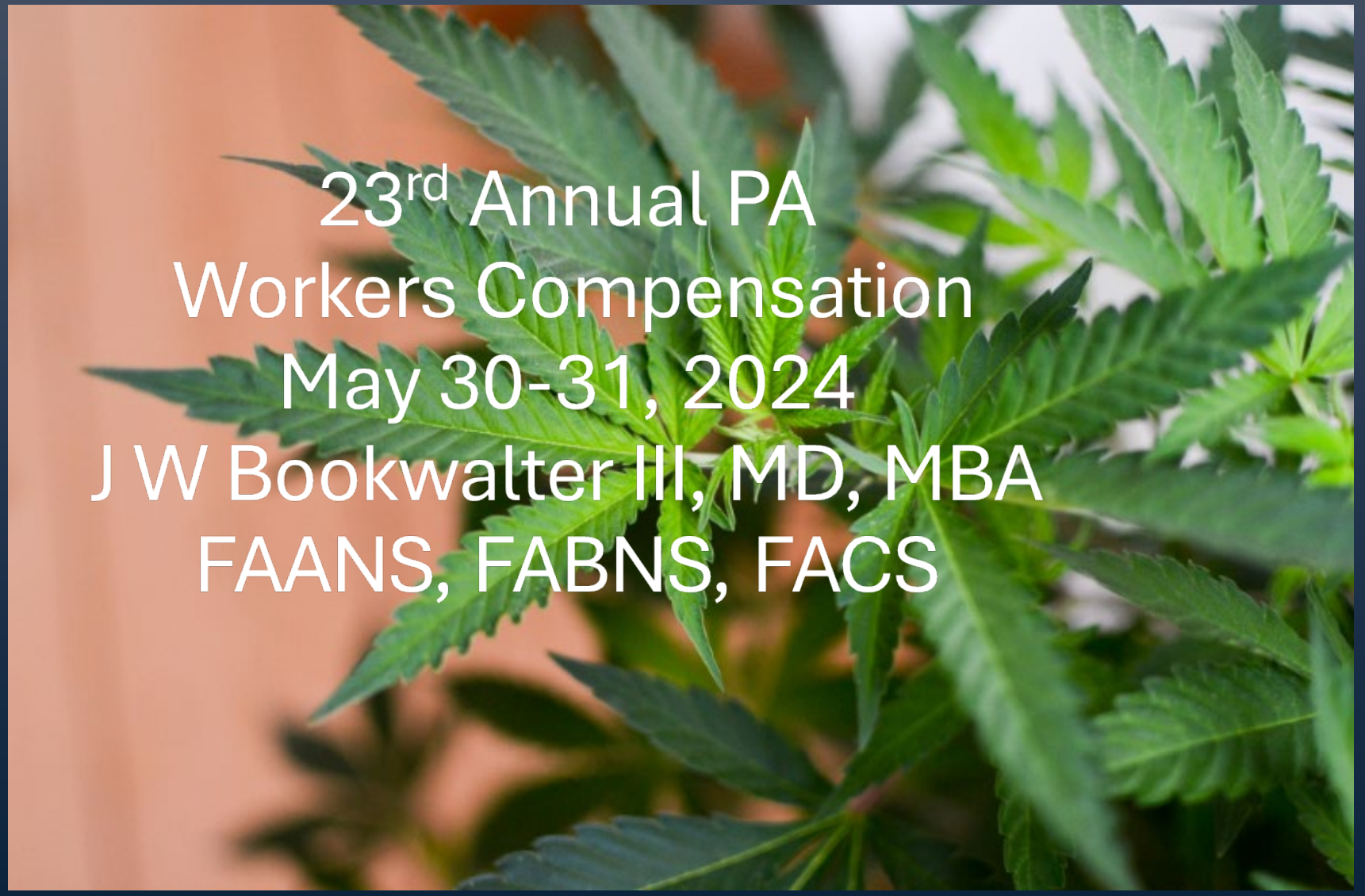

23rd Annual PA
Workers Compensation
May 30-31, 2024
J W Bookwalter III, MD, MBA
FAANS, FABNS, FACS

TALK AGENDA

- Speaker
- Getting a Card
- THC (Delta-8 &-9) and CBD
- Endocannabinoid system
- Does it work?
- Adverse effects
- Regulation
- Delta-8
- Comp and Weed

Speaker

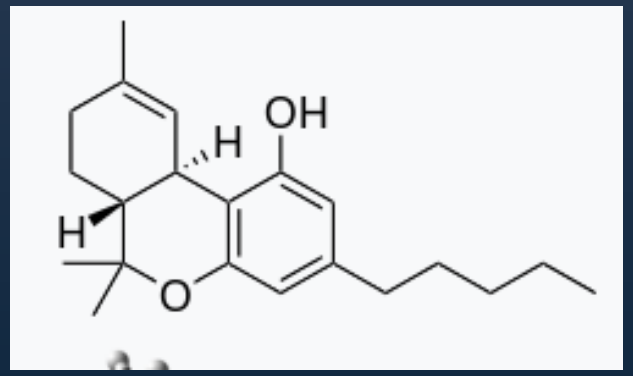
- Board Certified in Neurosurgery
- MBA in Pharmaceutical and Healthcare Management
- Years of clinical experience in managing pain problems
  - Narcotics are not the best treatment
  - Alternative options
- Supporter of exploring MJ as a treatment alternative
- Former Co-CEO of Medical Marijuana Dispensary Group
- Decades of experience in the medical-legal arena

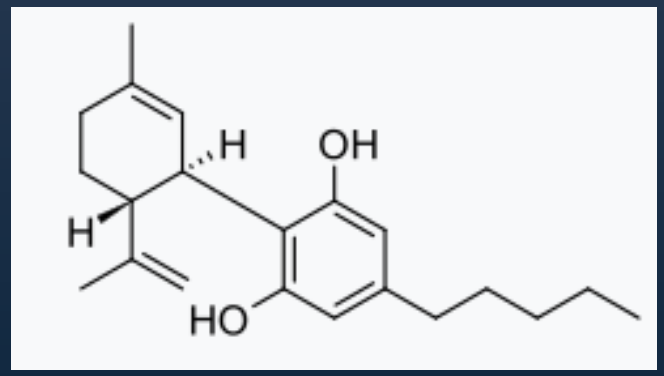
GETTING A CARD

- DOH website and apply
- Appointment with a certifying physician
- Get card
- Go to dispensary
- Consult with the pharmacist, NP, PA, or physician
- BUY ANYTHING YOU WANT

THC (left) and CBD (right) have the same chemical formula, $C_{21}H_{30}O_2$. They are structural isomers. Delta 9 is on the left, and CBD is on the right.

The key structural difference between the two molecules is that there is an oxygen-containing closed ring in THC that is open in CBD. This one structural difference leads to significantly different pharmacological effects of the two substances.

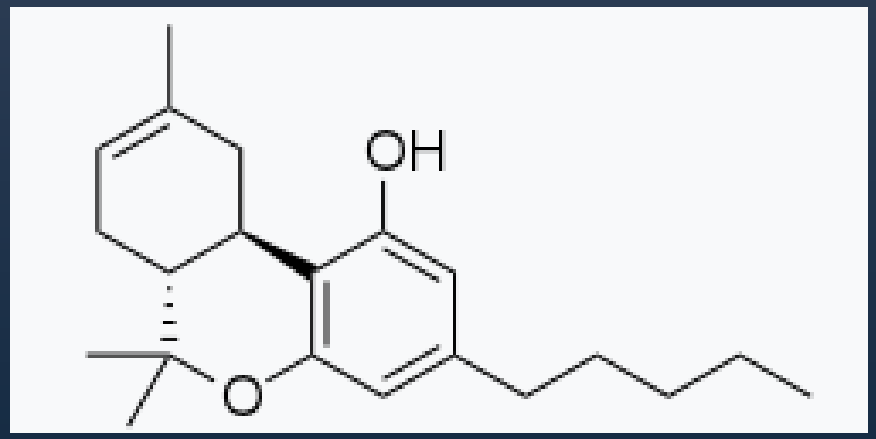




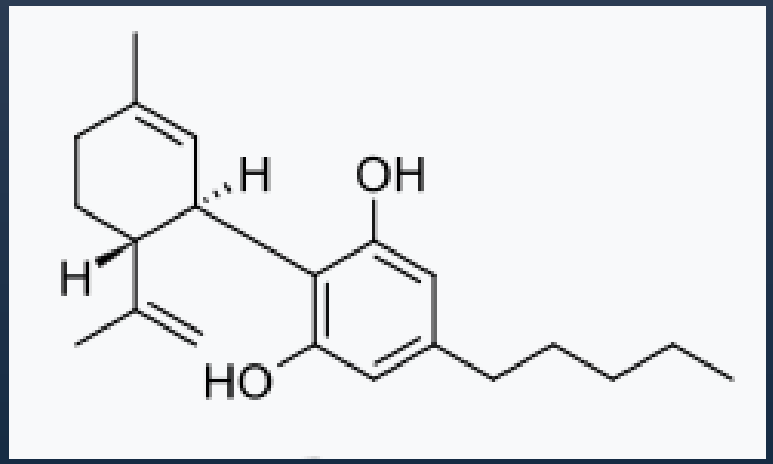
de Meijer EP, Bagatta M, Carboni A, et al. The inheritance of chemical phenotype in Cannabis sativa L. Genetics. 2003;163(1):335-346. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1462421/

