

Clinical Pearls

- Routinely ask about cannabis use in primary care (just like tobacco and alcohol), & monitor for cannabis use disorder.
- After failure of ≥3 other drugs, a trial of prescription cannabinoids (rather than cannabis) may be reasonable for treating neuropathic pain.²
- Approach cannabinoids with similar caution as opioids – see box below.
- Start cannabinoids at a low dose, and gradually titrate. A few clinical trials suggest some efficacy even at very low doses.^{21,22} Adverse effects are common; monitor; stop or taper if not tolerated.
- Inhaled cannabis is not a preferred route of administration due to difficulty dosing, risk of respiratory damage, and multi-component composition.
- Cannabis is not recorded on PIP in Saskatchewan (Rx-cannabinoids are).
- The potential harms of cannabis are often underappreciated by patients. Informed consent and patient education are advisable. The RxFiles Cannabis Patient Booklet may be a useful tool (available online [📖](#)).

Definitions and Background Information

Cannabinoid receptors: CB1 receptors (primarily in the central and peripheral nervous systems) and CB2 receptors (primarily in the immune system) are part of an endocannabinoid system in humans.¹

Cannabinoids: compounds that activate cannabinoid receptors. Endogenous cannabinoids in humans include AEA & 2-AG. Two studied, although still poorly understood, cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).

Cannabis: aka marijuana. Contains 400+ compounds, including 120+ cannabinoids. Often marketed based on THC & CBD concentrations, although it is uncertain if these are the most important compounds in cannabis.

Prevalence (2018): 14% of Canadian adults used cannabis in last 3mos, 6% used daily, & 1% were registered for medical use.^{16,30}

Challenges with the evidence: *limited & small RCTs*, of short duration, studying differing routes, forms & types of cannabinoids results in low confidence in assessing benefits & harms. Trials with *longer duration* tend to show less benefit,¹¹ implying that if an effect exists, it may wear off over time. Further, few cannabinoid trials are *adequately blinded* due to the psychotropic effects of cannabinoids (~90% of patients can guess their allocation),¹¹ which is thought to bias results towards benefit.¹⁷

Current (2018) legal status in Canada: Rx cannabinoids are Schedule II (controlled substances). Dried cannabis & oils are legal from a licensed producer with prescriber authorization, or from a cannabis retail store. Cannabis edibles aren't legal for purchase (yet).

Do Cannabinoids Work (Medicinally)?

Note: See "Challenges with the evidence" comments, above

Compared to placebo, cannabinoids may (limited, low quality evidence):

- ↓ chronic neuropathic pain **NNT=11** for ≥30% reduction over ~4 wks.^{2,15}
- ↓ chemotherapy-induced nausea & vomiting
NNT=3 for control of nausea/vomiting over ~1 day.²
- ↓ spasticity of multiple sclerosis or spinal cord injury
NNT=10 for ≥30% ↓ spasticity over ~6wks.⁶⁸
- ↓ seizures in Lennox-Gastaut & Dravet syndrome with **CBD**
NNT=4-7 for ≥50% reduction in seizure frequency over ~14 wks.²
- ↓ cachexia in HIV/AIDS, cancer, palliative care: weak evidence.

Are Cannabinoids Safe?

Adverse effects are very common with cannabinoids. Approximately 8-9 patients out of 10 will develop an adverse effect to cannabinoid therapy and ~1 patient in 10 will stop therapy because of an adverse effect.² Notable adverse effects include feeling “high” **NNH=4**; sedation **NNH=5**; speech disorders **NNH=5**; dizziness **NNH=5**; and ataxia/muscle twitching **NNH=6**.² Additional concerns include driving impairment, addiction risk, euphoria, and psychosis. Some cannabinoids may be safer than others, but **this is generally unstudied** (including specific THC/CBD ratios). See next page of this chart.

