From Evidence to Conversation

How to talk to patients about medical cannabis

Tiffany R Buckley, PharmD, BCPP

Director of Pharmacy of Spring Grove Hospital Center

Advanced Practice Psychiatric Pharmacist

University of Maryland School of Pharmacy

Disclosures

- Dr. Buckley does not have financial or other relationship with the manufacturer(s) of any commercial product(s) or provider(s) of any commercial service(s) discussed in this CE activity.
- Dr. Buckley is the owner and employee of TRB Speaks LLC, a public speaking company devoted to education about cannabis and mental health
- This presentation will include discussion of off-label, experimental, and /or investigational use of drugs or devices: (if yes, list here)
  - Cannabis
  - Cannabidiol

All relationships have been mitigated

Learning Objectives

- Conduct a patient-centered assessment of cannabis use by asking clinically relevant questions about the patient's reasons for use, cannabis products, THC/CBD content, route, frequency, perceived benefits, adverse effects, and impact on psychiatric symptoms and functioning.
- Demonstrate effective, nonjudgmental communication strategies for discussing cannabis use with patients in real time, including how to respond when patients report benefits, concerns, or reluctance to change their cannabis use.
- Develop individualized harm-reduction recommendations based on a patient's cannabis use patterns, psychiatric history, medications, and goals, including strategies to reduce risks related to high-potency products, frequent use, impairment, medication interactions, and worsening psychiatric symptoms.

Introduction

Why is this important?

- Patients are using cannabis
- Our goal is to create a safe and comfortable place for patients to discuss cannabis consumption to reduce potential harms from cannabis use
- It is important to understand:

1. What types of cannabinoid products are available?

2. How do you assess cannabis use?

3. How do I communicate with my patients about safe cannabis consumption?

1. What types of cannabinoid products are available?

What is cannabis?

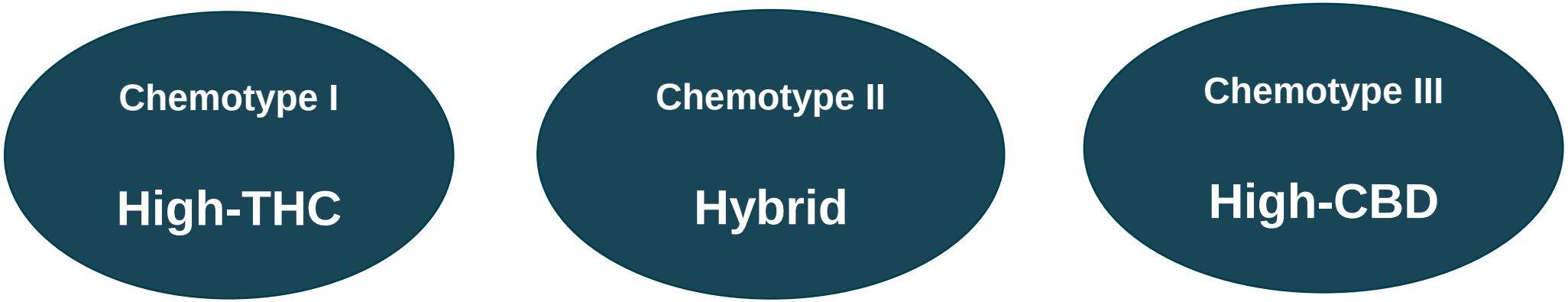
- Cannabis used for thousand years for medicinal, recreational, & spiritual purposes
- Contains over 500 unique substances:

Phytocannabinoids	Terpenes	Flavonoids
Fat-soluble compounds only made in the cannabis plant Protect cannabis from UV light	Contribute to smell of cannabis Anecdotal thoughts they are therapeutic but no solid evidence	Contribute to color of cannabis Full role still being delineated
Delta-9-Tetrahydrocannabinol (THC)* Responsible for "high" **Cannabidiol (CBD)*** Not intoxicating	Limonene Linalool β-myrcene β-caryophyllene α-pinene	Orientin Vitexin Isovitexin Apigenin Luteolin

Hudak J. *Marijuana: A Short History*. Vol Second edition; 2020.
Fischedick JT. *Cannabis and Cannabinoid Research*. 2017;2(1):34-47

What is the standard classification system for cannabis?

