Answering your Cannabis FAQ's

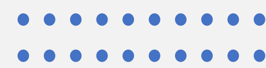
So much Content for a 20 minute talk

Disclosures

- **Faculty:** Michael Boivin, Rph
- **Relationships with financial sponsors:**
  - **Speakers Bureau/Honoraria:** J & J, Astra-Zeneca, SDM, Pfizer, Abbvie, Valneva, Sanofi, Novo-Nordisk
  - **Consulting Fees:** Merck, Teva, Pfizer, Abbott Diabetes, Valneva, Novo Nordisk, Khiron, Tilray, Canopy, Purdue, Ascensia

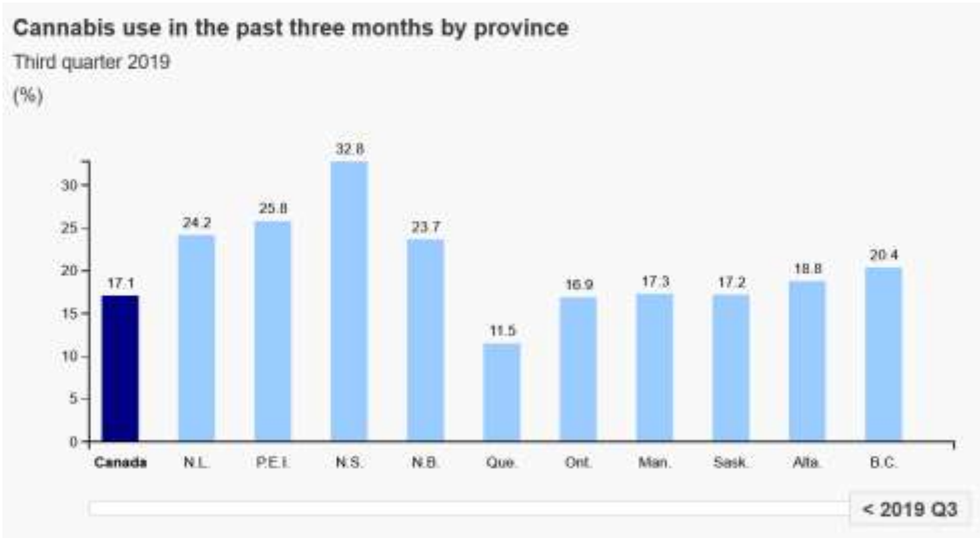
Learning Objectives

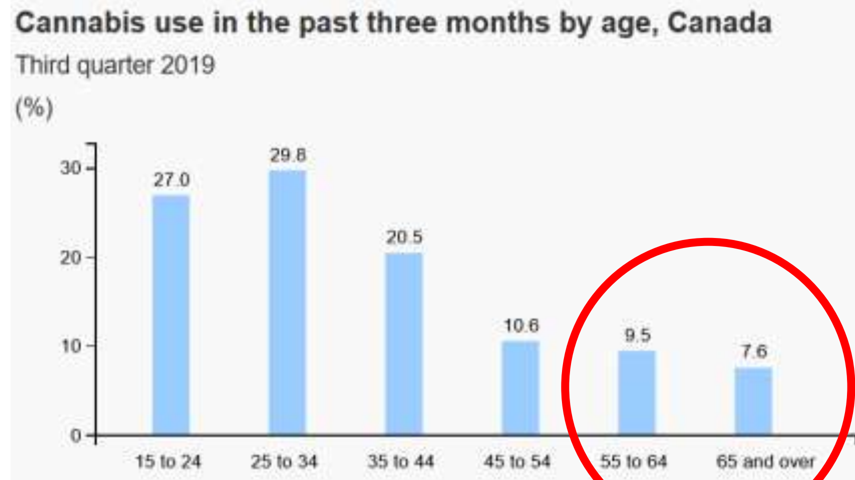
1. Review some of the most commonly asked patient questions regarding medical cannabis
2. Describe how the latest research provides some clarity in the role of medical cannabis
3. Determine the potential role of cannabis for patients with chronic pain



1. With legal recreational cannabis, is medical even an issue?

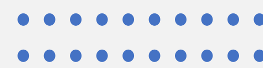
Cannabis Use in Canada





- ↑ Active Medical Clients despite legalization
  - October 2018 – 345,520
  - September 2019 – 369,614
- Medical cannabis stats:
  - 73% of medical users don't obtain authorization
  - 61% report they stop or ↓ other meds
  - 50% obtain medical cannabis from illegal source
  - Average authorization has stayed at 2 g for last year

