



Lunch & Learn



Cannabis – What Does it Mean for your Practice?

September 25, 2019

Theresa Mallick-Searle, MS, RN-BC, ANP-BC, Stanford
Health Care

Presented in partnership by:



American Association of
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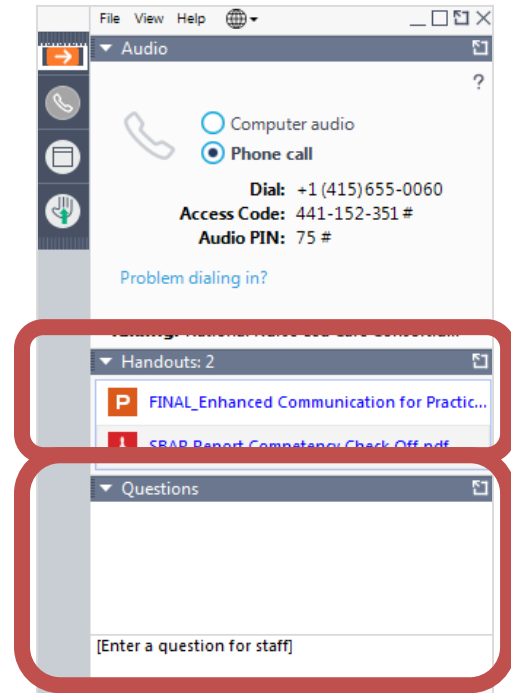
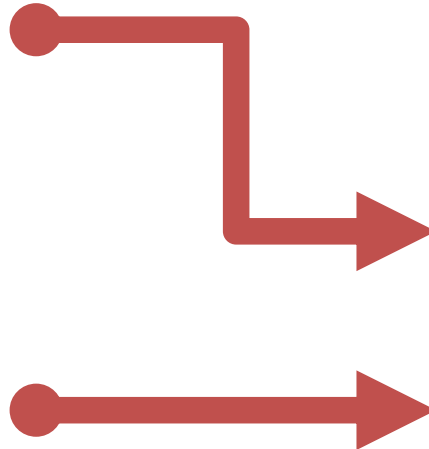


Transforming Clinical
Practices Initiative

Housekeeping Items

To **download materials**, go to the Handouts section on your GoToWebinar control panel.

To **ask a question**, type it into the Question pane in the GoToWebinar control panel and it will be relayed to the presenter.



Steps to Receive Free CE Credit

AANP will review attendance list after webinar is complete.

Participants who attend entire live presentation qualify for CE credit – 1.0 CE / 1.0 Pharm

- **REQUIRED:** attend at least **55 minutes** of presentation
- **REQUIRED:** access & connect to presentation slide-deck
- Phone-in-only participants **DO NOT** qualify

Participants who qualify for CE will receive a detailed email on how to obtain CE credit using the AANP CE Center.

Passcode and completion of an evaluation will be required to receive CE credit.

Questions can be directed to: calrich@aanp.org



National Investment in Quality Improvement

- Changes to the health care system are here
- Nurse practitioners (NPs) will play a key role during the critical transition from Fee-for-Service to **Value-Based Reimbursement**
- **NNCC** and the **AANP** have partnered together to create the **Nurse Practitioner Support & Alignment Network (NP SAN)**:
 - Prepare NPs for the upcoming changes to the health care system
 - Provide free continuing education & professional development centered around value-based health care practices
 - Offer key training opportunities that ready practices for **Value-Based Reimbursement**

Preparing NPs for Value-Based Reimbursement

What is the Quality Payment Program?

Began in 2017 as a result of the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) and requires CMS by law to implement an incentive program referred to as the *Quality Payment Program*, that provides for two participation tracks:

Merit-based Incentive
Payment System (MIPS)]

MIPS

If you decide to participate in MIPS, you will earn a performance-based payment adjustment through MIPS.

OR

Advanced Alternative
Payment Models (APMs)

Advanced
APMs

If you decide to take part in an Advanced APM, you may earn a Medicare incentive payment for participating in an innovative payment model.

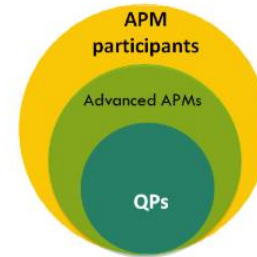
MIPS

vs.