Differing Health Care Perspectives on Medical Cannabis

Cannabis is useful?	Cannabis should be avoided?
<ul style="list-style-type: none"> • <i>Some patients have tried a dozen or so standard medications without success, and now want to try cannabis. If these patients find success with cannabis, and we help them do so safely, we will have done a great service for them.</i> • <i>When patients say a medication helps, we should listen to them, just as we listen when patients tell us the antidepressant or anti-emetic we prescribed are helping.</i> • <i>By developing products with different THC-to-CBD ratios, perhaps tolerability concerns can be addressed.</i> • <i>If cannabis helps our patients use less opioids, that's an attractive tradeoff.</i> 	<ul style="list-style-type: none"> • <i>Every other medication we prescribe has standard dosing and potency; no other medication is smoked. Inhaled cannabis contains 400+ compounds, and it's unclear which are important and how they interact. On top of that, each inhaled puff can be different from the last.</i> • <i>There is no evidence that cannabis is superior to prescription cannabinoids; therefore regulated & approved prescription cannabinoids should always be preferred.</i> • <i>In clinical trials, benefits are typically small and may just be a placebo effect. Meanwhile, adverse events are common. We have a professional duty to only prescribe medications when it can be done safely, and with cannabis the harms almost always outweigh the benefits. These harms may not be fully appreciated by patients.</i> • <i>If we routinely authorize cannabis today, will we mirror the opioid crisis tomorrow?</i>
<p>A final thought: <i>If a patient told you they were getting benefit from ibuprofen over-the-counter, you might recommend they continue taking it. You might even prescribe it. But would you feel the same way if the patient was using 6 grams of ibuprofen per day? Or if the patient insisted that the ibuprofen was improving their blood sugar control? Or if the patient had a history of GI bleeds?</i></p>	

Cannabinoids for pain, or Opioids ...

Trial evidence comparing cannabinoids and opioids is limited.⁵⁷ But they do have some similarities and differences to consider:

- **Efficacy:** For both drug classes, RCT evidence is of low quality and short duration, and tends to show only a modest reduction in pain. Longer trials tend to show less benefit. However, despite the relative lack of quality evidence, patients often have strong beliefs about the value of each drug class.
- **Adverse effects:** Nausea, sedation, and euphoria are adverse effects of both drug classes. Opioids can cause constipation;²⁵ cannabinoids can cause psychiatric disturbances (e.g. anxiety, agitation, amotivation, psychosis).²⁷ Adverse effects appear dose-related (↑dose = ↑AE). Both drug classes may be used by patients as an “escape”.
- **Addiction risk:** With prescription opioids, estimated to be 5.5%.²⁵ With *non-medical* cannabis, estimated to be 9%.²⁶ (The risk with medical cannabinoids is unstudied.)
- **Fatal overdose risk:** With prescription opioids, 0.23% with >100mg morphine per day (↑risk with ↑dose).²⁵ With cannabis, fatal overdose risk appears to be negligible.¹
- For both drug classes, the concept of a **trial with an exit strategy is important**. Not all patients will respond to these medications.

... Or Something Better?

If patients are wanting an escape from pain – physical or emotional – there are better choices! Non-pharmacological approaches to coping and living well with pain will be essential for success!

Miscellaneous info: **Synthetic illicit cannabinoids:** e.g. K2, Spice – highly potent CB1/CB2 receptor agonists; case reports of severe acute toxicity.⁵² **Phytocannabinoid:** a cannabinoid derived from cannabis (e.g. THC, CBD, & others). **THC:** a partial CB1 & CB2 agonist. **CBD:** uncertain mechanism of action. **Entourage effect:** an unproven hypothesis that efficacy of cannabinoids is increased (or adverse effects decreased) when they are used in combination and/or in particular ratios and/or with flavonoids, terpenoids. **Topical cannabis** e.g. creams: an unproven dosage form, promoted as local analgesia without systemic effect, but currently without trials to support. **Concentrated Cannabis** e.g. hash, shatter, budder, wax: contains THC as high as 90%. **Dabbing:** vaping small amounts of concentrated marijuana. **Travelling with cannabis outside of Canada:** not recommended. **Non-medical cannabis:** aka "recreational". **Is cannabis opioid-sparing?:** Evidence is still unclear.⁵⁸⁻⁶⁶

