Medical Uses of Cannabis and CBD

- Alan Ehrlich, MD FAAFP
- Associate Professor of Family and Community Medicine
- UMass Chan Medical School
- Worcester, MA

Objectives

- Be familiar with which medical conditions have evidence a therapeutic effect of cannabis and cannabis-derived medications
- Be able to counsel patients about use of cannabis and cannabidiol (CBD) for medical purposes
- Be familiar with the risks of cannabis and CBD use

Disclosure

The following relevant financial relationships have been disclosed by faculty, and all have been mitigated.

- **Alan Ehrlich, MD:** No relevant financial relationships disclosed.
- Moderators and non-faculty contributors involved in the planning, development, editing and review of the content have disclosed no relevant financial relationships.

Off-Label/Investigational Discussion:

- Faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices, as well as topics that are new and evolving, during the course of their presentations.

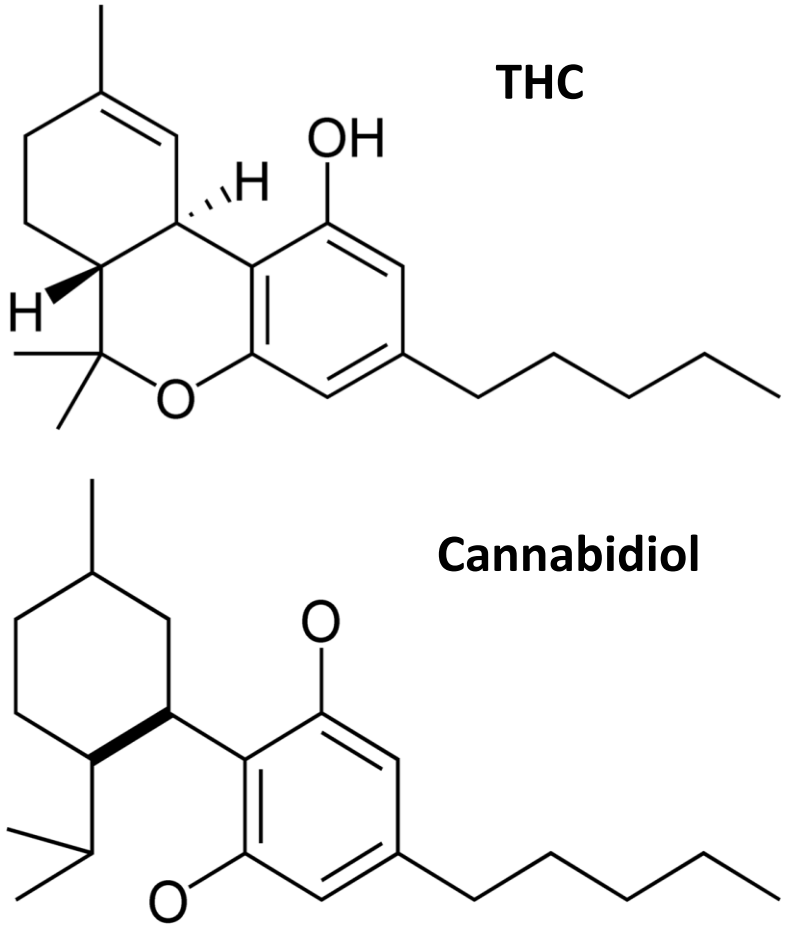
The only FDA approved use for anything discussed today is the use of a proprietary cannabidiol product (Epidiolex) for the treatment of pediatric epilepsies. All other uses should be considered experimental.

Terminology

- The term ‘medical cannabis’ (or ‘medical marijuana’) should be used for cannabis plants and plant material, for example flowers, marijuana, hashish, buds, leaves or full plant extracts used for medical reasons
- Registered medicinal cannabis extracts with defined and standardized THC and THC/CBD content should be classified as ‘cannabis-derived ’ or ‘cannabis-based’ medicines

THC vs. Cannabidiol

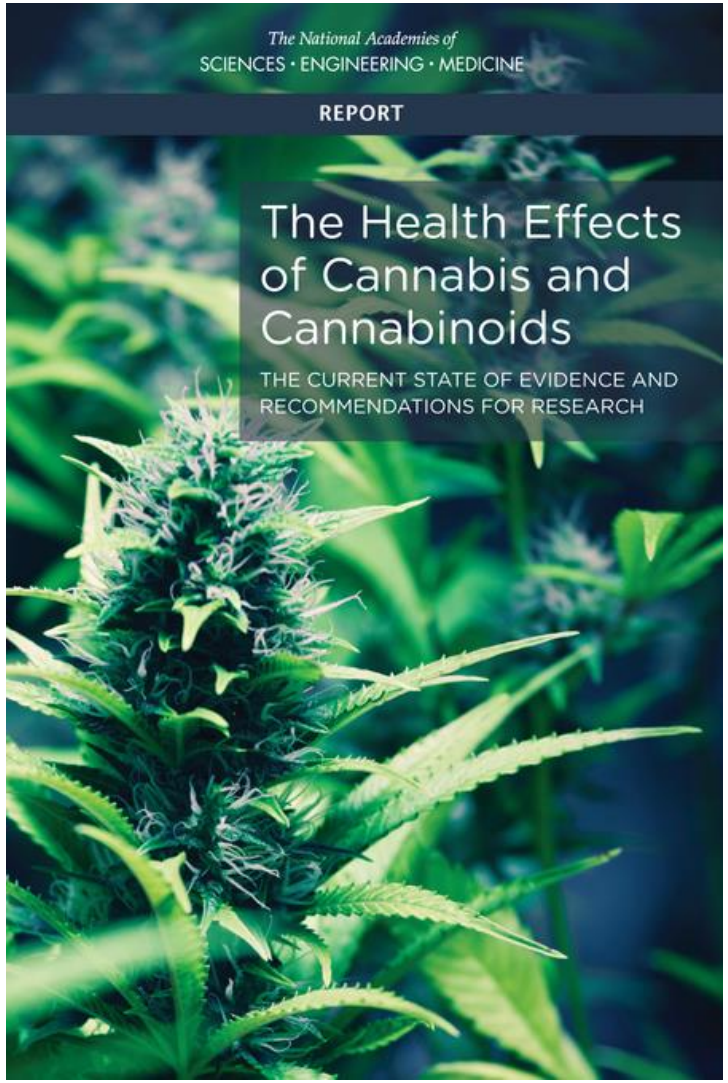
- THC (Delta-9 tetrahydrocannabinol)
  - Responsible for the “high” of marijuana
  - Short term effects include:
    - Euphoria
    - Altered senses and altered sense of time
    - Impaired body movement
    - Memory impairment
- Cannabidiol
  - Regulates response to THC
  - Decreases psychoactivity
  - Reduces craving and risk of addiction



Images courtesy of cacycle https://commons.wikimedia.org/wiki/File:Delta-9-tetrahydrocannabinol.png

Niesink RJ, van Laar MW. Does Cannabidiol Protect Against Adverse Psychological Effects of THC?. Front Psychiatry. 2013;4:130. Published 2013 Oct 16.

