UVM Project ECHO: Chronic Pain

Facilitators:
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Agenda

• Introductions and announcements
• Session objectives
• Didactic presentation (20-25 min)
  • Q & A
• Case presentations
  • Clarifying questions
  • Discussion
    • First, participants – then program faculty
  • Summary of recommendations
• Session parking lot items for follow up
• Closing reminders
  • Complete session evaluation (session recording info included in this email)
  • Session slides posted at www.vtahec.org
  • Submit a new case, template posted at www.vtahec.org
CME Disclosures

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UVM Project ECHO Chronic Pain: Cannabinoids for Chronic Pain

Speaker: Mac Abernathy, MD
April 3, 2020
Medical Cannabis for Chronic Pain

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Objectives

● Educate medical professionals on the basics of cannabis and the pharmacology of the cannabinoid system.

● Understand the evidence for medical cannabis in the treatment of chronic pain.

● Teach medical professionals the nuances of the medical cannabis law and application process in Vermont.

● Discuss the different formulations of medical cannabis and how to best utilize them for symptom management.

● Understand harm reduction strategies with medical cannabis and how to detect and treat cannabis use disorder.
I have no conflicts of interest or financial relationships to disclose.
Cannabis is a family of flowering plants with three species:

- **Cannabis sativa**
  - Very tall
  - Long branches with large distances between nodes
  - Expansive root system
  - Long, thin leaves

- **Cannabis indica**
  - Small, compact size
  - Condensed root system
  - Robust stalks
  - Wide leaves
  - Dense, heavy buds

- **Cannabis ruderalis**
  - Small in size and wild-looking
  - Fewer branches that Sativa or Indica specimens
  - Conical shape
The Ancient History of Cannabis

- Hemp (a cultivar of cannabis) has been used for fiber and rope since the Neolithic Age (12,000 years ago). Fibers have been found embedded in pottery dating to ~5000 BC.

- Incense burners from ~2500 BC were discovered in funerary tombs from the Pamir mountains in Central Asia. These burners contained residue high in CBN, the oxidative product of THC.

- From The Histories by Herodotus in 440 BC: “The Scythians...take some of this hemp-seed flower, and, creeping under the felt coverings, they throw it upon the red-hot stones; immediately it smokes, and gives out such a vapour as no Grecian vapour-bath can exceed; the Scyths, delighted, shout for joy..."
Ancient Medical Cannabis

- Cannabis was used as medication by many ancient civilizations including China, India, Egypt, Greece, and Arabia
- Indications included diarrhea, nausea, cramps, spasms, convulsions, pain, inflammation, fever and hemorrhoids.

The Eber’s Papyrus, dated to 1500 BC, contains a cannabis prescription for inflammation.
“Medical” Cannabis: mid-1800’s to 1920’s
Cannabinoid Receptor System Basics

- There are two major cannabinoid receptors: CB1 and CB2.
- CB1 receptors are mostly expressed within the central and peripheral nervous system.
- CB1 is the major receptor that produces the subjective and objective effects of cannabis.
- CB2 receptors are mostly expressed in the immune system.
Cannabinoid Receptor System: CB1

- **CB1 receptors** are G-protein coupled receptors expressed predominantly in the **central and peripheral nervous system**.

- Activation of CB1 receptors leads to **DECREASED cAMP production** which leads to a total relative decrease in peripheral and central neurotransmission (**CNS depression**).

- CB1 receptors are expressed highly on GABAergic neurons of the hippocampus. CB1 activation suppresses glutamate release in the hippocampus and likely plays a significant role in **memory selectivity**.
Cannabinoid Receptor System: CB1

- CB1 receptors are found on interneurons of the **dorsal horn of the spinal cord** as well as the **periaqueductal grey** - both of these areas are heavily involved in **pain processing**.

- CB1 receptors are also present in the basal ganglia, cerebellum, and neocortex. This receptor distribution indicates a role for cannabinoids in the **motor system**.
Cannabinoid Pharmacology: Endocannabinoids

- **Anandamide** is a fatty acid neurotransmitter derived from the metabolic breakdown of arachidonic acid. Along with other fatty acids, anandamide binds to cannabinoids receptors.

