

Cannabis and Cannabinoid-Based Medicine: Clearing the Smoke for Patients and Providers

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Disclosures

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Learning Objective 1

Describe practical considerations when recommending cannabis or cannabinoid-based medicine to patients.



Evidence for a Medicinal Benefit of Cannabis

Conclusive

- Chronic pain
- Nausea
- Spasticity in multiple sclerosis (MS)
- *Severe intractable epilepsy (cannabidiol)

Moderate

- Sleep (short-term)

Limited

- HIV/AIDS wasting
- Tourette syndrome
- Spasticity in MS (clinician rating)
- Anxiety related to public speaking (cannabidiol)
- PTSD
- Outcomes after TBI
- *Schizophrenia (cannabidiol)

*Modified

AIDS = acquired immunodeficiency syndrome; HIV = human immunodeficiency virus; PTSD = post-traumatic stress disorder; TBI = traumatic brain injury.
National Academies of Sciences, Engineering, and Medicine. 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/24625>. Accessed February 17, 2020.

Cannabis-Associated Harms

Conclusive	Moderate	Limited
Respiratory symptoms and more frequent chronic bronchitis episodes	Overdose injuries, including respiratory distress, among pediatric populations	Non-seminoma-type testicular germ cell tumors
Motor vehicle crashes	Lower newborn birth weight	Myocardial infarction
Development of schizophrenia or other psychoses	Mood, anxious, suicidal ideation, and suicide completion	Ischemic stroke or subarachnoid hemorrhage
*Less high school completion	Other substance abuse	Pregnancy complications
*Cannabis use disorder		Chronic obstructive pulmonary disorder (COPD)

*Modified

National Academies of Sciences, Engineering, and Medicine. 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/24625>. Accessed February 17, 2020.

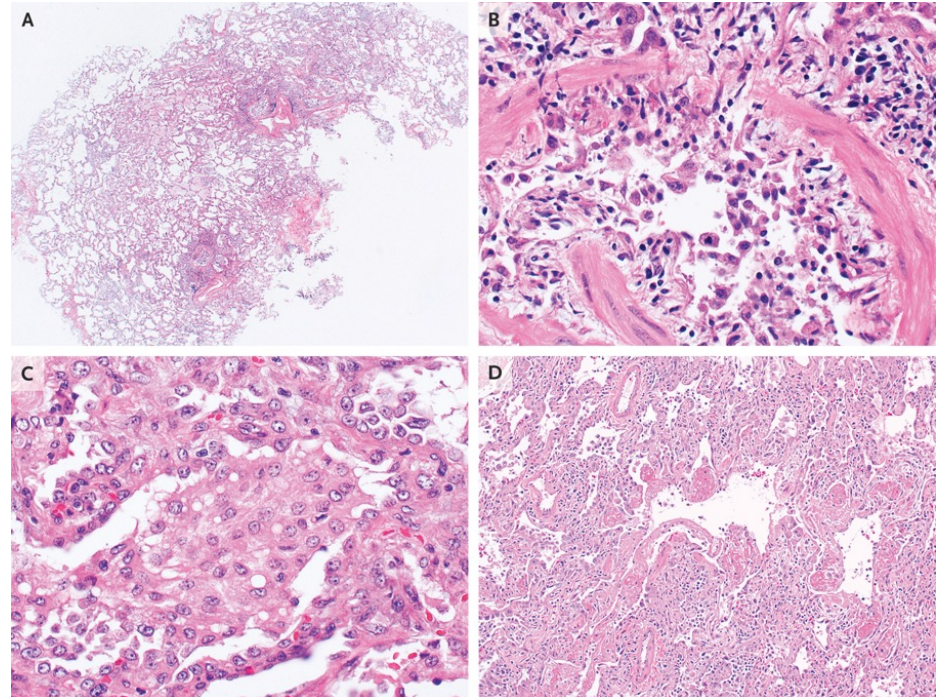
Cannabis-Associated Harms



- Evidence of cannabis-associated harms is largely derived from observational studies
 - Smoking
 - Uncertain potency and purity
 - Recreational use