- Three subspecies of cannabis*: Sativa, Indica*, and *Ruderalis*, but there has been so much cross-breeding or cross-pollination; it is hard to separate them
- At dispensary, consumers told *Sativa* strains are activating and *Indica* strains produce more relaxation, but **there is no standard classification system**
- **Chemotypes** are commonly classified according to their ratio of total THC to ratio of total CBD
  - Total THC = sum of THC + THCA normalized to their molecular weight
  - Total CBD = sum of CBD + CBDA normalized to their molecular weight
  - Cultivars from a similar class may have different levels of terpenes



Birenboim M, et al. *Phytochemistry*. 2022;200:113215
Hudak J. *Marijuana: A Short History*. Vol Second edition; 2020.

What are typical cannabis chemotypes?

Chemotype I	Chemotype II	Chemotype III
High THC THC greater than CBD More impairing	More balanced THC to CBD ratio THC approximately equal to CBD Somewhat impairing	High CBD CBD greater than THC Least impairing
Common ratios of THC to CBD (THC:CBD) 5:1, 20:1, 50:1	**Common ratios of THC to CBD (THC:CBD)** 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1	**Common ratios of THC to CBD (THC:CBD)** 1:25, 1:15, 1:8, 1:4

What is THC and CBD dosing seen in clinical trials?

	THC	CBD
Micro Dose	~0.3 mg	N/A
Low Dose	0.5 mg to 5 mg	0.4 mg to 19 mg
Medium Dose	6 mg to 20 mg	20 mg to 99 mg
High Dose	21 mg to 50+ mg *Most medical patients do not require doses over 40 mg of THC*	100 mg to 800+ mg

What dosage forms of cannabis are available?

- The average content of THC has increased over time
- States with medicinal and adult use cannabis have products with average THC potency of 16 – 35%

Form	THC potency (% THC) = Total mg THC divided by Total weight of product in mg
Fresh or dried flowers	Up to 30%
Cannabis oil	Up to 3%
Chemically concentrated extracts (hash, oil, shatter, budder, wax)	Up to 90%
Physically concentrated extracts (hash/kief)	Up to 60%
Edibles	Varies
Tinctures/sprays	Varies
Creams	Varies

Smart R, et al. *Addiction*. 2017;112(12):2167-2177
Health Canada. About cannabis. Published March 2, 2018. Accessed February 28, 2024

How is cannabis administered?

Smoking	Smoking with joints or spliff; most common route
Vaporizing	Breathing in dried cannabis or liquid cannabis vapors through a vaping device
Dabbing	Breathing in very hot vapors from heated cannabis concentrate
Sublingually	Putting oils or tinctures under the tongue
Orally	Eating or drinking teas, soda, pills, oils, baked goods, gummies
Topically	Creams or lotions

Health Canada. About cannabis. Published March 2, 2018. Accessed February 28, 2024

Pharmacokinetics of Cannabis

	Smoking/ Vaporization	Oral	Sublingual	Topical
Onset (min)	5 – 10	60 – 180	15 – 45	Varies
Duration (h)	2 - 4	6 - 8	6 - 8	Varies
Pro	• Rapid onset of action • Widely available • **Avoids first pass metabolism**	• Less odor than smoking • Discrete	• **Avoids first pass metabolism:** Provides more consistent dosing than oral • Discrete	Less systemic effects
Cons	• Odor • Can be difficult to administer • Smoking can generate hydrocarbons • Avoid in patients with CVD, asthma, and COPD	• Difficult to titrate due to delayed onset • THC converted to more potent metabolite by first pass metabolism	• Costly • Not always available	Only exerts effects locally

MacCallum CA, et al. *European Journal of Internal Medicine*. 2018;49:12-19.

Pharmacokinetics of Cannabis

	THC		CBD	
Administration Method	**Smoking/ Vaporization**	**Oral**	**Smoking/ Vaporization**	**Oral**
Bioavailability	• 10 – 35% • Depends on smoking technique	• 4 – 12% • Undergoes first pass metabolism	• 11 – 45% (mean 31%) • Depends on smoking technique	• 6% • Undergoes first pass metabolism
Metabolism:	• Mostly Hepatic (CYP2C and CYP3A) • Metabolized to 11-OH-THC or 11-COOH • **Via oral route:** 11-OH-THC is 3 – 4 x more potent than THC		• Hepatic • Metabolized to 7-OH-CBD and 7-COOH-CBD	
Plasma Half-life	• Occasional use: 1 to 3 days • Chronic use: 5 to 13 days		• 18 to 32 hours	
Distribution	• Highly lipophilic		• Highly lipophilic	

1.

