




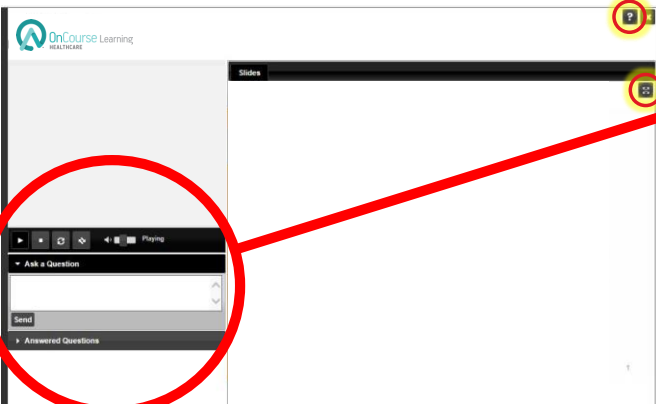
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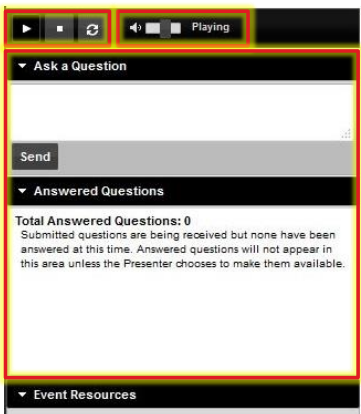
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OnCourse Learning
 HEALTHCARE

MEDICINAL CANNABIS

What Healthcare Professionals Need to Know

Carey S. Clark, PhD, RN, AHN-BC, RYT
 Associate Professor of Nursing at University of Maine at Augusta
 President, American Cannabis Nurses Association

Course Description and Objectives

- This course prepares the healthcare professional with a basic overview of cannabis as medicine. Contents include a brief history of cannabis use and prohibition, safety/ethical/legal concerns, the human endocannabinoid system, an overview of the cannabis plant's components, and cannabis as an evidence-based medicine. Implications for various healthcare professions are explored, and professional guidelines, ethics, and advocacy are highlighted.
- Learners will explore the endocannabinoid system, ways cannabis can be ingested, dosing approaches, side effects, medication interactions, ethics, legal issues, and safety.

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Presenter



Carey S. Clark, PhD, RN, AHN-BC, RYT has been a nurse since 1994, with a wide range of practical-clinical experience, including acute medical-surgical, pediatrics, inpatient psychiatric, home health nursing, parish nursing, and hospice nursing. Dr. Clark has taught across all levels of nursing in the traditional, online, and hybrid classroom settings.

- Board certified advanced holistic nurse
- Member of board of directors of the American Cannabis Nurses Association since 2016, current President
- Speaker at the Oncology Nursing Society National Congress and Regional Conferences
- Speaker at the national conference for the American Holistic Nursing Association



U.S. History and Cannabis Prohibition



1600s-1890: Hemp products produced for personal and commercial use. In 1619, every farmer in Virginia was required to grow hemp, and hemp was valued as legal tender in PA, VA, and MD.

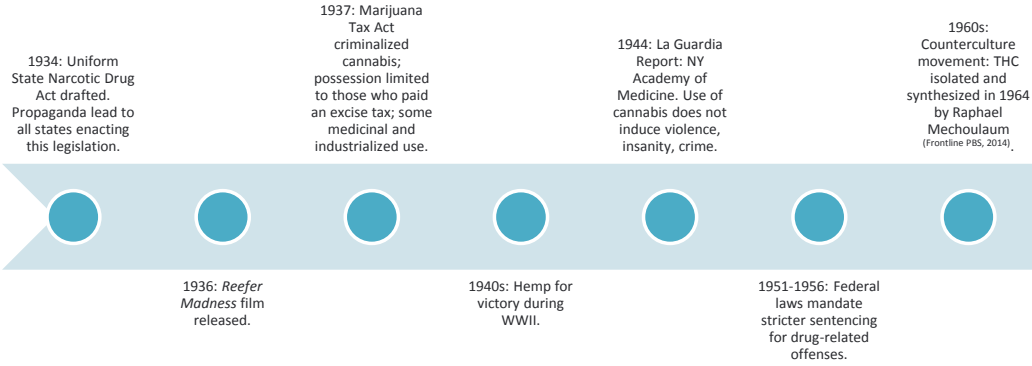
1906: Pure Food and Drug Act requires cannabis products to be labeled.