APMs



MIPs vs. APMs Timeline



- Designed for individuals & small practices
- Four (4) performance areas
- Replaces all current incentive programs
- Exempt if practice DOES NOT meet low volume threshold.

- Higher risk model
- Risk is shared throughout the APM
- Number of acceptable payment models is limited
- Rules to being considered a qualified provider (QP)

Where Can I Go to Learn More?

1. CMS QPP website www.qpp.cms.gov
2. NPI Lookup for participation status <https://qpp.cms.gov/participation-lookup>
3. AANP <https://www.aanp.org/legislation-regulation/federal-legislation/macra-s-quality-payment-program>



Cannabis: What Does it Mean for Your Practice?

Theresa Mallick-Searle, MS, RN-BC, ANP-BC
Stanford Health Care, Division Pain Medicine

Tmallick@stanfordhealthcare.org

 @tmallic

 <https://www.linkedin.com/in/theresa-mallick-searle>

Disclosures

- ❑ Speakers bureau: Amgen & Lilly Pharmaceuticals
- ❑ Any unlabeled/unapproved uses of drugs or products referenced will be disclosed.
- ❑ Covering a very LARGE topic in a short amount of time.

Learning Objectives

- Define the endocannabinoid system.
- Discuss evidence for cannabinoids in pain management.
- Review practical clinical basics & safety considerations.

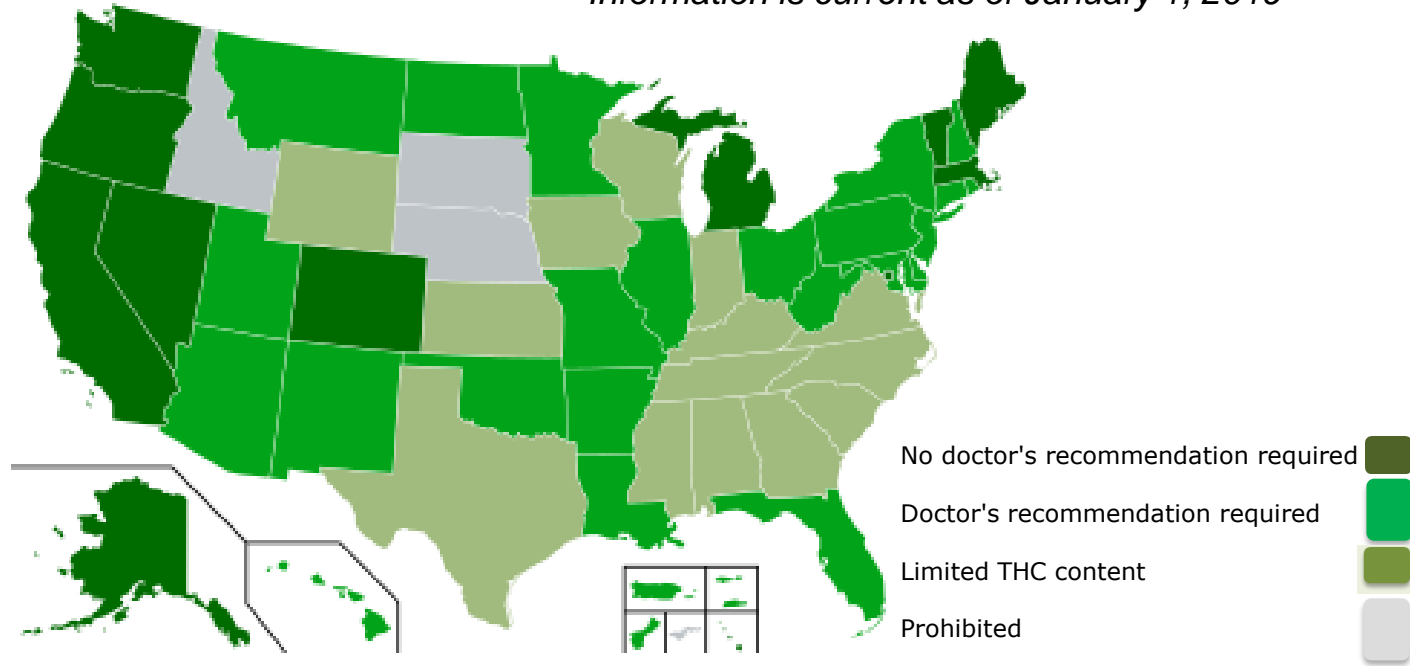
Is this really a big deal?