CBD and D8

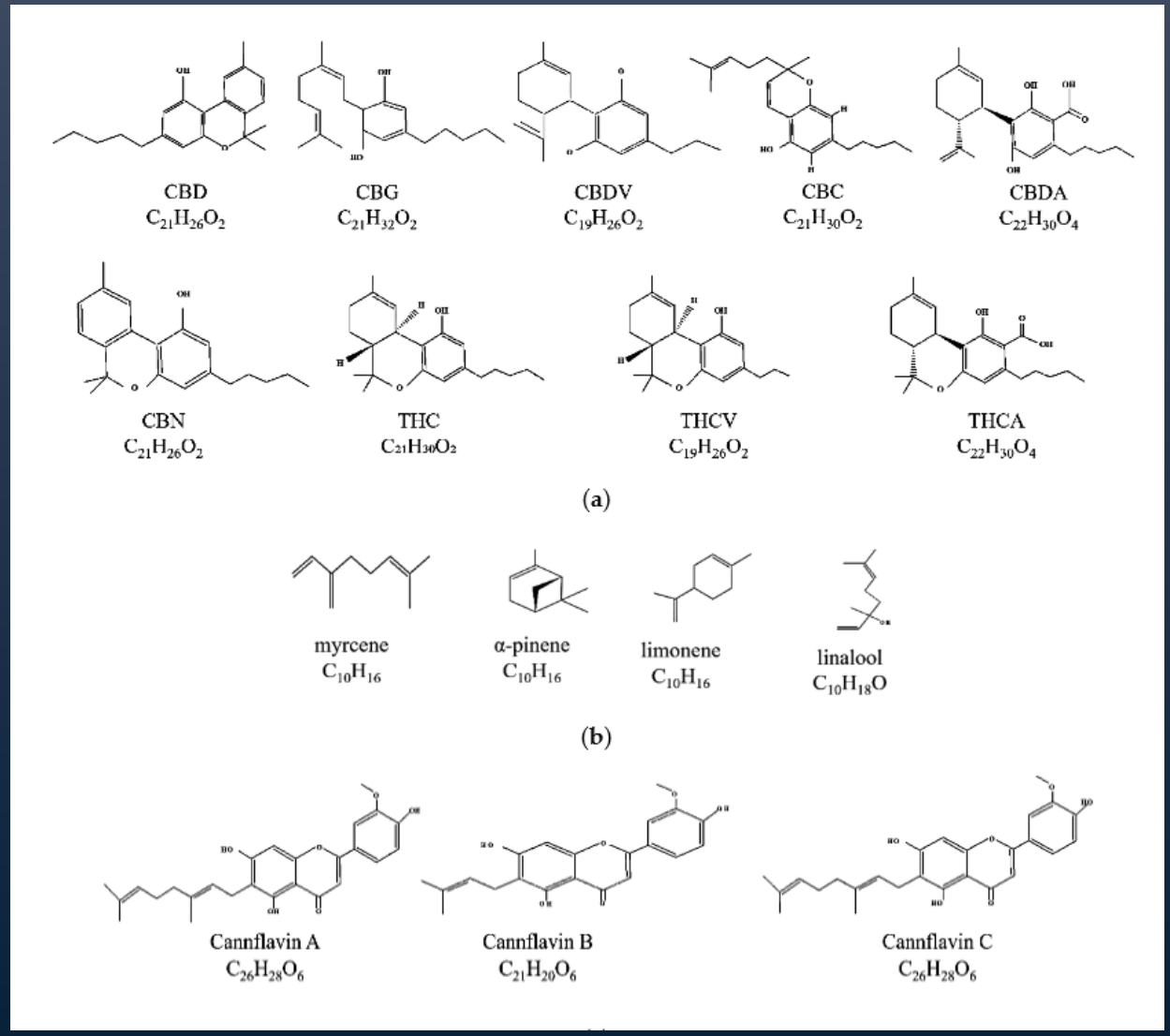
D8



CBD



The Variety of Cannabinoids



- THC and CBD are psychoactive by affecting receptors in the endocannabinoid system. By definition, a psychoactive drug is a substance that acts on the central nervous system where it alters brain function and neurotransmitter function, resulting in temporary changes in perception, mood, consciousness, and behavior.

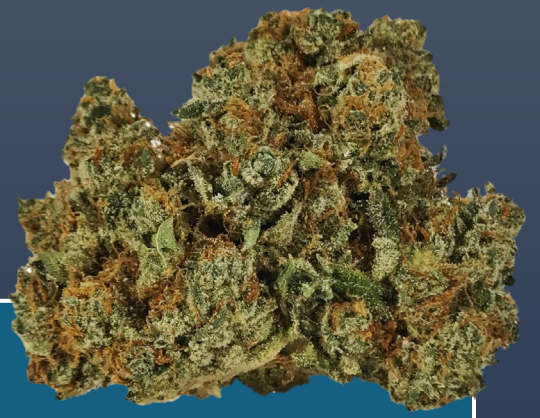
  Unlike THC, CBD does not induce euphoric feelings (a high) or induce hallucinations.

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/psychoactive-substance

PURPOSE

- Should cannabis be considered a medicine?
- What is the mechanism for its action?
- Impact on performance?

Cannabis



- Long history of medicinal use
- Approved medicinal use in 36 US states plus DC, Guam, and Puerto Rico
- Remains in Schedule I Federally – “No” recognized medicinal value
- Approved indications vary by state but include chronic pain, anxiety, epilepsy, nausea, wasting syndrome, pain, glaucoma, PTSD, ALS, Parkinson’s Disease, inflammatory bowel disease, MS
- Federal restrictions preclude meaningful research

ECS OVERVIEW

- The ECS (Endocannabinoid System) is comprised of receptors throughout your body that can utilize:
- Endocannabinoids - Cannabinoids produced by your body
- Botanical Cannabinoids or phytocannabinoids- Cannabinoids derived from plants
- Manufactured Cannabinoids - Cannabinoids synthesized in labs
- Receptors already in the body are affected by endocannabinoids and exogenous cannabinoids

Endocannabinoid System

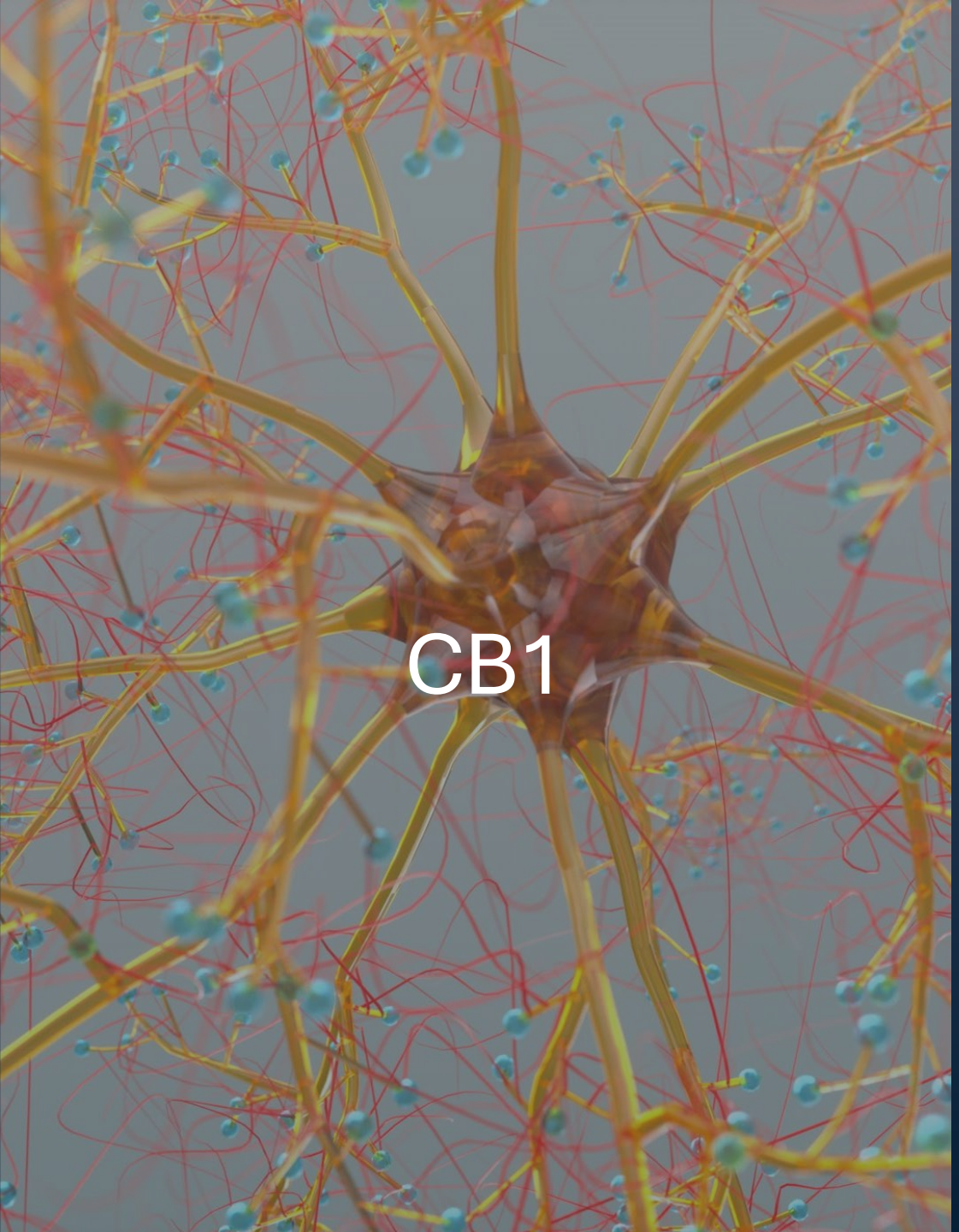
Two recognized CB receptors

CB_1

CB_2

More?

Number of identified endogenous signaling molecules



Discovered in 1988, CB1 receptors modulate pain through receptors in the central nervous system.

It also potentiates an anti-inflammatory effect on mast cells as an additional pain modulator.