1930: Harry Anslinger becomes commissioner of the new Federal Bureau of Narcotics (Frontline PBS, 2014).

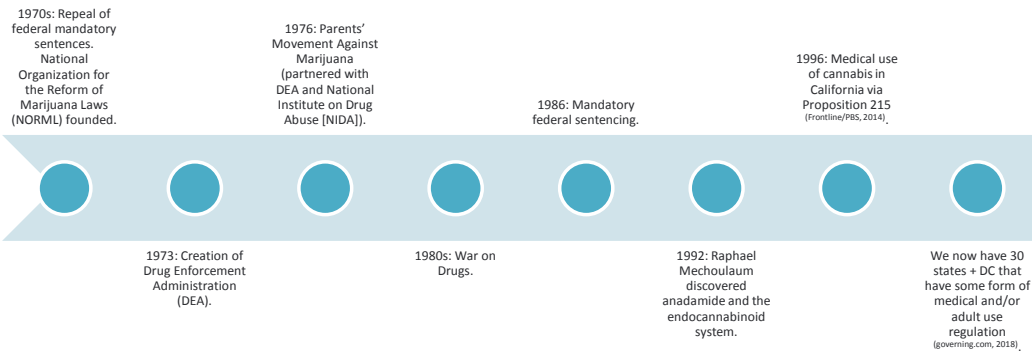
After the Civil War: decrease in hemp use, with new products and imports emerging.

1920s-1930s: Mexican immigrants brought cannabis to U.S. for recreational use, racist roots with prohibition during the Great Depression; began the stereotype of Mexicans linked with violence and crime (Frontline, PBS, 2014).

U.S. History and Cannabis Prohibition



U.S. History and Cannabis Prohibition



The Endocannabinoid System (ECS): What Is It?



- Human signaling system composed of:
 - Cellular cannabinoid receptors CB1 and CB2 (most studied; there are possibly many receptors in the ECS as yet to be identified).
 - Endogenous agonists of the receptors, mainly anandamide (N-arachidonoyl-ethanolamine) and 2-AG (2-arachidonoyl-glycerol). These are the physiological ligands (molecules that transmit signals in or between cells) that the body produces for the endocannabinoid receptors, and they create similar effects to cannabis in the body.
 - Enzymes and proteins that regulate endocannabinoid levels through degradation and inactivation of the endocannabinoids (DiMarzo, 2011).

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The Endocannabinoid System: What Does It Do?



- The ECS main role is to maintain homeostasis (Sulak, 2015).
- The ECS controls central and peripheral nervous systems, as well as other mammalian physiology such as energy uptake, immune responses, processing and storage, reproduction, and cellular fate (DiMarzo, 2011).
- Endo- and exogenous cannabinoids help create balance via inhibition and excitation of the nervous system, bone formation and resorption, inflammatory/ anti-inflammatory signaling, fat storage and release, supporting the management of blood sugar levels, blood pressure, and hormone levels (Viperman, 2014).

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The Endocannabinoid System: Where Is It?



CB-1 and CB -2 g-protein receptors

	CB1-R	CB2-R
Endogenous Ligands (EC)	AEA, 2-AG	2-AG
Major Tissue Location	Brain, peripheral nervous system	Immune system
Other Tissues	Pituitary, thyroid, adrenals, male-female reproductive, adipocytes, lung, liver, kidney	Spleen, tonsils, thymus, GI tract, osteocytes
General Action	Inhibits release of glutamate and GABA	Modulates cytokine release and immune response

Table based on Griffing & Thai (2015)

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The Endocannabinoid System: Where Is It?