- Most states (Guam & DC) in the US that have legislation allowing for the medicinal use of cannabinoids.
- Federally illegal! Major confusion?!
- Canada → Cannabis Act
- UK → Legalize medicinal marijuana
- FDA 2018 approved EPIDIOLEX® (cannabidiol) oral solution, schedule V.
- Global financial impact

Is this really a big deal?

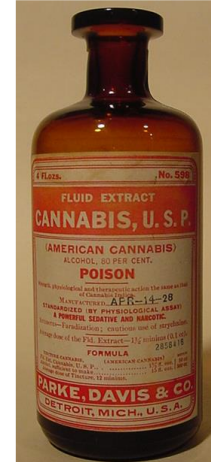
Map shows current state laws and recently-approved ballot measures legalizing marijuana for medical or recreational purposes.

Information is current as of January 1, 2019



Background

- USP 1850-1942
- 1930s U.S. Federal Bureau of Narcotics
“marijuana is a gate-way drug to narcotics addiction”
- 1937 Marijuana Tax Act
- The Controlled Substances Act of 1970
- Agriculture Act 2014/Hemp Farming Act 2018



Endocannabinoid System

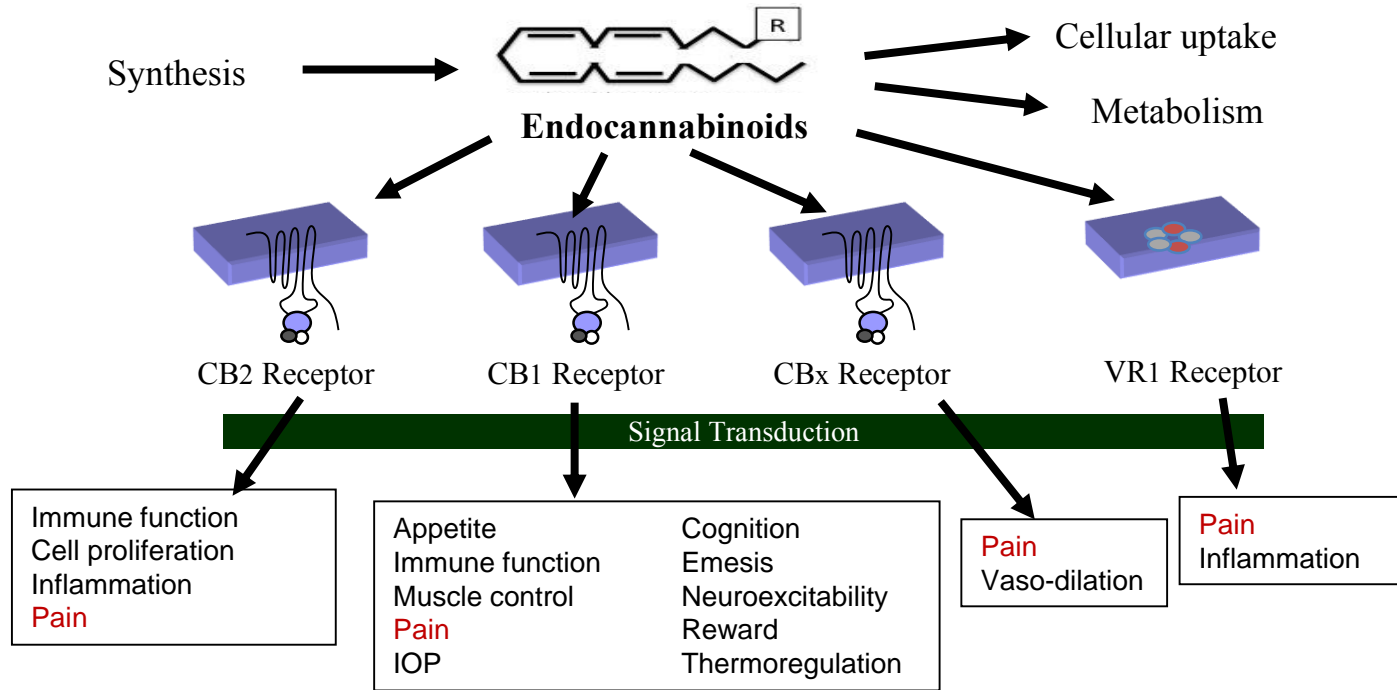
Endogenous - homeostatic regulatory system inherited by all mammals.