Widely present in vertebrates

Present mostly in the CNS, but also peripheral and enteric

Marcu I, Gee A, Lynn B. Cannabinoids and chronic pelvic pain in women: Focus on endometriosis. Journal of Endometriosis and Pelvic Pain Disorders. 2021;13(3):155-165. https://journals.sagepub.com/doi/abs/10.1177/22840265211011277?journalCode=peva

CB1 anti-neuroinflammatory activity

- Produces anti-inflammatory cytokines
- Promotes apoptosis (cell death) in T cell-driven inflammation
- Increases population of regulatory T cells
- Analgesic, anti-inflammatory, and neuroprotective effects

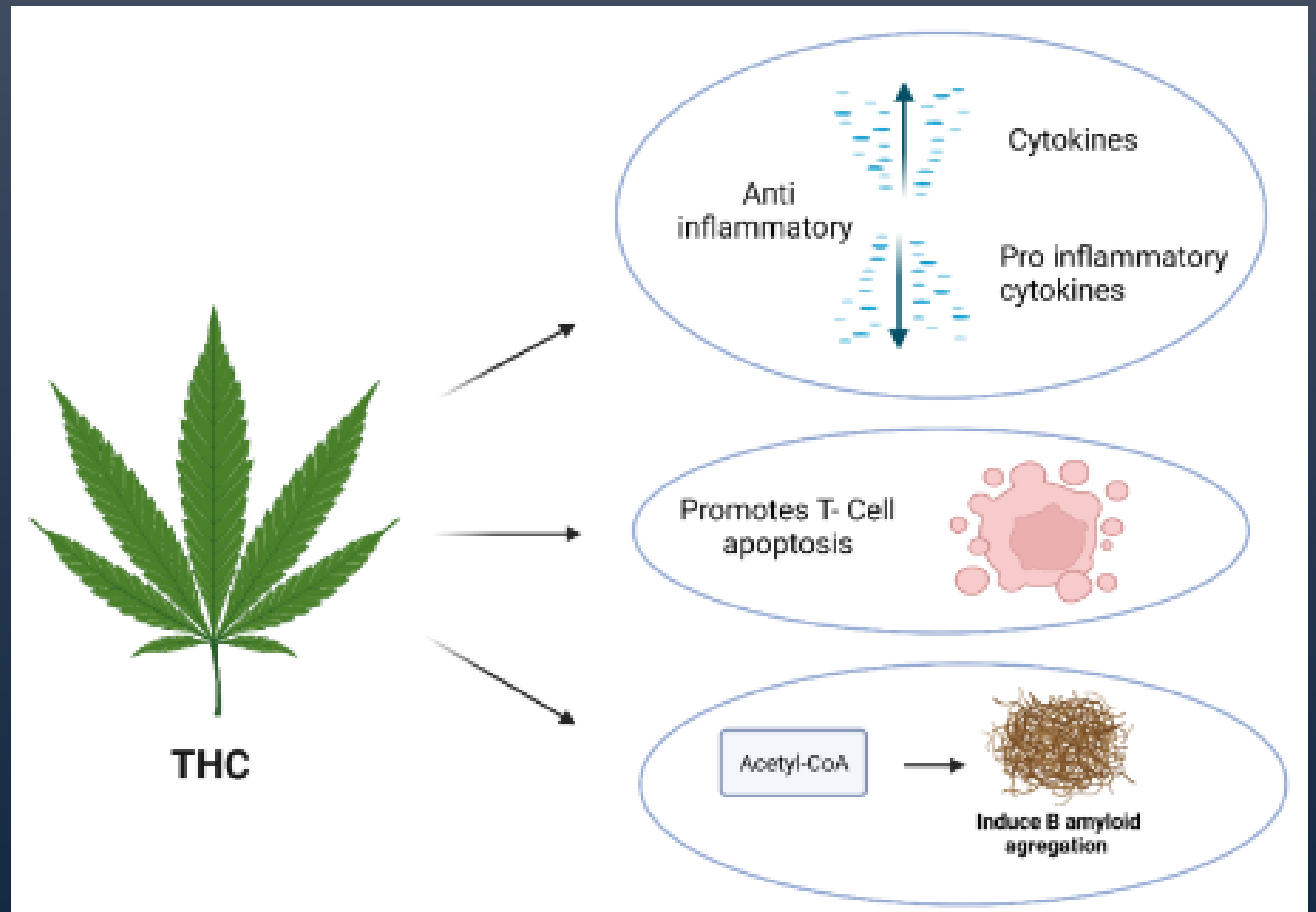


Figure 4. The anti-neuroinflammatory activity of THC.

In 1990, researchers mapped the locations of the CB1 Receptors and determined that the CB1 receptor is very highly expressed throughout the brain. In humans, the CB1 receptor is 10 times more prevalent in the CNS, as compared to the mu-opioid receptor

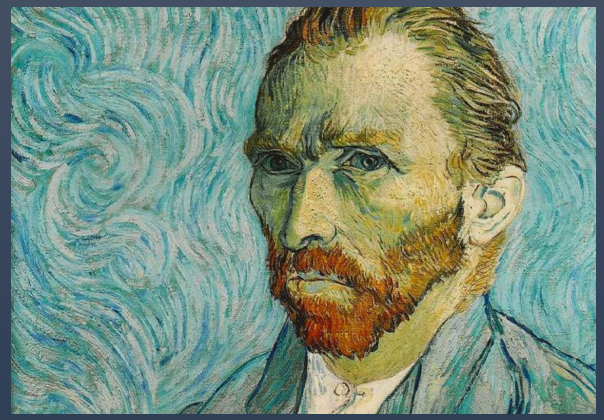
Burns HD, Van Laere K, Sanabria-Bohorquez S, et al. [18F]MK-9470, a positron emission tomography (PET) tracer for in vivo human PET brain imaging of the cannabinoid-1 receptor. Proc Natl Acad Sci USA. 2007;104:9800–9805.
https://pubmed.ncbi.nlm.nih.gov/17535893/

Endogenous Endocannabinoids

- Anandamide or AEA
- 2-arachidonyl glycerol (2-AG)
- Noladin ether
- Virodhaine
- N-arachidonlyl dopamine (NADA)

Śmiarowska M, Białecka M, Machoy-Mokrzyńska A. Cannabis and cannabinoids: pharmacology and therapeutic potential
Neurologia i Neurochirurgia Polska Polish Journal of Neurology and Neurosurgery 2022, DOI: 10.5603/PJNNS.a2022.0015
 ISSN: 0028-3843, e-ISSN: 1897-4260

Other Cannabinoid Sources

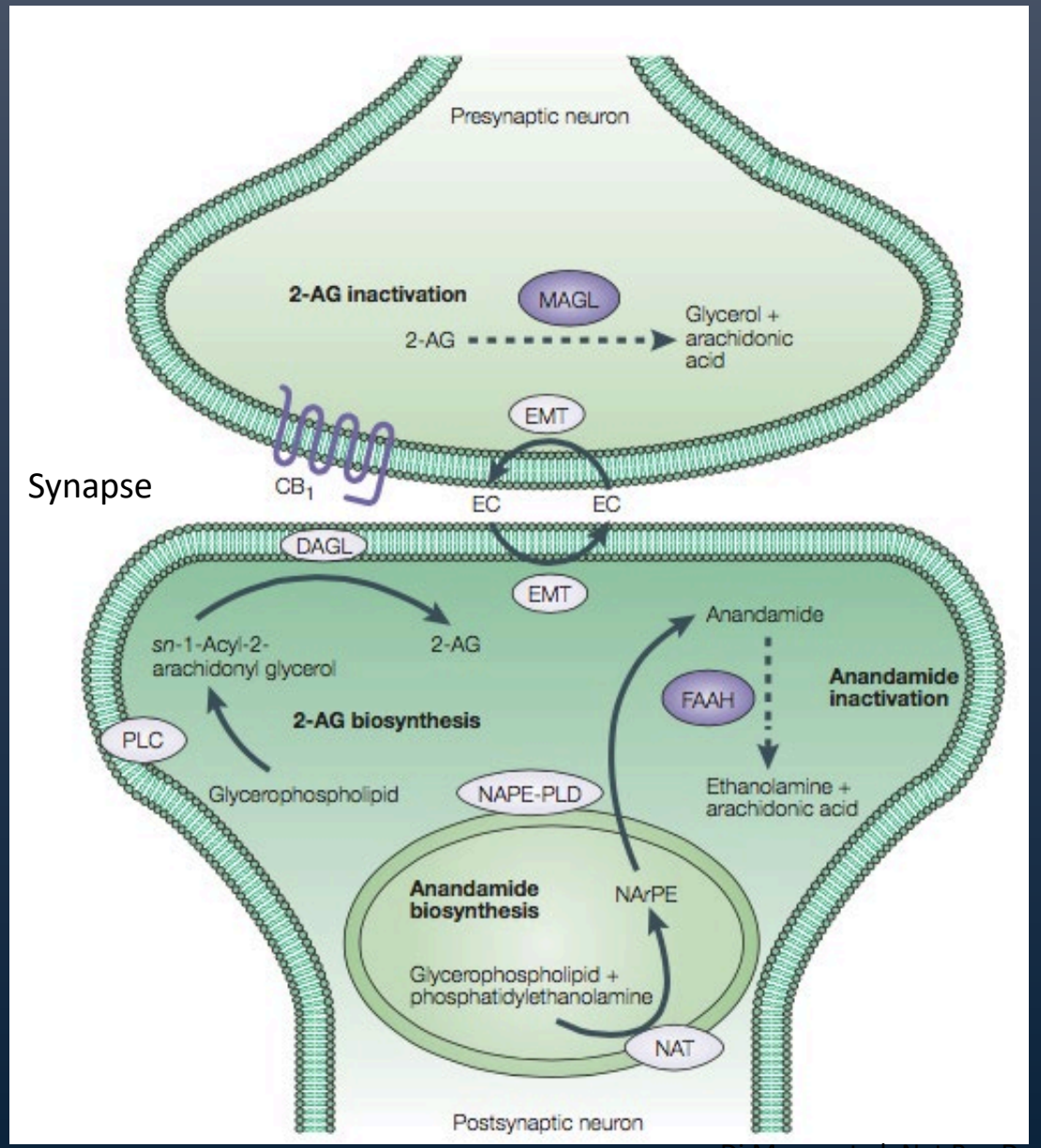


- Endocannabinoid-like compounds
- Black truffles
  - Anandamide
  - 0.54 ± 0.20 to 6.64 ± 1.85 pmol/mg protein
- Chocolate
  - *N*-oleoylethanolamine, *N*-linoleoylethanolamine and anandamide (0.5-57 µg/g)
- Other:
  - *Piper methysticum* – Yagonin – modest CB_1 agonist (0.72 µM)
  - *Echinacea* – alkamides – CB_2 affinities
  - *Camellia sinensis* – catechins – weak CB_1 affinity (>30 µM)
  - *Artemisia absinthium* – Thujone –WEAK CB_1 affinity (165 µM)
  - *Radula marginata* - Perrottetinene

How does marijuana work?