Physiologic Actions	CB1-R	CB2-R
GI Motility	Decreases gut motility	Reduces bowel inflammation
Peripheral Nervous System	Nociceptive interneurons in the dorsal horn of the spinal cord	Anti-inflammatory action with mast cells in spinal cord
Reproductive	Male: Leydig cells Female: ovary, ducts, uterus, etc.	Placenta, embryo, T-cell cytokine release
Cardiovascular system	Hypotension, bradycardia	Atherosclerotic plaque inflammation

Griffing & Thai (2015)

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Endocannabinoid Deficiency

- **Cannabinoid Deficiency Syndrome:**

It should be clear that everybody makes cannabinoids and everybody needs cannabinoids to function.

- People who do not make enough cannabinoids need to supplement with exogenous cannabinoids through cannabis ingestion, in much the same way that a diabetic needs insulin supplementation.
- Dr. Ethan Russo's (2004) publication on Clinical Endocannabinoid Deficiency explains this particularly well:
http://www.nel.edu/pdf /25_12/NEL251204R02_Russo_.pdf

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Cannabinoids in Cannabis Plant

- Over 500 compounds in cannabis plant, many of them are potentially therapeutic and interact with the ECS.
- Well over 100 cannabinoids are found in the plant. When cannabis is heated, it loses the acid form by release of a carbon dioxide molecule: i.e., decarboxylation. This changes how the components interact with the ECS.



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Cannabis and Exogenous Cannabinoids



- The exogenous phytocannabinoid THC — the psychoactive compound in cannabis — works primarily on CB1 receptors (hence the “high feeling” in the brain), but also has indirect interactions with CB2-R.
- The cannabinoid CBD works primarily with the immune system and CB 2 receptors, as it creates homeostasis around the inflammatory response through influencing neurotransmitters; however, it does not technically have psychoactive effects. It also modulates effects of THC by changing the shape of the CB1 receptor so there is less affinity for THC (Clark, 2015).

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Cannabis and Exogenous Cannabinoids



- Other cannabinoids and their actions are still being studied, such as the non-psychoactive cannabinoid CBN, also found in cannabis.
- Our bodies react to both our own production of endogenous cannabinoids and to the ingestion of phytocannabinoids found in the cannabis plant, as well as other non-psychoactive plants such as echinacea (Clark, 2015).

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Other Cannabinoid Plants



Wilcox, 2016

BLACK PEPPERCORNS, ROSEMARY, COPAIBA

Contain beta-caryophyllene. CB2 agonist, supports immune system function.

BLACK TRUFFLES

Plant, but creates anandamide.

CHOCOLATE

Contains substances that inhibit FAAH enzyme (therefore inhibits the breakdown of anandamide).

ECHINACEA

Components interact with CB2 receptors to support immune system, decrease inflammation.

KAVA

Sedation, pain relief. Interactions with CB1.

LIVERWORT

Perrottetinene, interacts with CB1 receptor, similar structure to THC.

HEMP

Primarily CBD.

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Terpenes

- Terpenes/Terpenoids: over 200 aromatic essential oils found in the cannabis plant. May protect plant from bacteria and fungus. Act on receptors and neurotransmitters. May serve to decrease THC intoxicating effect, allowing for a wider range in therapeutic effects.
- Terpenoids are generally recognized as safe by USFDA.
- They share a precursor with phytocannabinoids.
- May account for strain therapeutic values differences.
- Lipophilic; interact with cell membranes, neuronal/muscle ion channels, neurotransmitter receptors, g-protein coupled receptors, second messenger systems, and enzymes (Russo,2011).



