Medical Cannabis for Symptom Management

Amy Allen Case MD, FAAHPM
Lee Foundation Endowed Chair Supportive and Palliative Care
Roswell Park Comprehensive Cancer Center
Associate Professor of Medicine
University at Buffalo Jacobs School of Medicine
Division of Geriatrics and Palliative Medicine
Objectives

• Describe the origin and history of cannabis
• Review the pharmacology of medical cannabis
• Examine the evidence for the medicinal uses for cannabis for pain and non-pain symptoms
• State the adverse effects of medical cannabis
• Interpret laws and process for prescribing and tips for use in practice

• Disclosures: None
• Acknowledgements:
  • Sidra Anwar MD, Laszlo Mechtler MD, FAAN, FASN, Eric Hansen MD
Case

• You are seeing a 70 year-old woman with metastatic NSCLC. She struggles with fatigue, musculoskeletal pain, constipation, and decreased appetite. You have also noticed her flat affect and depressed mood. Today she is reporting worsening chronic peripheral neuropathy from her diabetes and increased nausea related to her ongoing chemo.

• She asks about medical marijuana. Do you:
  A. Recommend it as you feel it might be beneficial for her
  B. Discourage
  C. Are unsure, want to learn more
United States of Marijuana

The state of the union is strong for marijuana, a $9 billion industry. Recreational weed is legal in nine states and Washington, D.C. Medical marijuana is legal in 30 states, but it’s still prohibited by the federal government.
Basic Terminology

• *Marijuana* is frequently a synonym for *cannabis* but technically the two terms are separate.

• Cannabis is the botanical term for the hemp plant cannabis sativa.

• Phytocannabinoids (THC and CBD) and terpenes are most important active components
  • Phytocannabinoids are found in leaves
  • Terpenes are aromatic components produced in glandular part of plant’s flower bud
The Entourage Effect

• The enhancement of cannabinoid effects by non-cannabinoid components of plant
• There are more than 480 natural components of the cannabis plant, 66 are cannabinoids
Cannabis Sativa

• Tall, and laxly branched with long and narrow leaves

• Provides a “high” feeling, an energetic buzz, uplifting

• ↑↑ THC: ↓ CBD

• “Recreational users” typically seek this strain
Cannabis Indica
“Kush” (Hindu Kush mountain range)

- Short, conical, dense branches with short, broad leaves
- Provides a “stoned” feeling, sedation
- Used for sleep, pain relief, anxiolysis
- ↑THC: ↑CBD
- “Medical users” typically seek this strain
History of Cannabis

- 2900 BC- Chinese emperor Fu Hsi references “Ma” (cannabis) as a “popular medicine”
- 2700 BC- Father of Chinese medicine Emperor Shen Nung discovers healing properties of cannabis
- 1213 BC- Egyptians use cannabis for glaucoma, inflammation
- 1000 BC- Bhang (mix of cannabis and milk) used as medicine in India
- 200 BC- Medical cannabis used in ancient Greece
History of Cannabis

• 1500s- The Spanish brought cannabis to the Americas
• 1839- Sir William O’Shaughnessy researched cannabis in India
• 1850- United States Pharmacopeia classifies marijuana as a legitimate medical compound
• 1937- Marijuana Tax Act banned cannabis use and sales
• 1970- Controlled Substances Act (CSA) Schedule I classification
• 2013- Cole Memorandum- U.S. DOJ defined enforcement priorities which made prosecution of medical cannabis unlikely (rescinded 2018 US Attorney General Jeff Sessions)
• Today- Medical cannabis is not FDA approved for any medical condition
Cannabinoids

Endocannabinoids
- Anandamide or AEA
- 2-AG

Phytocannabinoids
- THC
- CBD
- CBC
- CBG
- THCV
- CBN

Synthetic Cannabinoids (THC)
- Dronabinol (Marinol®)
- Nabilone (Cesamet®)
CBD

Antibacterial
Inhibits cancer cell growth
Neuro-protective
Promotes bone growth
Reduces seizures and convulsions
Reduces blood sugar levels
Reduces function in the immune system
Reduces inflammation
Reduces risk of artery blockage
Reduces small intestine contractions
Reduces vomiting and nausea
Relieves pain
Relieves anxiety
Slows bacterial growth
Suppresses muscle spasms
Tranquilizing
Treats psoriasis
Vasorelaxant
Endocannabinoid system