Delta-9 THC is an agonist (stimulates) CB1 receptors, to produce its effects. This inhibits synaptic transmission

Synapse



Di Marzo et al. Nat Rev Drug Dis 2004;3.9:771.

CB_2

- Cloned in 1993
- 44% sequence homology with CB_1
- Role in the immune system
- Stimulated by CBD
- Lower levels expressed than CB_1

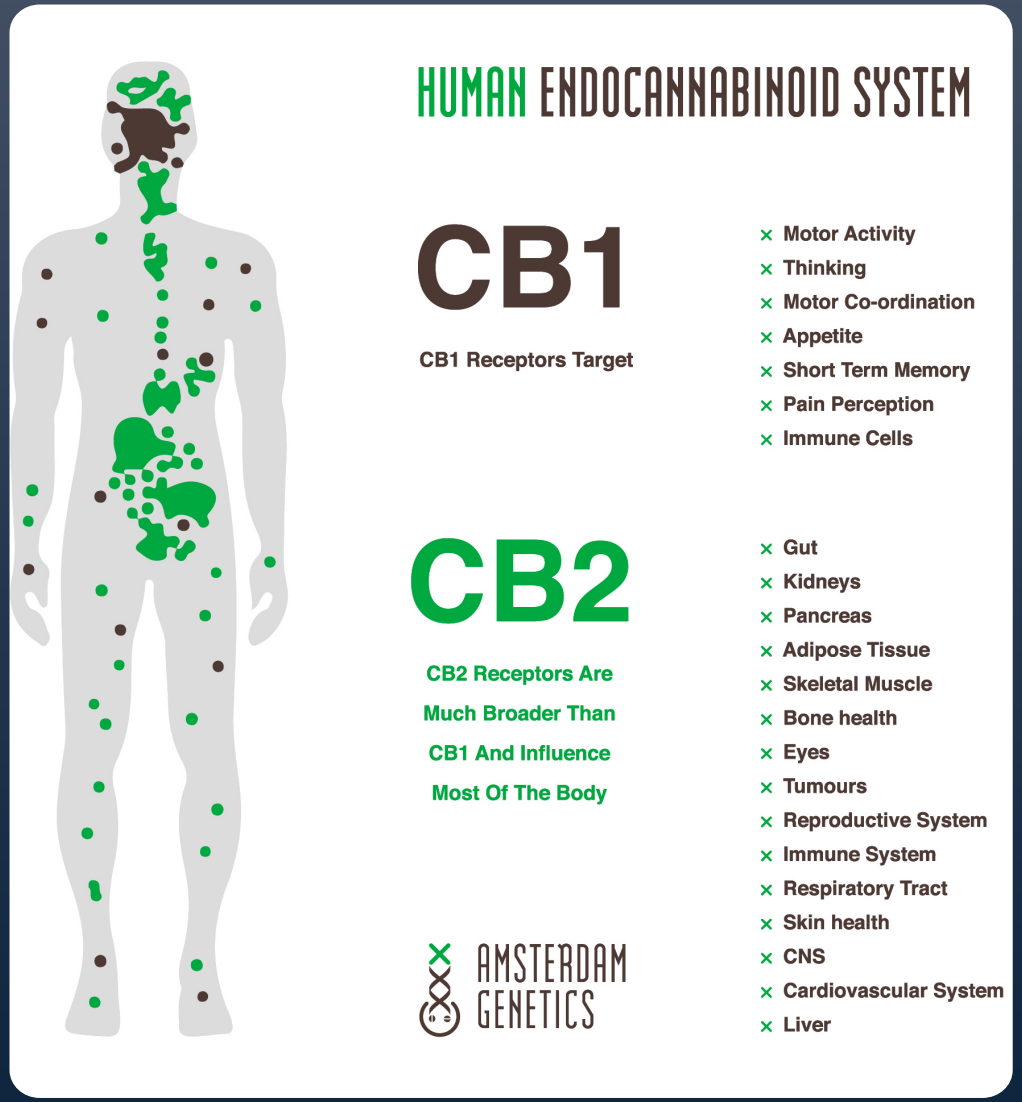
CB2 and Pain Modulation

CB2 leads to the release of endogenous opioids.

CB2 receptor activation inhibits proinflammatory signals near nociceptive (pain-perceiving) nerve cells.

These receptors are often activated when there is active inflammation or injury.

Emanuele, N. et al. The effects of cannabis and cannabinoids on the endocrine system. Rev Endocr Metab Disord (2021). Aug 30, 2021 https://doi.org/10.1007/s11154-021-09682-w



Receptors

- Cb1: Less prevalent
- THC only binds to Cb1

- Cb2: More prevalent
- Accepts broader range of cannabinoids

- Discovering others

CNS Endocannabinoid System Summary

ECs produced on demand

ECs modulate excitatory and inhibitory synaptic signaling

Modulate other neurotransmitters systems including DA, 5-HT, NE, ACh, and opioid

Pre- and postsynaptic feedback

Generally, inhibit NT release

Significance

Physiological

Chemical transmission and communication

Regulation of synaptic plasticity

Cell survival

Behavioral

Appetite and feeding

Motivation/Reward

Pain

Cognition, learning and memory

Mood

Motor activity

Immune and inflammation

Takeaways

- Endocannabinoid system
- Rich and complex physiological roles
- Lots to learn
- Phytocannabinoids (exogenous)
    - Diverse pharmacology
        - CB_1, CB_2, TRP
- Clinical
    - Several approved cannabinoid agents and a number are being actively investigated in clinical trials

Entourage Effect

- THC and CBD work synergistically.
  - THC/CBD ratio important in medicinal effects
- Chemical analysis
    - Major phytocannabinoids are THC and CBD
    - Most other phytocannabinoids are <1%
    - Terpenes
    - No clear *C. indica* vs *sativa* species
    - Variable chemical content between batches, suppliers, etc.
- Hypothesis states there is an interaction between phytocannabinoids and/or terpenes to alter the psychoactive and medicinal actions
- Alternate hypothesis –experienced differences result from variable THCA content, user expectations, and setting of use

Entourage Effect Research

- 20 healthy adults completed 9 double-blind sessions
- D-limonene alone, no difference from placebo
- THC (15mg & 30mg) alone typical effects
- Anxiety-like subjective effects qualitatively decreased with increasing doses of d-limonene
- Concurrent administration of 30mg of THC + 15mg d-limonene significantly reduced anxious/nervous and paranoid feelings compared to 30mg of THC alone
- D-limonene did not alter THC pharmacokinetics

Spindle, T. R., C. Austin Zamarripa, Russo, E., Pollak, L., Bigelow, G., Ward, A. M., Tomspon, B., Sempio, C., Touraj Shokati, Klawitter, J., Christians, U., & Vandrey, R. (2024). Vaporized D-Limonene Selectively Mitigates the Acute Anxiogenic Effects of Δ9-Tetrahydrocannabinol in Healthy Adults Who Intermittently Use Cannabis. *Drug and Alcohol Dependence*, 111267–111267. https://doi.org/10.1016/j.drugalcdep.2024.111267

Entourage Effect

- Romanian Study
- Other cannabinoids with different chemical structures interacts differently with the ECS
- This may lead to tailored therapeutic effects for specific conditions
- CBG and CBN may have antibacterial effects
- CBN may be mildly sedative\THC-V may as as an appetite suppressant
- Terpenes have been shown to have pharmacological properties

Adlin, B. (2024, May 6). Interaction Of Marijuana Terpenes And Cannabinoids Offers “Hope” For “Novel” Treatments, Study Says. Marijuana Moment. https://www.marijuanamoment.net/interaction-of-marijuana-terpenes-and-cannabinoids-offers-hope-for-novel-treatments-study-says/?

Adlin, B. (2024, February 7). New Study Shows How Marijuana Compounds Like Cannabinoids, Terpenes And Flavonoids Interact For Medical Benefits. Marijuana Moment. https://www.marijuanamoment.net/new-study-shows-how-marijuana-compounds-like-cannabinoids-terpenes-and-flavonoids-interact-for-medical-benefits/

Does It Work?

Most Common Qualifying Conditions

- Chronic pain (61%)
- Anxiety (57%)
- Depression (40%)
- PTSD (17%)

Kevin F. Boehnke, Owen Dean, Rebecca L. Haffajee, et al; U.S. Trends in Registration for Medical Cannabis and Reasons for Use From 2016 to 2020: An Observational Study. Ann Intern Med. [Epub 14 June 2022]. doi:10.7326/M22-0217
https://doi.org/10.7326/M22-

Patient View of Cannabis for Chronic Pain

- Effective for pain relief and functional improvement
- Allowed reduction in the use of prescription medications
- Insufficient on its own
- Modest side effects associated with use, but benefits exceeded the harms
- Adverse effects were often less than those of prescription medications
- Cost of cannabis for therapeutic purposes and lack of coverage by governmental agencies and insurers were a barrier to use.