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Terpenes



Boyar K, 2016

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Common Terpenes in Cannabis

A-PINENE	LINALOOL	BETA-CARYOPHYLLENE	MYRCENE	LIMONENE
Anti-inflammatory Bronchodilator Memory Antibacterial	Anesthetic Anti-convulsant Analgesic Anti-anxiety Calming Sedation	Anti-inflammatory Analgesic GI cell protectant Antifungal	Sedative effects Sleep aid Muscle relaxant Calming Anti-spasm	Treats acid reflux Anti-anxiety Antifungal Antibacterial Anticarcinogenic
Also found in pine needles	Also found in lavender	Also found in black pepper; other herbs and spices, cloves	Also found in hops Smells like cloves	Also found in citrus Smells like citrus
Counteracts effects of THC; helps with memory		Activates CB2 receptors	Most common one found in cannabis; increases THC psychoactivity	Usually second to fourth most present

Based on SCLabs (n.d.)

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The Entourage Effect

- All components of cannabis work together to interact with the ECS.
- Implications for future strains, with new combinations of cannabinoids and terpenoids, to create effective personalized medicines for specific health issues (Russo, 2011).
- Consider the benefits of whole plant medicine vs. selected synthetic cannabinoids.

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Supporting Patient Use of Cannabis as Medicine

CHALLENGES

Prohibition, complexity of the plant, quality control, dearth of RCT (MacCallum & Russo, 2018).

THE PLANT

Sativa (taller, thinner, lankier, thin-pointed leaves: alert, head-high, increased energy, daytime, Mycerene < 0.5%) vs. Indica (short, stalky, broad/chunky leaves; body-high, relaxation, sleep/pain, nighttime, Mycerene > 0.5%) vs. hybrid (mixing strains; may be indica dom or sativa dom) (Crescolabs, n.d.).

STRAINS

Can vary from region to region; personalized medicine. N-of-1; based on symptomology management, efficacy, and side effects (MacCallum & Russo, 2018).

CANNABIS MEDICINE

Cultivated organically, extracted/processed using Good Manufacturing Practice, tested with information on cannabinoid and terpene profile, free of pesticides and contaminants (microbial and heavy metals) (MacCallum & Russo, 2018).



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Ingestion Methods



MacCallum & Russo, 2018

RAW PLANT, JUICING

THCA (anti-inflammatory, anti-emetic, neuroprotective, anticonvulsant) and CBDA (anti-emetic, anti-anxiety).

TOPICALS

Use nano- or ionized particles or omega fats. Variable onset duration; localized.

ORAL INGESTION

20%-30% absorption. Oils, capsules, edibles. Onset 60-180 minutes, duration 6-8 hours.

OROMUCOSAL

Nabiximol spray (1 CBD:1 THC), tinctures, lozenges. Onset 15-45 minutes, duration 6-8 hours.

INHALATION

10%-60% absorption. Smoking vs. vaping. Onset 5-10 minutes, duration 2-4 hours.

SUPPOSITORIES

May be helpful for specific GI symptoms.

CONCENTRATES

Shatter, dabs, high THC increases side effects (recreational).

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Dosing

- If cannabis plant is legal in the state, start with cannabis vs. trial of synthetics.
- Dosing, considering THC mg: "Start low, go slow, stay low."
- Inhalation: One inhalation, wait 15 minutes. Proceed with one inhalation every 15-30 minutes until symptoms are relieved. Slowly titrate to avoid side effects. Duration 2-4 hours.
- Use CBD dominant to avoid side effects of THC.
- Euphoria state is not needed for relief of symptoms.

MacCallum & Russo, 2018

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Titration

- Start with oral preparations at bedtime
 - Day 1-2: 1.25-2.5 mg THC
 - Day 3-4: increase by 1.25-2.5 mg THC
 - Days 5-6: increase again by 1.25-2.5 mg THC every two days until symptom relief is achieved
 - Side effects: reduce back to best-tolerated dose
- Daytime strategy: dose 2-3 times/day
 - Day 1-2: 2.5 mg THC once/day
 - Day 3-4: 2.5 mg THC/BID
 - Increase as tolerated up to a max of 15 mg THC, divided BID or TID
 - Doses > 20-30 mg may increase adverse effects or cause tolerance with no increase in efficacy.
- CBD: 5-20 mg, divided BID or TID.