Cannabinoid receptors
- CB1 R - CNS
- CB2 R - Immune cells
  - Inhibit B and T cell activation

Endogenous agonists:
- Anandamide (AEA)
- 2-AG

Binds to pre-synaptic neuron and inhibits the release of other neurotransmitters:
- Glutamate
- NE
- GABA
- Acetylcholine

Figure from: Information for Health Care Professionals Cannabis (marihuana, marijuana) and the cannabinoids- Prepared by Health Canada. Feb 2013
Pharmacologic effects of THC

- Psychotropic
  - Initial euphoria and relaxation followed by depressant period
  - Alterations in memory and cognitive perceptual abilities
- Immunosuppressive/immunomodulatory
- Cardiovascular
  - Tachycardia, orthostatic hypotension, peripheral vasodilation
  - Analgesic
  - Anti-emetic
  - Appetite stimulation
Pharmacologic actions of CBD

- Anticonvulsive
- Analgesic
- Anti-anxiety
- Anti-depressant
- Anti-psychotic
- Anti-inflammatory
- Immunosuppressive
- Inhibits FAAH enzyme
CBD and THC synergism

• CBD reduces psychoactive effects of THC and improves tolerability

• CBD alters metabolism of THC and works synergistically

• High CBD:THC products are less associated with psychotic symptoms when compared to low CBD:THC cannabis
CB1 receptors

• Primarily in brain
• Not significant in brainstem (no effect on respirations or heart rate)
• Other locations: adipocytes, endocrine and exocrine glands, hepatocytes

• Anti-nociceptive effects
• Parasympathetic- anti emetic effects
• Neuroprotection
• Neuroplasticity

CB2 Receptors

• Immunomodulation:
  • Monocytes
  • Macrophages
  • B cells
  • T cells
• Liver, spleen, tonsils
• Microglia

• Expressed 100 fold less in neurons relative to $\text{CB}_1$ receptors.
  • Activation reduces neuroinflammation from cytokines or neuropathic injury
- Partial Agonist of CB1
- Euphoria
- Relaxation
- Anxiety
- Memory Impairment

- CB1 negative allosteric modifier
- Inhibits THC for binding to CB1
- Decrease THC psychotoxicity
  - ↓ anxiety, ↓ memory effects
- May prevent degradation of 2-AG (natural endocannabinoid)
THC: CBD Chemotypes or preparations

• THC predominant
  • 50:1, 19:1, 16:1

• Balanced/intermediate THC:CBD
  • 1:1, 4:1

• CBD dominant
  • CBD only, 1:>20

Psychoactivity
Medical cannabis products

• New York State
  • Oral oil tinctures
  • Oils for vaporization
  • Capsules

• Available in other states
  • Patches
  • Suppositories
  • Topical creams
Approved Cannabinoid Medicines

• Dronabinol THC
  • Chemo-induced nausea/vomiting (1985)
  • Anorexia associated with weight loss from AIDS (1992)

• Nabilone THC
  • Chemo-induced nausea/vomiting (1986)
  • Nabiximols 1:1 THC:CBD (US Phase III clinical trials)

• Sativex®- Oromucosal spray approved in 21 countries outside US for:
  • Spasticity from MS
  • Neuropathic pain in MS patients
  • Intractable cancer pain
Cannabinoids improve chronic pain

• True

• False
Institute of Medicine Report, 1999

- The Institute of Medicine issued a report based on a summary of the peer-reviewed literature addressing the efficacy of therapeutic marijuana use.

- The 1999 study found at least some benefit for smoked marijuana:
  - Stimulating appetite, particularly in AIDS-related wasting syndrome
  - Chemotherapy-induced nausea and vomiting
  - Severe pain
  - Some forms of spasticity

- **Strong evidence**
  - Chronic pain
  - Chemotherapy induced nausea and vomiting
  - Spasticity in multiple sclerosis (patient reported)

- **Moderate evidence**
  - Sleep disorders related to chronic illnesses

- **Limited evidence**
  - Appetite stimulation in AIDS
  - Anxiety, PTSD, depression in those with chronic disease
  - Spasticity in multiple sclerosis (clinician reported)

- **No evidence**
  - Anti-cancer effect in humans
Cannabis for neuropathic pain- Mücke et al Cochrane Database Review 2018