AminiLari M, Kithulegoda N, Strachan P, MacKillop J, Wang L, Pallapothu S, Neumark S, Sharma S, Sethi J, Zacharias R, Blain A, Patterson L, Busse JW. Benefits and Concerns Regarding Use of Cannabis for Therapeutic Purposes Among People Living with Chronic Pain: A Qualitative Research Study. Pain Med. 2022 Jun 2:pnac085. doi: 10.1093/pm/pnac085. Epub ahead of print. PMID: 35652734. https://pubmed.ncbi.nlm.nih.gov/35652734/

Medical cannabis safely helps alleviate cancer-related pain, may reduce opioid use

- Analyzed data from 358 patients with cancer in the Quebec Cannabis Registry
- Statistically significant decreases at 3, 6, and 9 months in
  - Worst pain
  - Average pain
  - Overall pain severity
  - Pain interference
- THC:CBD-balanced strains were associated with better pain relief as compared with THC-dominant or CBD-dominant strains
- Decreases in morphine equivalent doses were also observed

Source: Aprikian S, et al. *BMJ Support Palliat Care*. 2023;doi:10.1136/spcare-2022-004003

Australian Study, Arkel, et al

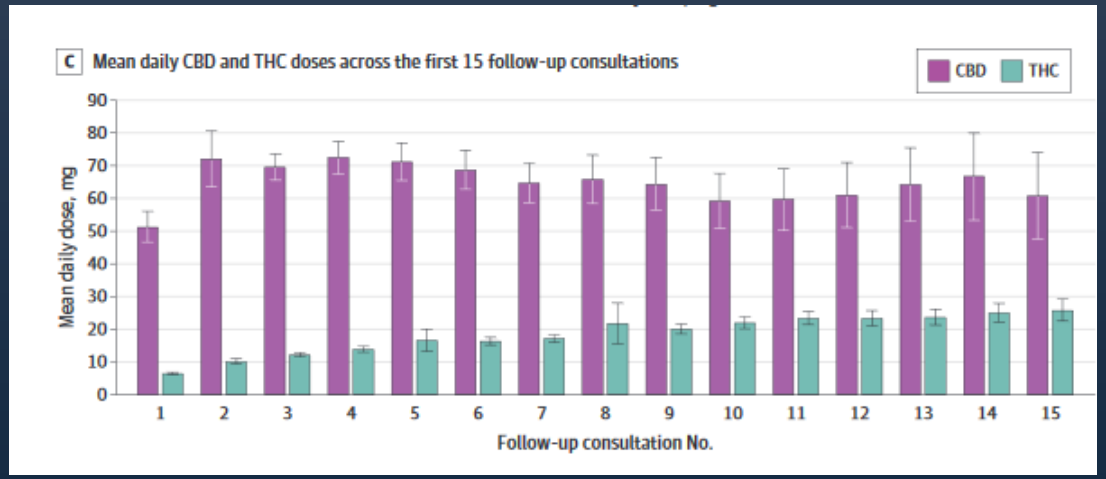
patients using medical cannabis improvements in health-related quality of life, which were mostly sustained over time.

Adverse events were rarely serious, but common, highlighting the need for caution with prescribing.

Mean daily CBD dose increased from 51 mg at initiation to 72 mg at 90 days then remained relatively constant.

THC dose did increase steadily from 6.5 mg to 26 mg over 675 days of treatment

THC dominant products were associated with largest improvements on the physical functioning domain



JAMA Network Open. 2023;6(5):e2312522. doi:10.1001/jamanetworkopen.2023.1252

Cannabis and Pain (NZ)

96% helped

- 49% reduce or stop prescription meds

Positive effects on pain relief, sleeplessness, and anxiety

98% with autism, ADHD, PTSD, and difficulty eating found taking cannabis helped

Medical cannabis cost high causing many to source on illicit market

Study results prompt call for medicinal cannabis policy evaluation | MDLinx. (2023). MDLinx. https://www.mdlinx.com/news/study-results-prompt-call-for-medicinal-cannabis-policy-evaluation/1Q5lENIPRZtZv5gwhFKDbj?show_order=2&utm_campaign=reg_daily-alert_230530_daily-nl-pm-v4_registered-users-a90&utm_source=iterable&utm_medium=email

According to a study appearing in JAMA Network in January 2023, “Among adults with chronic pain in states with medical cannabis laws, 3 in 10 persons reported using cannabis to manage their pain. Most persons who used cannabis as a treatment for chronic pain reported substituting cannabis in place of other medications including prescription opioids”

Bicket, M. C., Stone, E. M., & McGinty, E. E. (2023). *Use of Cannabis and Other Pain Treatments Among Adults With Chronic Pain in US States With Medical Cannabis Programs*. *6*(1), e2249797–e2249797. https://doi.org/10.1001/jamanetworkopen.2022.49797

According to a large cross-sectional survey (n=1661) involving adults with chronic pain who lived in the 36 states (and Washington, D.C.) with active medical cannabis programs in March to April 2022, “more than half of adults who used cannabis to manage their chronic pain reported that use of cannabis led them to decrease use of prescription opioid, prescription nonopioid, and over–the–counter pain medications, and less than 1% reported that use of cannabis increased their use of these medications.”

Bicket MC, Stone EM, McGinty EE. Use of Cannabis and Other Pain Treatments Among Adults With Chronic Pain in US States With Medical Cannabis Programs. JAMA Netw Open. 2023;6(1):e2249797. doi:10.1001/jamanetworkopen.2022.49797

5 Most Common Mental Health Reasons Patients Use Medical Marijuana

- Anxiety (57%)
- Depression (40%)
- PTSD/Trauma (17%)
- Managing other drug or alcohol use (11%)
- Psychosis (4%)

Leung, J., Chan, G., Stjepanović, D. et al. Prevalence and self-reported reasons of cannabis use for medical purposes in USA and Canada. Psychopharmacology (2022). https://doi.org/10.1007/s00213-021-06047-8

PTSD

- Theory – PTSD causes an imbalance in the endocannabinoid system, which can be restored with exogenous cannabinoids
- Cannabis can reduce nightmares and hyperarousal
- Can help reduce anxiety
- May change memory processing
- Issues around gun ownership
  - No evidence that cannabis uniquely puts individuals at risk of firearm harm

Adverse Effects

Common Short Term Adverse Effects

- Dry Mouth
- Nausea/vomiting
- Fatigue/drowsiness
- Euphoria
- Hallucinations
- Disorientation/confusion
- Loss of balance
- Impairment in hand-eye coordination

Śmiarowska M, Białecka M, Machoy-Mokrzyńska A. Cannabis and cannabinoids: pharmacology and therapeutic potential. Neurologia i Neurochirurgia Polska Polish Journal of Neurology and Neurosurgery 2022, DOI: 10.5603/PJNNS.a2022.0015

Clinical Toxicology

- Not a single documented death due to *cannabis* overdose
- Behavioral risks
    - Motor vehicle accidents
- Chronic high frequency usage
    - Cognitive
        - Impairment of memory and attention
        - Schizophrenia association (causative?)
    - Cardiovascular
        - MI and stroke risk (causative?)
        - Arrhythmias
    - Gastrointestinal
        - Cannabinoid hyperemesis syndrome
    - Hepatic
        - Elevated serum liver enzymes
    - Respiratory (smoked)
        - Inflammation
        - Metaplasia
        - Cancer – probably not
    - Reproductive
        - Lowered sperm count

Increased risk of major adverse cardiac and cerebrovascular events in elderly non-smokers who use cannabis (Poster Abstract MDP249)

- 20% had an increased chance of having a major heart or brain event while hospitalized, compared to the group who did not use cannabis.
- 13.9% of cannabis users with cardiovascular risk factors had a major adverse heart and brain event while hospitalized compared to non-cannabis users.
- Additionally, the cannabis users in comparison to non-cannabis users had a higher rate of heart attacks (7.6% versus 6%, respectively) and were more likely to be transferred to other facilities (28.9% vs. 19%).
- High blood pressure (defined as greater than 130/80 mm Hg) and high cholesterol were predictors of major adverse heart and brain events in marijuana users.
- Study details:
  - 2019 National Inpatient Sample health records were reviewed for 28,835 adults with cannabis use disorder and high blood pressure, Type 2 diabetes or high cholesterol. The comparison group included 10,680,000 adults with the same risk factors who did not use marijuana.
  - Researchers examined hospitalization records to analyze the incidence of in-hospital cardiovascular disease events for adults in both groups.
  - 69.5% of participants in the cannabis use disorder group were male and 30.5% were female. In contrast, 45.8% were males in the non-cannabis use group versus 54.2 in the female non-use group.
  - Health records of race according to cannabis use versus non-use , respectively was: 70.2% versus 76.4 among white adults; 20.1% versus 10.8% among Black adults; 5.6% versus 7.4% among Hispanic adults; 0.70% versus 2.7% among Asian or Pacific Islander adults; and 1% versus 0.40% among Native American adults.

Cannabis Use and Serious Mental Disorders

Lancet Psychiatry

Schizophrenia and bipolar disorder have high degrees of heritability

A subgroup of individuals might have a high genetic risk of developing a psychotic disorder and using cannabis.

May want to reduce cannabis use in individuals at high risk or patients with psychotic disorders.

