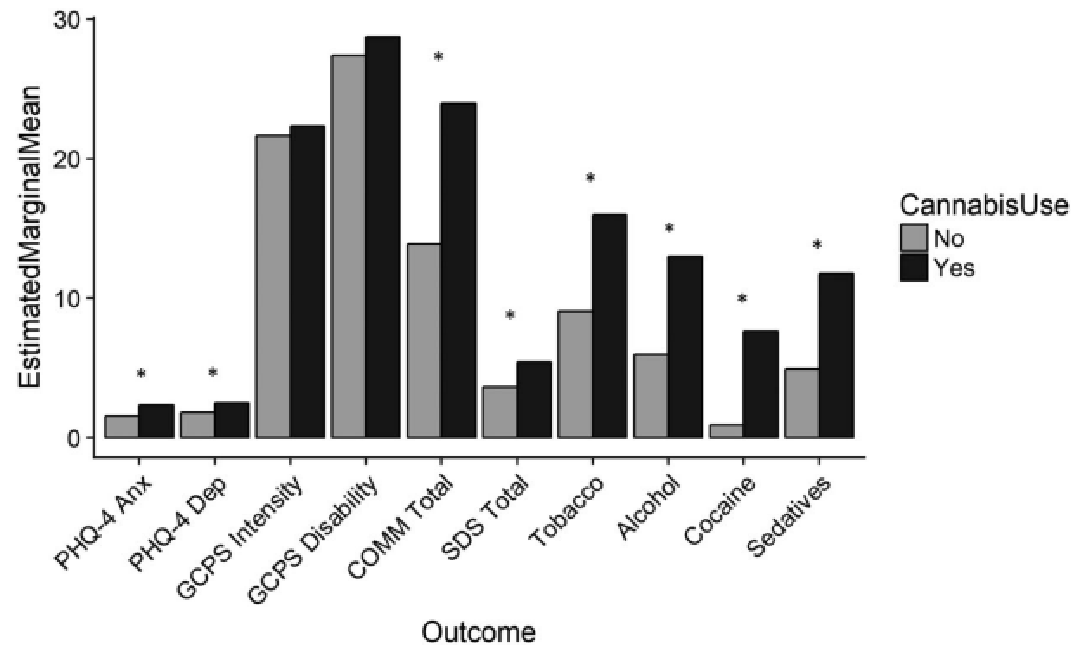


FIGURE 1. Group Estimated Marginal Mean Comparison. Note: * indicates a significant difference at the $P < 0.005$ level. PHQ-4 Anx—Anxiety, PHQ-4 Dep—Depression, GCPS Intensity—pain intensity, GCPS Disability—pain disability, COMM Total—Current Opioid Misuse, SDS Total—Severity of Opioid Dependence.

Examined use of opioids alone compared to use of opioid and cannabis co-use in a **cross-sectional** study.

Opioid and cannabis co-use associated with increased anxiety and depression symptoms, as well as tobacco, alcohol, cocaine, and sedative use problems, but not pain experience.