• 16 studies, 1750 subjects
• 2 to 26 weeks long
• Compared an oromucosal spray with a plant-derived combination of tetrahydrocannabinol (THC) and cannabidiol (CBD) (10 studies), nabilone (two studies), inhaled herbal cannabis (two studies) and dronabinol (two studies) against placebo (15 studies) and an analgesic (dihydrocodeine) (one study).
• 50% or greater pain relief compared with placebo (21% versus 17%; 95% confidence interval (CI) 0.00 to 0.09) NNT 20
• 30% or greater compared with placebo (39% versus 33%; RD 0.09 (95% CI 0.03 to 0.15); NNT 11
• 10% of cannabis versus 5% of placebo withdrew due to AEs; NNTH 25
• Cannabis increases nervous system AEs compared with placebo (61% versus 29%; RD 0.38 (95% CI 0.18 to 0.58); NNTH 3
Systematic Review (SR) for neuropathic pain-Petzke et al 2016

• 15 RCTs
• 1619 participants
• 10 used a plant-derived oromucosal spray with THC/CBD, 3 studies used a synthetic cannabinoid (2 with nabilone and 1 with dronabinol) and 2 studies used medicinal cannabis.
• Meaningful pain relief response cutoff >30%
• NNT 14
Cannabinoids for medical use- Pain
SR- Whiting et al. JAMA 2015

• 28 randomized trials- 2,454 participants

• Medical conditions: Neuropathy (17 trials); other conditions included cancer pain, multiple sclerosis, rheumatoid arthritis, musculoskeletal issues, and chemotherapy-induced pain.

• 22 of these trials evaluated plant-derived cannabinoids, 5 trials evaluated synthetic THC

• All but 1 of the selected primary trials used a placebo control, while the remaining trial used an active comparator (amitriptyline)
SR for neuropathic pain- Whiting et al. JAMA 2015

• Patients who reported a reduction in pain of at least 30% was greater with cannabinoids than with placebo (OR, 1.41 [95% CI, 0.99-2.00])

• One trial assessed smoked THC and reported the greatest beneficial effect (OR, 3.43 [95% CI, 1.03-11.48])

• SAEs: Cannabinoids were associated with a much greater risk of any AE, serious AE, withdrawals due to AE, and a number of specific AEs
SR for neuropathic pain- Andrea et al, 2015

- 5 RCTs of the effect of inhaled cannabis
- 178 patients
- OR 3.22 for pain relief vs placebo (95% CI 1.59- 7.24) tested across 9 THC concentrations
- Meaningful pain relief response cutoff >30%
- NNT 5.6
- Possible dose dependent effect
Cannabis for joint pain

• Cannabis is commonly used for joint pain

• High frequency of satisfaction with cannabis
  • 63% with arthritis
  • 77% with fibromyalgia

• Many state that cannabis limits their opioid use- 94% fibromyalgia, 81% arthritis.

• In the limited RCT of commercial cannabis no analgesic benefits were seen in those with osteoarthritis or rheumatoid arthritis.

# Cannabis for Cancer Pain-RCT from 2010 to 2017

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number/Duration</th>
<th>Cannabis</th>
<th>Comparator</th>
<th>Primary Outcome</th>
<th>Secondary Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichtman/2017</td>
<td>397/5 weeks Opioid tolerant</td>
<td>Nabiximols</td>
<td>Placebo</td>
<td>NRS wk3,5; NS P=0.085</td>
<td>Improved sleep p=0.027, improved PGIC, SGIC, PSQ</td>
</tr>
<tr>
<td>Johnson/2010</td>
<td>177/4 weeks Opioid tolerant</td>
<td>THC spray THC/CBD spray</td>
<td>Placebo</td>
<td>Change in NRS THC/CBD p=0.014, THC p=0.32</td>
<td>EORTC-QLQ-NS Increased nausea with THC/CBD Rescue doses-NS</td>
</tr>
<tr>
<td>Portenoy/2012</td>
<td>360/ 5 weeks Opioid tolerant</td>
<td>Nabiximols low, medium, high dose</td>
<td>Placebo</td>
<td>30% decrease in pain intensity p=0.32, better response with low dose</td>
<td>Improved sleep-low dose No difference PGIC, PAC-QOL Increased nausea with nabiximols</td>
</tr>
<tr>
<td>Cote/2016</td>
<td>56/4weeks HN cancer undergoing therapy</td>
<td>Nabilone</td>
<td>Placebo</td>
<td>EORTC QLQ p=0.43</td>
<td>VAS pain, analgesic consumption, nausea, appetite, sleep-NS</td>
</tr>
</tbody>
</table>