Includes:

- CB1 & CB2 receptor sites
{CBx & VR1 receptor sites}
- Endocannabinoids
 - *Anandamide*
 - *2-arachidonylglycerol (2AG)*
 - *Nolan ether*
 - *Virodhamine*
 - *NADA*
- Synthesizing & degrading enzymes

- Cognition & memory
- Appetite & digestion
- Stress response
- Inflammation
- Motor ~~control~~ **relax**
- Sleep **eat**
- Exploration **sleep** social behavior **forget** anxiety
- Immune **per/fect** endocrine function
- Autonomic nervous system
- Antinociception

Endogenous Cannabinoid System



Courtesy of Donald Abrams, MD

Clinical Endocannabinoid Deficiency

Ethan Russo, MD (2004/2016)

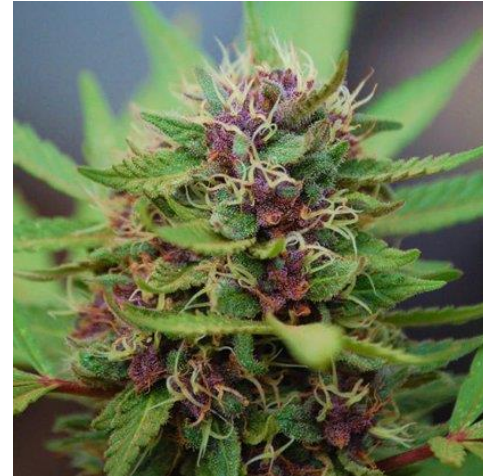
- The ECS theory of disease.
- Lack of sufficient endocannabinoids/
dysregulation of the ECS.
- Result in higher susceptibility
(fibromyalgia, irritable bowel syndrome,
depression, anxiety, migraine).
- Phytocannabinoids (THC, CBD) can
bind to the cannabinoid receptor sites
(CB1, CB2), and mimic the physiological
processes seen with binding of the endocannabinoids.



What is cannabis sativa (aka marijuana)?

It is a Plant w/over 400 different chemicals:

- >60 types of cannabinoids
 - delta-9-tetrahydrocannabinol (THC)
 - Cannabidiol (CBD)
 - Cannabinol (CBN)
 - Cannabichromene (CBC)
 - Cannabigerol (CBG)
 - Tetrahydrocannabivarin (THCV)
- Flavonoids, Terpenes, Terpenoids
- Fungus? Bacteria? Pesticides?
- Byproducts of manufacturing (solvents, heavy metals)

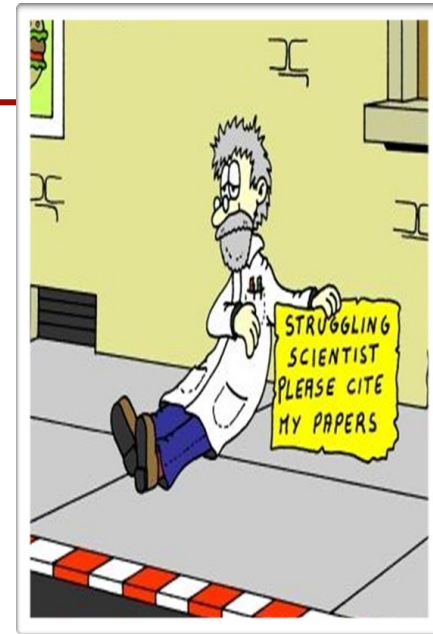


Research

- Center for Medicinal Cannabis Research
 - National Center for Natural Products Research (NCNPR) at the University of Mississippi
 - National Institute on Drug Abuse (NIDA)
 - National Institutes of Health (NIH)
-
- Canadian Institutes of Health Research
 - Canadian Consortium for the Investigation of Cannabinoids (CCIC)

Europe

- The Medicinal Cannabis Research Foundation (MCRF): UK
- Spain, Germany, Italy
- ICRS: [http:// www.cannabinoidsociety.org](http://www.cannabinoidsociety.org)



<https://clinicaltrials.gov/>

Cannabinoids for Medical Use

A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidtkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

- Moderate-quality evidence support use of cannabinoids in chronic pain & spasticity.
- Low-quality evidence: CINV, HIV weight loss, insomnia, Tourette's.
- Use of cannabinoids were associated with increased risk of short-term adverse effects.