Cannabis Stats Hub - https://www150.statcan.gc.ca/n1/pub/13-610-x/cannabis-eng.htm
Canadian Cannabis Survey - https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/canadian-cannabis-survey-2019-summary.html
Data on cannabis for medical purposes - https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/medical-purpose.html



2. Who should be considered for cannabis?

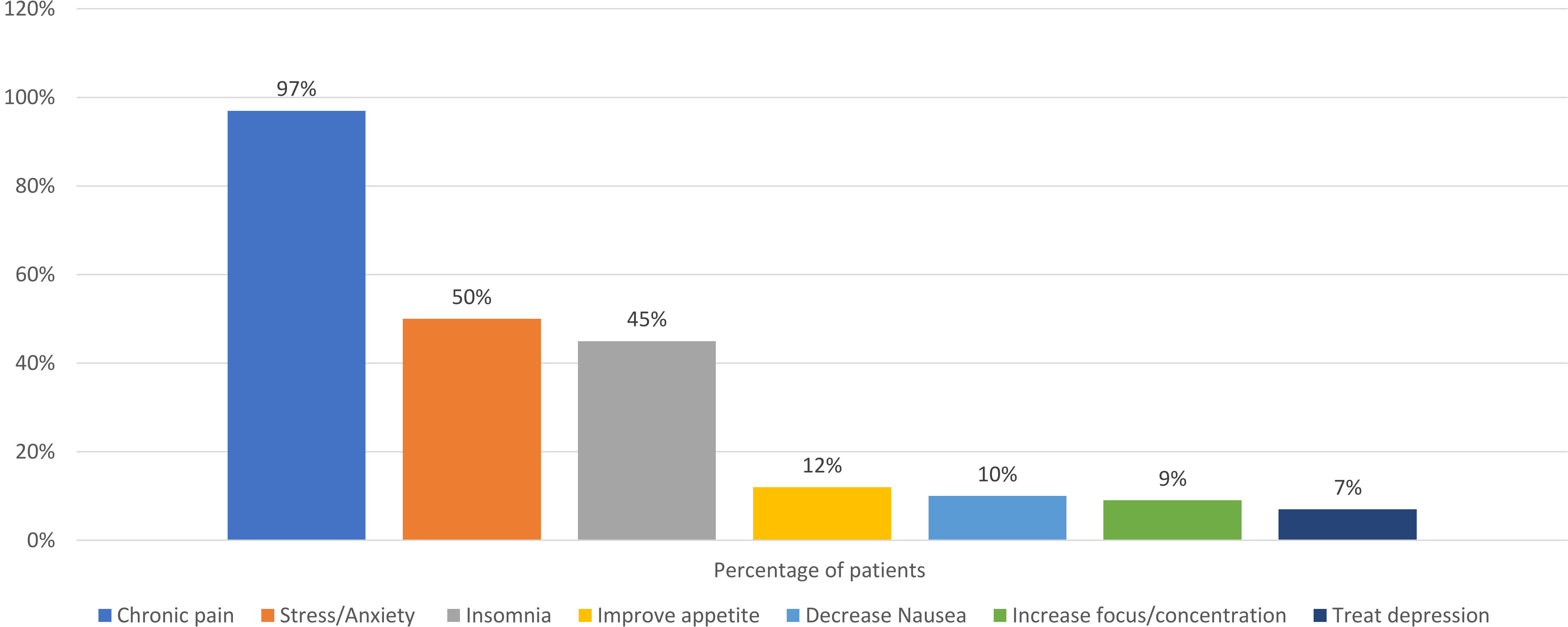
Key Points to Remind Patients

- Cannabis is not a first-line treatment
- Used for symptom management
- Given to patients who are not reaching goals with current therapy
- May be able to reduce other medications but don't normally stop them
- Current data does not support it as a cure for any condition
- Have to help patients frame cannabis role, not a magic bullet

https://www.cureyourowncancer.org/the-kelly-hauf-story-how-she-beat-brain-cancer-naturally-with-cannabis-oil.html

30K Shares! https://www.dailymail.co.uk/health/article-3043607/Cannabis-oil-cured-bowel-cancer-claims-father-33-given-just-18-months-live.html

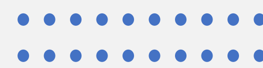
The Vast Majority of Patients Use Cannabis for Pain, Sleep and Anxiety



Webb CW, Webb SM. Therapeutic Benefits of Cannabis: A Patient Survey. *Hawaii J Med Public Health*. 2014;73(4):109-111.