NRS= Numerical rating scale, PGIC= Patient global impression of change, SGIC= Subject global impression change, NS= Not significant
Chronic pain- Conclusion 4-1

• There is substantial evidence that cannabis is an effective treatment for chronic pain in adults

• Best evidence for neuropathic pain
Chemotherapy induced nausea and vomiting (CINV)
Cannabis for nausea and vomiting

- Central regulation of emesis occurs via the:
  - Dorsal Vagal Complex (DVC)
  - Area Postrema – located outside BBB, provides communication between blood-borne signals
  - Nucleus of the solitary tract
  - Dorsal motor nucleus of the vagus

}
SR- CINV Tramer et al BMJ 2001

- 30 RCT
- 1366 patients receiving chemotherapy
- Oral and IM synthetic THC
- Cannabinoids were more effective antiemetics than prochlorperazine, metoclopramide, chlorpromazine, thiethylperazine, haloperidol, domperidone, or alizapride
- RR 1.38 (95% CI 1.18-1.62)
- NNT nausea-6
- NNT vomiting- 8
- THC did not add to ondansetron as prophylaxis
SR- CINV Tramer et al BMJ 2001

• Harmful side effects also occurred more often with cannabinoids:
  • Dizziness 2.97 (2.31 to 3.83), NNTH 3
  • Dysphoria or depression 8.06 (3.38 to 19.2), NNTH 8
  • Hallucinations 6.10 (2.41 to 15.4), NNTH 17
  • Paranoia 8.58 (6.38 to 11.5), NNTH 20
  • Arterial hypotension 2.23 (1.75 to 2.83), NNTH 7
Cochrane Review CINV- Smith et al. 2015

- 23 trials for CINV with synthetic THC
- Mix of placebo and active comparators
- All favored cannabinoids, though not all statistically significant
- There was no difference in outcome between patients who were cannabis naïve and those who were not
Cannabis for chemotherapy induced nausea and vomiting

• No head-to-head comparisons with current standard CINV treatments: 5HT3 R antagonists, NK1 inhibitors
• No RCT for nausea secondary in advanced cancer— case report (GI mets), isolated case series
• In selected patients, cannabinoids may be useful as mood enhancing adjuvants for the control of chemotherapy related sickness
• Cannabinoids should be considered as useful adjunctive treatment for people on moderately or highly emetogenic chemotherapy that are refractory to other antiemetic treatments, when all other options have been tried
• Despite incidence of SE, cannabinoids seems to be patient preference
Chemotherapy induced nausea and vomiting

Conclusion 4-3

• There is substantial evidence that oral cannabinoids are effective antiemetics in the treatment of chemotherapy-induced nausea and vomiting.
Anorexia
MARIJUANA

PROUD SUPPORTERS OF THE SNACK FOOD INDUSTRY!
How does cannabis stimulate appetite?

• CB1R are present in the hypothalamus (controls food intake) and in mesolimbic reward system which may be involved in the motivational/reward aspects of eating.

• Endocannabinoids and CB1 agonists inhibit vagal fibers to promote eating.
RCT Anorexia in advanced cancer- Jatoi et al. JCO 2002

• RCT 485 patients with advanced cancer
• Loss of appetite or weight was a problem and reported the loss of 5 pounds or more during 2 months and/or a daily intake of less than 20 calories/kg of body weight
• 3-arms: megestrol acetate, THC and both
• O-FAACT
  • FACCT response 75% megestrol vs. 49% THC
  • Cannabis did not add to megestrol
RCT Anorexia in advanced cancer- Strasser, et al. JCO 2016

• 164 patients with advanced cancer and weight loss of greater than 5 percent over 6 months were randomized 2:2:1 to receive treatment with a cannabis extract (standardized to THC 2.5 mg and cannabidiol 1.0 mg), THC 2.5 mg, or a placebo twice daily for 6 weeks.

• Appetite, mood, and nausea were monitored daily. Cancer-related quality of life and cannabinoid-related toxicity were also monitored.