Vaping-Associated Lung Injury

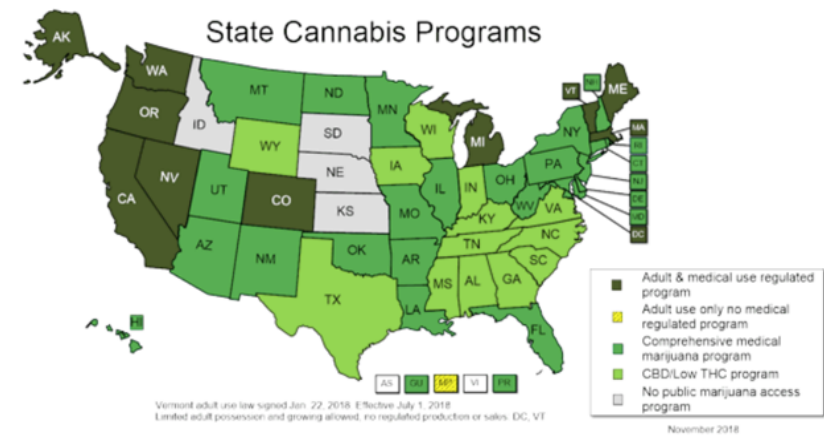
- Electronic-cigarette, or vaping, product use–associated lung injury (EVALI)
- Foamy macrophages and pneumocyte vacuolization on biopsy
- Vitamin E acetate found in bronchoalveolar-lavage (BAL) fluid
- Airway-centered chemical pneumonitis from Vitamin E acetate and/or other inhaled toxic substances



Butt YM, et al. *N Engl J Med.* 2019;381(18):1780-1782.; Blount BC, et al. *MMWR Morb Mortal Wkly Rep.* 2019;68(45):1040-1041.

Legalization of Cannabis

- All but four states allow some form of medicinal cannabis product
 - Improved verification of drug potency and purity
- Farm Bill of 2018 legalized hemp-derived cannabidiol (CBD)
 - In 2019, FDA issued warnings to 15 companies for improper marketing of hemp
- Prevalence of medicinal cannabis use is increasing
 - 1.6% 12-month prevalence of medicinal use (18 years and older; 2015)
 - Significant increase since 2013 (up from 1.2%)



Patient Evaluation



Who is the patient?

- Presenting problem
- Medical history
 - Age?
 - Comorbidities (e.g., immunosuppression)?
 - Experienced user?
- Physical exam and vital signs
- Labs (recommended for CBD)

What would you recommend?

- Prescription or medical marijuana card?
- Recommendation for THC, CBD, or both?
- Dosing recommendations?
- Oral or inhalation?

THC = tetrahydrocannabinol.