More dosing guidelines:
<http://cannabisclinicians.org/wp-content/uploads/2012/02/Dosing-Guidelines-Carter-et-al.pdf>

- Chronic conditions: long-acting oral preparations with vaping for breakthrough; 60-80 minute onset, 6-8 hour duration
- Most medicinal patients use 1-3 grams of cannabis/day without escalating doses (MacCallum & Russo, 2018).
- Patients can keep a cannabis diary: time of ingestion, dose, strain, effectiveness, side effects (Clark, 2018)



The people in this photograph are models, and the scenario is fictitious.

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Pharmacokinetics

- Absorption, distribution, metabolism determine onset and duration,
- Absorption has the most variability: lipophilicity, bioavailability, which organ is processing.
- Topical/oral: best absorbed with some fat (omegas) or polar solvent: ethanol.
- Nano-ionized particles may help with absorption.
- Recent meal time, depth of inhalation, temperature of vaporization.
- 20%-30% oral absorption; 10%-60% inhalation.

MacCallum & Russo, 2018

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Contraindications



- Pregnancy and lactation.
- Psychosis.
- Unstable cardiac conditions (angina, tachycardia).
- Vulnerable populations: children, teens, people with history of addiction.
- Patients with COPD and asthma should avoid smoking. (MacCallum & Russo, 2018)

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Side Effects

Safe medicine: No overdose due to lack of CB1 receptors in the brainstem

- Most Common
 - Drowsiness
 - Fatigue
 - Dizziness
 - Dry mouth
 - Cough/phlegm/bronchitis (smoking related)
 - Anxiety
 - Nausea
 - Cognitive effects
- Common
 - Euphoria
 - Blurred vision
 - Headache
- Rare
 - Orthostatic hypotension
 - Toxic psychosis/paranoia
 - Depression
 - Ataxia
 - Tachycardia
 - Cannabis hyperemesis
 - Diarrhea

MacCallum & Russo, 2018

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Drug Interactions



May increase bleed time; caution with NSAIDs and blood thinners.

No medication that can't be used with cannabis.

Metabolized by CYP450 liver cytochrome; serum levels may increase with inhibitors or decrease with enzyme inducers.

Rare drug interactions. (MacCallum & Russo, 2018)

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Safety Issues



- Diversion
- Children and pets
- Social and work life: some patients may use CBD in day, THC at night.
- Driving: first become accustomed to the medication. Wait 4 hours post inhalation, 6 hours after ingested, or 8 hours post euphoria. User should not drive if he/she feels high
- Daily use, low doses, develop tolerance

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Cannabis Use Disorder

- Greater in men, highest risk late teens to mid-20s, associated with other substance use and mental health disorders (NIH, 2016).
- DSM-5 criteria:
 - A problematic pattern of cannabis use leading to clinically significant impairment or distress as manifested by at least two of the following occurring in a 12 month period:
 1. Cannabis is often taken in larger amounts over a longer period than was intended.
 2. There is a persistent desire or insignificant effort 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 failure to fulfill major role obligations at work, school or home.
 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 situations which is physically hazardous.
 9. Cannabis use is continued despite knowledge of having persistent or recurrent physical or psychological problems that are unlikely to have been caused or exacerbated by cannabis.
 10. Tolerance, as defined by either:
 - 1) A need for markedly increased amounts of cannabis to achieve intoxication and desired effect, or
 - 2) A markedly diminished effect with continued use of the same amount of cannabis.
 11. Withdrawal, as manifested by either:
 - 1) The characteristic withdrawal symptoms for cannabis, or
 - 2) A closer related substance is taken to relieve or avoid withdrawal symptoms.