• No difference between the groups in appetite, quality of life, or toxicity.
SR anorexia/cachexia in HIV/AIDS- Whiting et al. JAMA 2015

- 4 RCT involving 255 patients
- All four studies included dronabinol, with one investigating inhaled cannabis as well.
- Three trials were placebo-controlled, and one used megestrol acetate as the comparator.

- The review authors concluded that there was some evidence suggesting that cannabinoids were effective in weight gain.
SR Anorexia/cachexia in HIV/AIDS Lutge et al. 2013

• 7 RCTs- trials compared dronabinol or inhaled cannabis with a placebo or with each other
• In one study the individuals’ weights increased significantly more on higher doses of cannabis and dronabinol than on lower doses
• In another trial, study with 88 evaluable patients failed to find any significant difference
• Changes in appetite, food, and caloric intake were not deemed to be evaluable in any of the studies
• Authors concluded the evidence is lacking for utility of cannabis in AIDS associated anorexia
Anorexia- Conclusion 4-4(a) and 4-4(b)

• 4-4(a) There is limited evidence that cannabis and oral cannabinoids are effective in increasing appetite and decreasing weight loss associated with HIV/AIDS.

• 4-4(b) There is insufficient evidence to support or refute the conclusion that cannabinoids are an effective treatment for cancer-associated anorexia-cachexia syndrome.
Anxiety
There is high level of evidence that cannabis improves anxiety and depression

• True

• False
RCT Anxiety- Bergamaschi et al 2011

• 24 never-treated patients with Social Anxiety Disorder were allocated to receive either CBD (600 mg) or placebo.

• Cannabidiol did help reduce anxiety score on Anxiety Visual Analogue Mood Scale 107 minutes after administration compared to placebo.
Chronic pain trials reporting on anxiety symptoms as secondary outcomes

• These trials suggested greater short-term benefit with cannabinoids than a placebo on self-reported anxiety symptoms.

• Trials suggested to have high bias.

• In contrast, evidence from observational studies found moderate evidence that daily cannabis use is associated with increased anxiety symptoms.
• There is limited evidence that cannabidiol is an effective treatment for the improvement of anxiety symptoms, in individuals with social anxiety disorders.
Depression

• 5 RCT involving 634 patients without cancer– chronic pain, multiple sclerosis.

• Found cannabis not better than placebo.

• One study that evaluated three doses of nabiximols found increased depressive symptoms at the highest dose, but no difference compared to the placebo at lower doses.
• There is limited evidence that nabiximols, dronabinol, and nabilone are ineffective treatments for the reduction of depressive symptoms in individuals with chronic pain or multiple sclerosis.
Insomnia

- 2 RCTs (54 participants) had sleep as primary outcome, one trial evaluated patients with OSA, and the other included patients with fibromyalgia.
- 19 trials (3231 participants) evaluated sleep as secondary outcome in patients with chronic pain and multiple sclerosis

Results:
- Sleep was improved in most trials
- In pain trials improved sleep may be the indirect analgesic effect of cannabis
- No clinical trials that has evaluated the effects of cannabinoids in patients with primary chronic insomnia.
• There is moderate evidence that cannabinoids, primarily nabiximols, are an effective treatment to improve short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis.
Seizures
Cannabis for seizures- Perucca et al 2017

• Activation of CB1 receptor has proven to dampen neurotransmission and produce an overall reduction in neuronal excitability.

• High quality randomized trials have demonstrated that cannabidiol in patients with Dravet and Lennox- Gastaut Syndrome reduces seizures

• Will cannabidiol become an antiseizure medication for acquired seizure disorders?
Dr. Sanjay Gupta:
Why I changed my mind on weed. Well I am here to apologize.

We have been terribly and systematically misled for nearly 70 years in the United States, and I apologize for my own role in that. I apologize because I didn’t look hard enough, until now I didn’t look far enough. I didn’t review papers from smaller labs in other countries doing some remarkable research, and I was too dismissive of the loud chorus of legitimate patients whose symptoms improved on cannabis.
A patient wants medical marijuana as they read online that it may help treat cancer. You:

A. Prescribe medical cannabis for the treatment of their cancer
B. Discuss the approved medical conditions in which medical cannabis is indicated
C. Explain that there are not high level evidence that medical cannabis is a treatment for cancer
D. All of the above
E. B and C
Cannabis and the treatment of cancer
Cannabis and the treatment of cancer