National Academies of Science Engineering and Medicine 2017 Report



There is conclusive or substantial evidence that cannabis or cannabinoids are effective for:

- Treatment of chronic pain in adults
- Treatment of chemotherapy-induced nausea and vomiting
- Improving multiple sclerosis spasticity symptoms

National Academies of Sciences, Engineering, and Medicine 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research

There is moderate evidence that cannabis or cannabinoids are effective for:

- Improving short-term sleep outcomes in individuals with sleep disturbance associated with
  - Obstructive sleep apnea
  - Fibromyalgia
  - Chronic pain
  - Multiple sclerosis

National Academies of Sciences, Engineering, and Medicine 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research

There is limited evidence that cannabis or cannabinoids are effective for:

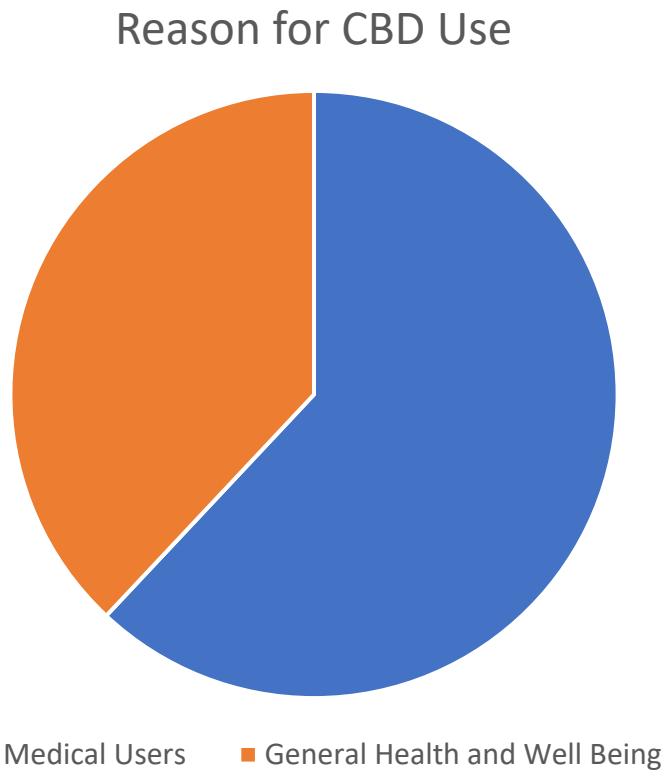
- Increasing appetite and decreasing weight loss associated with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)
- Improving clinician-measured multiple sclerosis spasticity
- Improving symptoms of Tourette syndrome
- Improving symptoms of posttraumatic stress disorder (PTSD)

National Academies of Sciences, Engineering, and Medicine 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research

What Are The Medical Benefits?

Image courtesy of https://www.flickr.com/photos/vaping360/38102409532 and vaping360.com/cbd-oil-cannabidiol-hemp-oil/

Why People Use CBD



Most Common Medical Indications

- Chronic pain
- Joint pain/arthritis
- Anxiety
- Depression
- Insomnia
- Migraines
- PTSD
- Nausea
- Cancer
- Asthma/Allergies

Moltke J, Hindocha C. Reasons for cannabidiol use: a cross-sectional study of CBD users, focusing on self-perceived stress, anxiety, and sleep problems. J Cannabis Res. 2021;3(1):5.

CBD For Epilepsy

- June 2018 Cannabidiol (Epidiolex) FDA approved for treatment of Dravet syndrome and Lennox-Gastaut syndrome in patients aged ≥ 2 years

- September 2018 DEA reclassifies CBD to schedule V

Efficacy Of CBD For Epilepsy

- 255 patients with Lennox-Gastaut syndrome and ≥ 2 drop seizures/week randomized to CBD (10 mg/kg or 20 mg/kg) vs. placebo
- Median % reduction from baseline in drop-seizure frequency
  - 41.9% in the 20-mg cannabidiol group
  - 37.2% in the 10-mg cannabidiol group
  - 17.2% in the placebo group

Devinsky O, Patel AD, Cross JH, et al. Effect of Cannabidiol on Drop Seizures in the Lennox-Gastaut Syndrome. N Engl J Med. 2018

Efficacy Of CBD For Epilepsy

- 120 children with Dravet syndrome randomized to CBD 20 mg/kg/d vs. placebo
- Efficacy based on change from baseline
- Adverse events more frequent in the cannabidiol group included:
  - Diarrhea
  - Vomiting
  - Fatigue
  - Fever
  - Somnolence
  - Abnormal liver-function tests

	CBD	Placebo
Seizure frequency at baseline	12.4/month	14.9/month
Seizure frequency during 14 weeks of treatment	5.9/month	14.1/month
Seizure free by end of trial	5%	0%

Devinsky O, Cross JH, Laux L, et al. Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. N Engl J Med. 2017

CBD For Autism Spectrum Disorders

- No RCTs yet
- Observational data suggests benefit
- CBD:THC used in studies typically 20:1