	Generic/TRADE	Indications & Comments	DOSING	\$/30d	Adverse Events AE / Contraindications CI / Drug Interactions DI / Monitor M
Prescription Cannabinoids (pharmaceutical grade)	Nabilone CESAMET, g THC analogue 0.5, 1mg cap ☹ ☹ ☹ 0.25mg cap ✗ ☹ ☹	Preferred over cannabis. ^{CFP¹⁸} ✓ severe nausea/vomiting from cancer chemotherapy ☹ off-label: AIDS-related anorexia ☹ Palliative pain ☹ Neuropathic pain • Not detected in SK urine drug screen	Initial: 0.25-0.5mg po HS Usual: 1-2mg po daily-BID for CINV 1mg BID for neuropathic pain Usual max: 6mg/day	\$22-18 g \$112-215 g \$112 g \$310 g ^{\$1200}	AE: Some notes on adverse effects: • percentages below are often “worst case scenarios” from systematic reviews, yet due to trial-design issues could also be underestimates. • adverse effects appear dose-related (↑dose = ↑AE) • it is difficult to compare AE rates between agents, due to few head-to-head trials. • THC appears to be the main component responsible for causing a “high” (low quality evidence). ⁴⁴ CBD possibly safer than THC, but some of its psychotropic effects are underappreciated (e.g. vs placebo in predominately pediatric trials: aggression/anger 3-5% vs <1%; irritability/agitation 5-9% vs 2%; somnolence 25% vs 8%). ³¹ drowsiness or sedation up to 50% across cannabinoids. ² dizziness up to 32% across cannabinoids. ² psychiatric disturbances up to 17% across cannabinoids, ² and up to 27% with inhaled cannabis. ^{COMPASS} including depression, anxiety, panic, paranoia, hallucination. euphoria up to 15%, and feeling “high” up to 35% across cannabinoids. ² acute psychosis or dissociation up to 5% across cannabinoids. ² speech disorders up to 32%, and ataxia up to 30% across cannabinoids. ² impaired memory up to 11% across cannabinoids. ² irritability or agitation up to 9%, and anger or aggression up to 5% with CBD. ³¹ appetite changes: decreased appetite in up to 22% of patients on CBD, ³¹ but conversely increased appetite in up to 38% of patients on dronabinol. ¹⁸ GI issues: dry mouth; diarrhea up to 20%, vomiting up to 15% with CBD. ^{19,31} Conversely ↓ nausea in up to 20% of pts with dronabinol. ¹⁸ SATIVEX: mouth irritation. pneumonia up to 8% with oral CBD. ³¹ ↑ LFTs up to 16% of pts on CBD; ³¹ ?related to concomitant valproate/clobazam. driving impairment: risk of fatal car crash approximately doubles with THC. ^{28,55} schizophrenia unmasking: cannabis may hasten first psychotic episode by 2-6yrs. ⁸ withdrawal with abrupt discontinuation (see withdrawal symptoms on next page) cannabis hyperemesis syndrome: severe abdominal pain/vomiting; requires drug discontinuation; relieved by hot shower; applying capsaicin to abdomen useful. ³² red eyes reported with non-medical use of oral and smoked THC. rare or uncertain: ?sexual problems, ?cancer testicular, ?↓BMD, ?pancreatitis. Harms specific to smoked cannabis: cough 7%, respiratory issues (e.g. development of COPD, pulmonary aspergillosis, ?lung cancer), ³⁵ cardiovascular issues (e.g. ↑HR, ¹ postural hypotension, ¹ ?↑MI 1 hour after smoking, ³⁹) ?steatosis with hepatitis C, ?gynecomastia, ?thrombophlebitis, contaminants in unregulated cannabis (e.g. lead, fentanyl, pesticides) CI: pregnancy; breastfeeding; age <21-25yrs (CBD exception: tx-resistant seizures?); psychosis or schizophrenia history. ⁶ Caution: in elderly, substance abuse history, driving (sometimes a contraindication) <4hrs after inhalation / <6hrs after ingestion / <8 hrs after euphoria (note: driving impairment studies have focused on THC component); history of seizures, psychiatric disorders (e.g. bipolar, anxiety), cardiovascular disease, or respiratory disease. ⁹ DI: A note on drug interactions: Interactions are not fully understood; many are theoretical. Cannabis has many compounds besides THC & CBD; these may have unknown drug interactions. Watch closely for pharmacodynamic (additive) interactions. All cannabinoids: additive CNS effects (e.g. sedation, confusion, impairment) with alcohol, anticholinergics, anti-epileptics, benzos, opioids, etc. [² disulfiram-rx if alcohol in product] THC-containing products 2C9 & 3A4 substrate: ↓ levels by CBZ, SJW, phenytoin, etc. ↑ levels by clarithromycin, fluoxetine, fluvoxamine, gemfibrozil, etc. CBD-containing products 2C19 & 3A4 substrate: ↓ levels by CBZ, SJW, phenytoin, etc. ↑ levels by clarithromycin, fluconazole, fluvoxamine, gemfibrozil, etc. 2C19 inhibitor: ↑ levels of citalopram, clobazam; ↓ levels of clobidogrel ?additive hepatotoxicity risk with valproic acid or clobazam. ^{19,20} Smoked cannabis: smoking may result in 1A2 induction; e.g. ↓ levels of antipsychotics, caffeine, TCAs, theophylline, warfarin Nabilone: while a THC-mimic, does not have THC drug interactions. M: HR, BP, CNS adverse effects, psych symptoms, tx agreement, CUD, LFTs (with EPIDIOLEX)