Selective Cannabinoids for Chronic Neuropathic Pain: A Systematic Review and Meta-analysis

Howard Meng, MD,* Bradley Johnston, PhD,†‡§|| Marina Englesakis, MLIS,¶|| Dwight E. Moulin, MD,#
and Anuj Bhatia, MBBS, MD, FRCPC, FRCA, FFPMRCA, FIPP, EDRA, CIPS*

- Selective cannabinoids provided a small benefit in chronic neuropathic pain.
- High degree of heterogeneity amongst included publications.
- Need for additional: well designed, large, RCT to better assess dosage/duration/effects on physical & psychological function.

High-quality evidence is lacking.

All cannabis-based medicine pooled together were better than placebo:

- Reducing pain intensity
- Reports of moderate pain relief
- Improvement in sleep
- Improvement in psychological distress
- Global improvement

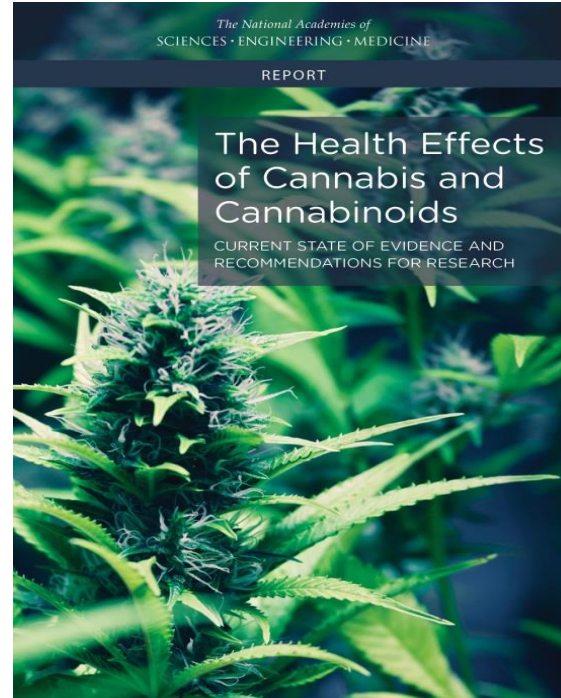
All cannabis-based medicine pooled together were
NO better than placebo:

- Improving health-related QOL
- Stopping medication because it was not effective
- Frequency of serious side effects

More people reported sleepiness, dizziness, cognitive problems and dropped out of studies because of side effects with all cannabis-based medicines pooled together versus placebo.

The Health Effects of Cannabis and Cannabinoids: Current State of Evidence and Recommendations for Research (2017)

- In adults with chemotherapy induced N/V, oral cannabinoids are effective antiemetics.
- Adults with chronic pain are more likely to experience clinically significant pain relief.
- Adults with MS related spasticity reported improvement of spasticity symptoms.



Suggested citation: National Academies of Sciences, Engineering, and Medicine. 2017. *The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research*. Washington, DC: The National Academies Press. "Used with permission"

Is Cannabis a Rational Solution to the Opioid Crisis?

Pro/Advocates

- Excellent alternative, less addictive, less likely to result in death.
- “Alternatives to Opioids Act of 2018” - Illinois
- NY - “adding any condition for which an opioid could be prescribed as a qualifying condition for medical marijuana.”
- The National Institutes of Health recently awarded a 5-year \$3.8 million grant. [*Albert Einstein College of Medicine - Chinazo Cunningham, M.D.*]

Con/Critics

- **Substitution of one addictive substance for another.**
- **Side effects under recognized (e.g. psychosis).**
- **Evidence hasn't proven benefit for pain.**

Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis (2017)

Purpose: Determine the opioid-sparing potential of cannabinoids.

Results: Studies included in qualitative synthesis (n = 28)

- Median effective dose of morphine administered in combination with delta-9-THC is 3.6 times lower than the of morphine alone.
- Codeine administered in combination with delta-9-THC was 9.5 times lower than of codeine alone.