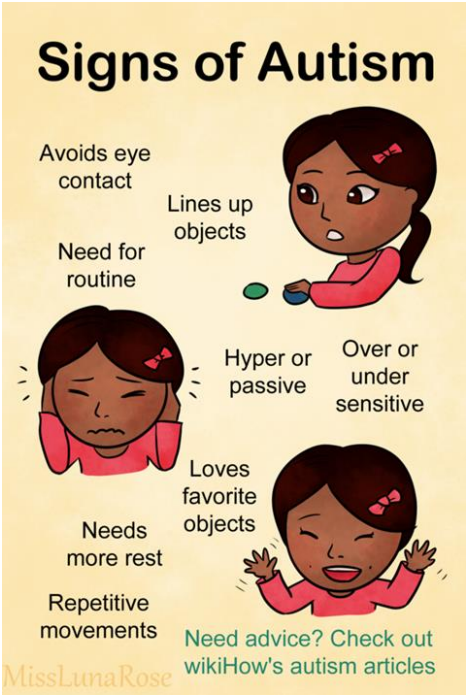


Image unchanged courtesy of https://commons.wikimedia.org/wiki/File:Signs_of_Autism.png

CBD For ASD

- 60 children with ASD given cannabis oil CBD/THC 20:1
- 77% low functioning
- Titrated up to max 10mg/kg/d
- Much improved or very much improved
  - Behavioral outbreaks (61%)
  - Anxiety (39%)
  - Communication (47%)

Aran, A., Cassuto, H. & Lubotzky, A. Cannabidiol Based Medical Cannabis in Children with Autism- a Retrospective Feasibility Study. Neurology 2018

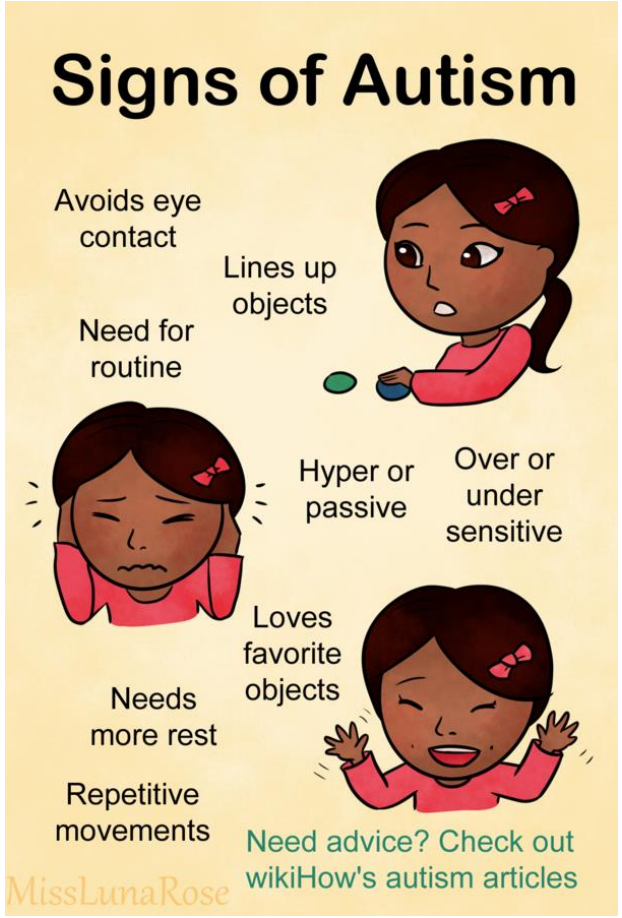
CBD For ASD

- 188 children with ASD (mean age 13) treated with cannabis oil (CBD:THC 20:1)
- Most common baseline symptoms
  - Restlessness (90.4%)
  - Rage attacks (79.8%)
  - Agitation (78.7%)
- 93 patients assessed after 6 months
  - 30% significant improvement
  - 54% Moderated improvement
  - 15% Slight improvement or no change

Bar-Lev Schleider L, Mechoulam R,et al. Real life Experience of Medical Cannabis Treatment in Autism: Analysis of Safety and Efficacy. Sci Rep. 2019

CBD For ASD

- 110 patients aged 5-25 years with ASD treated with CBD rich oil
  - Treatment consisted of 5.7 mg CBD and 0.3 mg THC/drop, starting at 1 drop twice a day ad titrating up
  - 12 stopped due to AE, 8 for lack of improvement, and 8 for other reasons
- Significant improvement seen with standardized assessment scales
- Greatest improvement seen in social communication abilities



Hacohen M, Stolar OE, Berkovitch M, et al. Children and adolescents with ASD treated with CBD-rich cannabis exhibit significant improvements particularly in social symptoms: an open label study. Transl Psychiatry. 2022;12(1):375.

Image unchanged courtesy of https://commons.wikimedia.org/wiki/File:Signs_of_Autism.png

CBD for Anxiety

- Case series of 72 patients with anxiety and/or sleep problems given 25-75 mg/day
- Assessments at 1 month
  - Anxiety improved in 79%
  - Sleep symptoms improved in 67%
- CBD tolerated by all but 3 patients

Shannon S, Lewis N, Lee H, Hughes S. Cannabidiol in Anxiety and Sleep: A Large Case Series. Perm J. 2019

CBD for Social Anxiety

- RCT of 24 patients with social anxiety disorder given CBD 600 mg or placebo 90 minutes before simulated public speaking
  - CBT group had reduced anxiety compared to placebo group
  - Placebo group did worse than healthy controls

Bergamaschi MM, Queiroz RH, et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naive social phobia patients. Neuropsychopharmacology. 2011

CBD For Arthritic Pain

- 136 patients with OA or Psoriatic arthritis randomized to CBD 20 mg, 30 mg, or placebo for 12 weeks
- Pain measured on 0-100 mm scale
- No differences in mean pain
- No differences in % achieving 30 mm reduction in pain

Vela J, Dreyer L, Petersen KK et al. Cannabidiol treatment in hand osteoarthritis and psoriatic arthritis: a randomized, double-blind, placebo-controlled trial. Pain. 2022

Does CBD Help Schizophrenia?