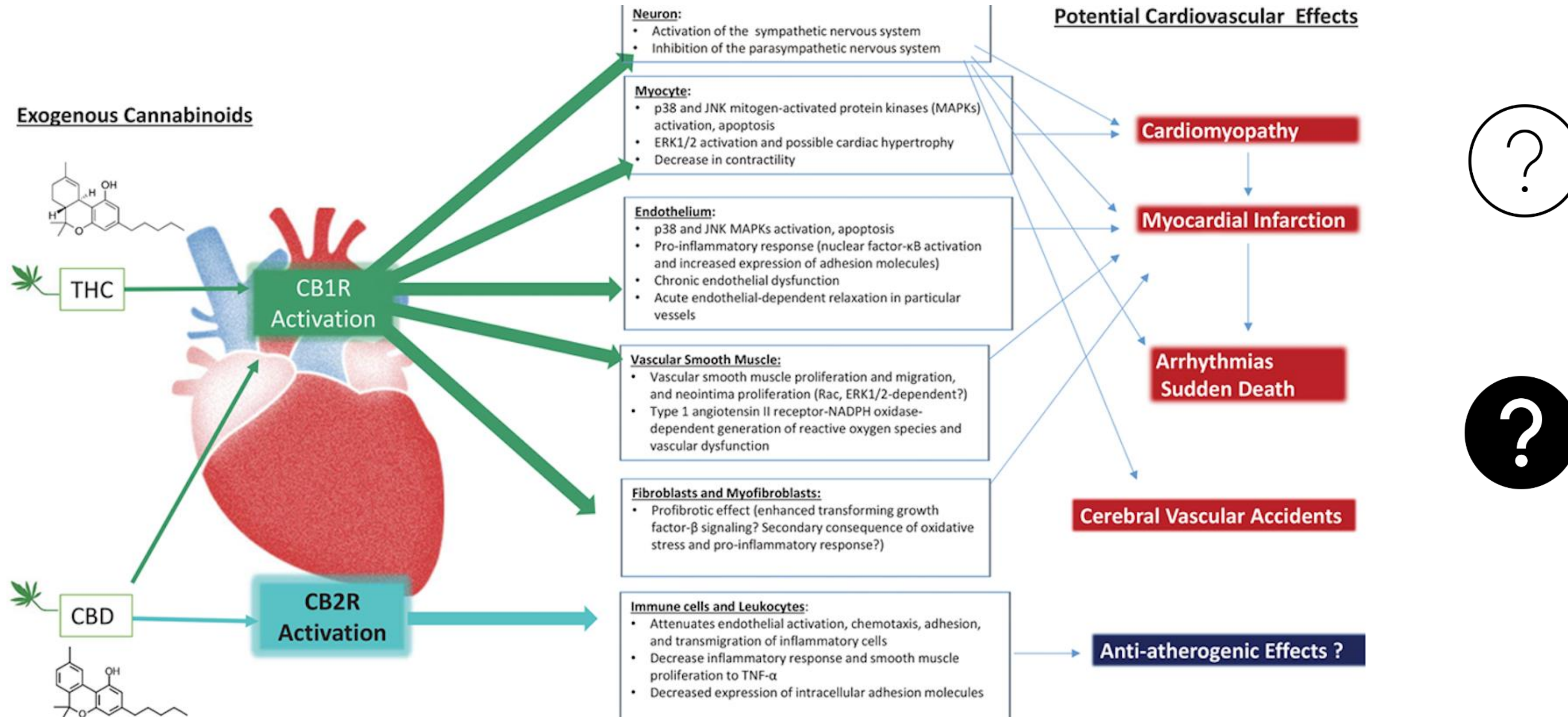
Rogers AH, et al. *J Addict Med.* Jul/Aug 2019;13(4):287-94.

Effect of Cannabis Use on Psychiatric Disorders

- National Epidemiologic Survey on Alcohol and Related Conditions participants interviewed 3 years apart in 2 waves
- Cannabis use assessed by whether there was cannabis use in the 12 months preceding interview
- Of 34,683 respondents, cannabis use was significantly associated with greater **prevalence** and **incidence** of substance use disorders in wave 2 but NOT any mood or anxiety disorder
  - Any SUD: OR 6.2; 95% CI, 4.1-9.4
    - Alcohol use disorder, cannabis use disorder, other drug use disorder, and nicotine dependence

Blanco C, et al. *JAMA Psychiatry.* 2016;73(4):388-395.

Effect of Cannabis on Cardiovascular Disease



Robert L. Page. Circulation. Medical Marijuana, Recreational Cannabis, and Cardiovascular Health: A Scientific Statement From the American Heart Association, Volume: 142, Issue: 10, Pages: e131-e152, DOI: (10.1161/CIR.0000000000000883)

Effect of Cannabis on Cerebrovascular Disease

- Population survey of nearly 7,500 people from Australia, examining risk of non-fatal stroke or transient ischemic attack
- 153 stroke/TIA cases
- Adjusting for age, those who had used cannabis during the past year (n=1,043) had 3.3 times the rate of stroke/TIA (95% CI 1.8-6.3, $p<0.001$)
- **Elevated stroke/TIA higher only for those who used cannabis weekly or more often**
- Smoking cannabis associated with peripheral artery disease

Hemachandra D, et al. *Aust N Z J Public Health.* 2016 Jun;40(3):226-30.