Original Investigation

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD, MS; Colleen L. Barry, PhD, MPP

The enactment of statewide medicinal marijuana laws is associated with significantly lower state-level opioid overdose mortality rates, according to data published in August 2014 in JAMA Internal Medicine.

Researchers reported, “States with medical cannabis laws had a 24.8 percent lower mean annual opioid overdose mortality rate compared with states without medical cannabis laws.”

I know nothing about cannabis!



Important Talking Points

- Encourage open/non-judgmental dialogue.
- Driving “under the influence”.
- Recommend obtaining medical marijuana card issued by state.
- Traveling considerations.
- Share the extend of the research that is known.
- Provide website resources.
- Discuss drug to plant interactions, side effects, risk of addiction.
- Recommend products & dispensaries?

Mental Health

Cannabinoids (THC) appear to effect the same reward system as alcohol, cocaine, opioids.

Evidence for cannabis dependence from epidemiological studies (*Miller & Plant 1996; Malhotra & Biswas 2006*).

- irritability, anxiety, disturbed sleep, craving

Mental wellness

- Worsen sub-clinical, stable mental illness
- Effective motivation
- Psychosis in genetically susceptible individuals

Tolerance & Adverse Effects (AEs)

Tolerance

- Mood, sleep
- Psychomotor performance
- Arterial pressure
- Antiemetic properties

Common AEs

- Anticholinergic effects (dry mouth, blurry vision, urinary retention, tachycardia, constipation, hypertension).
- CNS effects (ataxia, cognitive dysfunction, hallucination).

Cannabis Hyperemesis Syndrome

Pharmacokinetics: delta-9-tetrahydrocannabinol

- THC psychoactive cannabinoid
- Highly lipophilic
- Rapidly absorbed through lungs after inhalation, quickly reaching high serum concentration
- Systemic bioavailability is ~23-27% for daily users, ~10-14% occasional users
- Extensive liver (first pass) metabolism; cytochrome P450
- >65% excreted in the feces, ~20% urine
- $t_{1/2}$ occasional users is 1-2 days, daily users up to 2 weeks

Stirring the Pot: Potential Drug Interactions

- CYP450 Enzymes: 1A2, 3A4, 2C9, 2C19.
- CNS depressants, antidepressants, central nervous system drugs – potentiate effects of THC.
- Any medications that are metabolized through the same pathways could result in less or more of the drug's effects.
- For scientific reviews: *Drug Metabolism Reviews*.
- Epocrates is a good quick reference for cannabidiol and synthetic THC.

Oral versus Inhaled

	INHALED	ORALLY INGESTED
Peak Blood Levels (min)	3-10	60-120
Bioavailability (%)	10-40	<15
Time to peak psychoactive activity (min)	20	120-240

Cannabidiol (CBD)

Defining Terms:

- CBD from Hemp (↑contaminants, ↓THC)
- CBD from cannabis sativa (↑THC, ↑purity)
- Hemp Oil (seeds of hemp plant, no CBD, no THC, +essential fatty acids, +omega three)

Research:

- Epidiolex®
- Other - preliminary research included studies of anxiety, cognition, movement disorders, and pain (anti-inflammatory).
- Efficacy most antidotal (discuss current animal studies).

Safety: Dosing toxicity? Anti-inflammatory effects? CYP450 metabolism.

Side Effects: Fatigue, diarrhea, changes of appetite/weight, dry mouth. Transaminase elevations (reported in Epidiolex studies).

How to Shop for CBD



- 1. Decide Why You Want to Use CBD, and in What Form**
- 2. Consider How Much THC the Product Contains**
- 3. For Products From Hemp, Find Where It Was Grown**
- 4. Ask for Test Results**
- 5. Look for Products That List the CBD Amount**
- 6. Know What Other Terms on the Label May Mean**
- 7. Avoid Products That Make Sweeping Health Claims**
- 8. Watch Out for Vaping Products With Propylene Glycol**

Practical Dosing

Recommend only products that are properly labeled.

- Label information should include the ingredients and the milligrams of each cannabinoid per dose.
- Recommend only products from companies that test for potency, pesticides, mold, and bacteria.
- Mindful of byproducts of production (e.g. solvents).