- Anandamide is believed to be involved in memory, motivation, feeding, embryonic implantation into the uterine wall, and the rewarding effects of exercise.

- Anandamide is the primary endogenous ligand for CB1 receptors.
Cannabinoid Receptor System: CB2

- **CB2 receptors** are G-protein coupled receptors expressed predominately in the immune system. This receptor plays a very sophisticated role in immune response. The receptors are found on hematopoietic stem cells, monocytes, T-cells, B-cells, and macrophages.

- CB2 receptors **mediate and/or modulate several immune functions** including cytokine release, immunosuppression, cell migration, gene transcription (through a reduction in cAMP) and immune cell apoptosis.
Cannabinoid Receptor System: CB2

- CB2 receptors are present on microglia of the central nervous system. It is generally believed that CB2 receptors are not found at high expression levels in the brain otherwise; this is an area of scientific debate.

- CB2 receptors are expressed in peripheral nerve terminals and there is substantial speculation they are involved in nociception.
Cannabinoid Pharmacology: Phytocannabinoids

- **Phytocannabinoids** can be defined as any plant-derived natural product capable of either directly interacting with cannabinoid receptors and/or sharing chemical similarity with cannabinoids.

- The major cannabinoids present in the cannabis plant are:
  - THCa (tetrahydrocannabinolic acid)
  - CBDa (Cannabidiolic acid)
  - CBNa (Cannabinolic acid)
  - CBGa (Cannabigerolic acid)
  - CBCa (Cannabichromenic acid)
  - CBLa (Cannabicyclol)
  - CBVa (Cannabivarin)
  - THCVa (Tetrahydrocannabivarin)
  - CBDVa (Cannabidivarin)
  - CBCVa (Cannabichromevarin)
  - CBGa (Cannabigerovarin)
  - CBGMa (Cannabigerol Monomethyl)
Cannabinoid Pharmacology: Phytocannabinoids

- However, there are ~113 different phytocannabinoids present in the cannabis plant...
Cannabis Pharmacology: Phytocannabinoids

- Female cannabis plants in active flowering (marijuana) contain the highest concentration of cannabinoids.

- **Trichomes** are sticky surface glands on the female cannabis plant that are designed to catch pollen. These glands contain **cannabis resin/oil which is the major source of cannabinoids in the female cannabis plant**. Leaves and stems have low cannabinoid content.
Phytocannabinoid Pharmacology: THC

- Tetrahydrocannabinol (THC) is the primary psychoactive constituent of cannabis and functions as a CB1 and CB2 receptor partial agonist.

- **Pharmacokinetics of THC** - vary as a function of its route of administration.
  - Inhaled THC causes a maximum plasma concentration within minutes, psychotropic effects start within seconds to a few minutes, reach a maximum after 15-30 minutes, and taper off within 2-5 hours.
  - Orally ingested THC has a delayed onset of psychotropic effects, typically 30-90 minutes. Maximum effects occur after 2-3 hours and last for about 4-12 hours, depending on dose.
  - THC has poor oral bioavailability (6-20%) but is absorbed at a higher rate when inhaled (10-35%). Oral THC has a half-life of 25-36 hours and is metabolized by the liver primarily by CYP2C9, CYP2C19, and CYP3A4.
# Phytocannabinoid Pharmacology: THC

**THC Effects**
- Intoxication, a varied syndrome
- Sedation
- Stimulation with some strains
- Bodily relaxation
- Increased appetite
- Nausea suppression
- Analgesia
- Suppression of seizure activity

**THC Adverse effects**
- Tachycardia/palpitations
- Anxiety/paranoia
- Hypotension
- Motor discoordination
- Xerostomia
- Nausea (at very high doses)
Phytocannabinoid Pharmacology: THC

- **Serious Adverse Reactions**
  - Cannabis Use Disorder
  - Exacerbation of prior existing mental illness
  - Psychosis/Hallucinations
  - Cannabis induced hyperemesis (years of daily use implicated)

- Long term and/or heavy cannabis use can cause **amotivational syndrome**.