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Cannabis Withdrawal

Anxiety
 Depression
 Decreased appetite
 Headaches
 Insomnia
 Irritability
 Muscle tension
 Nausea
 Nightmares/vivid dreams
 (Miller, Oberbarnscheidt, & Gold, 2017)

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Generally agreed that alcohol, heroin, crack, and tobacco are the most harmful substances when it comes to addiction. Cannabis is far less addictive and harmful (Van Amsterdam, Nutt, Phillips, & Van Den Breek, 2015; Lachenmeier & Rehm, 2015).

Comparing Addictive Qualities of Popular Drugs
(Higher score indicates more serious effect)

Drug	Dependence	Withdrawal	Tolerance	Reinforcement	Intoxication
Nicotine	6	4	5	3	2
Heroin	5	5	6	5	5
Cocaine	4	3	3	6	4
Alcohol	3	6	4	4	6
Caffeine	2	2	2	1	1
Marijuana	1	1	1	2	3

Henningfield & Hills, 1994

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Recreational vs. Medicinal

Intent

Biphasic medicine; increased dosing does not mean more efficacy of the medications; increasing tolerance

Safer alternative to more dangerous drugs/medications

May be an exit drug (Walsh et al, 2017)

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Legal and Ethical Issues



- Smoke/secondhand smoke
- Social justice issues
- Right to autonomy
- No harm/decreasing harm
- Advocacy
- Know your state practice act
- Education!



Cannabis Concerns



EXIT VS. ENTRY DRUG

NIDA vs harm reduction tool. (Lau, Sales, Averill, Murphy, Sato, & Murphy, 2015)

FORMING BRAIN IN ADOLESCENCE

Memory issues with inconclusive data as to degree of impairment (smaller hippocampus), may negatively impact size of amygdala, rat studies show poorer cognitive performance. Earlier, more frequent use leads to brain structural changes. (Jacobus & Tapert, 2014)

MENTAL HEALTH ISSUES

Depression (heavy use related). (Lev-Ran, Roerecke, LeFoll, George, McKenzie, & Rehm, 2014)

SUICIDALITY

May be related to difficulties with interpersonal functioning. (Buckner, Lemke, Walukevich, 2017)

SCHIZOPHRENIA

Meta-analysis with mixed results, consider family history, stress of environment, and childhood abuse; most studies look at one to two symptoms, psychosis vs. schizophrenia diagnosis. (Australian Government, Department of Health, 2016)

Cannabis Effectiveness: Levels of Evidence

Level of Evidence of Efficacy	Conclusive or substantial evidence	Moderate evidence	Limited evidence	Insufficient evidence
Benefits	<ul style="list-style-type: none"> • Adult chronic pain • Multiple Sclerosis/spasticity • Chemotherapy-induced nausea/vomiting • Intractable seizures • Dravet and Lennox-Gestaut syndromes (CBD) 	<ul style="list-style-type: none"> • Sleep disturbances related to pain, MS, fibromyalgia, sleep apnea • Decreasing intraocular pressure in glaucoma 	<ul style="list-style-type: none"> • Dementia • Parkinson's • Schizophrenia symptoms • PTSD symptoms • Appetite/weight issues • HIV/AIDS • Traumatic brain injury • Anxiety (CBD) • Tourette syndrome 	<ul style="list-style-type: none"> • Depression • Addiction abstinence • IBS symptoms • Cancer-treatment • Cancer-associated anorexia • ALS symptoms • Dystonia

MacCallum & Russo, 2018

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Cancer



- National Cancer Institute (NCI) recognizes potential for cannabis cure; still have mostly in vivo and in vitro studies. (NCI, 2017)
- Early palliation: Pain, nausea, sleep issues, nutritional issues, depression. (Abrams, 2016)
- Minimal body of scientific evidence that human cancer can be cured by cannabis: animal-mice studies and in vitro studies are very promising.
- Anecdotal evidence of people curing cancer with cannabis oil (high potency, concentrated). (Abrams)
- Does seem to enhance effectiveness of chemotherapy. (NCI)
- Glioblastoma multiforme seems to be most receptive to cannabis treatment, possibly due to great concentration of CB1 receptors in brain; affinity for THC. (Abrams; NCI)