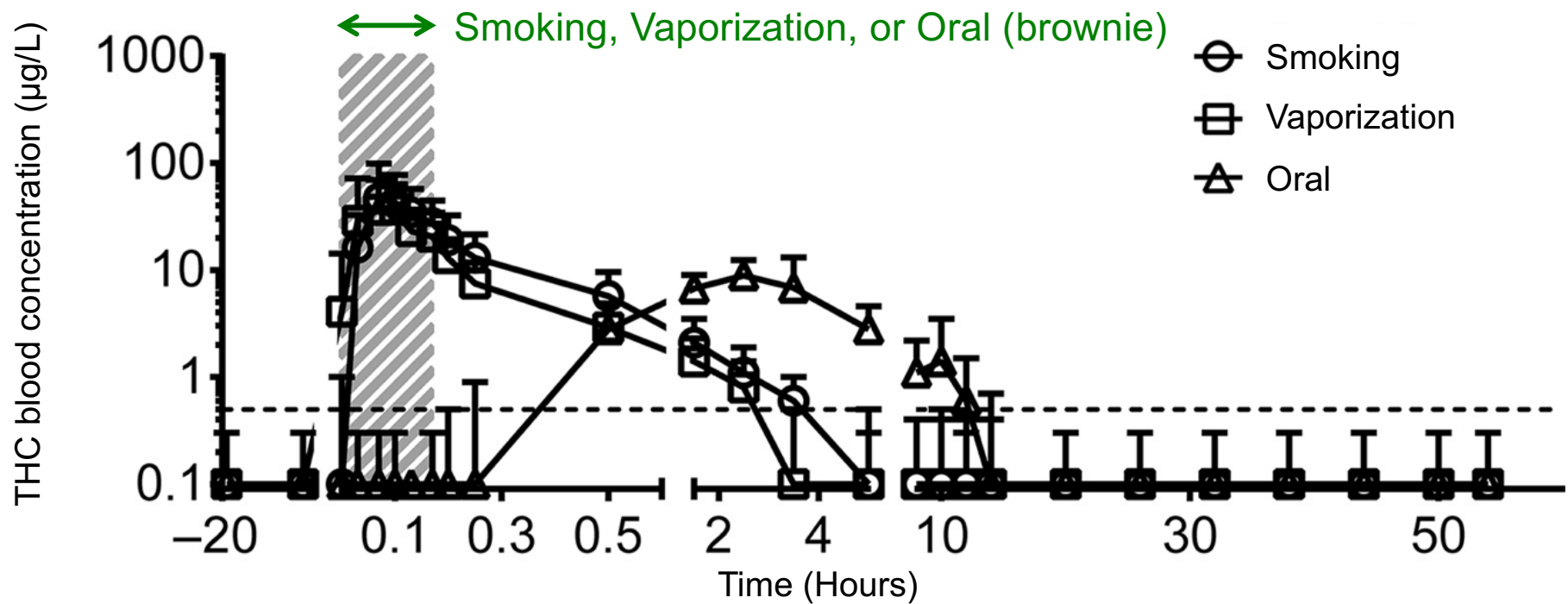
FDA-Approved Cannabinoids



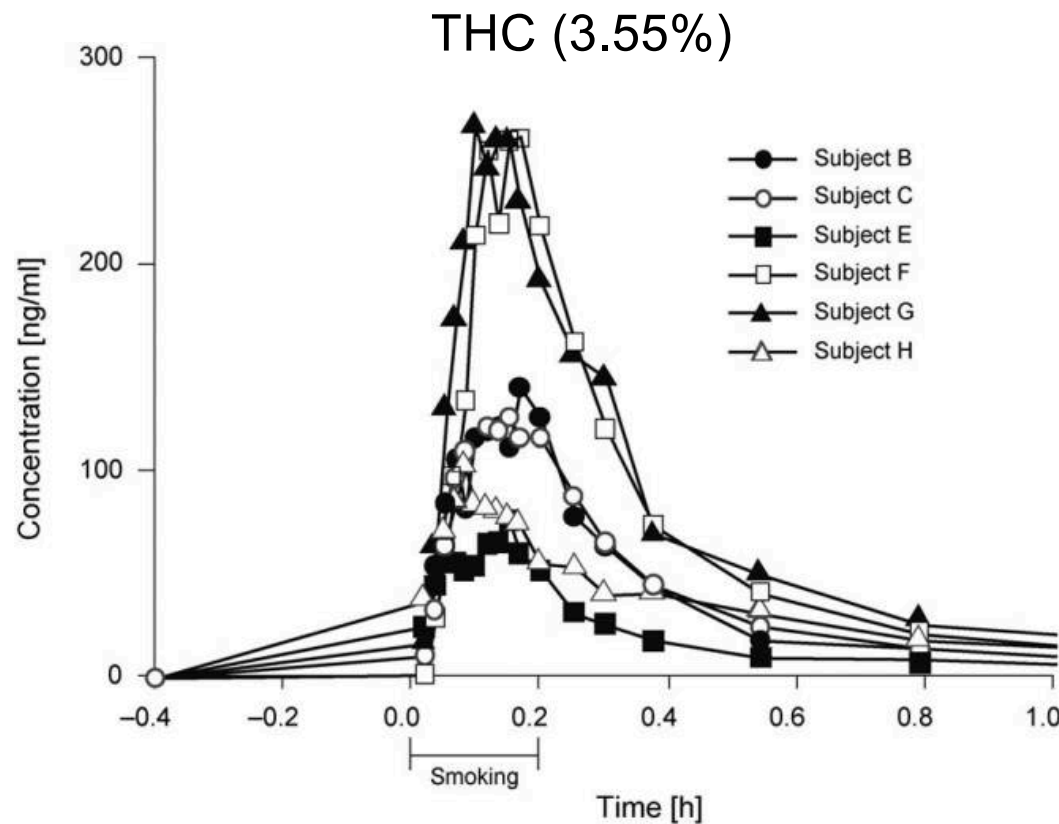
- Prescribing information is available for these medications on their package inserts which are available online¹⁻³
- Be mindful of warnings and precautions
 - Class risks (e.g., suicidal ideation and CBD)
 - Adverse reactions that are specific to the drug or a result of drug-drug interactions (e.g., hepatocellular injury with CBD)

1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/018651s029lbl.pdf; 2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s011lbl.pdf; 3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210365lbl.pdf.