Chayasirisobhon S. *Perm J.* 2020;25:19.200. doi:10.7812/TPP/19.200

What are the side effects of cannabis?

Short term effects

- Feeling high, a sense of well-being, relaxation, heightened sensory experiences
- Dry mouth, dry/red eyes, dizziness, confusion, sleepiness
- Difficulty remembering/concentrating/paying attention quickly
- Postural hypotension, tachycardia, paranoia, delusions, hallucinations

Long term effects

- Possible increased chance of addiction
- Effects on memory, concentration, ability to think and make decisions
- Risks to lungs for smoked cannabis: bronchitis, lung infections, long-term cough, and increased mucus build up in chest
- Cannabis hyperemesis syndrome

Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. Accessed February 28, 2024

What are synthetic cannabinoids?

Delta-8-THC

- Cannabinoid that only occurs naturally in tiny amounts in cannabis
- Made in a lab from CBD from hemp
- Has psychoactive and "intoxicating" effects
- **Side effects:** Hallucinations, vomiting, tremors, anxiety, dizziness, confusion, loss of consciousness

WARNINGS

- FDA has NOT looked at products for safety or approved them for medical use
- Often mislabeled as "hemp" derived

Spice/K2

- Synthetic version of THC
- Mix of plant matter sprayed with synthetic psychoactive chemicals
- Often looks like potpourri
- **Side effects:** Paranoia, anxiety, panic attacks, hallucinations, giddiness, convulsions, organ damage, death

WARNINGS

- FDA has NOT looked at products for safety or approved them for medical use
- Almost impossible to know the ingredients and strength

1. Commissioner O of the. 5 Things to Know about Delta-8 Tetrahydrocannabinol – Delta-8 THC. *FDA*. Published online January 30, 2023. Accessed January 31, 2023. https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc

1. Spice/ K2, Synthetic Marijuana. Accessed January 31, 2023. https://www.dea.gov/factsheets/spice-k2-synthetic-marijuana

2. How do you assess cannabis use?

How do you assess cannabis use?

“Do you use cannabis?” is the beginning of the assessment, not the end.

1. **Why?** What symptoms or goals are driving the patient's use?
2. **What?** What products are they using? THC, CBD, or both? Do they know the potency?
3. **How?** Smoking, vaping, edibles, tinctures, concentrates, etc.
4. **How much and how often?** Include frequency, dose when known, and changes in use over time.

How do you assess cannabis use?

5. **When?** When do they use relative to symptoms, medications, work, sleep, or other activities?
6. **What happens when they use?** Explore both perceived benefits and adverse effects.
7. **What happens when they don't use?** Ask about cravings, withdrawal, sleep disturbance, irritability, or difficulty cutting back.
8. **How is it affecting functioning?** Work, school, relationships, cognition, driving, and daily activities.

How do you assess cannabis use?

Clinical pearl:

Ask about cannabis with the same curiosity and specificity that you would use when taking a medication history.

What do you actually say?

“Cannabis is the only thing that works for me.”

“How do we respond without dismissing the patient's experience or automatically endorsing cannabis as treatment?”

What do you actually say?

Demonstrate a patient-centered approach:

1. **Acknowledge**
   “I hear that you feel cannabis has been helping your anxiety.”
2. **Explore**
   “Tell me what you notice before you use it and what changes afterward.”
3. **Share**
   “Would it be okay if I shared some of what we know about cannabis and anxiety?”
4. **Connect**
   “I’m wondering whether the cannabis could be helping in the short term but also contributing to some of the symptoms you've been experiencing.”
5. **Collaborate**
   “Given what cannabis is doing for you and the concerns we've discussed, what changes would you be willing to consider?”

What do you actually say?

Key message:

The goal isn't to win an argument about cannabis.

The goal is to keep the patient engaged enough to have an ongoing conversation about benefits, risks, and safer use.