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Oncology Patients

“Cannabis use among patients at a comprehensive cancer center in a state with legalized medicinal and recreational use,” *Cancer*, 25 Sept 2017; Pergam et al

Cross-sectional survey of over 927 patients

66% patients had used cannabis previously
(24% last year, 21% in last month).

Use for both physical and neuro-psych symptoms.

222 active users

74% weekly, 56% daily, 31% multiple times/ day.

51% felt cannabis provided major benefits; 39% moderate

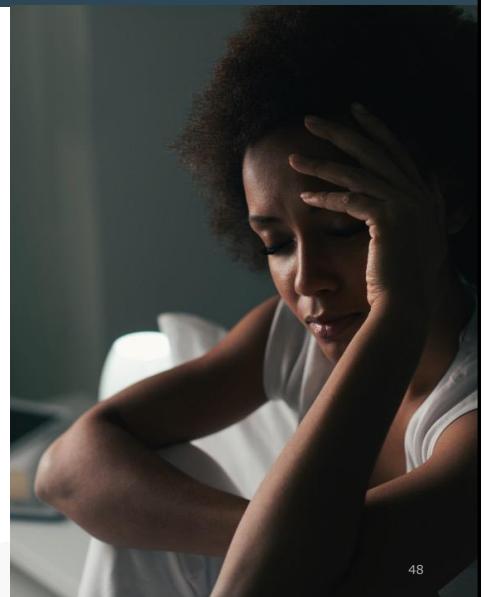
Inhaled (70%), medibles (medicated edible products) (70%)

74% indicated wanting info about cannabis from healthcare providers: only 15% did get info from HCP

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PTSD

- Dampen the strength or emotional impact of traumatic memories through synergistic mechanisms.
- Make it easier for people with PTSD to rest or sleep, to feel less anxious and less involved with flashback memories.
- The presence of endocannabinoid-signaling systems within stress-sensitive nuclei of the hypothalamus, as well as upstream limbic structures (amygdala), point to the significance of this system for the regulation of neuroendocrine and behavioral responses to stress. Passie et al, 2012



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PTSD

- Cannabinoids might play a role in fear extinction and anti-depressive effects. Further studies are warranted in order to evaluate the therapeutic potential of cannabinoids in PTSD. (Passie et al, 2012)
- A study in New Mexico with 80 PTSD patients showed a 75% decrease in Clinician-Administered PTSD Scale (DSM-IV) when cannabis was introduced. (Greer, Grob, & Halberstadt, 2014)
- May be an increased risk for cannabis use disorder for PTSD patients. (Kanasagra et al, 2017).

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Pain



Manzanares, Julian, & Carrascosa, 2006

Cannabinoid receptors and endocannabinoids are present in the pain circuits throughout the nervous system: CB1 receptors modulate pain sensitivity (nociception). CB2 receptors activation may support decreased inflammation.

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Pain



- Cannabis and chronic pain: better than opiates (fewer risks, fewer side effects). Most studies have had small N due to prohibition effect.
- *Co-agonists*: Cannabis increases the pain-relieving effects of morphine, as discovered by researchers at UCSF. The two medications are synergistic, and this provides great hope for patients suffering intractable pain at end of life, chronic pain sufferers, and opiate addicts.

Abrams & Guzman, 2015

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Multiple Sclerosis



Nielsen et al, 2018

- Review of 11 systematic reviews: 32 studies, including 10 moderate- to high-quality RCT.
- Recent reviews show effective to modestly effective for pain and spasticity.
- Gap of studies with non-cannabinoid comparators.