Doses Taken Orally are Delayed and More Difficult to Self-Titrate



Exposure to Drug After Vaping or Smoking Varies as a Result of Depth of Inhalation



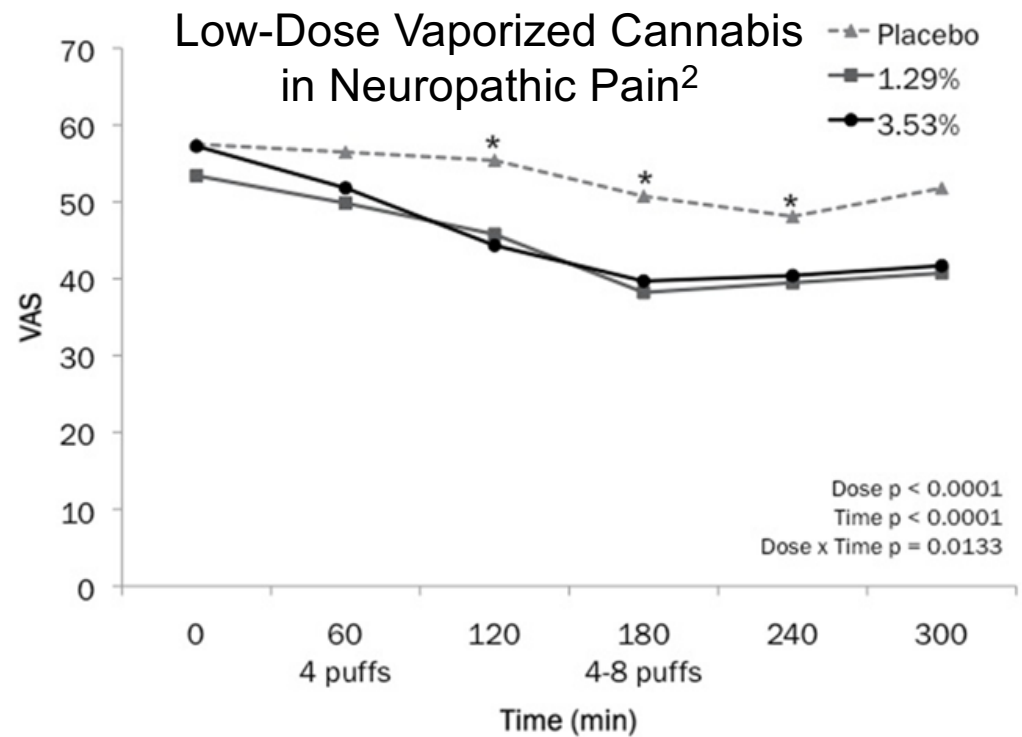
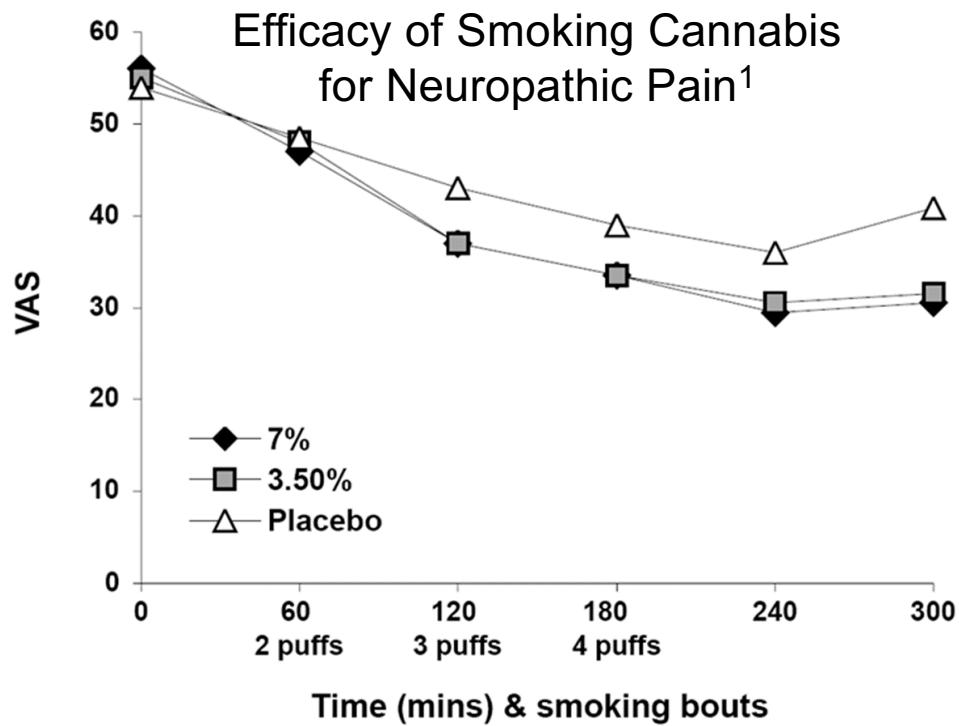
n = 6

Huestis MA, et al. *J Anal Chem.* 1992;16:276-282.