• High expression of CB1 receptors on cancers particularly if anaplastic
• Animal studies suggest that cannabis has anti-neoplastic activity but can also stimulate cancers in immunocompetent animals
• Only 1 clinical study of 9 patients with GBM with direct instillation of THC
• FDA issued a warning in November 2017 to companies marketing cannabis as cancer treatment/cures, concern for patients forgoing treatments in pursuit of “miracle cure"
• Immunosuppression (CB2 receptors)- ? Interactions with checkpoint inhibitors
• Risks of aspergillosis with smoked cannabis and other infections which may particularly important in the immunosuppressed

Adverse effects and interactions
Adverse effects of cannabis

- Distorted perception
- Loss of motor coordination
- Difficulty with concentration/problem solving
- Dry mouth
- Tachycardia
- Psychosis and Schizophrenia (increased risk with personal/family history)
- Infertility
  - In vivo and in vitro studies have shown that cannabis may disrupt the hypothalamus pituitary-gonadal axis, spermatogenesis, and sperm function
- Cannabinoid hyperemesis syndrome
- Impaired driving
**TABLE 4. Proposed Clinical Criteria for Cannabinoid Hyperemesis**

<table>
<thead>
<tr>
<th>Essential for diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term cannabis use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Major features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe cyclic nausea and vomiting</td>
</tr>
<tr>
<td>Resolution with cannabis cessation</td>
</tr>
<tr>
<td>Relief of symptoms with hot showers or baths</td>
</tr>
<tr>
<td>Abdominal pain, epigastric or periumbilical</td>
</tr>
<tr>
<td>Weekly use of marijuana</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supportive features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age less than 50 y</td>
</tr>
<tr>
<td>Weight loss of &gt;5 kg</td>
</tr>
<tr>
<td>Morning predominance of symptoms</td>
</tr>
<tr>
<td>Normal bowel habits</td>
</tr>
<tr>
<td>Negative laboratory, radiographic, and endoscopic test results</td>
</tr>
</tbody>
</table>
BOX 9-1
Summary of Chapter Conclusions*

There is substantial evidence of a statistical association between cannabis use and:

- Increased risk of motor vehicle crashes (9-3)

There is moderate evidence of a statistical association between cannabis use and:

- Increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal (9-4b)

There is no or insufficient evidence to support or refute a statistical association between cannabis use and:

- All-cause mortality (self-reported cannabis use) (9-1)
- Occupational accidents or injuries (general, nonmedical cannabis use) (9-2)
- Death due to cannabis overdose (9-4a)
IS IT SAFE TO SMOKE MARIJUANA WHILE YOU ARE PREGNANT?

Rumors abound that marijuana has no effect on the unborn child, and that it is safe to smoke while pregnant. But research has shown that marijuana use by mom can cause numerous adverse effects on newborns and growing children. Some effects can linger into adulthood.

**Birth**
- Newborns:
  - Low birth weight and premature delivery
  - Increased anxiety and depression symptoms
  - Increased emotional reactions
  - Reduced separation anxiety

**3 Years**

**The Developmental Years:**
- Less branching in nerve cells
- Reduced ability to pay attention
- Diminished problem-solving skills
- Difficulty with detail-oriented memory
- Decreased ability to organize and prioritize

**18 Years**

**Adulthood:**
- Altered brain functions and problems using working memory

**22 Years and Beyond**

No research has shown any safe level of marijuana use while a woman is pregnant.

Cannabis Use Disorder (CUDIT-SF)

How often in the past 6 months:

1. Did you find you were unable to stop using cannabis once you had started?
2. Have you devoted a great deal of your time to getting, using or recovering from cannabis?
3. Have you had a problem with memory or conversation after using cannabis?

Never (0) Less than monthly (1) Monthly (2) Weekly (3) Daily (4)

CUD present with ≥ 2
Factors that contribute to adverse effects of cannabis

• Dose
• THC:CBD ratio of product
• Route of administration
• Time since consumption
• Comorbidities
• Age
• Co-administration of other medicines or substances
• Duration of use (long-term versus naïve)
Drug interactions with cannabis-Clinical pearls

• Opioids- may need to decrease opioid dose

• Anxiolytics- may need to decrease anxiolytic dose

• Tricyclic antidepressants- try to avoid concurrent use

• SSRIs- monitor for increased side effects of SSRIs

• Anti-retrovirals- may need to decrease cannabis dose

• Anti-seizure meds- may need to decrease dose
  • If CYP inducer used, may not see full effects of marijuana
Impact of cannabis on opioid use