- RCT of 36 patients with schizophrenia given CBD 600 mg/day or placebo
  - No benefit seen
- RCT of 88 patients with schizophrenia given CBD 1,000 mg/day or placebo
  - Decreased positive psychotic symptoms
  - More likely to be rated as improved
  - Less likely to be rated as unwell
- Both trials used CBD as add-on therapy, not a replacement for antipsychotics

Boggs DL, Surti T, et al. The effects of cannabidiol (CBD) on cognition and symptoms in outpatients with chronic schizophrenia a randomized placebo controlled trial. Psychopharmacology (Berl). 2018
McGuire P, Robson P, et al. Cannabidiol (CBD) as an Adjunctive Therapy in Schizophrenia: A Multicenter Randomized Controlled Trial. Am J Psychiatry. 2018;

Topical CBD

- Proposed for various dermatologic conditions
  - Atopic dermatitis
  - Psoriasis
  - Contact dermatitis
  - Acne
  - Seborrhea

- Case series of 14 patients with venous leg ulcers
- All wounds were chronic; median duration of wound was 191.5 days
- Proprietary CBD based cream applied to wound area prior to compression bandage
- Complete wound closure achieved in 11 (79%) after median 34 days

Maida V, Shi RB, Fazzari FGT, Zomparelli L. Topical cannabis-based medicines - A novel adjuvant treatment for venous leg ulcers: An open-label trial. Exp Dermatol. 2021

Notable Adverse Effects of CBD

- Drowsiness/Somnolence
- Fatigue
- Weight gain
- Elevated transaminases
- Diarrhea
- Worsening of epilepsy
- Fetal mortality and birth abnormalities (animal studies only)

Huestis MA, Solimini R et al. Cannabidiol Adverse Effects and Toxicity. Curr Neuropharmacol. 2019

Partial List of Drug Interactions

- CBD is metabolized via the CYP3A4 enzyme
- CBD inhibit CYP2C19, CYP2D6, and CYP2C9, and may inhibit some CYP3 enzymes
- Use drug interaction checker if CBD use will be chronic

Drugs That Raise CBD Levels	Drug Levels Raised By CBD	Drug Levels Decreased By CBD
Clarithromycin	Antihistamines	Carbamazepine
Ketoconazole	Atorvastatin	Oxycarbazepine
Itraconazole	Simvastatin	Phenobarbital
Ritonavir	Cyclosporine	Phenytoin
	Antiretrovirals	
	Haloperidol	
	Sildenafil	
	Warfarin	
	Benzodiazepines	
	Morphine	

Balachandran P, Elsohly M, Hill KP. Cannabidiol Interactions with Medications, Illicit Substances, and Alcohol: a Comprehensive Review. J Gen Intern Med. 2021

What About Cannabis?

Image courtesy of Tomas de Aquino
https://www.flickr.com/photos/warrantedarrest/68481352

Cannabinoids for Chronic Pain

Cochrane Review: Cannabis for Chronic Neuropathic Pain

- Interventions:
  - Smoked cannabis
  - Cannabis-based medicines
- Systematic search:
  - 16 RCTs
  - 1,750 participants

Outcome	Number of participants	Cannabinoid vs. placebo	NNT/NNH
≥ 50% ↓ in pain	1,001	20.9% vs. 17.3%	20
≥ 30% ↓ in pain	1,586	37.7% vs. 30.4%	11
Serious AE	1,876	6.6% vs. 5.2%	
Withdrawals due to AE	1, 848	10.4% vs. 4.7%	25

Mücke M, Phillips T et al. Cannabis-based medicines for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2018;3(3):CD012182.

SR Cannabinoids For Noncancer Chronic Pain

Condition	Number of trials (participants)	Odds Ratio (OR) For 30% Pain Reduction Cannabis vs. Placebo
Any Pain Type	9 (1,734)	1.46 (1.16-1.84)
Neuropathic Pain	7 (1,105)	1.31 (1.02-1.69)
Multiple Sclerosis (MS) Nonneuropathic Pain	2 (502)	2.38 (1.35-4.22)

- Pooled event rates
  - 30% reduction in pain 29% with cannabinoids vs. 25.9% with placebo (NNT 24)
  - Any adverse events in 81.2% with cannabinoids vs. 66.2% with placebo (NNH 6)

Stockings E, Campbell G, et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain. 2018;159(10):1932-1954.

Can Cannabis Decrease Opioid Use?

- 8,165 persons in state of NY treated with long-term opiates and medical cannabis (2017-2019)
- NY PMP data used for opioid prescriptions and medical cannabis dispensing
- Cannabis users > 30 days compared to those with ≤ 30 days exposure

Daily MME	Decrease in MC User Cohort	Decrease in MC Non-user Cohort
< 50	48%	4%
50-90	47%	9%
>90	51%	14%

Nguyen T, Li Y, et al. Changes in Prescribed Opioid Dosages Among Patients Receiving Medical Cannabis for Chronic Pain, New York State, 2017-2019. JAMA Netw Open. 2023

Can Cannabis Decrease Opioid Use?

- 131 chronic pain patients seeking the first annual renewal of their New Mexico Medical Cannabis Program (NMMCP) license
  - 76% reported using prescription opioids prior to enrollment in the NMMCP
  - Prescription Monitoring Program (PMP) records showed that only 49% of the patients were actually prescribed opioids in the six months prior to enrollment
- At time of renewal, of the 64 patients with verifiable opioid prescriptions prior to MCP enrollment
  - 35 (55%) reported stopping use of prescription opioids
  - 26 patients (41%) showed no prescription opioid activity at their first annual renewal

Vigil JM, Stith SS, Reeve AP. Accuracy of Patient Opioid Use Reporting at the Time of Medical Cannabis License Renewal. Pain Res Manag. 2018

Can Cannabis Decrease Opioid Use?

- National cohort of 1,514 people with chronic noncancer pain who were being treated with opioids
- Over next 4 years 24% used cannabis for pain
- No evidence that cannabis use reduced prescribed opioid use or increased rates of opioid discontinuation

Campbell G, Hall WD, Peacock A, et al. Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: findings from a 4-year prospective cohort study. Lancet Public Health. 2018

Cannabis and Opioids

- Data is conflicting on change in opioid use
- Reasonable to set expectation that reduction in opioid dosing should be considered

https://sc.wikipedia.org/wiki/File:20050613-019-poppy.jpg
https://www.publicdomainpictures.net/en/view-image.php?image=91243&picture=cannabis-sativa-leaf

IDSA Recommendation For HIV Neuropathy

- Medical cannabis may be an effective treatment in appropriate patients (Weak recommendation, Moderate evidence)
- Medical cannabis may be more effective for patients with a history of prior cannabis use
- Potential benefits of cannabis need to be balanced with risks
  - Neuropsychiatric adverse effects at higher doses
  - Harmful effects of smoked forms of cannabis in patients with severe lung disease
  - Addiction risk in patients with cannabis use disorder