Cannabis Dosing Recommendations are Consistent for THC But Vary Widely for CBD

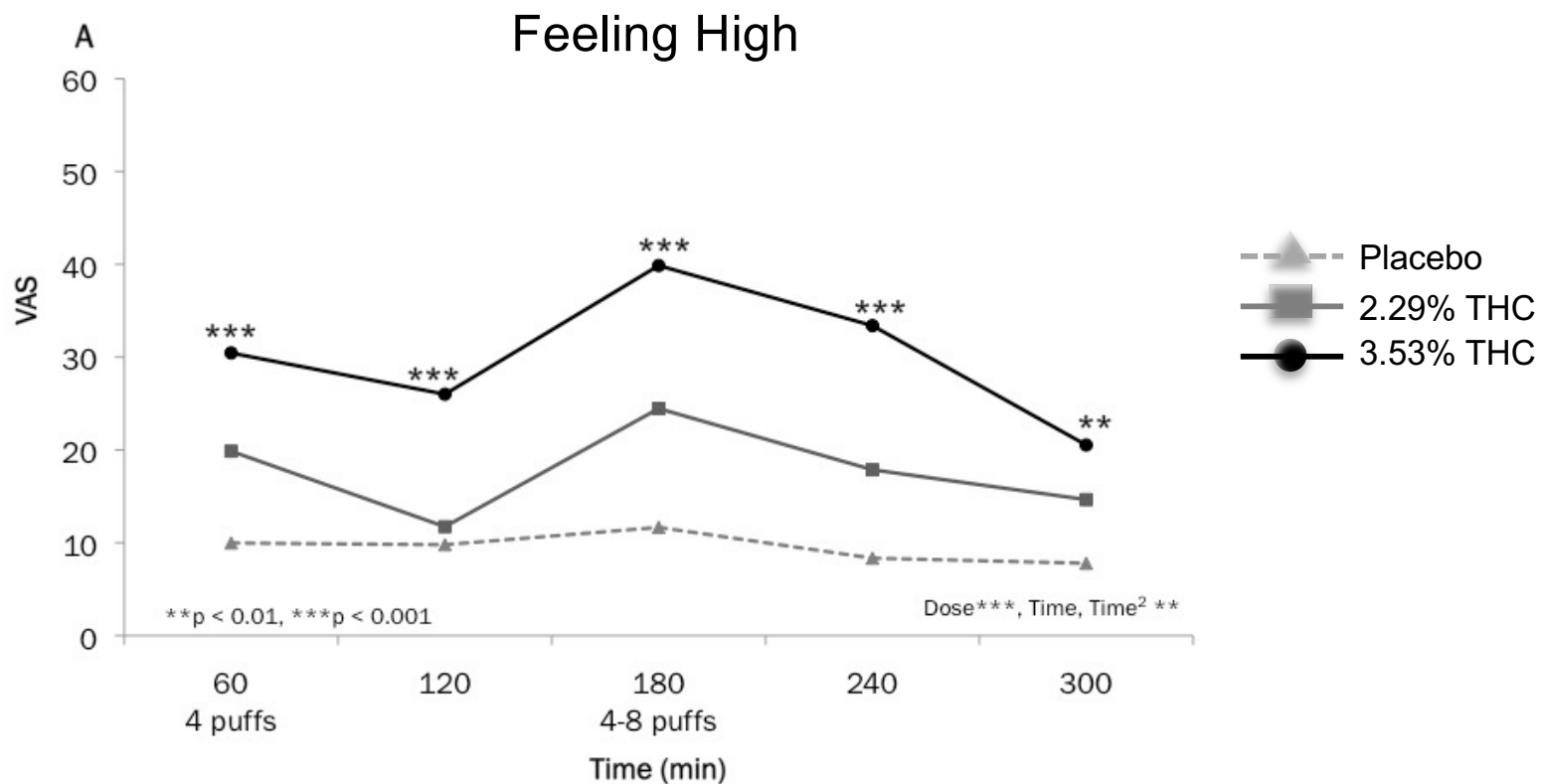
- State recommendations for oral THC dosing
 - WA and CO: No more than 10 mg THC initially
 - OR: No more than 5 mg THC initially
- Wide variations in CBD dosing
 - Oral doses of 5 mg are commonly recommended at dispensaries
 - Oral doses of 20 mg/kg/day were used in the Lennox-Gastaut syndrome and Dravet syndrome clinical trials
- Inhalation
 - “Dose” often refers to the strength of the cannabis