Same genes found to be related to both cannabis use and serious mental disorders | MDLinx. (2023). MDLinx. https://www.mdlinx.com/news/same-genes-found-to-be-related-to-both-cannabis-use-and-serious-mental-disorders/2bszdlTRBjtjdyMpPIdM4W?show_order=4&utm_campaign=reg_evening-edition_230602_daily-nl-pm-v4_registered-users-a90&utm_source=iterable&utm_medium=email

Contribution of Cannabis Use to Variation in the Incidence of Psychotic Disorder

- Strongest independent predictor:
  - Daily users (3.2x higher than never users)
  - High potency users (1.6x higher than never users)
  - Starting use before age 15 (mild)
- Multicenter European Center Study

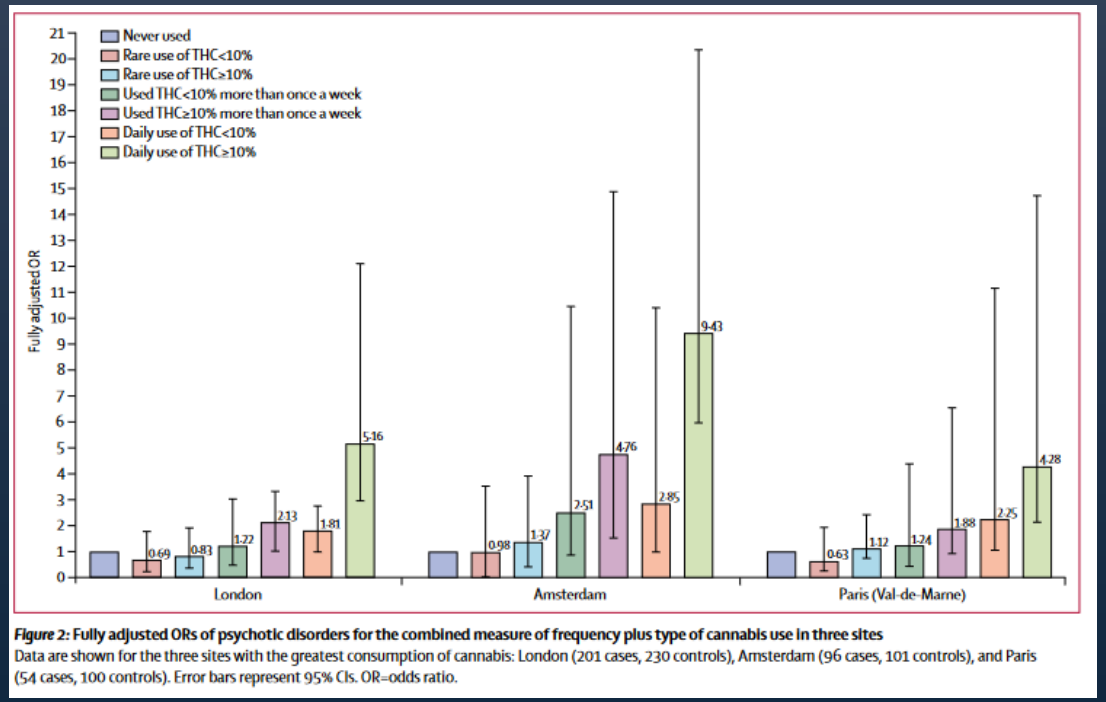


Figure 2: **Fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in three sites**
Data are shown for the three sites with the greatest consumption of cannabis: London (201 cases, 230 controls), Amsterdam (96 cases, 101 controls), and Paris (54 cases,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

www.thelancet.com/psychiatry Vol 6 May 2019

Psychotic Episode from Marijuana

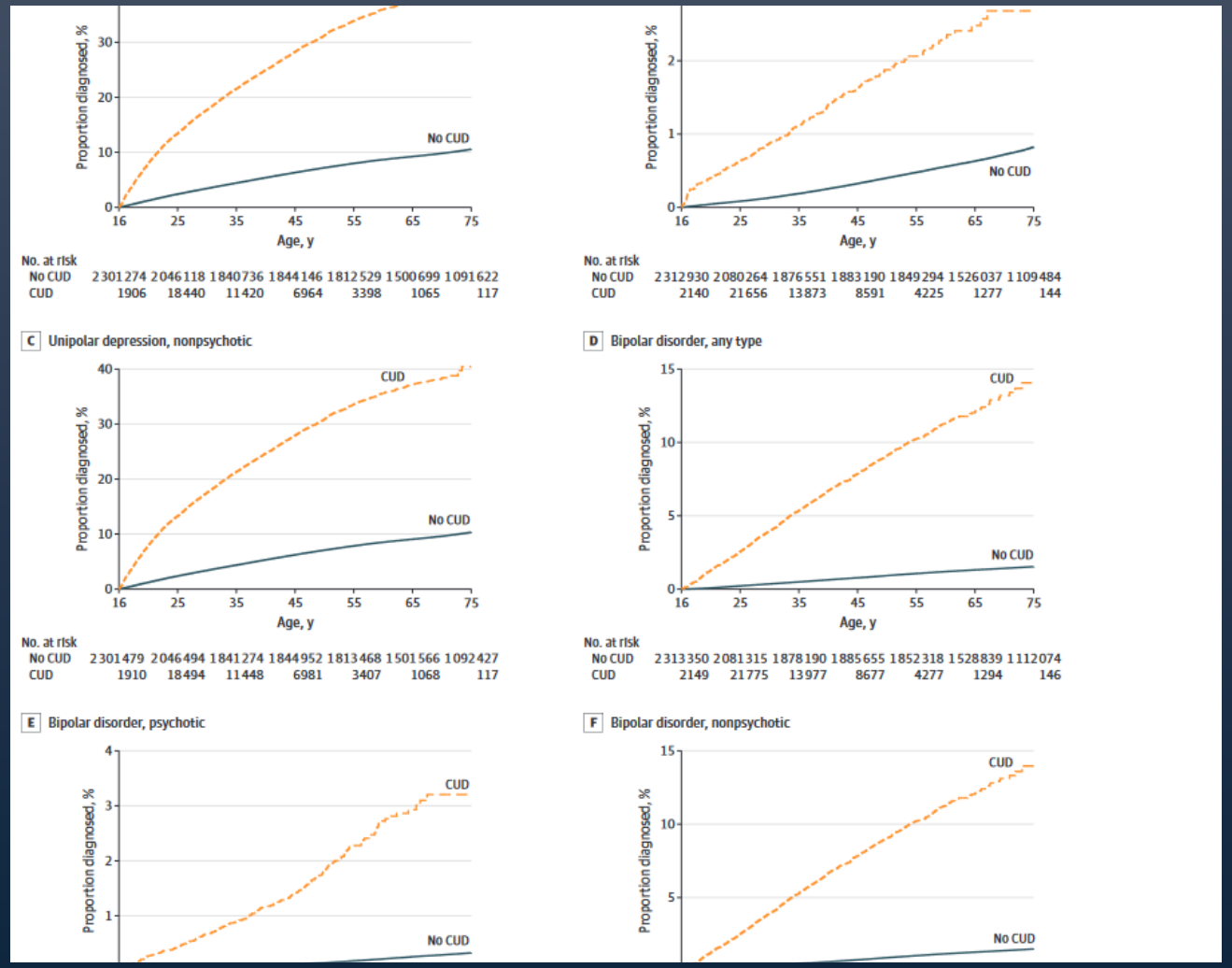
- Daily use of cannabis and use of high-potency cannabis increase the risk of a psychotic disorder.
  - Self-reported
- Starting use by age 15
- Data not validated by blood, urine, or hair samples
- No direct measure of THC %
- Does not differentiate licit versus illicit market
- No data on CBD content, which may modify Delta-9 effects
- London 45.7 cases/100,000; Amsterdam 37.9/100,000

- www.thelancet.com/psychiatry Vol 6 May 2019

Cannabis Use Disorder and Depression

- Danish Study
  - Evaluated 6,651,765 individuals in the national medical database who were at least 16 years of age between 1/1/1995 and 12/31/2023

Cannabis use disorder may represent an independent factor associated with both unipolar depression and bipolar depression



JAMA Psychiatry. 2023;80(8):803-810. doi:10.1001/jamapsychiatry.2023.1256
Published online May 24, 2023

Does the passage of medical and recreation MJ laws lead to an increase in teen MJ use?

- NO
- Youth Risk Behavior Survey 1993-2019
  - There was little evidence that the legalization of medical and recreational marijuana encourages youth marijuana use
  - The overall association between recreational marijuana legalization and marijuana use among adolescents was statistically indistinguishable from zero.
- They are already using drugs and marijuana from the illicit market
- Legalization allows access to safe, unadulterated products the illicit market cannot provide, just as the control of alcohol does not decrease underage use, but simply provides products of known provenance.

Anderson DM, Rees DI, Sabia JJ, Safford S. Association of Marijuana Legalization With Marijuana U
School Students, 1993-2019. JAMA Netw Open. 2021;4(9):e2124638. doi:10.1001/jamanetworkope
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783850

Underage Use

- Among 898,271 students' recreational cannabis legalization was not associated with adolescents’ likelihood or frequency of cannabis use
- Associated with modest decreases in cannabis, alcohol, and e-cigarette use.
  - Each subsequent year is associated with an 8% percent higher odds of zero cannabis use
- Negative total effect estimate for alcohol use
- More significant results emerged for cigarettes

Rebekah Levine Coley, Carey, N., Kruzik, C., Summer Sherburne Hawkins, & Baum, C. F. (2021). Recreational Cannabis Legalization, Retail Sales, and Adolescent Substance Use Through 2021. *JAMA Pediatrics*. https://doi.org/10.1001/jamapediatrics.2024.0555

Underage Use

- Cross-sectional study
  - Cross-sectional studies are observational studies that analyze data from a population at a single point in time. They are often used to measure the prevalence of health outcomes, understand determinants of health, and describe features of a population
- In this repeated cross-sectional study, there was no evidence that RMLs were associated with encouraging youth marijuana use, based on both the logistic regression and interaction-weighted models.