Bruce RD, Merlin J, et al. 2017 HIVMA of IDSA Clinical Practice Guideline for the Management of Chronic Pain in Patients Living With HIV. Clin Infect Dis. 2017

Parkinson Disease

- **Venderova 2004 N = 85 (all cannabis-naïve)**
  - Mild or substantial symptom relief in 46%
  - Improved bradykinesia in 45%
  - Improved muscle rigidity in 38%
  - Improved rest tremor in 31%
  - Improved L-dopa induced dyskinesia in 14%
  - Symptoms worsened in 5%

Balash 2017 (N = 47)

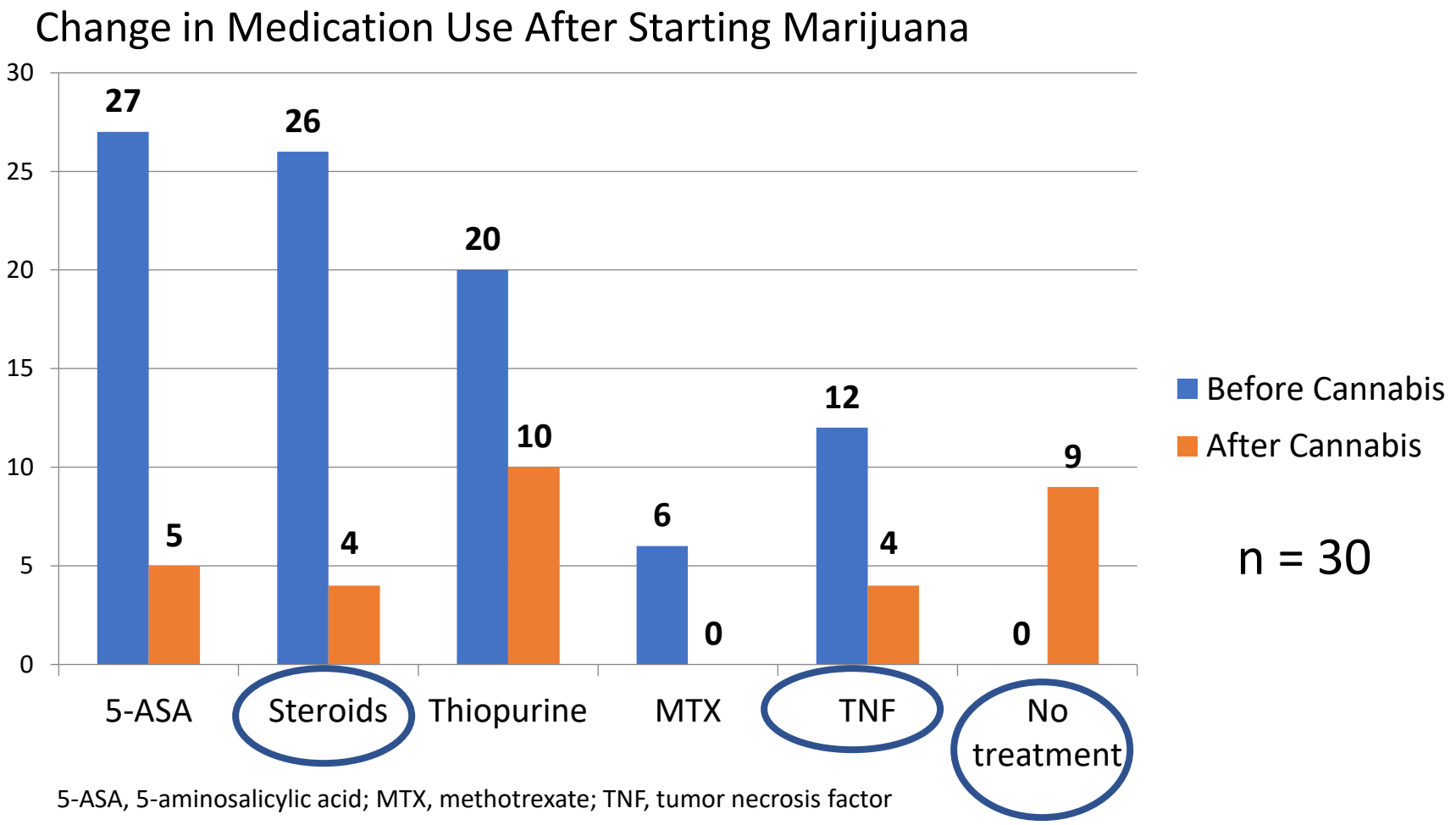
- ↓Falls
- ↓ Depression
- ↓ Tremor
- ↓ Muscle stiffness
- ↑ Sleep
- ↑Pain relief

Benefits not seen till 1.7 months on average and more consistently reported by those using for > 3 months

RCTs fail to find clear benefit in motor symptoms

Venderová K, Růzicka E, et al. Survey on cannabis use in Parkinson's disease: subjective improvement of motor symptoms. Mov Disord. 2004
Balash Y, Bar-Lev Schleider L, Korczyn AD, et al. Medical cannabis in Parkinson disease: real-life patients' experience. Clin Neuropharmacol 2017