- Cannabis use during pregnancy is associated with lower birth weight in the infant.
Phytocannabinoid Pharmacology: CBD

- Cannabidiol (CBD) has complex allosteric effects at CB1 and CB2 receptors. CBD has low binding affinity for CB1/CB2 and behaves as an antagonist of CB1/CB2 agonists despite this low affinity.

- CBD has been shown to act as a serotonin 5-HT1A receptor partial agonist.

- CBD allosterically modulates the μ-opioid and δ-opioid receptors.

- Cannabidiol has poor oral bioavailability (<7%) but is absorbed at a higher rate when inhaled (median 31%). CBD has a half-life of 18-30 hours and is metabolized by the liver and gut, primarily by CYP2C19 and CYP3A4 and secondarily by glucuronidation.
Phytocannabinoid Pharmacology: CBD

- CBD (Epidolex) was approved in June 2018 by the FDA to decrease seizure frequency in two severe forms of childhood epileptic encephalopathy, Dravet and Lennox-Gastaut Syndrome.

- The vast majority of studies done with CBD are preclinical and pilot studies. Medical professionals have little guidance on how to counsel patients taking CBD because of this paucity of evidence.

- CBD has been associated with elevated liver enzymes during the Epidolex trial, so caution should be utilized in patients with hepatic impairment.
Medical Cannabis and Cannabinoid Ratios

- While the exact percentages are hotly debated, there is general consensus that cannabis has increased in THC potency over time. This is due to selective breeding and market demand.

- Medical cannabis has on average 18% THC and 1% CBD by weight. The strongest medical cannabis has around 23-25% THC and may have no detectable CBD.

- THC to CBD ratios matter because CBD can ameliorate the more negative effects of THC due to the previously discussed allosteric modulation and antagonist action at CB1 receptors.
Cannabinoid Pharmacology Summarized

CBD, CBN, and THC fit like a lock and key into existing human receptors. These receptors are part of the endocannabinoid system which impacts physiological processes affecting pain modulation, memory, and appetite plus anti-inflammatory effects and other immune system responses. The endocannabinoid system comprises two types of receptors, CB1 and CB2, which serve distinct functions in human health and well-being.

**CB1 receptors** are primarily found in the brain and central nervous system, and to a lesser extent in other tissues.

**CB2 receptors** are mostly in the peripheral organs especially cells associated with the immune system.

**THC** Tetrahydrocannabinol

CBD does not directly "fit" CB1 or CB2 receptors but has powerful indirect effects still being studied.

**CBD** Cannabidiol

**CBN** Cannabinol

**Common Effects:**
- euphoria
- relaxation
- anxiety
- short term memory impairment

**Common Effects:**
- decreases negative side effects of THC
- decreased anxiety
- decreased short term memory impairment
The Health Effects of Cannabis and Cannabinoids

THE CURRENT STATE OF EVIDENCE AND RECOMMENDATIONS FOR RESEARCH

March 31, 2017

PDF for free at
https://www.nap.edu/24625

Committee on the Health Effects of Marijuana:
An Evidence Review and Research Agenda

Board on Population Health and Public Health Practice

Health and Medicine Division

A Report of
The National Academies of
SCIENCES • ENGINEERING • MEDICINE
DEFINITIONS OF WEIGHTS OF EVIDENCE USED BY THE NATIONAL ACADEMY

- **CONCLUSIVE** evidence - strong evidence from randomized controlled trials to support the conclusion, supportive findings from multiple good-quality studies with no credible opposing factors “A firm conclusion can be made, and the limitations to the evidence, including chance, bias, and confounding factors, can be ruled out with reasonable confidence.”

- **SUBSTANTIAL** evidence - supportive findings from good-quality studies with very few or no credible opposing factors, “minor limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.”

- **MODERATE** evidence - some evidence to support the conclusion, several good to fair quality studies with few or no credible opposing findings, “A general conclusion can be made but limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.”

- **LIMITED** evidence - weak evidence to support the conclusion, supportive findings from fair studies or mixed findings with one conclusion being favored “A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors.”

- **No evidence**...self explanatory
Conclusive or substantial evidence that cannabis or cannabinoids are effective:

- For the treatment for chronic pain in adults (cannabis)
- For antiemetic therapy in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)
Substantial evidence of a statistical association between:

- Cannabis use and the development of schizophrenia and other psychoses with the highest risk among the most frequent users.