D. Mark Anderson, Fe, H. T., Liang, Y., & Sabia, J. J. (2021). Recreational Marijuana Laws and Teen Marijuana Use, 1993-2021. JAMA Psychiatry. https://doi.org/10.1001/jamapsychiatry.2024.0698

Adult Use

- The real critical issues are related to safety
  - HHS report
  - Do not get respiratory depression, so death is not a consequence
  - Over time (hours) symptoms spontaneously remit
  - Driving impairment has been studied
    - Enforcement must be legislated
  - Physical and Psychological dependence can occur but are mild compared to other intoxicating substances
  - Adverse reactions are substantially less than other substances, including alcohol
- A regulated market for all cannabis products is necessary for consumer safety
- Underage consumption is going to occur in spite of legislation
- Eliminating the illicit market is the only strategy for safe use at any age

WHAT, IF ANY, RISK THERE IS TO THE PUBLIC HEALTH

The risks to public health posed by marijuana are low compared to other drugs of abuse (e.g., heroin, cocaine, benzodiazepines), based on an evaluation of various epidemiological databases for ED visits, hospitalizations, unintentional exposures, and most importantly overdose deaths.

For overdose deaths, marijuana is implicated when present with other drugs

Although abuse of marijuana produces clear evidence of a risk to public health, that risk is relatively lower than that posed by most other comparator drugs, e.g. alcohol or narcotics

Regulation

Data Insights

Program Data: Q1 2022 v. Q1 2023		
	Q1 2022	Q1 2023
Active Patients Certificates	406,454	425,367
Approved Practicioners	1,779	1,825
Dispensing Events	20M	31M
Products Dispensed	56.8B	87.9
Total Sales	4.8B	7.3B
G/Ps to Dispensaries	1.9B	2.9B
Dispensaries to Patients	2.9B	4.4B
Operational Dispensaries	155	173
Retail Price per Gram	$13.40	$9.81
Wholesale Price per Gram	$6.65	$4.09

$2.1 B Legal Medical Market

$2.9 Billion Illicit Market

Problems Without Regulation

Actual quantity of melatonin ranged from 74% to 478% of the declared quantity (1.3-mg to 13.1mg)

As little as 0.1-mg to 0.3-mg of melatonin can increase plasma concentrations into the normal nighttime range.

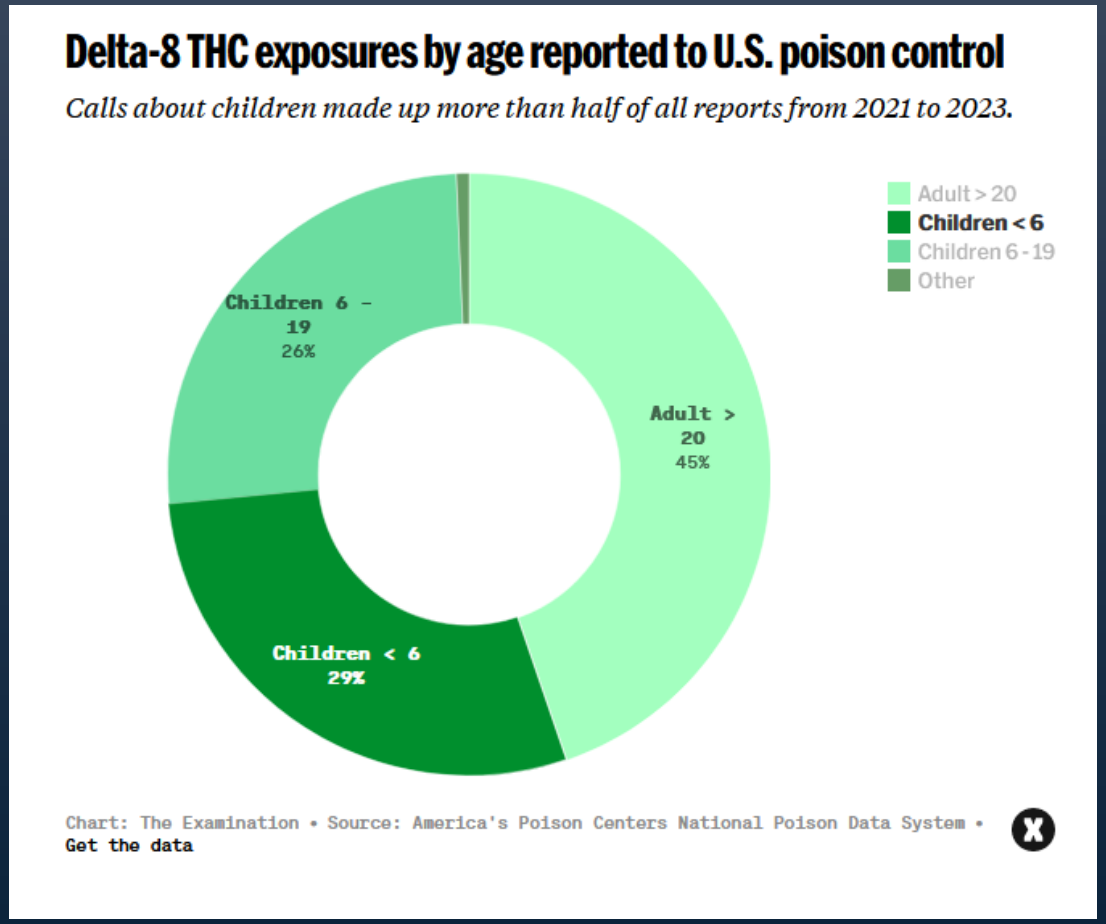
88% were inaccurately labeled

In products containing CBD, the actual CBD content was 104%-118% of labeled

JAMA April 25, 2023 Volume 329, Number 16

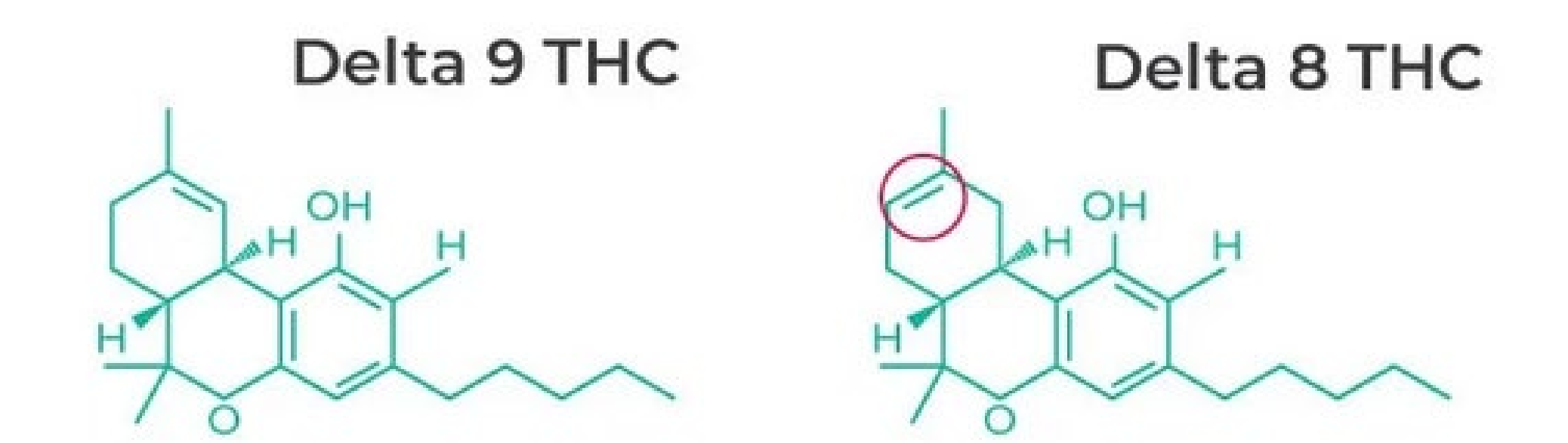
- Delta 8
- Some manufacturers may use potentially unsafe household chemicals
- From January 1, 2021, Poison Control to February 28, 2022:
  - 2362 exposure cases
  - 41% pediatric
    - 82% unintentional
  - 45% requiring healthcare facility evaluation were pediatric
  - One pediatric fatality

Delta 8


Delta-8 THC exposures by age reported to U.S. poison control
Calls about children made up more than half of all reports from 2021 to 2023.
Adult > 20
Children < 6
Children 6 - 19
Other
Children 6 - 19 26%
Adult > 20 45%
Children < 6 29%
Chart: The Examination • Source: America's Poison Centers National Poison Data System •
Get the data

What Is Delta-8?

Delta 8



Delta 9 has a double bond at the ninth carbon atom and Delta 8 at the eighth

HubSpot, I. (2023). Hs-Sites.com. https://9128848.hs-sites.com/share/hubspotvideo/118302416719?utm_medium=email&_hsmi=260711079&_hsenc=p2ANqtz-9Doy4knUcvmfWtd96xpSHHn3n8M5hPS8ro9tw65J6UnOyRozinESG9-QbPUDy391653sFMj4XEqB08jhCWNnKVWq2LgQ&utm_content=260711079&utm_source=hs_email

Marijuana Economic Impact on Regulated Market from Unregulated Cannabinoid Sources for Nonmedical and Medical Use

- The proliferation of CBD based products, primarily Delta-8 has adversely affected the regulated market.
- Glass shops and “CBD Boutiques” are providing misleading advertising representing they are selling the same product as Medical Marijuana without having to get a card.
- Currently, research on Delta-8 is lacking, as well as other THC products produced from CBD.
- Lack of process supervision, laboratory control, and testing prevents accurate awareness of dosing.