Low Doses of THC When Used for Neuropathic Pain are Equianalgesic



1. Wilsey B et al. *J Pain*. 2008;9(6):506-521.; 2. Wilsey B, et al. *J Pain*. 2013;14(2):136-148.

Low-Dose THC Causes Less High



Wilsey B, et al. *J Pain*. 2013;14(2):136-148.

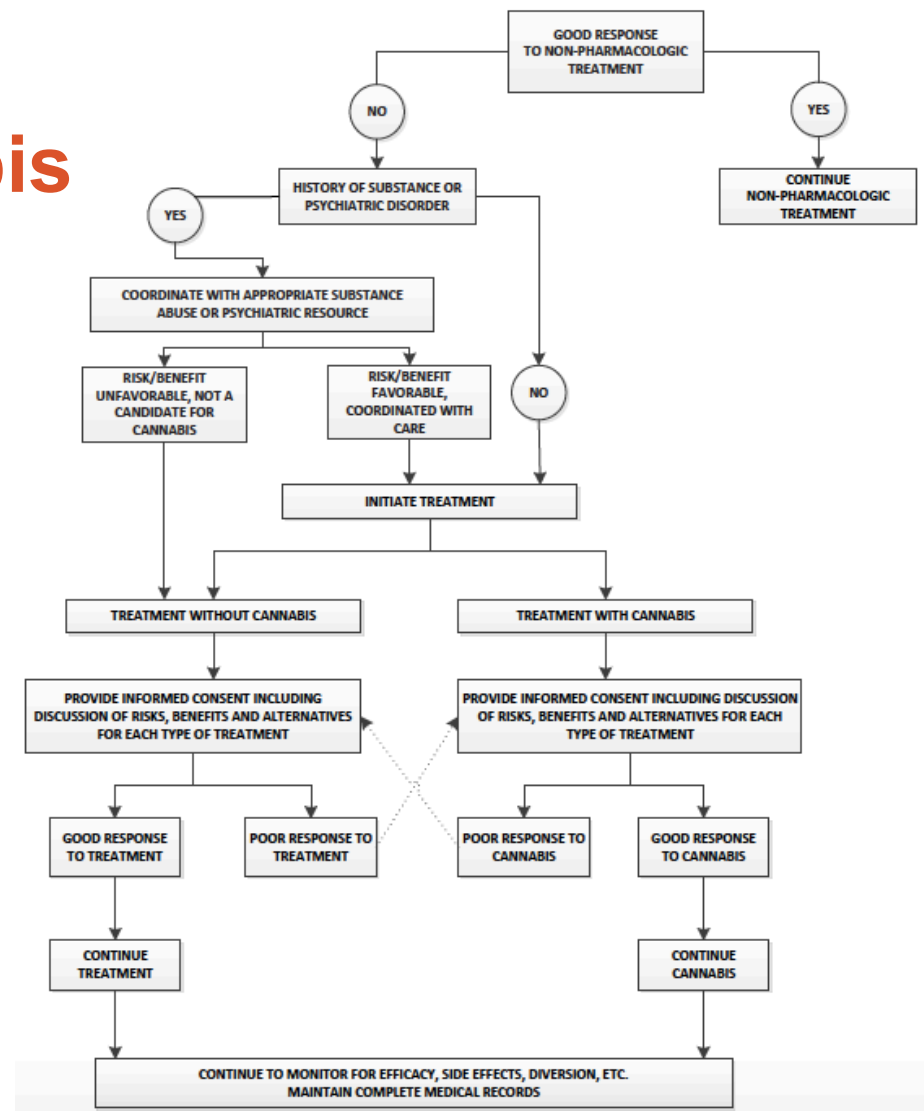
Less Cognitive Impairment with Low-Dose THC