	Nabiximols SATIVEX x extracted THC/CBD 2.7mg THC & 2.5mg CBD per spray (peppermint flavour; poor taste) (contains alcohol) * refrigerate prior to dispensing Not available in USA.	Preferred over cannabis. ^{CFP¹⁸} ✓ advanced cancer pain (adjunctive) ✓ multiple sclerosis neuropathic pain or spasticity (adjunctive) • Spasticity may require lower doses than pain (e.g. 4-5 sprays vs >8 sprays per day).	• Spray under the tongue or into side cheek (may alternate sides). • Shake vial gently. Device requires priming (3 sprays). Initial: 1 spray sublingually HS Usual: 1 spray sublingually q4h Usual max: 12 sprays per day	3 vial pack = \$700 (\$2.60/spray) (90 spray/vial) \$84 \$504 \$1008	
	Cannabidiol EPIDIOLEX extracted CBD 100mg/mL solution ^{FDA¹⁸} (contains alcohol & sesame oil)	✓ Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients ≥2 years of age	Seizures (Lennox-Gastaut or Dravet): ≥2yrs: 2.5-10mg/kg/dose po BID usually give before a meal • Food ^{fat/caloric} increases absorption.	Not available in Canada	
	Dronabinol MARINOL synthetic THC USA only: 2.5, 5mg, 10 cap (in sesame oil) 5mg/mL solution SYNDROS (contains alcohol)	✓ severe nausea/vomiting from cancer chemotherapy ✓ AIDS-related anorexia	Initial: 2.5mg po HS Usual: 2.5-5mg po TID-QID for chemo nausea/vomiting (~5mg/m ²) 2.5mg po BID ac lunch and supper for anorexia ^{AIDS³} Max: 20mg/day	D/C from Canadian market	
Medical Cannabis	Oral Cannabis Oils x THC/CBD in various ratios, e.g.: 25mg THC / 0mg CBD per mL 1mg THC / 20mg CBD per mL 3mg THC / 3mg CBD capsule many other formulations & potencies available. Veteran's Affairs: coverage available for some patients	No official indications. May be medically authorized in Canada to any patient for any indication. • THC detected in urine drug screen up to 4 weeks after last dose (esp. chronic/heavy users) • Oral vs inhaled: Oral has lower bioavailability (~10% vs ~25%), ¹ slower onset (30-60min vs 5-10min), ⁴ longer duration (4-8 hrs vs 2-4 hrs), ¹ & does not have respiratory risk. • Smoked vs vaped: smoking speculated to have more respiratory risk (but data limited). Vaping ~2x more potent (smoking destroys some drug via combustion). • Vaping devices: Consider a Health Canada approved vaporizer. "Marijuana Math" note: estimate only – some uncertainty! What is the estimated THC dose if 1 joint, containing 0.5 grams of 10% THC dried cannabis, is smoked? Answer: 500mg cannabis x 10% THC x 50% loss to combustion ≈ 25mg THC	Initial: 2-3mg of CBD +/- THC po HS (e.g. 0.1mL of 20mg/mL CBD) Usual: Uncertain due to lack of randomized trials. Titrate slowly. (Consider: dronabinol & nabiximols labelling suggest max doses of 25-30mg THC per day.) • Food increases absorption. • Consider 1 st dose at 7p.m. to leave time for assessing effect. • Consider weekend trial start (or when impairment less disastrous). Guidelines recommend avoiding smoked cannabis. ^{2,7} Initial: 1-2 puffs inhaled HS. (1 puff of joint ≈ 1-10mg THC. Variation is due to inhalation depth, puff size, THC potency, smoked vs vaped, joint size, etc.) Usual: Uncertain due to poor quality evidence. Titrate slowly. Based on market data for 2017 in Canada, medical cannabis patients titrated themselves to an average dose of 750mg dried cannabis per day. ¹⁶	\$7 e.g. 60mL bottle of oil containing 1200mg CBD ≈ \$130	
	Dried Cannabis x THC/CBD in various ratios, often to smoke/vape, e.g.: 12.5% THC 4% THC / 10% CBD 1% THC / 13% CBD many other potencies available. * refrigerate for max stability Veteran's Affairs: coverage available for some patients Trend: towards ↑ potency products. ⁵⁴ (e.g. 4% THC in 1995 → 12% in 2014) Average joint: ~0.5g dried cannabis. ^{WHO} Medical use in USA: 33 States & D.C. Recreational use USA: 10 States & D.C.			In 2017 in Canada, the average medical price was \$8/g and the average street price was \$7.5/g \$12-24 for 1-2 puff HS \$180 for 750mg/day \$720 for 3g/day	