Cannabaceutical™ Facts		Afghani X Sour Diesel	
★★★★★		Tested On: November 11, 2013	
Total Aerobic Count	GOLD	Total Yeast & Mold	GOLD
Total Enterobacteria	GOLD	Pesticides Screen	PASS
Δ ⁹ -THC Max:	18.57 %	Sum of Top Terpenes	22.5 mg/g
Δ ⁹ -THCA	20.89 %	β-Caryophyllene	7.5 mg/g
Δ ⁸ -THC	0.25 %	Myrcene	3.5 mg/g
CBD Max:	0.35 %	Limonene	3.2 mg/g
CBDA	0.08 %	α-Humulene	2.8 mg/g
CBD	0.27 %	α-Pinene	2.6 mg/g
CBG Max	1.82 %	β-Pinene	1.5 mg/g
Δ ⁹ -THCVA	0.13 %	Germacrene B (tl)	1.5 mg/g
CBN	ND %		

The Vape Pen

- Avoid with products that contain propylene glycol (solvent).
- Propylene glycol can degrade to formaldehyde.
- Recommend vape pens that contain “solvent-free oils”.



The image is a screenshot of a news article from SFGATE. At the top left, there is a back arrow icon and the SFGATE logo. To the right, there is a weather icon showing a sun and a cloud with the temperature 55°, and a hamburger menu icon. Below this is a blue navigation bar with the text 'BAY AREA & STATE' and a 'SUBSCRIBE' button. The main headline of the article is '7 Californians hospitalized in ICU after vaping cannabis or CBD oils'. Below the headline, it says 'Mike Moffitt, SFGATE | on August 16, 2019'. There is a row of social media sharing icons: an envelope, Facebook, Twitter, Pinterest, Reddit, and a red square icon. To the right of these icons is a comment icon with the number '48' below it. The main image of the article shows a close-up of many yellow and black vape pens. At the bottom left of the image, it says 'Photo: Contributed Photo'. At the bottom right, there are two icons: a 3x3 grid and a double arrow icon.

Hemp CBD Scorecard: An Evaluation of Hemp CBD Producers

HEMP CBD SCORECARD	
GRADE	COMPANY
A	   
B	       
C	         
D	       
F	         

Center for Food Safety (CFS) is a national non-profit public interest and environmental advocacy organization

<https://www.centerforfoodsafety.org/reports/5719/hemp-cbd-scorecard-an-evaluation-of-hemp-cbd-producers>

Practical Dosing

Regardless of the specific physiological system, the effects of cannabis are dependent on many factors:

- Dose, variety
- Route (Inhalation, oral, transmucosal, transdermal, topical)
- Timing
- General health (medical co-morbidities), Age
- Use of other substances/medications
- Chronic user of cannabis versus naive

Practical Dosing

Average adult dosing of THC:

- Cannabis-naïve individuals 2.5-5 mg
- Daily - weekly users 10-20 mg
- Daily+ 25 mg+
- Doses exceeding 20–30 mg/day may increase adverse events or induce tolerance without improving efficacy.

<https://www.leafly.com/news/cannabis-101/cannabis-edibles-dosage-guide-chart>

MacCallum & Russo, 2018

Average adult dosing of CBD:

- 300-1500 mg/day

<https://www.webmd.com/vitamins/ai/ingredientmono-1439/cannabidiol>

Practical Dosing

Sativex® (1:1 THC/CBD): Spasticity due to multiple sclerosis.

➤ **2.7mg/2.5mg BID**

(max 32.4mg/30mg/day)

<https://www.medicines.org.uk/emc/product/602>

Epidiolex® (CBD): Seizures (Dravet/Lennox-Gastaut)

➤ **5 mg/kg oral BID**

(max 20 mg/kg/day)

https://www.epidiolex.com/sites/default/files/EPIDIOLEX_Full_Prescribing_Information.pdf

LACK OF STANDARDIZATION MAKES DOSING A CHALLENGE FOR PATIENTS & PRACTITIONERS

Overconsumption:

- Re-dosing too soon
- Delayed on-set with oral dosing (>120 minutes)
- Hostile behavior/erratic speech/mild psychosis

The L.E.S.S. Method: A measured approach to oral cannabis dosing

Start **L**ow

- **E**stablish potency
- Go **s**low
- **S**upplement as needed

(Erowid & Erowid, 2011)

Tips

- Familiarize yourself with
 - THC, CBD dosing.
 - drug : drug (plant) interactions, side effects, withdrawal.
 - local dispensaries and counsel patient to accordingly.