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Interprofessional Work

EMS

No overdose on natural cannabis: supportive care.

SOCIAL WORKERS

Evidence-based treatment, concerns with addiction, teen use, workplace issues, and diversion. Finding support for medicinal patients.

PHARMACISTS

Work in dispensaries (required in CT, MN, NY, PA). Help patients with dose, strain choice, education, registration process.

NUTRITIONISTS

Holistic nutrition, supporting the ECS through nutrition.

CANNABIS CLINICIANS GUIDELINES

<http://cannabisclinicians.org/scc-practice-standards/> MDs/APRNs develop relationship with patient; recommend as per state guidelines.

AMERICAN CANNABIS NURSES ASSOCIATION SCOPE/STANDARDS

<https://cannabisnurses.org/page-1765547> Support patients holistically



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End the Stigma

- Educate yourself, educate others, educate your professional societies and organizations.
- Work with patients; support autonomy.
- Advocate for cannabis law reforms.
- Consider social justice issues, political action.
- Call it cannabis.

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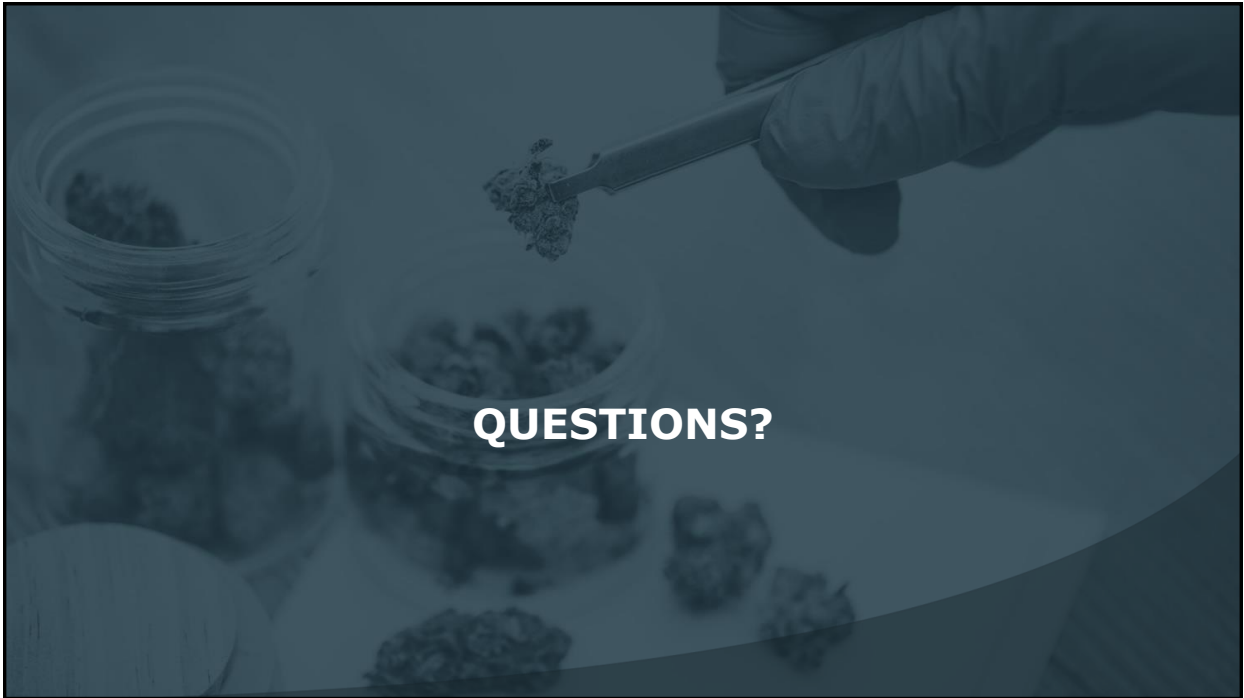
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QUESTIONS?



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