‘Typical’ First Medical Cannabis Patient

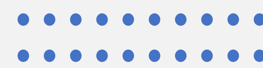
- > 45 years of age
- Chronic pain patient
  - Not reaching goals
  - Being considered for opioids or approaching opioid max dose in guidelines
- Has tried approved therapies
- Has tried cannabis with success
- Approaches clinician to ask about cannabis



3. What strain do I use?

Strain Selection

- Each strain can lead to a slightly different response
  - High THC: Low CBD
  - Balanced THC: CBD
  - High CBD: Low THC
- Many will start with CBD predominant
  - Increases NNH and if response – bonus
  - Especially in elderly and poly pharmacy patients
- Most of the data is with THC
  - THC provides many of the therapeutic effects and not just recreational
  - The goal is symptom reduction and not to get ‘high’



4. Administration and dosing

Inhaled or Oral?

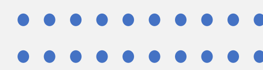
	Smoking	Vaporization	Oral
Onset (min)	5-10	5-10	60-180
Duration (h)	2-4	2-4	6-8
Benefits	Rapid onset	Rapid onset, less waste than smoking	Less odour, convenient, discreet
Cons	Carcinogens, loss of cannabinoids to side smoke, dexterity required	Cost of vaporizer, dexterity to prepare doses, may not be portable	Titration can be more challenging due to delayed onset
Role in therapy	Rarely recommended as more risks with no benefits over vaporization	Ideal for patients with episodic acute symptoms (fast onset)	Ideal for chronic conditions as long-acting requiring less dosage frequency

MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *European Journal of Internal Medicine*. January 2018. doi:10.1016/j.ejim.2018.01.004

Dosing and Titration

- No guideline recommended dosing for medical cannabis
- Fundamental principle is to 'start low, go slow, then go'
- For oils:
  - CBD predominant – 2.5-5 mg HS, ↑ by 2.5-5 mg every 1 to 3 days
  - THC– 1.25-2.5 mg HS ↑ by 1.25-2.5 mg every 1 to 3 days
- For inhalation:
  - Start with 1 inhalation, wait 15 minutes to several hours, may increase by 1 inhalation every 15-30 minutes until therapeutic response or adverse effects
- Titrate until therapeutic response or adverse effect
  - Don't titrate until impairment
  - 30:50 dosing suggestion – max 30 mg/day THC, if 50 mg not effective need to adjust

MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *European Journal of Internal Medicine*. January 2018. doi:10.1016/j.ejim.2018.01.004



5. Vape pens, are you kidding me?

Not All Vapes are Created Equal

- Smoking cannabis
  - Releases same harmful chemicals in tobacco smoking (PAH, CO, tar)
  - Not linked to lung cancer, but exacerbation of respiratory conditions
- Vapourization
  - Vapourization of dried cannabis flower or non-additive extract pens
  - Different than illegal extract pens associated with harm in the US
- Strong reason for promotion of legal products

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Statement from the Council of Chief Medical Officers of Health on vaping in Canada

From: Public Health Agency of Canada

Statement

October 11, 2019

We are increasingly concerned by the substantial rise of vaping among Canadian youth. As nicotine in any form is highly addictive, non-smokers who vape products containing nicotine are at risk of going on to use tobacco products such as cigarettes.

As we stated in April 2019, Canada has seen the rates of youth smoking decline significantly in recent years, but youth are now turning to vaping in large numbers. We are very concerned that a new generation of youth addicted to nicotine will lead to a resurgence in smoking—reversing decades of progress and creating new public health problems.

Youth are particularly susceptible to nicotine's negative effects, which can include altering their brain development and affecting their memory and concentration.

While the harms of vaping products are starting to emerge, researchers are still gathering data on their potential effectiveness as a means of helping smokers quit smoking. What we do know is that, regardless of a person's age, vaping can lead to nicotine addiction and can increase exposure to harmful chemicals for people who are non-smokers.