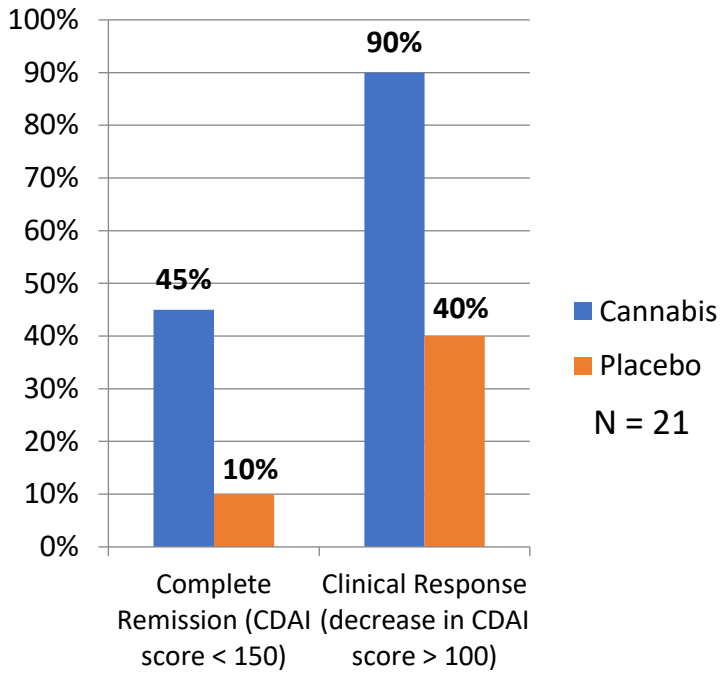
Intractable Crohn's Disease



5-ASA, 5-aminosalicylic acid; MTX, methotrexate; TNF, tumor necrosis factor

Cannabis For Intractable Crohn's Disease

- 21 patients with refractory disease
- Cannabis smoking twice a day vs. placebo
- 8 week study
- Crohn's Disease Activity Index (CDAI) used as outcome
- Differences not significant



Naftali T, Bar-Lev Schleider L, et al. Cannabis induces a clinical response in patients with Crohn's disease: a prospective placebo-controlled study. Clin Gastroenterol Hepatol. 2013

Benefits Reported BY IBD Patients

Effect on Medication	% Reporting
Allowed me to decrease my conventional IBD medications	19.6%
Allowed me to stop my conventional IBD medications	12.5%
Made me need to increase my conventional IBD medications	3.6%
Allowed me to avoid surgery that was recommended to me	10.7%
Cured my inflammatory bowel disease	7.1%
Caused only side effects	5.4%
Was a waste of my money	1.8%

Storr M, Devlin S, Kaplan GG, et al. Cannabis use provides symptom relief in patients with inflammatory bowel disease but is associated with worse disease prognosis in patients with Crohn's disease. Inflamm Bowel Dis. 2014

Cannabis and IBD – CCF White Paper

- There appears to be a role for medicinal cannabis as complementary therapy for refractory or resistant symptoms
- More research is required to understand the short- and long-term benefits and risks of this therapy and to develop approaches to understanding dosing and monitoring patients
- We support policy changes that would facilitate further research into the potential therapeutic benefits of medicinal cannabis, including revising cannabis' status as a federal Schedule I controlled substance

Swaminath A, Berlin EP, Cheifetz A, et al. The Role of Cannabis in the Management of Inflammatory Bowel Disease: A Review of Clinical, Scientific, and Regulatory Information. Inflamm Bowel Dis. 2019

Concerns With THC Use

Image unchanged courtesy of Topher i:
https://www.flickr.com/photos/74655092@N00/101851123/

Adverse Effects of Cannabis

- Short-term effects
  - Dizziness
  - Impaired motor coordination
  - Altered judgment
  - Euphoria, disorientation
  - Increased appetite
  - ↑ HR & BP; Vasodilation
  - Psychosis
  - MVA
- Long-term effects
  - Addiction
  - Psychosis
  - Pulmonary effects
  - Hyperemesis

Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. N Engl J Med. 2014
Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. Lancet. 2009

Acute Psychosis

- Risk of acute cannabis psychosis while intoxicated that can last 24-48 hours
  - Persistent psychotic symptoms lasting beyond the period of acute intoxication
  - Paranoia, disorganized thinking, persecutory and grandiose delusions, hallucinations, and cognitive impairment
- Risk of psychosis related to THC concentration and THC/CBD ratio
- Increased risk for schizophrenia in at-risk users

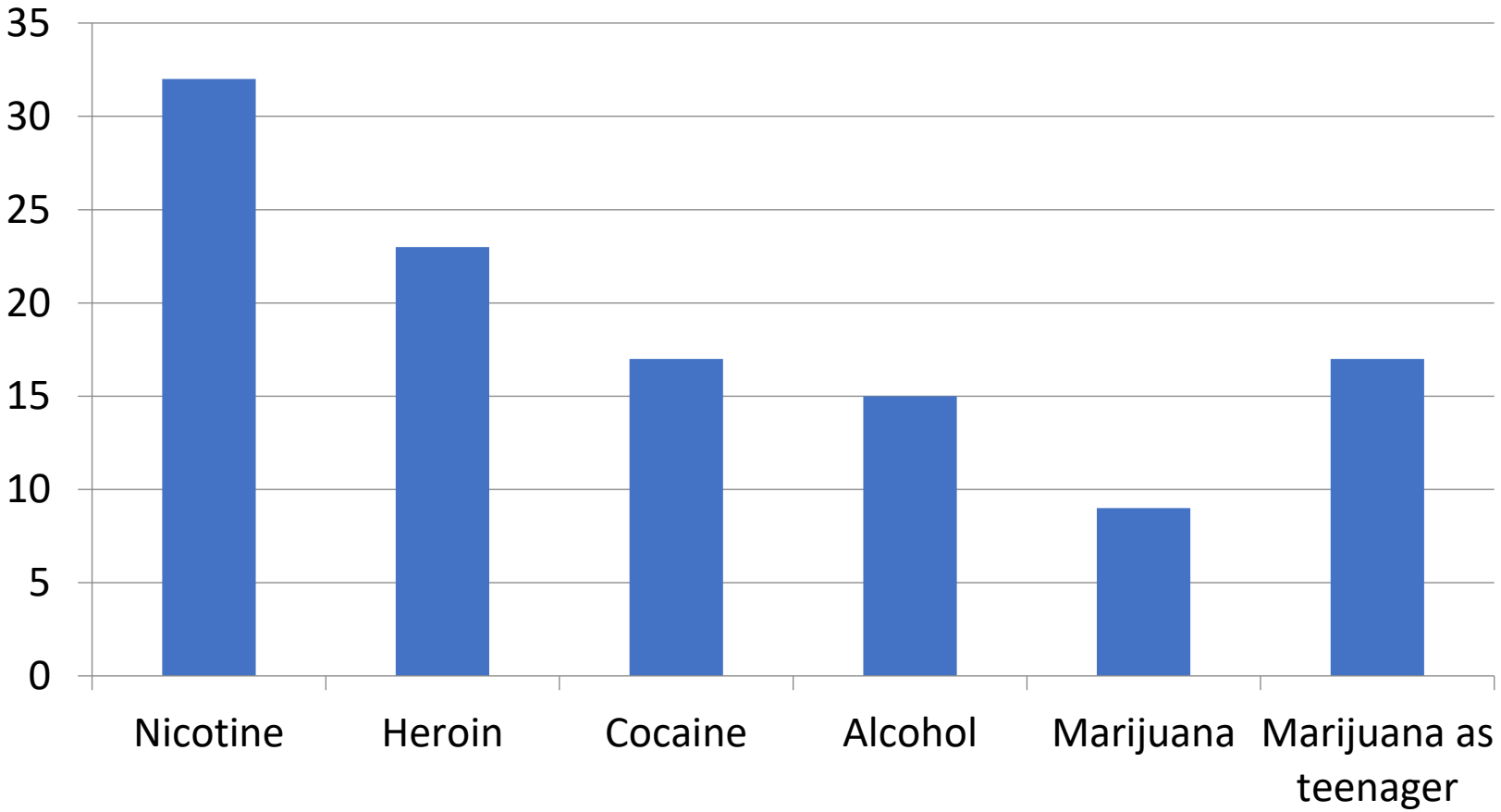
Bui QM, Simpson S, Nordstrom K. Psychiatric and medical management of marijuana intoxication in the emergency department. West J Emerg Med. 2015;16(3):414-417. doi:10.5811/westjem.2015.3.25284