3. How do I communicate to my patients about safe cannabis consumption?

Clinical Considerations

- Everyone will respond differently to cannabis
- How clients respond to cannabis depends on:
  - Age, sex, and pre-existing health conditions
  - Experience with cannabis
  - Other foods, drinks, medications, or drugs client is taking
  - Type of cannabis they take and how they take it
  - THC and CBD content
- Clients' response can change each time they use cannabis
- Important to weigh the risk and benefit of cannabis in each client
- Monitor the patient for changes in mental status, behavior, usage, and side effects

Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. Accessed February 28, 2024

Patient-related variables

- Age
- Other diseases or conditions
  - Including lung disease, severe liver, severe kidney disease, severe cardiovascular disease
- Pregnant or breastfeeding
- Past mental health history
- Family history of psychotic disorders
- Substance use disorder history
- Polypharmacy
- Support systems
- Health literacy
- Access to healthcare
- Financial status
- Driving or safety sensitive job

Medication-related variables

- Mechanism of action
- Formulations
- Administration
- Pharmacokinetic properties
  - Onset, peak, duration of action, metabolism, elimination
- Adverse effects
- Cost

Patient-related variables

- Collect relevant data about medical history

Age

Older adults

- May be more sensitive to the effects of THC
- Greater risk of drug-drug interactions (DDIs) because on more medication therapy

Younger than 25 years old

- Brain develops until a person is 25
- Higher levels of THC linked to an increased chance of psychiatric symptoms including psychosis, addiction, suicide, cognitive impairment in learning, memory, and executive functioning



1.

MacCallum CA, et al. European Journal of Internal Medicine. 2018;49:12-19.
MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. .
Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. Can Fam Physician. 2018;64(2):111-120
Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. May 29, 2014. Available at: https://jcpp.net/wp-content/uploads/2016/03/PatientCareProcess-with-supporting-organizations.pdf.

Patient-related variables

- Collect relevant data about medical history

Other Health Conditions

Respiratory Disease

- Cannabis smoke may irritate & damage the lungs. Unclear if vaping is healthier than smoking.
- Use carefully in patients with asthma or chronic obstructive pulmonary disorder (COPD)

Unstable Cardiovascular Disease (CVD)

Congestive heart failure, critical aortic stenosis, poorly controlled atrial fibrillation, severe coronary artery disease

- THC can cause acute effects such as postural hypotension or tachycardia. **Avoid in patients with unstable CVD. Avoid smoked formulations in anyone at risk for or with CVD**

Severe Kidney Disease

- Cannabinoids generally safe in severe kidney disease
- Some cannabis may be contaminated with heavy metals, pesticides and solvents which could be problematic in patients with kidney disease

Severe Liver Disease

- Cannabinoids are hepatically metabolized. Patients may be more sensitive to the effects

Dexterity Issues: Person may have difficulty administering certain forms of cannabis

Patient-related variables

- Collect relevant data about medical history

Mental Health	• Causal link not established between cannabis and mental illness • Data from adult-use cannabis populations shows there may be a link between cannabis use and mental illness • People with anxiety, depression, and PTSD are more likely to use cannabis
Family History of Psychosis	• Chronic use of high potency, THC-predominant cannabis at a young age linked to increased risk of psychosis in people with genetic disposition for psychosis • **Always look for family history of psychosis**
SUD	• Chance of addiction higher with THC-predominant chemovars in patients with pre-existing substance use disorders
Pregnancy/ Breastfeeding	• More research is needed, but parts of cannabis may affect the developing baby in pregnant women • Using cannabis during pregnancy is linked to lower birth weight and increased risk of both brain and behavioral problems in babies • THC can pass through breast milk; **Avoid in pregnancy/breastfeeding**

Patient-related variables

- Collect information about lifestyle habits, preferences & beliefs, health and functional goals, socioeconomic factors that affect access to medication

Support Systems

Financial Status
Insurance does not cover medical cannabis

Access to Healthcare

Driving or Safety Sensitive Job

Health Literacy

MacCallum CA, et al. European Journal of Internal Medicine. 2018;49:12-19.
MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. .
Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. Can Fam Physician. 2018;64(2):111-120
Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. May 29, 2014. Available at: https://jcpp.net/wp-content/uploads/2016/03/PatientCareProcess-with-supporting-organizations.pdf.

Drug-Drug Interactions

- Screen for DDIs
  - Use the Penn State Cannabis and Drug Interaction Tracker to check for DDIs
    - https:/cann-dir.psu.edu/
  - Cannabis is a CNS depressant
    - THC is competitively inhibited at CYP1A2, CYP2B6, CYP2C9, and 2D6
    - CBD is competitively inhibited at CYP3A4, CYP2B6, CYP2C9, CYP2D6, and CYP2E1
    - CBN is competitively inhibited at CYP2B6, CYP2C9, and CYP2E1

Important clinical implications

- Most drug interactions are associated with using cannabis with other CNS depressants
- Cannabis dose or other medications may need to be decreased
- May result in higher levels of warfarin (Cannabis may block metabolism CYP2C9)
- May prevent transformation of clopidogrel its active prodrug (cannabis may block metabolism of CYP2C19)

1.