Impact of Legalization on Cannabis Use

Association Between Recreational Cannabis Legalization and Changes in Cannabis Use/Disorder

- 506,000 respondents comparing cannabis use before and after legalization of recreational cannabis across several states

Table 2. Past-Month Marijuana Use, Frequent Marijuana Use, and CUD in the Past 12 Months Among 495 796 Respondents Before vs After RML Enactment From 2008 to 2016[a]

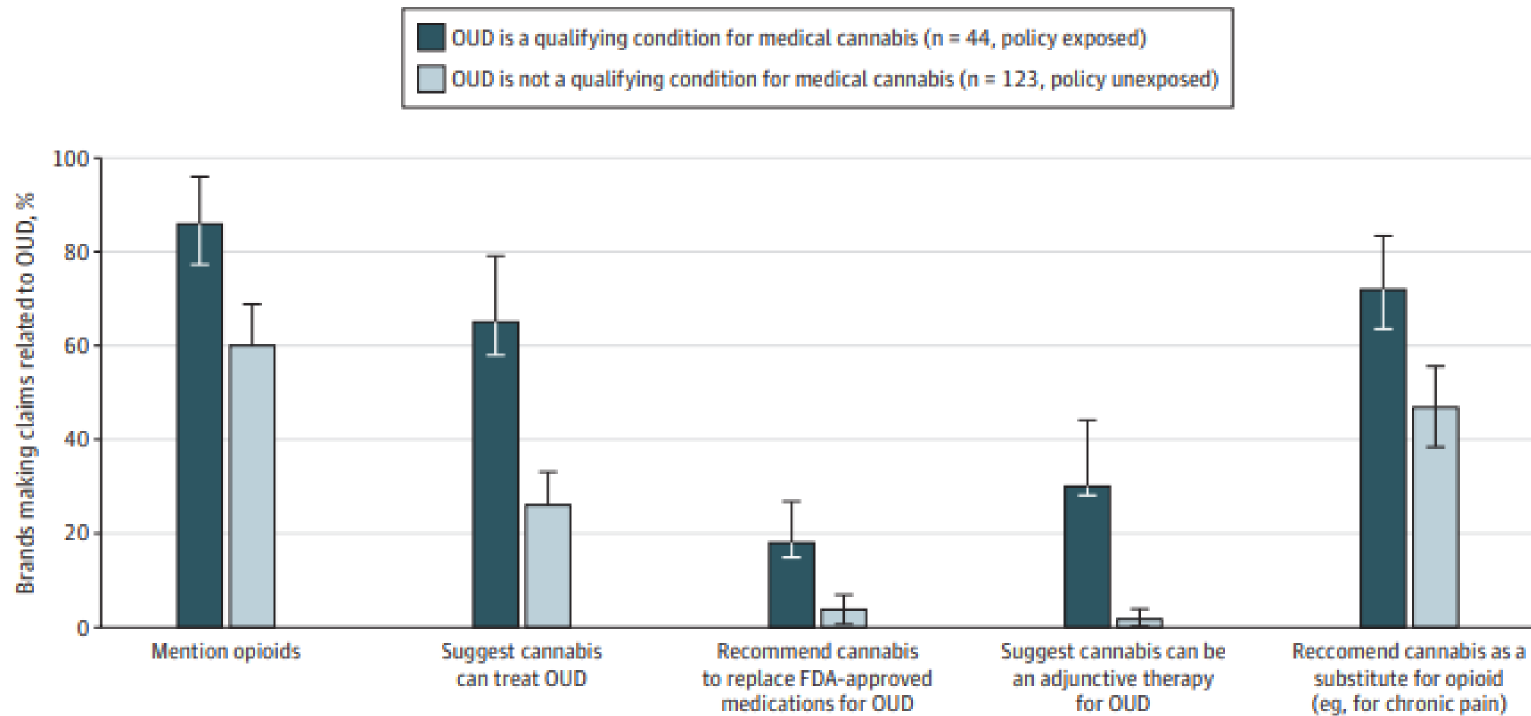
	Marijuana Use						CUD in the Past 12 mo		
	Past Month			Frequent					
	% Who Reported Use			% Who Reported Frequent Use			% Who Met Criteria for CUD		
Age Group, y	Before RML[b]	After RML[c]	AOR (95% CI)[d]	Before RML[b]	After RML[c]	AOR (95% CI)[d]	Before RML[b]	After RML[c]	AOR (95% CI)[d]
12-17	4.76	5.28	1.12 (0.97-1.28)	1.07	1.19	1.12 (0.87-1.43)	2.18	2.72	1.25 (1.01-1.55)
18-25	13.06	14.03	1.09 (0.99-1.20)	4.64	5.08	1.10 (0.97-1.25)	3.62	3.48	0.96 (0.80-1.14)
≥26	5.65	7.10	1.28 (1.16-1.40)	2.13	2.62	1.24 (1.08-1.41)	0.90	1.23	1.36 (1.08-1.71)