- Consider The Treatment Agreement.
- Continue to remember Federally illegal.
- Mindful of addiction, abuse, mental health issues.

Final Takeaways

- Cannabinoids emerging as valid option for refractory chronic pain management.
- Innovative solutions to opioid crises needed.
- Cannabinoid-opioid synergy deserves attention.
- Clinical trials challenging to design but necessary to conduct.
- Can no longer refuse to discuss.
- State laws ...



Resources

Dispensary Information:

Voluntary Patient Focused Certification

<http://patientfocusedcertification.org/certification/>

- Addresses product & distribution safety
- Based on quality standards for medical cannabis products and businesses issued by the **American Herbal Products Association** (AHPA) and the **American Herbal Pharmacopoeia** (AHP) Cannabis monograph

<http://camcd-acdcm.ca/>

Resources

Canadian Consortium for the Investigation of Cannabinoids (CCIC): www.ccic.net

- Accredited cannabinoid education (ACE) programs
- Informed by needs assessments, expert faculty

International Cannabinoid Research Society (ICRS):
www.icrs2014.org

International Association for Cannabinoid Medicine (IACM):
www.cannabis-med.org

University of Washington & Alcohol and Drug Abuse Institute (ADAI)

<http://adai.uw.edu/mcacp/index.htm>

Society of Cannabis Clinicians: www.cannabisclinicians.org

Physician/Clinician Training

New York:

https://www.health.ny.gov/regulations/medical_marijuana/practitioner/

Florida:

http://www.flhealthsource.gov/ommu/physician_requirements

All licensed MDs/DOs – some states require specialty practice (e.g. pain management, palliative care, etc.)

MS in Medical Cannabis Science and Therapeutics at the School of Pharmacy should contact

[**msmedicalcannabis@rx.umaryland.edu**](mailto:msmedicalcannabis@rx.umaryland.edu)

NPs: OR, WA, NY, MA, NM, ME, NJ

<http://adai.uw.edu/mcacp/index.htm>

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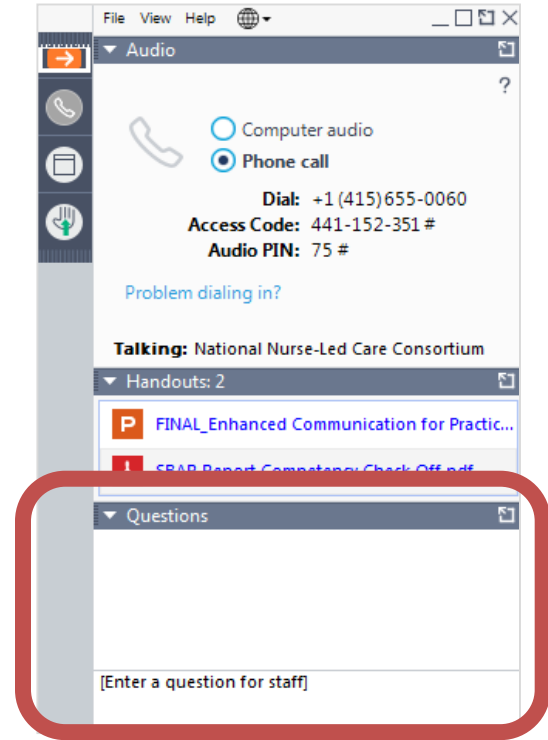
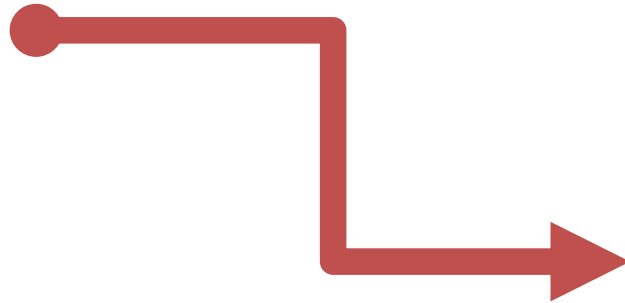
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