- Cannabis use frequency and the progression to developing problem cannabis use.

- Severity of problem cannabis use and being male, but the recurrence of problem cannabis use does not differ between males and females.
Other Relevant Medical Evidence for Patients with Chronic Pain

- Medical cannabis use is associated with a decrease in opioid use in a majority (64%) of surveyed patients and is associated with improved quality of life (45%). Boehnke et al. 2016 “Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain.” *The Journal of Pain* 17(3).p739-744

- An anonymous survey of medical cannabis users (n=95) indicated that *cannabis indica* (vs. *sativa*) was preferred for the following types of pain: non-migraine headache, neuropathy, spasticity, and arthralgias. Pearce et al. 2014 “Discriminating the Effects of Cannabis sativa and Cannabis indica: A Web Survey of Medical Cannabis Users.” *The Journal of Alternative and Complementary Medicine* 20(10)

- A meta analysis of individual patient data from 178 participants with 405 observations in five RCTs demonstrated that inhaled cannabis produced a decrease in neuropathic pain in one out of 5 to 6 patients (NNT 5.6 [3.4, 14] CRI95%).** Andreae et al. 2015 “Inhaled Cannabis for chronic neuropathic pain: an individual patient data meta-analysis.” *The Journal of Pain* 16(12).p1221-1232
Other Relevant Medical Evidence for Patients with Chronic Pain

- The short term effects of smoking cannabis resemble COPD with coughing, wheezing, sputum production, etc but a small number of high-quality studies have demonstrated there is no causal relationship between smoking cannabis and long-term lung function. Owen et al. 2014. "Marijuana: respiratory tract effects". Clinical Reviews in Allergy & Immunology. 46 (1): 65–81.

Vermont Medical Cannabis Law

~4,500 people in the VT Medical Cannabis Registry according to VT DPS.

Qualifying Conditions:
- Any patient receiving hospice care
- Cachexia or wasting syndrome
- Cancer
- Crohn's disease
- Glaucoma
- HIV or AIDS
- Multiple Sclerosis
- Parkinson's disease
- PTSD
- Seizures
- Severe or chronic pain
- Severe nausea

- **Possession Limit:** 2 ounces (56 grams) of usable cannabis

- **Home Cultivation:** No more than 9 total plants, only 2 of which may be mature.

- Patients may have registered caregivers through the application process.

- The fee is $50 and requires annual renewal.

- **Providers do not “prescribe” medical cannabis.**
Vermont Medical Cannabis Law

If a patient asks about firearms and the medical cannabis registry, the Vermont Department of Public Safety does not file the registry with the NICS, the background checking system that is used for firearm purchases. Directly from the website:

“Information about individuals (patients, caregivers, dispensary personnel, etc.) regardless of their statutes on the Registry is NOT part of the National Instant Criminal Background Check System (NICS).”
6) BONA FIDE HEALTH CARE PROFESSIONAL-PATIENT RELATIONSHIP INFORMATION

(A) Have you completed a full assessment of the patient applicant’s medical history and current medical condition, including a personal physical examination?
   [] Yes  [] No

(B) Do you have a treating or consulting relationship with the patient applicant of at least three (3) months?
   [] Yes  [] No

(C) Has the patient applicant been diagnosed with a terminal illness and/or currently under hospice care?
   [] Yes  [] No

(D) Was the patient applicant diagnosed in another state or jurisdiction where they formally resided and moved to Vermont within the last three (3) months?
   [] Yes  [] No

(E) Was the patient applicant diagnosed with the debilitating medical condition specified on the previous page within the last three (3) months?
   [] Yes  [] No

(F) Was the patient applicant referred to you by another health care professional because of your advanced education and clinical training specific to the debilitating medical condition specified on the previous page?
   [] Yes  [] No

7) HEALTH CARE PROFESSIONAL SIGNATURE

I certify that:

(A) I am a health care professional;
   A) Licensed to practice medicine under 26 V.S.A Chapter 23 or Chapter 33;
   B) Licensed as a naturopathic physician under 26 V.S.A. Chapter 81;
   C) Certified as a physician assistant under 26 V.S.A. Chapter 31; or
   D) Licensed as an advanced practice registered nurse under 26 V.S.A. Chapter 28; or,
   E) Professional licensed under substantially equivalent provisions in NH, MA, or NY

(B) I am in good standing with the state (VT, NH, MA, NY) regulating my professional license, and that the facts stated on this Health Care Professional Verification Form are true and accurate to the best of my knowledge and belief.