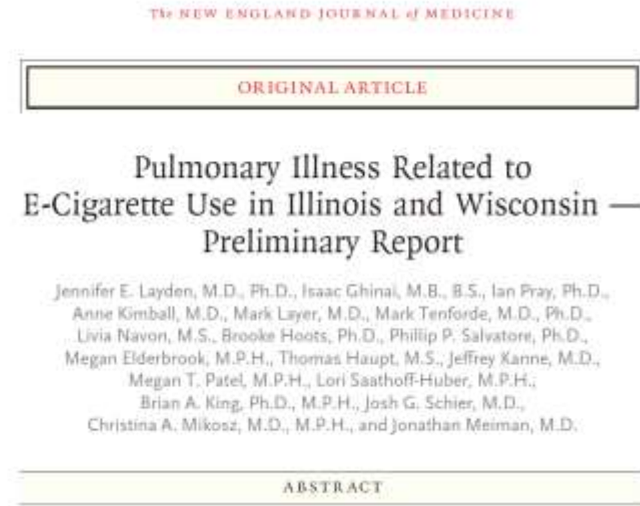
Individuals who use vaping products breathe in a mixture of chemicals, which include harmful and potentially harmful substances such as nicotine, solvents, cancer-causing chemicals (e.g., formaldehyde), heavy metals and flavourings. It is also not clear what underlying risk there may be from inhalation of ultra-fine particles created by the mechanism of vaping technology that permits inhalation deep into the lung.

Some chemicals (e.g., flavourings) in vaping products may be safe to eat, but have not necessarily been tested for safety when inhaled. Limited information is available on the health effects of inhaling glycerol (a common vaping diluent) and the majority of flavourings used in vaping liquids.

We cannot stand by and watch a new generation of Canadians become dependent on nicotine or be exposed to products that could have significant negative consequences for their health.

https://www.canada.ca/en/public-health/news/2019/10/statement-from-the-council-of-chief-medical-officers-of-health-on-vaping-in-canada.html?fbclid=IwAR3P4hC0TTNIDu0_OvhY_RFLf_jMeILo9mHyEBBBMjJ-jfkWV9VF7hUIfVQ

Two NEJM Publications



The NEW ENGLAND JOURNAL of MEDICINE

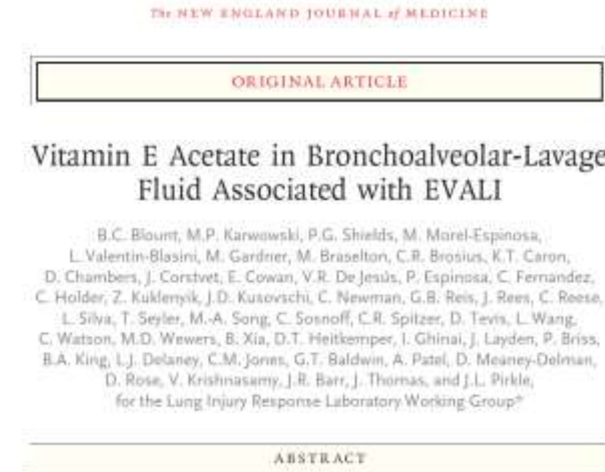
ORIGINAL ARTICLE

Pulmonary Illness Related to
E-Cigarette Use in Illinois and Wisconsin —
Preliminary Report

Jennifer E. Layden, M.D., Ph.D., Isaac Ghinai, M.B., B.S., Ian Pray, Ph.D.,
Anne Kimball, M.D., Mark Layer, M.D., Mark Tenforde, M.D., Ph.D.,
Livia Navon, M.S., Brooke Hoots, Ph.D., Phillip P. Salvatore, Ph.D.,
Megan Elderbrook, M.P.H., Thomas Haupt, M.S., Jeffrey Kanne, M.D.,
Megan T. Patel, M.P.H., Lori Saathoff-Huber, M.P.H.,
Brian A. King, Ph.D., M.P.H., Josh G. Schier, M.D.,
Christina A. Mikosz, M.D., M.P.H., and Jonathan Meiman, M.D.