Driving Issues

- Risk of MVA ↑ 2-2.6X based on 2 SR
- THC disrupts perception of time, concentration, movement, memory and coordination
- Slower reaction time and slower decision making, lane drift, trouble judging distances, reduced peripheral vision
- Drivers will compensate with slower driving and larger following distance

Asbridge M, Hayden J A, Cartwright J L. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis BMJ 2012
Pearlson GD, Stevens MC, D'Souza DC. Cannabis and Driving. Front Psychiatry. 2021

Lifetime Addiction Risk (%)



Bostwick JM. Blurred boundaries: the therapeutics and politics of medical marijuana. Mayo Clin Proc. 2012

Cannabinoid Hyperemesis Syndrome

- Cyclic vomiting
- Abdominal pain
- Compulsive showering
- Improvement of symptoms with cessation of cannabis
- Typically, cannabis used at least weekly, and for > 1 year
- Rates doubled in CO following legalization

Image courtesy of Richard Masoner via flickr:
https://www.flickr.com/photos/bike/with/566364513/

Lapoint J, Meyer S, Yu CK, et al. Cannabinoid Hyperemesis Syndrome: Public Health Implications and a Novel Model Treatment Guideline. West J Emerg Med. 2018

Cognitive Impairment

- Longitudinal cohort in New Zealand with 1,037 followed from birth to age 45
- Study members interviewed about substance use at ages 18, 21, 26, 32, 38, and 45
- Long-term cannabis users (86) at age 45 defined as:
  - Using at least weekly in the past year or were dependent on
  - Also used weekly or more frequently at one or more previous assessments
- Cannabis users compared to never-users (202), long-term tobacco users (75), long-term alcohol users (57), mid-life recreational cannabis users (65) and cannabis quitters (60)

Meier MH, Caspi A, R Knodt A, et al. Long-Term Cannabis Use and Cognitive Reserves and Hippocampal Volume in Midlife. Am J Psychiatry. 2022

IQ Assessment At Age 45

- Long-term cannabis users had average IQ as children (99.3) but below-average IQ as adults (93.8)
- 5.5-point childhood-to-adulthood IQ decline was significantly larger than
  - Lifelong cannabis non-users (+ 0.70)
  - Long-term tobacco users (− 1.5)
  - Long-term alcohol users (− 0.50)
- Not statistically different from
  - Midlife recreational cannabis users (− 3.5)
  - Cannabis quitters (− 3.3)

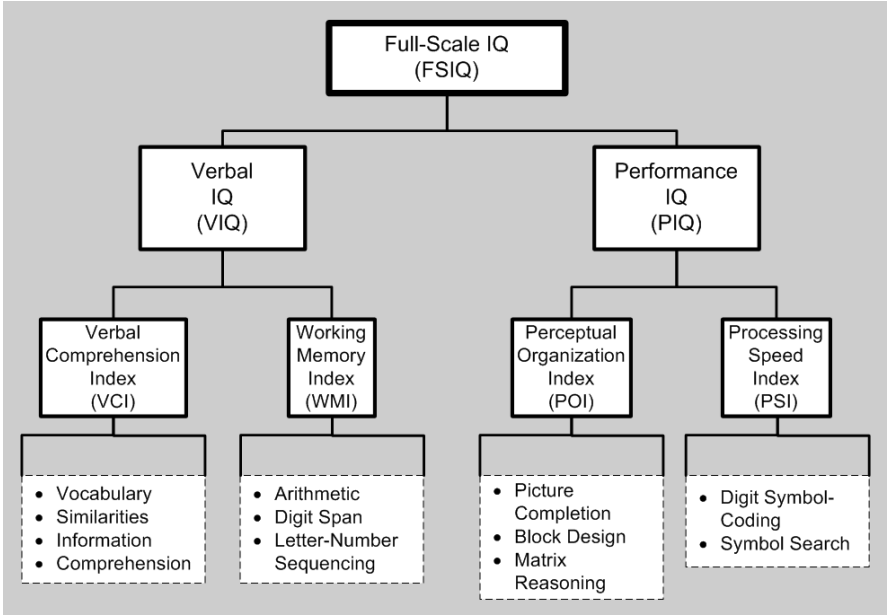


Image unchanged courtesy of Shelley Adams: https://commons.wikimedia.org/wiki/File:Wechsler_Adult_Intelligence_Scale_subscores_and_subtests.svg

Meier MH, Caspi A, et al. Long-Term Cannabis Use and Cognitive Reserves and Hippocampal Volume in Midlife. Am J Psychiatry. 2022

Pulmonary Effects Of Smoking Cannabis

- Chronic bronchitis symptoms may develop
- Chronic use
  - No increase in airway obstruction or COPD
  - No clear association with lung or upper airway cancer
  - May increase risk for URI and pneumonia
  - Significantly lower risks than tobacco
- Symptoms usually resolve with abstinence

Image unchanged courtesy of Elsa Olosson
https://www.flickr.com/photos/elsaolofsson/50610713028