Data from the National Survey on Drug Use and Health

Cerda M, et al. *JAMA Psychiatry.* 2020 Feb 1;77(2):165-71.

Study included >500,000 respondents
RML = Recreational Marijuana Legaliation

Association of State Policies Allowing Medical Cannabis for OUD And Dispensary Marketing

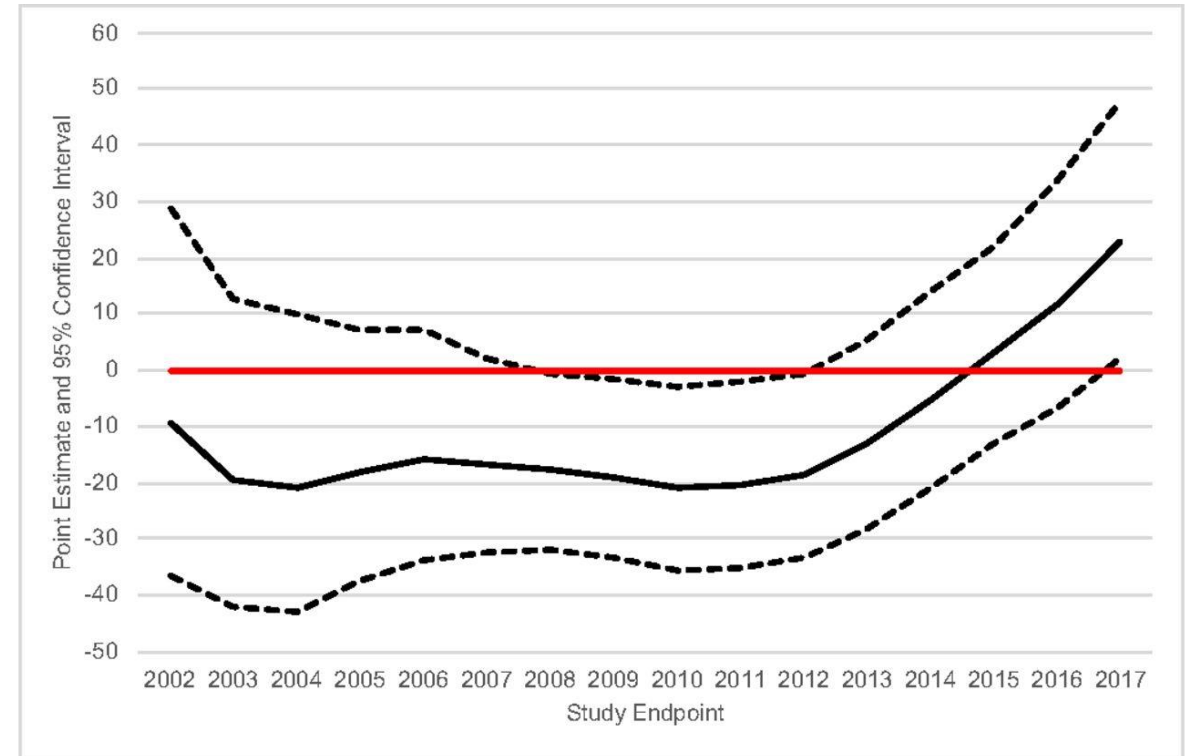


Whiskers indicate 95% CIs. FDA indicates US Food and Drug Administration.

Shover CL, et al. *JAMA Netw Open.* 2020 Jul;1:3(7):e2010001.