• When used in conjunction with opioids, cannabis can lead to greater cumulative relief of pain and potential reduction of opioid use

• Prevent development of tolerance to and withdrawal from opioids

• Potentially enhance opioid analgesia after a prior dosage has become ineffective

• Potentially less dangerous than opioids (minimal mortality)
Contraindications

• Absolute Contraindications
  • Acute psychosis and other unstable psychiatric conditions

• Relative Contraindications
  • Severe cardiovascular, immunological, liver or kidney disease
  • Cannabis may exacerbate arrhythmia or a history of arrhythmias
Medical cannabis use in practice
Qualifying conditions for medical cannabis-New York State

- Cancer
- HIV or AIDS
- Amyotrophic lateral sclerosis (ALS)
- Parkinson's disease
- Multiple sclerosis
- Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity
- Epilepsy
- Inflammatory bowel disease
- Neuropathy
- Chronic pain as defined by 10 NYCRR §1004.2(a)(8)(xi)
- Post-traumatic stress disorder
- Huntington's disease
- Any condition for which an opioid could be prescribed (provided that the precise underlying condition is expressly stated on the patient’s certification)
Patients must also have one of the following associated or complicating conditions:

• Cachexia or wasting syndrome
• Severe or chronic pain
• Severe nausea
• Seizures
• Severe or persistent muscle spasms
• PTSD
• Opioid use disorder (only if enrolled in a treatment program certified pursuant to Article 32 of the Mental Hygiene Law).
Process for patient to obtain medical cannabis

1. **Contact your practitioner**
   - to see if medical marijuana may help. Practitioners must be registered with DOH in order to issue you a certification.

2. **Obtain patient certification**
   - from a registered practitioner if appropriate for your condition.

3. **Register online**
   - A Registry ID Card will be mailed after the application is approved.

4. **Purchase Product**
   - from a registered organization's dispensing facility.
A month supply of medical cannabis (out of pocket) on average is:

- A. $20-40
- B. $40-80
- C. $800-120
- D. $240-480
Back to the case

• You are seeing a 70 year-old woman with metastatic NSCLC. She struggles with fatigue, musculoskeletal pain, constipation, and decreased appetite. You have also noticed her flat affect and depressed mood. Today she is reporting worsening chronic peripheral neuropathy from her diabetes and increased nausea related to her ongoing chemo.

• She asks about medical marijuana. Do you:
  A. Recommend it as you feel it might be beneficial for her
  B. Discourage
  C. Are unsure, want to learn more
**Summary**

**Cannabinoids**
- Cannabidiol "CBD"
  - Exogenous cannabinoid
  - Antagonist CB1, CB2
  - Less analgesia, antiemetic than THC
  - May block psychoactive s/e and potentiate other effects of THC
  - Possible anti anxiety, anticonvulsant, neuroprotective effects

**Delta-9 THC**
- Exogenous cannabinoid
- Partial agonist CB1, CB2
- Psychosis
- Impaired cognition
- Euphoria, anxiety
- Sedation
- Muscle relaxation
- Analgesia
- Antiemetic

**Potential Harms**
- Conclusive evidence
  - Chronic bronchitis, respiratory sx
  - Motor vehicle crash
  - Low birth weight
  - Assoc. w/schizophrenia, other psychosis
- Moderate evidence
  - "Problem cannabis use" if depressed
  - No inc risk lung, or head & neck cancer
- Limited evidence
  - Inc. ischemic CVA
  - Inc. MI ❤
  - COPD risk

**Benefits**
- Conclusive evidence
  - Chronic pain
  - Chemo-induced N/V
  - MS related spasticity
- Moderate evidence
  - Sleep, short term
- Limited evidence
  - HIV/AIDS wasting
  - Tourette’s syndrome
  - Anxiety, social
  - HIV neuropathic pain
  - Chronic neuropathic pain


Created by Matthew Watto, MD
I would prescribe or support the use of medical cannabis for approved conditions

• Yes. I would prescribe or support the use of medical cannabis for approved conditions for my patients

• No. I would not prescribe or support the use of medical cannabis for my patients.
Thank you!

Questions?

Amy.Case@RoswellPark.org