MacCallum CA, et al. European Journal of Internal Medicine. 2018;49:12-19.
MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. .
Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. Can Fam Physician. 2018;64(2):111-120
Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. May 29, 2014. Available at: https://jcpp.net/wp-content/uploads/2016/03/PatientCareProcess-with-supporting-organizations.pdf.

Cannabis Dosing for Harm Reduction

Select Chemovar

- To minimize harm, recommend using CBD-dominant cannabis with no or lower levels of THC from a legitimate source

Select Dosage Form & Route of Administration

- Oral oil or capsules recommended
- **For fast onset:** Consider vaporization of dried flower; Consider pre-rolls for patients with dexterity issues
  - Generally, not recommended for patients with respiratory disease
- Avoid chemically concentrated extracts due to potential contamination and high potency of THC
- Insufficient evidence on safety of recommendations for other dosage forms

Dosing Regimen

- No recommended guidelines for dosing in patients with mental illness; Start low and go slow

1.

MacCallum CA, et al. European Journal of Internal Medicine. 2018;49:12-19.
MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. .
Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. Can Fam Physician. 2018;64(2):111-120

Strategies to Minimize Risk from Cannabis

1. Let doctor or pharmacist know you are using cannabis.
   Your medications may need adjustment.
2. Cannabis can vary in concentration and quality. Obtain cannabis from a verified source.
   Make sure that cannabis is tested. Read labels carefully. Avoid synthetic products.
3. Use products with higher ratio of CBD to THC. Avoid THC pre-dominant preparations because they may increase anxiety and are linked to more side effects
4. Products are difficult to dose. Start with a low dose of CBD and slowly increase
5. Avoid smoked formulations. Smoking may irritate lungs.
6. Monitor the type, how often, and how much cannabis you consume.
   Track chemovar, terpenes, dose, administration method, frequency, and the effects
7. If you notice changes in your thoughts, behavior, or start using cannabis products more frequently, let your healthcare provider know

MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018..
Fischer B, et al. Lower-Risk Cannabis Use Guidelines (LRCUG) for reducing health harms from non-medical cannabis use: A comprehensive evidence and recommendations update. *Int J Drug Policy*. 2022;99:103381.

Strategies to Minimize Risk from Cannabis

8	There is a chance you could develop CUD. CUD is more likely if you use products with high potency THC often.
9	Cannabis is linked to psychosis, especially in people with a genetic predisposition who start using high-potency THC products at an early age and consume cannabis often.
10	Cannabis may have negative cognitive effects on children and young adults
11	Cannabis can be sedating and make it harder to think. Avoid tasks that require mental effort. Monitor older adults for falls and dizziness
12	Avoid driving. Before driving wait at least 3 - 4 h after inhaled, 6 h after oral, 8 if “high” noted
13	Avoid cannabis in pregnancy and breastfeeding
14	Medical cannabis products are only intended for the person who is certified

MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018..
Fischer B, et al. Lower-Risk Cannabis Use Guidelines (LRCUG) for reducing health harms from non-medical cannabis use: A comprehensive evidence and recommendations update. *Int J Drug Policy*. 2022;99:103381.

Follow Up & Monitor

- Medication appropriateness, effectiveness, and safety and patient adherence through available health data and patient feedback.
  - Monitor initially every 2 to 4 weeks
  - Can increase interval to monthly every six months, depending on patient
    - Factors to consider:
      - How comfortable they are using cannabis
      - Comorbid medical conditions
      - Ability to adhere for the treatment plan
      - Ability to keep inventory of cannabis efficacy - recommend they keep track of type, dose, route, and frequency of cannabis use
  - If no progress or minimal progress after 3 months, consider discontinuing therapy
  - At appointments, assess new medications, usage, and side effects
- Clinical endpoints that contribute to the patient's overall health.
  - Consider baseline screening with validated measure to objectively measure anxiety[1]

MacCallum CA, et al. European Journal of Internal Medicine. 2018;49:12-19.
MacCallum CA, et al. European Journal of Internal Medicine. 2021;89:10-18.
Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. May 29, 2014. Available at: https://jcpp.net/wp-content/uploads/2016/03/PatientCareProcess-with-supporting-organizations.pdf.
Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. Can Fam Physician. 2018;64(2):111-120.
Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018.