ABSTRACT

- 53 patients, mean 19 years
  - 98% resp Sx's
  - 81% GI Sx's
  - 100% constitutional Sx's
- 84% used a product with THC in it



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

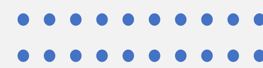
Vitamin E Acetate in Bronchoalveolar-Lavage
Fluid Associated with EVALI

B.C. Blount, M.P. Karwowski, P.G. Shields, M. Morel-Espinosa,
L. Valentin-Blasini, M. Gardner, M. Braselton, C.R. Brosius, K.T. Caron,
D. Chambers, J. Corstvet, E. Cowan, V.R. De Jesús, P. Espinosa, C. Fernandez,
C. Holder, Z. Kuklenyik, J.D. Kusovschi, C. Newman, G.B. Reis, J. Rees, C. Reese,
L. Silva, T. Seyler, M.-A. Song, C. Sosnoff, C.R. Spitzer, D. Tevis, L. Wang,
C. Watson, M.D. Wewers, B. Xia, D.T. Heitkemper, I. Ghinai, J. Layden, P. Briss,
B.A. King, L.J. Delaney, C.M. Jones, G.T. Baldwin, A. Patel, D. Meaney-Delman,
D. Rose, V. Krishnasamy, J.R. Barr, J. Thomas, and J.L. Pirkle,
for the Lung Injury Response Laboratory Working Group*

ABSTRACT

- 51 patients with electronic-cigarette, or vaping, product use–associated lung injury (EVALI)
- 94% of bronchoalveolar lavage cases found vitamin E acetate

Blount, Benjamin C., Mateusz P. Karwowski, Peter G. Shields, Maria Morel-Espinosa, Liza Valentin-Blasini, Michael Gardner, Martha Braselton, et al. "Vitamin E Acetate in Bronchoalveolar-Lavage Fluid Associated with EVALI." *New England Journal of Medicine* 0, no. 0 (December 20, 2019): null. https://doi.org/10.1056/NEJMoa1916433. Layden, Jennifer E., Isaac Ghinai, Ian Pray, Anne Kimball, Mark Layer, Mark Tenforde, Livia Navon, et al. "Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin — Preliminary Report." *New England Journal of Medicine*, September 6, 2019, NEJMoa1911614. https://doi.org/10.1056/NEJMoa1911614.



6. Cannabis drug interactions

Pharmacodynamic Drug Interactions with Cannabis

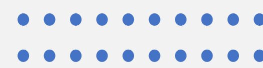
- Can worsen sedation and cognitive impairment with cannabis
  - Alcohol
  - Opioids
  - Antipsychotics
  - Benzodiazepines
  - Tricyclic antidepressants
  - Anti-epileptics

Lucas P., Catherine J., Peter Galettis, and Jennifer Schneider. "The Pharmacokinetics and the Pharmacodynamics of Cannabinoids." *British Journal of Clinical Pharmacology* https://doi.org/10.1111/bcp.13710.

More Pharmacokinetic Interactions – Mainly with CBD

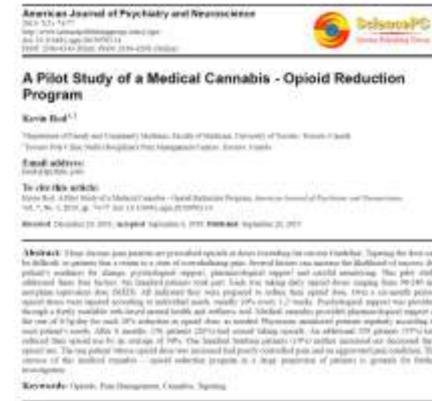
- CYP 3A4
  - Inducers ↓ THC and/or CBD
    - Carbamazepine, phenobarbital, phenytoin, rifampin, St. John's wort
  - Inhibitors ↑ THC and/or CBD
    - Azole antifungals, grapefruit, macrolides, mifepristone, protease inhibitors
  - CBD is an inhibitor of CYP 3A4 and could ↑ 3A4 substrates
    - Clobazam, tacrolimus, buprenorphine cyclosporine and phenytoin
- CBD – inhibits CYP 2C19, CYP 2D6
- Smoking induces CYP 1A1 and 1A2 – caffeine, theophylline

Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. aem. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html. Published October 12, 2018. Accessed October 15, 2018. Canadian Pharmacists Association. Cannabis (CPhA Monograph). https://www.e-therapeutics.ca/. Accessed May 5, 2019. Rong C, Carmona NE, Lee YL, et al. Drug-drug interactions as a result of co-administering Δ9-THC and CBD with other psychotropic agents. *Expert Opinion on Drug Safety*. 2018;17(1):51-54. doi:10.1080/14740338.2017.1397128. Alsherbiny MA, Li CG. Medicinal Cannabis—Potential Drug Interactions. *Medicines (Basel)*. 2018;6(1). doi:10.3390/medicines6010003"Evidence of a Clinically Significant Drug-Drug Interaction between Cannabidiol and Tacrolimus: A Case Report." *ATC Abstracts* (blog). Accessed May 16, 2019. https://atcmeetingabstracts.com/abstract/evidence-of-a-clinically-significant-drug-drug-interaction-between-cannabidiol-and-tacrolimus-a-case-report/.



7. Cannabis for opioid crisis?

Too Early to Tell – Early Signs Look Good



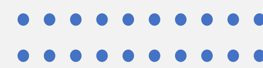
American Journal of Psychiatry and Neuroscience

A Pilot Study of a Medical Cannabis - Opioid Reduction Program

- Preclinical data demonstrated, when combined with THC:
  - Effective dose of morphine 3.6 X lower
  - Effective dose of codeine is 9.5 X lower
- New study from US demonstrated that cannabis laws led to reduction in MED, # opioid Rx's, patients on opioids

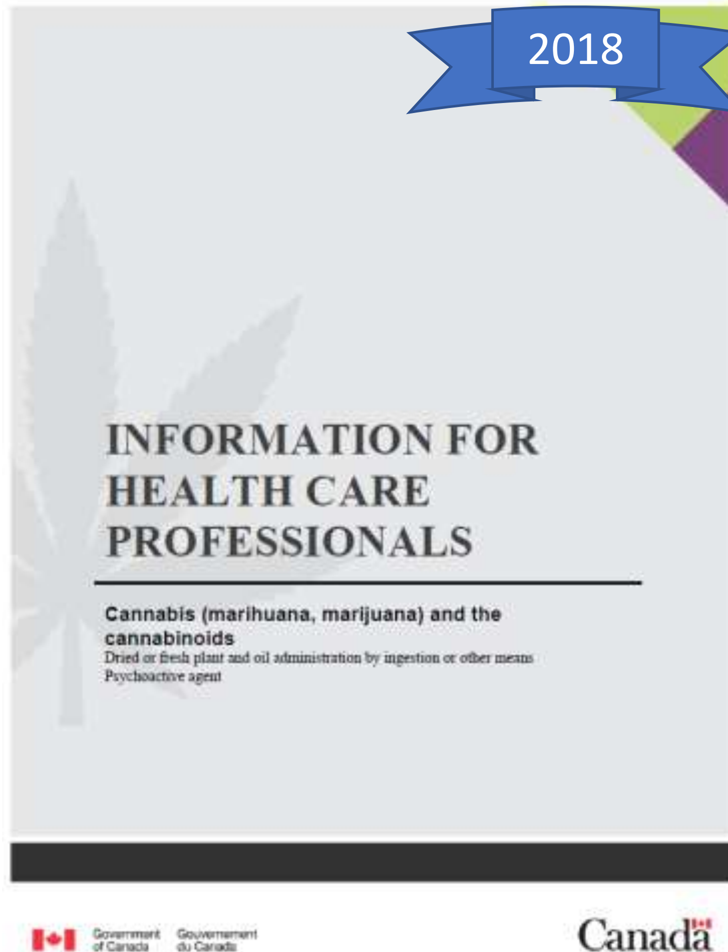
- Pilot study (n-=600)
  - MEQ = 90-240 mg
  - 4-6% THC and CBD
  - 0.5 g/day for each ↓ 10% MED
- Results
  - 26% stopped opioid
  - 55% decreased opioid MED by average 30%
  - 19% had no increase or decrease in opioid

Nielsen, Suzanne, Pamela Sabioni, Jose M. Trigo, Mark A. Ware, Brigid D. Betz-Stablein, Bridin Murnion, Nicholas Lintzeris, et al. "Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis." *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology* 42, no. 9 (August 2017): 1752–65. https://doi.org/10.1038/npp.2017.51. McMichael, Benjamin J., R. Lawrence Van Horn, and W. Kip Viscusi. "The Impact of Cannabis Access Laws on Opioid Prescribing." *Journal of Health Economics* 69 (January 1, 2020): 102273. https://doi.org/10.1016/j.jhealeco.2019.102273. Rod, Kevin. "A Pilot Study of a Medical Cannabis - Opioid Reduction Program." *American Journal of Psychiatry and Neuroscience* 7, no. 3 (2019): 74–77.