Trend Towards Increase in Opioid Overdose Deaths

- Bachhuber, et al –
  - 1999-2010 – states enacting medical cannabis laws had lower-than-expected opioid overdose mortality rates (24.8% reduction)
- Shover, et al -
  - 2010-2017 – 32 states eneacted medical cannabis laws, including 17 allowing only low levels of THC
  - 8 states enacted recreational cannabis laws
  - 23% increase in opioid overdose deaths



Bachuber MA, et al. *JAMA Intern Med.* 2014;174(10):1668-1673.
Shover CL, et al. *Proc Natl Acad Sci USA.* 2019 Jun 25;11^(26):12624-12626.

The “How” of Cannabis Use

Approaching the Patient on Cannabis Use

Opening the dialogue to cannabis

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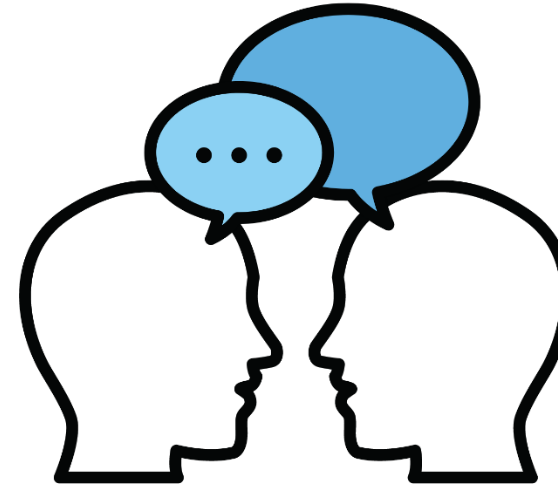
Cannabis Use – Talking Points

- General use
  - Is it being used alternatives to treat your indication?
- Indication for use
- Route of use
  - Avoid smoking which contains many of the same carcinogens as tobacco smoke
- Quantity and frequency of use
- Source of use
- Perceived benefit of use
- Risk for addiction



Be patient-centered

Harm Reduction

- Focus on reducing the negative consequences of drug use vs. drug use is ”bad”
- Emphasize the importance of knowing the content and concentration of the cannabis product
- Set patient-centered goals
- Suggest alternative routes of administration that may reduce harm

BE OPEN-MINDED AND AVOID STIGMATIZING THE USE OF CANNABIS

Jaffe SL. *Emerging Trends in Drugs, Addictions, and Health.* 1 (2021) 100011.

Assessment for Cannabis Use Disorders

- 1) How often do you use cannabis?
- 2) How many hours were you “stoned” on a typical day when you had been using cannabis?
- 3) How often during the past 6 months did you find that you ere not able to stop using cannabis once you had started?
- 4) How often during the past 6 months did you fail to do what was normally expected form you because of using cannabis?
- 5) How often in the past 6 months have you devoted a great deal of your time to getting, using, or recovering form cannabis?
- 6) How often in the past 6 months have you had a problem with your memory or concentration after using cannabis?
- 7) How often do you use cannabis in situations that could be physically hazardous, such as driving, operating machinery, or caring for children?
- 8) Have you ever thought about cutting down, or stopping, your use of cannabis?

Adamson SJ, et al. *Drug Alcohol Depend.* 2010 Jul1;110(1-2):137-43.

Role as a Medical Provider

- Synthesize the available information
- Discuss the risks of use of cannabis
- Warn of highly potent products containing high levels of THC
- Emphasize that many conditions not supported by evidence for **medical benefit**
  - HIV/AIDS
  - PTSD
  - Migraines
  - Parkinson's Disease
- Understand that many studies have variable outcome measures

Summary

- The growth of highly potent THC-containing products is fraught with risks
- The medical literature for cannabis has not kept up with the fervor of cannabis use, resulting from both legalization and commercialization
- Gaps exist particularly related to:
  - Appropriate dosing
  - Content of THC vs. CBD
  - Route of administration and associated bioavailability
- Harm reduction may be an essential strategy to employ especially amongst those with, or at high risk, for co-morbid psychiatric and substance use disorders
- Further longitudinal research is necessary to justify using cannabis more broadly and for specific indications

Questions & Discussion

Thank you to everyone who joined and participated today!