Conclusion

ASK → RESPOND → RECOMMEND

1. **ASK**
   Understand the **why, what, how, how much, and what happens** when the patient uses cannabis.
2. **RESPOND**
   Acknowledge the patient's experience, explore perceived benefits and harms, share evidence without judgment, and identify areas of concern together.
3. **RECOMMEND**
   Develop realistic recommendations based on the patient's psychiatric risks, cannabis use pattern, medications, and willingness to change.

Take Home Message

The most effective cannabis conversation is not simply “Do you use?” or “You should stop.”

It is:

- What are you using?
- Why are you using it?
- What is it doing for you?
- What risks are we seeing?
- And how can we work together to make your use safer?

Questions?

Thank you for attending!

References

- Smart R, Caulkins JP, Kilmer B, Davenport S, Midgette G. Variation in cannabis potency and prices in a newly legal market: evidence from 30 million cannabis sales in Washington state. *Addiction*. 2017;112(12):2167-2177. doi:10.1111/add.13886
- UMMC Midtown Campus. University of Maryland Medical Center. Accessed February 28, 2024. https://intra.umms.org/midtown
- Ergisi M, Erridge S, Harris M, et al. UK Medical Cannabis Registry: an analysis of clinical outcomes of medicinal cannabis therapy for generalized anxiety disorder. *Expert Review of Clinical Pharmacology*. 2022;15(4):487-495. doi:10.1080/17512433.2022.2020640
- Legare CA, Raup-Konsavage WM, Vrana KE. Therapeutic Potential of Cannabis, Cannabidiol, and Cannabinoid-Based Pharmaceuticals. *Pharmacology*. 2022;107(3-4):131-149. doi:10.1159/000521683
- D'Souza DC, Perry E, MacDougall L, et al. The Psychotomimetic Effects of Intravenous Delta-9-Tetrahydrocannabinol in Healthy Individuals: Implications for Psychosis. *Neuropsychopharmacol*. 2004;29(8):1558-1572. doi:10.1038/sj.npp.1300496
- Lowe H, Toyang N, Steele B, Bryant J, Ngwa W. The Endocannabinoid System: A Potential Target for the Treatment of Various Diseases. *International Journal of Molecular Sciences*. 2021;22(17):9472. doi:10.3390/ijms22179472
- Spice/ K2, Synthetic Marijuana. Accessed January 31, 2023. https://www.dea.gov/factsheets/spice-k2-synthetic-marijuana
- Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. *Can Fam Physician*. 2018;64(2):111-120.
- Peters BA, Lewis EG, Dustman RE, Straight RC, Beck EC. Sensory, perceptual, motor and cognitive functioning and subjective reports following oral administration of delta9-tetrahydrocannabinol. *Psychopharmacologia*. 1976;47(2):141-148. doi:10.1007/BF00735812
- Fakhoury M. Role of the Endocannabinoid System in the Pathophysiology of Schizophrenia. *Mol Neurobiol*. 2017;54(1):768-778. doi:10.1007/s12035-016-9697-5
- Lu HC, Mackie K. Review of the Endocannabinoid System. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. 2021;6(6):607-615. doi:10.1016/j.bpsc.2020.07.016
- Boehnke KF, Gangopadhyay S, Clauw DJ, Haffajee RL. Qualifying Conditions Of Medical Cannabis License Holders In The United States. *Health Affairs*. 2019;38(2):295-302. doi:10.1377/hlthaff.2018.05266
- MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *European Journal of Internal Medicine*. 2018;49:12-19. doi:10.1016/j.ejim.2018.01.004
- Brown JD. Potential Adverse Drug Events with Tetrahydrocannabinol (THC) Due to Drug–Drug Interactions. *Journal of Clinical Medicine*. 2020;9(4):919. doi:10.3390/jcm9040919
- Crippa JAS, Derenusson GN, Ferrari TB, et al. Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report. *J Psychopharmacol*. 2011;25(1):121-130. doi:10.1177/0269881110379283
- Birenboim M, Chalupowicz D, Maurer D, et al. Multivariate classification of cannabis chemovars based on their terpene and cannabinoid profiles. *Phytochemistry*. 2022;200:113215. doi:10.1016/j.phytochem.2022.113215
- Sarris J, Sinclair J, Karamacoska D, Davidson M, Firth J. Medicinal cannabis for psychiatric disorders: a clinically-focused systematic review. *BMC Psychiatry*. 2020;20(1):24. doi:10.1186/s12888-019-2409-8
- Beaulieu P, Boulanger A, Desroches J, Clark AJ. Medical cannabis: considerations for the anesthesiologist and pain physician. *Can J Anesth/J Can Anesth*. 2016;63(5):608-624. doi:10.1007/s12630-016-0598-x