Time (Minutes)	Dose (% THC)	Effect Size Compared to Placebo				
		Pegboard Dominant	Pegboard Nondom	WAIS III Digit Symb	HVLT - Sum of All Trials	HVLT - Delay
0	1.29	.10	.13	-.11	-.27	-.13
	3.53	.02	.03	-.10	-.07	-.11
60	1.29	.21	.08	-.18	-.13	-.04
	3.53	.07	.09	-.24	-.26	.02
120	1.29	.02	.27	-.11	.00	-.02
	3.53	-.03	.25	-.14	-.17	-.22
180	1.29	-.01	.17	-.30	-.17	-.08
	3.53	-.05	.20	-.33	-.46	-.42
240	1.29	.18	.20	-.13	-.28	.12
	3.53	.07	.20	-.15	-.43	-.20
300	1.29	.03	-.02	-.12	-.02	-.15
	3.53	-.09	.08	-.06	-.09	-.15

HVLT = Hopkins Verbal Learning Test- Revised; WAIS = Wechsler Adult Intelligence Scale.
 Wilsey B, et al. *J Pain*. 2013;14(2):136-148.

Guidelines for Physicians Who Recommend Cannabis

- Establish a physician-patient relationship
- Evaluate the patient
- Document the presence of a qualifying condition
- Conduct informed and shared decision making
- Create a “Treatment Agreement”
- Provide ongoing monitoring
- Consult a specialist or refer if needed
- Keep and maintain adequate medical records



Cannabis Treatment Agreement



- Keep in secure location
- Consult doctor if starting to use cannabis recreationally
- Caution if pregnant
- Caution if heart disease or heart rhythm problem
- Abstain if serious mental illness
- Minimize exposure to smoke
- Do not use in public unless legal
- Use minimal amount of cannabis to achieve relief
- Do not drive a car or operate machinery for 3-4 hours after using
- Consider alternative treatments, including prescribed cannabinoids
- Look out for withdrawal
- Re-evaluate regularly
- Avoid combining with narcotics, sedatives, and alcohol

Cannabis Next Steps



- Larger scale clinical trials on cannabis, administered via several routes, and specific constituents, plus their combinations
- Make cannabis and a range of cannabinoid-based medications available by prescription, in accordance with agreed protocols, and subject to availability from trusted sources that confirm potency and purity, and regulated dispensing

Current CMCR Studies

PI	Condition	Sponsor	Design	N	Treatment
Thomas Marcotte Barth Wilsey	Low Back Pain	National Institutes of Health (NIH)	Parallel Groups Randomized Controlled Trial (RCT)	120	Vaporized cannabis Oral Dronabinol Oral / Vaporized Placebo
Doris Trauner	Severe Autism	Noorda Foundation	Crossover RCT	30	Oral CBD Oral Placebo
Fatta Nahab	Essential Tremor	Essential Tremor Foundation Tilray Pharmaceuticals	Crossover RCT	16	Oral CBD/THC Oral Placebo
Kristin Cadenhead	Early Psychosis	Krupp Family Foundation	Crossover RCT	78	Oral CBD Oral Placebo
William Perry Jared Young	Bipolar Disorder Healthy Volunteers	NIH	Parallel Groups RCT	144	Oral CBD Oral THC Oral Placebo
Brook Henry	HIV Sensory Neuropathy	NIH	Within Subjects Crossover	100	Vaporized Cannabis Vaporized Placebo
Thomas Marcotte	Driving Impairment	State of California	Parallel Groups RCT	180	Smoked Cannabis Smoked Placebo

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Questions & Answers

Thank You!



Resources

- The Health Effects of Cannabis and Cannabinoids. National Academies of Sciences, Engineering, and Medicine (Free):
 - <https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state>
- Monitoring Health Concerns Related to Marijuana in Colorado: 2016. State of Colorado (Free):
 - <https://www.colorado.gov/pacific/cdphe/marijuana-health-report>
- Wilsey, et al. (2015) The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients Through a Written Document. *Clin J Pain*.
- Guidelines for the Recommendation of Cannabis for Medical Purposes
 - https://www.mbc.ca.gov/Publications/guidelines_cannabis_recommendation.pdf
- The University of California Center for Medicinal Cannabis Research (Link to Research):
 - <http://cmcr.ucsd.edu>
 - cmcr@ucsd.edu