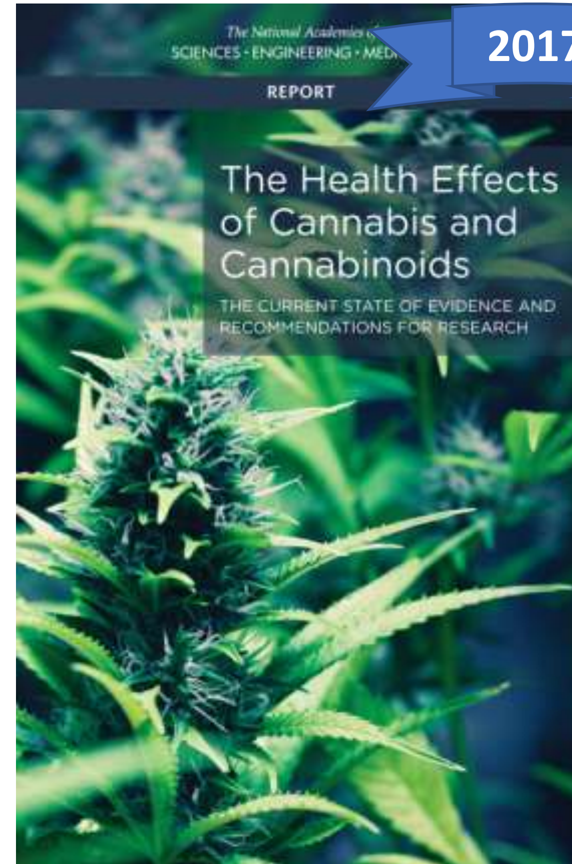


8. Where can I find more information?

Learn as Much as You Can – Systematic Reviews



https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html



https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state

https://www.cfp.ca/content/cfp/64/2/111.full.pdf

Practical Considerations for Medical Cannabis

- Quick summary
- Strongly recommended for you to download
- Can access through Dr. MacCallum's website:
  - https://www.drcarolinemaccallum.com/cannabis-resources/
- Can answer questions where you may have trouble finding answers

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Review Article

Practical considerations in medical cannabis administration and dosing

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ARTICLE INFO

Keywords:
Cannabis
Cannabinoids
Marijuana
Drug abuse
Psychopharmacology
Adverse events

ABSTRACT

Cannabis has been employed medicinally throughout history, but its recent legal prohibition, biochemical complexity and variability, quality control issues, previous dearth of appropriately powered randomised controlled trials, and lack of pertinent education have conspired to leave clinicians in the dark as to how to advise patients pursuing such treatment. With the advent of pharmaceutical cannabis-based medicines (Sativex/nabiximols and Epidiolex), and liberalisation of access in certain nations, this ignorance of cannabis pharmacology and therapeutics has become untenable. In this article, the authors endeavour to present concise data on cannabis pharmacology related to tetrahydrocannabinol (THC), cannabidiol (CBD) et al., methods of administration (smoking, vaporisation, oral), and dosing recommendations. Adverse events of cannabis medicine pertain primarily to THC, whose total daily dose-equivalent should generally be limited to 30 mg/day or less, preferably in conjunction with CBD, to avoid psychoactive sequelae and development of tolerance. CBD, in contrast to THC, is less potent, and may require much higher doses for its adjunctive benefits on pain, inflammation, and attenuation of THC-associated anxiety and tachycardia. Dose initiation should commence at modest levels, and titration of any cannabis preparation should be undertaken slowly over a period of as much as two weeks. Suggestions are offered on cannabis-drug interactions, patient monitoring, and standards of care, while special cases for cannabis therapeutics are addressed: epilepsy, cancer palliation and primary treatment, chronic pain, use in the elderly, Parkinson disease, paediatrics, with concomitant opioids, and in relation to driving and hazardous activities.

MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *European Journal of Internal Medicine*. January 2018. doi:10.1016/j.ejim.2018.01.004

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