(C) I understand, notwithstanding any law to the contrary, a person who knowingly provides false information on this application may be guilty of perjury and imprisoned for not more than one year or fined not more than $1,000.00 or both. This penalty shall be in addition to any other penalties that may apply.

This verification form is not considered a prescription and that the only purpose of this verification form is to confirm that the applicant/patient has a debilitating medical condition.

Health Care Professional’s Signature: __________________________ Date: __________
Cannabis as Medicine

Approach Cannabis using principles of pharmacology.

- **Strain** – sativa, indica, or hybrid
- **Formulation** – flower/bud, concentrate, tincture, edible
- **Potency/Cannabinoid ratio** - THC% and/or CBD% if applicable
- **Dose** – how much THC is in the product
- **Frequency** - how often to administer
Cannabis as Medicine

Strain selection is a very inexact science.

- **Sativas** tend to be more activating and energetic. They can be anxiety/paranoia inducing for some patients. They may have lower CBD content.

- **Indicas** tend to be more relaxing and produce some sedation. They may make patients more lethargic with more motor discoordination. They may have higher CBD content.

- **Hybrids** can give the effects of both types of cannabis, it depends on the genetics.

- THC, CBD, and other cannabinoid content can vary a lot by strain, dispensary, grower, etc.
Cannabis as Medicine

**Smoked (inhaled) whole cannabis** – the dried flower (bud) of the female cannabis plant. 10-25% THC,

### Smoked/Vaporized Cannabis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Duration</td>
<td>1 - 4 hrs</td>
</tr>
<tr>
<td>Onset</td>
<td>0 - 10 mins</td>
</tr>
<tr>
<td>Come Up</td>
<td>5 - 10 mins</td>
</tr>
<tr>
<td>Plateau</td>
<td>15 - 30 mins</td>
</tr>
<tr>
<td>Come Down</td>
<td>45 - 180 mins</td>
</tr>
<tr>
<td>After Effects</td>
<td>2 - 24 hrs</td>
</tr>
</tbody>
</table>

**Dosing Flower:** start with 0.1g to 0.15g and go up from there, wait 3-5 minutes between inhalations, inhale deeply but briefly.
Cannabis as Medicine

Cannabis concentrates – 40 to 90% THC, many extraction methods

Dosing Concentrates: complex, take as small “a puff as possible”, repeat in 5 minutes, exercise caution due to potency

Vaping associated pulmonary injury (VAPI) is a potentially serious side effect of using vaporized cannabis.
Cannabis as Medicine

**Edibles** – active cannabinoids inside of food products
Cannabis as Medicine

Edible (ingested) Cannabis

- **Total Duration**: 4 - 10 hrs
- **Onset**: 0.5 - 2 hrs
- **Come Up**: 1 - 1.5 hrs
- **Plateau**: 2-5 hours
- **After Effects**: Up to 16 hrs

- **Dosing Edibles**: 5 mg for first dose in cannabis naive patients

- Edibles may have increased nausea vs. inhaled cannabis.

- **Do not re-dose edibles.** It may take up to 2 hours for them to start working.
Cannabis as Medicine

- **Tinctures** – active cannabinoids (decarboxylated) typically in food-grade ethanol, can be absorbed sublingually or ingested. Sublingual cannabinoids have a more rapid onset than edibles and a shorter duration of action.

- **Dosing Tinctures:** \(?\) mg THC/per mL, eye dropper 1 mL (20 drops), 5mg to start
Cannabis as Medicine

Strategy for Counseling Patients

- Extensive harm reduction counseling done first, including acknowledging the limitations/implications of the evidence.

- Encourage starting at low doses!

- Achieving positive benefit and mitigating negative effects via strain selection, vaporization, product formulation, careful dosing, and cannabinoid ratio control. Experimentation may be required.