Tashkin DP. Effects of marijuana smoking on the lung. Ann Am Thorac Soc. 2013

Cardiovascular Effects

- Physiologic Effects
  - Increased myocardial oxygen demand
  - Reduced oxygen supply
  - Prothrombotic state
  - Regional vasospasm
- Clinical Outcomes
  - AMI risk ↑ nearly 5X within 1 hour of exposure (may have no other RF)
  - 2.3 X increased risk of ischemic stroke (higher with weekly use)
  - Increased stroke may be due to reversible cerebrovascular spasm (RCVS)
  - 32% of 67 patients with RCVS had positive toxicology for cannabis

Singh A, Saluja S, Kumar A, et al. Cardiovascular Complications of Marijuana and Related Substances: A Review. Cardiol Ther. 2018

American Society of Regional Anesthesia and Pain Medicine (2023)

- Universal screening for cannabinoids should be performed prior to surgery and should include type of cannabis or cannabinoid product, time of last consumption, route of administration, amount, and frequency of use. (Grade A)
- Delay elective surgery for a minimum of 2 hours after cannabis smoking because of increased perioperative risk of acute MI

Shah S et al Regional Anesthesia & Pain Medicine Published Online First: 03 January 2023

ACOG Guidance (2021 Reaffirmed)

- Before pregnancy and in early pregnancy, ask about use of marijuana
- Users should be counseled regarding potential adverse health consequences of continued use during pregnancy
- Women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use
- There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged

Image in the pubic domain: https://commons.wikimedia.org/wiki/File:Pregnant-woman.jpg

ACOG COMMITTEE OPINION Number 722 • October 2017

Concerns In the Elderly

- Aging leads to changes in pharmacokinetics
  - Changes in liver metabolism and renal clearance
  - Elderly have greater percentage of fat where cannabinoids accumulate
- Drug-drug interactions
- Adverse effects may be increased, such as risk of falls
- Only small number of trials include elderly patients, and none analyze this population separately

Abuhasira R, Ron A, Sikorin I, Novack V. Medical Cannabis for Older Patients-Treatment Protocol and Initial Results. J Clin Med. 2019

Elderly Users in Israel

- 2,736 patients ≥ 65 years old
  - 56% 65-74
  - 32% 75-84
  - 12% ≥ 85
- Indications for cannabis
  - 37% Cancer pain
  - 30% Other pain
  - 24% Chemotherapy symptoms
  - 5.3% Parkinson disease
- 31.7% reported at least 1 adverse event (dizziness and dry mouth most common)

Abuhasira R, Schleider LB, Mechoulam R, Novack V. Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly. Eur J Intern Med. 2018

Mary

Mary is a 44-year-old office worker with a history of low back pain for several years. The pain is not severe, but it can cause trouble with sleeping, and she is frustrated by it. She has tried various non-narcotic medications, which have had limited effect, and has also been to physical therapy. She tried acupuncture but that did not give her long-term relief either. She does not have any surgically correctable lesions.

At her most recent visit, she tells you she has gotten a medical cannabis card and has tried smoking marijuana a few times and finds it helpful.

What additional information would you like to know?

- How did she get the medical cannabis card?
- What advice was she given about using cannabis for this?
- Has she considered alternatives to smoking cannabis to get relief?
- Who is going to manage this going forward?
- Why did she want a cannabis card instead of just going to a dispensary for recreational cannabis?

Advising Patients

- What are the therapeutic goals?
- What mode of consumption is best?
- How should this be dosed?

Pharmacokinetics of Different Forms

Mode of Consumptions	Onset of Action	Peak plasma Concentration	Duration of Effect
Smoking/Vaping	5-10 min after inhalation (varies with depth of inhalation, breath holding etc)	20-30 minutes	2-3 hours
Edible	30-90 minutes after ingestion (very unpredictable)	120-180 min after ingestion (very unpredictable)	4-12 hours
Sublingual/oromucosal including oral dissolving films	5-30 minutes	15-60 minutes	4-12 hours

Other routes of administration include rectal suppositories and topical

https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids-eng.pdf

A Few Words About Edibles

Problems With Edibles

- Delay in onset of effect
  - Titration difficult
  - May lead to excessive dosing
- Accidental ingestion
- Inaccurate labeling
  - 17% accurately labeled
  - 23% under labeled
  - 60% over labeled

Vandrey R, Raber JC, et al. Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products. JAMA. 2015

Accidental Ingestion

- Colorado Regional Poison Center had reports of 163 children with unintentional cannabis exposure 2009-2015
- Mean rate of marijuana-related visits to the children's hospital:
  - 1.2 per 100 000 population 2 years prior to legalization
  - 2.3 per 100,000 population 2 years after legalization
- Half of exposures due to edibles
- Median stay in ED 11 hours and for inpatients 26 hours

Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional Pediatric Exposures to Marijuana in Colorado, 2009-2015. JAMA Pediatr. 2016

Advice On Dosing Cannabis

- Dosing based on THC content
- Many uses are for managing symptoms
- With inhalation, rapid effect makes titrating easy
  - Have patient look for strains with more CBD to minimize adverse effects
  - Start on weekends or other times when functioning the next day is less critical
- Sublingual can also be titrated but need to start with low dose, especially in those naïve to cannabinoids or the elderly
  - 2.5 mg THC is reasonable starting dose
  - Increase 1.25-2.5 mg every few days as needed if patient tolerating
- Edibles hardest to titrate; again start at 2.5 mg and increase slowly
- Start at bedtime, if possible, especially edibles

Monitoring

- Have patient keep a symptom diary along with amounts of cannabinoids used
- Have them note adverse effects and severity
- Follow up in 1-2 weeks and have them bring in product or pictures of the labels
- Determine THC mg/day being used. Over 20-30 mg/day often associated with significant adverse effects

Practice Recommendations

- Be open to talking with your patients about cannabis and CBD
- Provide your patients with balanced information about cannabis/CBD use for medical reasons
- For patients who are going to start cannabis for medical reasons, counsel them on starting low and progressing as needed
- Advise patients on driving risks with THC

Questions?

Saturday 12:30pm – 1:30pm

CME: Medical Uses of Cannabis and CBD

Please scan this QR code on you mobile

or tablet device to access the session feedback survey

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