False Positives

- Delta-8 is quasi-legal but can result in a positive THC test if no specific differentiation between it and Delta-9 is made
- Action pending before the US Supreme Court and the Court agreed to take it up
  - Trucker used hemp-derived CBD product for pain management
  - Filed RICO suit against the company promoting the product
  - Trucker alleges that Medical Marijuana, Inc. committed mail and wire fraud
  - Lost his job, wages, insurance, and pension benefits
- DEA rehired and provided back pay to a special agent who was fired after testing positive for THC that he attributed to CBD he took as an opioid alternative for chronic pain

Jaeger, K. (2024, April 29). U.S. Supreme Court Takes Up Case Of Trucker Fired Over THC Test He Says Was Caused By CBD Product. Marijuana Moment. https://www.marijuanamoment.net/u-s-supreme-court-takes-up-case-of-trucker-fired-over-thc-test-he-says-was-caused-by-cbd-product/?

Comp pays for weed

Cost: Oxycontin vs Cannabis

Oxycontin

- 10-mg is $464/ 100
- 40-mg is $1400/100
- 80 mg is $2600/100

Weekly cost

- 10-mg twice daily $64.96
  - Three per day $97.44
  - Four per day $129.92
- 40-mg twice daily $196

- Cannabis
  - $100 to find the right product
  - Low tolerance $25/week
  - High tolerance $100/week
  - Stretch an RSO for a month and the cost is $15/week
  - Half an ounce of flower per week would be $200
  - Proposed law for reimbursement of $250/month, $3000/year

Driving and Cannabis

CONCLUSIONS AND RELEVANCE

Smoking cannabis ad libitum by regular users resulted in simulated driving decrements.

However, when experienced users control their own intake, driving impairment cannot be inferred based on THC content of the cigarette, behavioral tolerance, or THC blood concentrations.

Participants' increasing willingness to drive at 1 hour 30 minutes may indicate a false sense of driving safety. Worse driving performance is evident for several hours post smoking in many users but appears to resolve by 4 hours 30 minutes inmost individuals.

Further research is needed on the impact of individual biologic differences, cannabis use history, and administration methods on driving performance.

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2021.4037

CONCLUSIONS AND RELEVANCE

- In a crossover clinical trial that assessed driving performance during on-road driving tests, the SDLP (standard deviation of lateral position/lane weaving) following vaporized THC-dominant and THC/CBD-equivalent cannabis compared with placebo was significantly greater at 40 to 100 minutes but not 240 to 300 minutes after vaporization;
- There were no significant differences between CBD-dominant cannabis and placebo.
- However, the effect size for CBD-dominant cannabis may not have excluded clinically important impairment, and the doses tested may not represent common usage.

JAMA. 2020;324(21):2177-2186. doi:10.1001/jama.2020.21218

Driving and Cannabis

- 947,604 Traffic injury ED Visits
  - 426 had cannabis involvement - 0.04%
  - 7564 had alcohol involvement – 0.8%
  - Annual visits did increase by 475.3%
  - 0.18/ 1000 in 2010 to 1.01/1000 in 2021
- In the same time frame alcohol involved accidents increased by 9.4%
  - 8.03/1000 to 8.79/1000
- Visits did increase with nonmedical cannabis commercialization, but the actual number of visits is rare and well below alcohol.

Myran, D. T., Gaudreault, A., Pugliese, M., Manuel, D. G., & Tanuseputro, P. (2023). Cannabis-Involved Traffic Injury Emergency Department Visits After Cannabis Legalization and Commercialization. JAMA Network Open, 6(9), e2331551–e2331551. https://doi.org/10.1001/jamanetworkopen.2023.31551

JAMA Psychiatry

RCT: Evaluation of Field Sobriety Tests (FSTs) for Identifying Drivers Under the Influence of Cannabis

POPULATION

117 Men, 67 Women

Adults 21-55 y with cannabis use ≥4 times in past month, willing to abstain from cannabis for 2 d

Mean age, 30 y

INTERVENTION

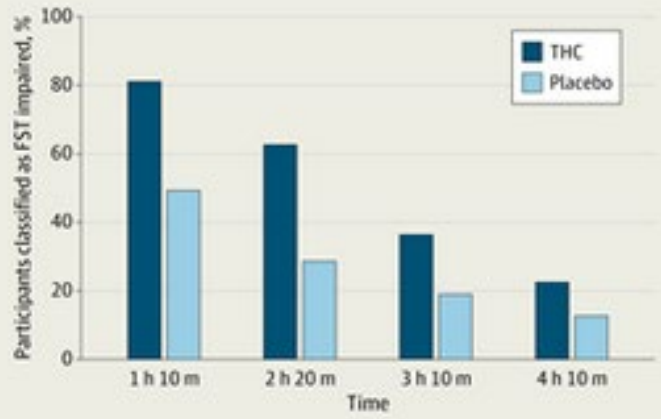
184 Participants analyzed

63 Placebo cannabis
0.02% THC placebo cigarette ad libitum before FST administration

121 Δ^9-Tetrahydrocannabinol (THC)
5.9% or 13.4% THC cannabis cigarette ad libitum before FST administration

FINDINGS

Officers classified a significantly higher proportion of participants as FST impaired in the THC group vs the placebo group at 3 of 4 time points measured after smoking



SETTINGS / LOCATIONS

Center for Medicinal Cannabis Research, University of California, San Diego, CA

PRIMARY OUTCOME

Proportion of participants classified as FST impaired by law enforcement officer-administered FSTs at 4 time points after smoking. FSTs included Walk and Turn, One Leg Stand, Finger to Nose, Lack of Convergence, and Modified Romberg

Marcotte TD, Umlauf A, Grelotti DJ, et al. Evaluation of field sobriety tests for identifying drivers under the influence of cannabis: a randomized clinical trial. *JAMA Psychiatry*. Published online August 2, 2023. doi:10.1001/jamapsychiatry.2023.2345

Interpreting the Results

- Field Sobriety Test (FST) did differentiate between individuals receiving THC vs Placebo
- High rate at which the participants receiving a placebo failed to adequately perform FSTs and the high frequency that poor FST performance was suspected to be due to THC-related impairment suggests that FSTs, absent other indicators, may be insufficient to denote THC-specific impairment

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2023.2345

Published online August 2, 2023.

Conclusions

FSTs are useful adjuncts but do not provide strong objective evidence of THC-specific impairment

Additional efforts to validate existing methods and provide law enforcement with new, effective tools foe identifying impairment are needed

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2023.2345
Published online August 2, 2023.

Analytics and Impairment

- Current analytical methodologies can readily identify cannabis use but
- There is no direct relationship between impairment and Delta9 concentrations in blood or saliva making legal “per se” limits scientifically unjustified.
- Signs of impairment and cannabis use do not rule out the involvement of other drugs.
- Compounding the matter is the hemp-derived cannabidiol (CBD) products.
- Many contain varying levels of Delta 9 as well as Delta 8 with differing degrees of psychoactivity.
- For accuracy, analytical methods must be able to distinguish the various THC isomers, which have identical masses and exhibit immunological cross-reactivity
- A new testing approach has been developed based on exhaled breath and blood sampling that incorporates kinetic changes and the presence of key cannabinoids to detect recent cannabis use within the impairment window without the false-positive result with other methods.

VDegregorio, M. W., Kao, C.-J., & Wurz, G. T. (2024). Complexity of Translating Analytics to Recent Cannabis Use and Impairment. *Journal of AOAC International*. https://doi.org/10.1093/jaoacint/qsae015

Which THC Is It?

- THC confirmation tests are usually designed to detect compounds related to the use of cannabis. If the confirmation test does not specifically search for delta-8 metabolites (and it does not do so routinely), testing will not detect the delta-8 metabolites and the original positive cannabinoid test may be erroneously reported as either positive or negative for THC
- smokable hemp plant products were analyzed for Δ8-THC, Δ9-THC, THCA, and total Δ9-THC by a previously established liquid chromatography with photodiode array detection (LC-PDA) method using a methanol extraction procedure
  - **76 % of it focused on floral hemp that is used to produce hemp-derived finished products such as smokable hemp**
  - **Over 90 % of the samples analyzed by NIST were determined to have a total Δ9-THC mass fraction above 0.3 % even though samples were being marketed as hemp**
  - **Surprisingly, often the associated online documentation reported total Δ9-THC mass fractions of ≥ 0.3 %**
  - **Measurements differed by ≈ 55 % for total Δ9-THC, ≈ 68 % for THCA, and ≈ 18 % for Δ9-THC**

- Determination of Δ9-THC, THCA, Δ8-THC, and Total Δ9-THC in 53 Smokable Hemp Plant Products by Liquid Chromatography and Photodiode Array Detection. (2024). National Institute of Justice. https://nij.ojp.gov/library/publications/determination-d9-thc-thca-d8-thc-and-total-d9-thc-53-smokable-hemp-plant?fbclid=IwAR0PrQ6WETwu3PAI7mvvORtMJaFaCeOt3BmzsRjM7YSomJjTay7gVDSG-_k

False Positives:

- Fasting – No
- Exercise –
  - Does increase endocannabinoid levels but does not show up in urine or blood as D9 or metabolite
  - THC-COOH levels—what urine tests look for—were *not* elevated following fasting and exercise in humans

Jikomes, N. (2024, January 18). Weed & exercise Part III: Can cardio make you fail a drug test? Retrieved April 4, 2024, from Leafly website:

https://www.leafly.com/news/science-tech/thc-fat-exercise-blood-levels

What If Comp Pays?

- Can’t treat like regular medications and reimburse pharmacy.
- Law proposing specific limits
- How to do a utilization review
- Side gig buying medical weed on comp dime and reselling to non-card users for less than the dispensary (buy on sale with comp dollars and resell with markup)
- Assessing impairment