- Train them how to decipher medical cannabis labels so they know what they are getting. Products at the dispensaries are expensive and the counseling at the medical dispensaries can be hit or miss.
Cannabis as Medicine

Strategy for Counseling Patients

- Smoked/vaporized cannabis as an “instant release” form; edibles/tincture as a “controlled release” form.
- Use a symptom tracking journal and encourage patients to keep up with it.
- Warn patients about tolerance and withdrawal, these are real phenomena. Tell them they can come to you if things get out of hand.
- Encourage tolerance breaks if possible. It can take 1-2 weeks to “reset.”
Pain Diary

You can complete the highlighted fields on this form online and then print the form for easy reference. Only text that is visible on the form is printed; scrolled text will not print. Any text you enter into these fields will be cleared when you close the form; you cannot save it.

A pain diary may help you and your doctor find out what makes your pain better or worse. Use the diary below to keep track of when you have pain, how bad it is, and what you are doing to treat it.

These faces show how much something can hurt. The face on the left shows no pain. The other faces show more and more pain. The face on the right shows very much pain. You can use these faces to know what number to use to show how much you or a child hurts right now.

### Daily pain diary

**Date:**

**Time:**

**Pain scale rating:**

**Medicine and dose:**

**Medicine side effects:**

**What made the pain better today?**

**What made the pain worse today?**

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### Experience Summary

Enter notes about your experience including details on the effect, side effects, dosage specifics, etc.

### Effects

- [ ] Pain Relief
- [ ] Mood Improvement
- [ ] Sedative
- [ ] Energetic
- [ ] Creative
- [ ] Anti-inflammatory
- [ ] Fatigue Reducing
- [ ] Intestinal Ease
- [ ] Appetite Stimulant
- [ ] Focused
- [ ] Anti-Depressant
- [ ] Other

**Nausea**

**Dry Eyes**

**Dry Mouth**

**Constipation**

**Diarrhea**

**Self-Report**

**Drowsy**

**Dizziness**

**Nausea**

**Headache**

**Drowsy**

**Other**

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### Overall Outcome

Enter your overall feeling of relief after taking your daily treatment:

- [ ] Much Worse
- [ ] No Change
- [ ] Much Better

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This information does not replace the advice of a doctor. Healthwise, Incorporated, disclaims any warranty or liability for your use of this information.
A Real Example Medical Cannabis Regimen

4 products total:
- Vaporizer cartridge with a *sativa*-based extract of medium strength (60%)
- Vaporizer cartridge with *indica*-based extract of high strength (85+%)  
- *Indica* whole flower  
- *Indica*-based tincture  

Schedule:
**Day time:** 2 days per week on average she will need 2 to 3 pulls on the *sativa* vaporizer due to waking up in pain. She will wait as long as she can before she does this so it doesn’t diminish her motivation. She never uses *indica*-based products during the day.

**Night time:** In the afternoon, if the pain is mild to moderate, she uses 0.5-1g of *indica* flower in a vaporizer built specifically for flower. If her pain is severe she will use the vaporizer pen instead and take pulls in 5 minute intervals until her pain is tolerable. She takes 10 drops of tincture (10mg of THC) 90 minutes before she goes to bed. She holds it under her tongue for as long as she can. This both helps her go to sleep and prevents her from waking up from pain in the middle of the night. She wakes with no after effects.
A Real Example Medical Cannabis Regimen

- It took 8 months to nail down this patient’s medical cannabis regimen.
- Lots of trial and error.
- She was able to eliminate medications for sleep (trazodone and zaleplon).
- Significant decrease in her opioids (180 MME to 20 MME).
- She grows her own *indica* plants for the flower and tincture, but she has to buy the vaporizer cartridges. On average, she spends about $90 a month buying medical cannabis products.
Cannabis Use Disorder
Cannabis Use Disorder

- Point prevalence of 0.19 percent in 2010 (13 million people), very likely higher now.

- Young men in urban areas are at highest risk.

- Roughly 1 in 8 cannabis users has a use disorder.