References

- Sachedina F, Chan C, Damji RS, de Sanctis OJ. Medical cannabis use in Canada and its impact on anxiety and depression: A retrospective study. *Psychiatry Res*. 2022;313:114573. doi:10.1016/j.psychres.2022.114573
- Hudak J. *Marijuana : A Short History*. Vol Second edition. Brookings Institution Press; 2020. http://survey.hshsl.umaryland.edu/?url=https://search.ebscohost.com/login.aspx?direct=true&db=nlebk&AN=2372317&site=eds-live
- Health Canada. MARIHUANA FOR MEDICAL PURPOSES REGULATIONS: *The Canadian Journal of Addiction*. 2014;5(4):20. doi:10.1097/02024458-201412000-00010
- Fischer B, Robinson T, Bullen C, et al. Lower-Risk Cannabis Use Guidelines (LRCUG) for reducing health harms from non-medical cannabis use: A comprehensive evidence and recommendations update. *Int J Drug Policy*. 2022;99:103381. doi:10.1016/j.drugpo.2021.103381
- Radwan MM, ElSohly MA, El-Alfy AT, et al. Isolation and Pharmacological Evaluation of Minor Cannabinoids from High-Potency Cannabis sativa. *J Nat Prod*. 2015;78(6):1271-1276. doi:10.1021/acs.jnatprod.5b00065
- MacCallum CA, Lo LA, Boivin M. "Is medical cannabis safe for my patients?" A practical review of cannabis safety considerations. *European Journal of Internal Medicine*. 2021;89:10-18. doi:10.1016/j.ejim.2021.05.002
- Fischedick JT. Identification of Terpenoid Chemotypes Among High (−)- *trans* -Δ^{9} - Tetrahydrocannabinol-Producing *Cannabis sativa* L. Cultivars. *Cannabis and Cannabinoid Research*. 2017;2(1):34-47. doi:10.1089/can.2016.0040
- Pertwee R. Handbook of Cannabis: Vol. First edition. Published 2014. Accessed February 16, 2024. http://survey.hshsl.umaryland.edu/?url=https://search-ebscohost-com.proxy-hs.researchport.umd.edu/login.aspx?direct=true&db=e025xna&AN=853248&site=eds-live&ebv=EB&ppid=pp_Cover
- Health Canada. For health care professionals: Cannabis and cannabinoids. Published October 12, 2018. Accessed February 28, 2024. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html
- Stampanoni Bassi M, Gilio L, Maffei P, et al. Exploiting the Multifaceted Effects of Cannabinoids on Mood to Boost Their Therapeutic Use Against Anxiety and Depression. *Frontiers in Molecular Neuroscience*. 2018;11:424. doi:10.3389/fnmol.2018.00424
- Epidiolex (cannabidiol) dosing, indications, interactions, adverse effects, and more. Accessed November 17, 2021. https://reference.medscape.com/drug/epidiolex-cannabidiol-1000225
- Hillard CJ, Beatka M, Sarvaideo J. Endocannabinoid Signaling and the Hypothalamic-Pituitary-Adrenal Axis. *Compr Physiol*. 2016;7(1):1-15. doi:10.1002/cphy.c160005
- Fusar-Poli P, Crippa JA, Bhattacharyya S, et al. Distinct Effects of Δ9-Tetrahydrocannabinol and Cannabidiol on Neural Activation During Emotional Processing. *Archives of General Psychiatry*. 2009;66(1):95-105. doi:10.1001/archgenpsychiatry.2008.519
- Bergamaschi MM, Queiroz RHC, Chagas MHN, et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. *Neuropsychopharmacology*. 2011;36(6):1219-1226. doi:10.1038/npp.2011.6
- Karniol IG, Shirakawa I, Kasinski N, Pfeferman A, Carlini EA. Cannabidiol interferes with the effects of Δ9-tetrahydrocannabinol in man. *European Journal of Pharmacology*. 1974;28(1):172-177. doi:10.1016/0014-2999(74)90129-0
- Cannabidiol (pharmaceutical): Drug information - UpToDate. Accessed June 14, 2023. https://www-uptodate-com.proxy-hs.researchport.umd.edu/contents/cannabidiol-pharmaceutical-drug-information?search=epidiolex&source=panel_search_result&selectedTitle=1~16&usage_type=panel&kp_tab=drug_general&display_rank=1#F51962069
- CANN-DIR. Accessed December 4, 2023. https://cann-dir.psu.edu/