- The more cannabis you use, the higher your risk of developing a use disorder.
DSM-5 Cannabis Use Disorder Diagnostic Criteria

A problematic pattern of cannabis use leading to **clinically significant impairment or distress**, need two of the following within 1 year:

1. **Cannabis is often taken in larger amounts** or over a longer period than was intended.

2. Persistent desire or **unsuccessful efforts to cut down** or control cannabis use.

3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.

4. **Craving**, or a strong desire or urge to use cannabis.

5. Recurrent cannabis use resulting in a **failure to fulfill major role obligations at work, school, or home**.
DSM-5 Cannabis Use Disorder Diagnostic Criteria

6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.

7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.

8. Recurrent cannabis use in physically hazardous situations.

9. Cannabis use is continued despite persistent or recurrent physical or psychological problems caused or exacerbated by cannabis.

10. Physical tolerance, requiring dose escalation to achieve desired effects.

11. Withdrawal or using cannabis to avoid withdrawal.
Cannabis Withdrawal

- Occurs within 6 to 48 hours of abrupt cessation of regular use.
- Withdrawal severity directly tied to frequency and amount of use.
- Daily cannabis use in one study led to a 70-96% likelihood of withdrawal upon abrupt cessation.

- **Cannabis Withdrawal Symptoms:**
  - Irritability/anger
  - Anxiety
  - Headache
  - Depressed Mood
  - Sleep difficulty
  - Poor appetite
The Common Sense Approach to Detecting Problem Cannabis Use

- Use the same assessment methods you use for patients taking any controlled substance with addiction/withdrawal potential.

- Are they using it or is it using them....

- Severe cannabis use problems can and do happen, consider ATP referral.

- Cannabis withdrawal looks opposite of the intoxication (as is the cast with most substances of abuse).
The only “legal” medical cannabis farm in America at my alma mater, the University of Mississippi in Oxford MS.

Thank You
Supplemental info follows
Phytocannabinoids as Approved medications

-Nabiximols (Sativex)
  - Standardized botanical drug/cannabis extract
  - Tetrahydrocannabinol (THC) and cannabidiol (CBD) in approximately 1:1 ratio
  - Each spray delivers a dose of 2.7 mg THC and 2.5 mg CBD
  - Not approved in the US, would be considered a Schedule I drug
  - Neuropathic pain, MS spasticity, overactive bladder, cancer-related pain

-Dronabinol (Marinol)
  - Pure (−)-trans-Δ⁹-tetrahydrocannabinol
  - Schedule III controlled substance
  - FDA approved for chemotherapy-induced nausea and HIV/AIDS anorexia
  - Dose formulations 2.5mg, 5mg, 10mg capsules; 5mg/ml solution

-Cannabidiol solution (Epidiolex)
  - Schedule V controlled substance (???)
  - Orphan drug FDA approval for Dravet Syndrome and Lennox-Gastaut Syndrome, two severe forms of epileptic encephalopathy of childhood
  - Starting dosage is 2.5 mg/kg taken twice daily (5 mg/kg/day). After one week, the dosage can be increased to a maintenance dosage of 5 mg/kg twice daily (10 mg/kg/day). Max is 20mg/kg/day
Cannabis Medical Evidence

National Academies of Sciences, Engineering, and Medicine. March 31, 2017

**Conclusive or substantial evidence** that cannabis or cannabinoids are effective:
- For the treatment for chronic pain in adults (cannabis) (4-1)
- Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) (4-3)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)

**Moderate evidence** that cannabis or cannabinoids are effective for:
- Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols) (4-19)

**Limited evidence** that cannabis or cannabinoids are effective for:
- Increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabis and oral cannabinoids) (4-4a)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)
- Improving symptoms of Tourette syndrome (THC capsules) (4-8)
- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol) (4-17)
- Improving symptoms of posttraumatic stress disorder (nabilone; one single, small fair-quality trial) (4-20)
Cannabis Medical Evidence


**Limited evidence** of a statistical association between cannabinoids and:
- Better outcomes (i.e., mortality, disability) after a traumatic brain injury or intracranial hemorrhage (4-15)

**Limited evidence** that cannabis or cannabinoids are ineffective for:
- Improving symptoms associated with dementia (cannabinoids) (4-13)
- Improving intraocular pressure associated with glaucoma (cannabinoids) (4-14)
- Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis

**Moderate evidence** of a statistical association between cannabis use and:
- The impairment in the cognitive domains of learning, memory, and attention (acute cannabis use) (11-1a)

**Limited evidence** of a statistical association between cannabis use and:
- Impaired academic achievement and education outcomes (11-2)
- Increased rates of unemployment and/or low income (11-3)
- Impaired social functioning or engagement in developmentally appropriate social roles (11-4)
Cannabis Medical Evidence

Moderate evidence of a statistical association between cannabis use and:
- The impairment in the cognitive domains of learning, memory, and attention (acute cannabis use) (11-1a)

Limited evidence of a statistical association between cannabis use and:
- Impaired academic achievement and education outcomes (11-2)
- Increased rates of unemployment and/or low income (11-3)
- Impaired social functioning or engagement in developmentally appropriate social roles (11-4)

Limited evidence of a statistical association between sustained abstinence from cannabis use and:
- Impairments in the cognitive domains of learning, memory, and attention (11-1b)
Cannabis Medical Evidence

National Academies of Sciences, Engineering, and Medicine March 31, 2017

Substantial evidence of a statistical association between cannabis use and:
• The development of schizophrenia or other psychoses, with the highest risk among the most frequent users (12-1)

Moderate evidence of a statistical association between cannabis use and:
• Better cognitive performance among individuals with psychotic disorders and a history of cannabis use (12-2a)
• Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use)
• A small increased risk for the development of depressive disorders (12-5)
• Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users (12-7a)
• Increased incidence of suicide completion (12-7b)
• Increased incidence of social anxiety disorder (regular cannabis use) (12-8b)
Cannabis Medical Evidence

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There is substantial evidence that:
• Stimulant treatment of attention deficit hyperactivity disorder (ADHD) during adolescence is not a risk factor for the development of problem cannabis use (13-2e)
• Being male and smoking cigarettes are risk factors for the progression of cannabis use to problem cannabis use (13-2i)
• Initiating cannabis use at an earlier age is a risk factor for the development of problem cannabis use (13-2j)

There is substantial evidence of a statistical association between:
• Increases in cannabis use frequency and the progression to developing problem cannabis use (13-1)
• Being male and the severity of problem cannabis use, but the recurrence of problem cannabis use does not differ between males and females (13-3b)

There is moderate evidence that:
• Anxiety, personality disorders, and bipolar disorders are not risk factors for the development of problem cannabis use (13-2b)
• Major depressive disorder is a risk factor for the development of problem cannabis use (13-2c)
• Adolescent ADHD is not a risk factor for the development of problem cannabis use (13-2d)
• Being male is a risk factor for the development of problem cannabis use (13-2f)
• Exposure to the combined use of abused drugs is a risk factor for the development of problem cannabis use (13-2g)
• Neither alcohol nor nicotine dependence alone are risk factors for the progression from cannabis use to problem cannabis use (13-2h)
• During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for the development of problem cannabis use (13-2k)

There is moderate evidence of a statistical association between:
• A persistence of problem cannabis use and a history of psychiatric treatment (13-3a)
• Problem cannabis use and increased severity of posttraumatic stress disorder symptoms (13-3c)

There is limited evidence that:
• Childhood anxiety and childhood depression are risk factors for the development of problem cannabis use (13-2a)
Cannabis Medical Evidence

National Academies of Sciences, Engineering, and Medicine March 31, 2017

There is moderate evidence of a statistical association between cannabis use and:
• The development of substance dependence and/or substance abuse disorder for substances including alcohol, tobacco, and other illicit drugs (14-3)

There is limited evidence of a statistical association between cannabis use and:
• The initiation of tobacco use (14-1)
• Changes in the rates and use patterns of other licit and illicit substances (14-2)
Cases/HIPAA

DO NOT INCLUDE:
• Names
• Address
• DOB
• Phone/Fax #
• Email address
• Social Security #
• Medical Record #

The discussion and materials included in this conference are confidential and privileged pursuant to 26VSA Section 1441-1443. This material is intended for use in improving patient care. It is privileged and strictly confidential and is to be used only for the evaluation and improvement of patient care.
• STOP RECORDING
Wrap-Up

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