References

- D'Souza DC, Ranganathan M, Braley G, et al. Blunted Psychotomimetic and Amnestic Effects of Δ-9-Tetrahydrocannabinol in Frequent Users of Cannabis. *Neuropsychopharmacology*. 2008;33(10):2505-2516. doi:10.1038/sj.npp.1301643
- Be More Engaged in Your Healthcare. Accessed February 29, 2024. https://www.ahrq.gov/questions/be-engaged/index.html
- Zamarripa CA, Spindle TR, Surujunarain R, et al. Assessment of Orally Administered Δ9-Tetrahydrocannabinol When Coadministered With Cannabidiol on Δ9-Tetrahydrocannabinol Pharmacokinetics and Pharmacodynamics in Healthy Adults: A Randomized Clinical Trial. *JAMA Netw Open*. 2023;6(2):e2254752. doi:10.1001/jamanetworkopen.2022.54752
- Masataka N. Anxiolytic Effects of Repeated Cannabidiol Treatment in Teenagers With Social Anxiety Disorders. *Front Psychol*. 2019;10:2466. doi:10.3389/fpsyg.2019.02466
- Rodriguez CEB, Ouyang L, Kandasamy R. Antinociceptive effects of minor cannabinoids, terpenes and flavonoids in Cannabis. *Behavioural Pharmacology*. 2022;33(2 & 3):130-157. doi:10.1097/FBP.0000000000000627
- Zuardi AW, Shirakawa I, Finkelfarb E, Karniol IG. Action of cannabidiol on the anxiety and other effects produced by delta 9-THC in normal subjects. *Psychopharmacology (Berl)*. 1982;76(3):245-250. doi:10.1007/BF00432554
- National Institute on Alcohol Abuse and Alcoholism. About Cannabis Policy | APIS - Alcohol Policy Information System. Published 2022. Accessed June 13, 2023. https://alcoholpolicy.niaaa.nih.gov/about/about-cannabis-policy
- Health Canada. About cannabis. Published March 2, 2018. Accessed February 28, 2024. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/about.html
- 21 USC 802: Definitions. Published February 15, 2024. Accessed December 3, 2023. https://uscode.house.gov/view.xhtml?req=(title:21%20section:802%20edition:prelim)%20OR%20(granuleid:USC-prelim-title21-section802)&f=treesort&edition=prelim&num=0&jumpTo=true
- 7 USC 1639o: Definitions. Accessed December 4, 2023. https://uscode.house.gov/view.xhtml?req=(title:7%20section:1639o%20edition:prelim)
- Commissioner O of the. 5 Things to Know about Delta-8 Tetrahydrocannabinol – Delta-8 THC. *FDA*. Published online January 30, 2023. Accessed January 31, 2023. https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc
- ElSohly MA, Gul W. 3Constituents of Cannabis Sativa. In: Pertwee R, ed. *Handbook of Cannabis*. Oxford University Press; 2014:0. doi:10.1093/acprof:oso/9780199662685.003.0001
- Agency for Healthcare Research and Quality, Rockville, MD. Be More Engaged in Your Healthcare. Published December 2020. Accessed February 29, 2024. https://www.ahrq.gov/questions/be-engaged/index.html
- State of Connecticut. How is total THC calculated. CT.gov. Published October 5, 2023. Accessed March 5, 2024. https://portal.ct.gov/cannabis/Knowledge-Base/Articles/How-is-total-THC-calculated
- Moreno-Sanz G. Can You Pass the Acid Test? Critical Review and Novel Therapeutic Perspectives of Δ9-Tetrahydrocannabinolic Acid A. *Cannabis Cannabinoid Res*. 2016;1(1):124-130. doi:10.1089/can.2016.0008