Who could be a candidate for cannabinoid therapy?

- Cannabinoids are generally not considered first- or second-line therapy for any indication. Reserve use for patients who have failed other therapies.²
e.g. may consider if tried ≥3 drugs for neuropathic pain or ≥2 drugs for palliative pain or if refractory to standard therapies for CINV, spasticity in MS or SCI, or cachexia [or refractory pediatric seizure]
- Watch for relative **contraindications** such as **pregnancy, breastfeeding**, age <21-25, a history of psychosis/schizophrenia, or substance abuse history. For more details, see [RxFiles Cannabis Q and A](#).

Prescribing/Authorizing Cannabinoids Safely

Cannabinoids are potential drugs of abuse; caution is needed when prescribing. In general, follow similar principles to prescribing opioids (see [RxFiles Prescribing Opioids Safely](#)). A summary of these principles is as follows:

- Optimize suitable non-cannabis therapies first (drug and non-drug)
- Check electronic health records (e.g. PIP in SK) at baseline and with each visit
Note: medical cannabis does not appear on PIP. Option to check order hx with Licensed Producer. Document cannabis use on local EMR (just like tobacco, alcohol, etc.).
- Baseline urine drug screen, and randomly thereafter
THC metabolite detected = THC-COOH. Note: urine drug screens in SK do not test for CBD.
- Assess risk of addiction, and monitor for cannabis use disorder →
- Ensure the patient understands cannabinoids are prescribed as a **trial**
Reasonable trial duration may be ~12 weeks.
- Obtain Treatment Agreement and Informed Consent
Search "agreement" at www.rxfiles.ca for a sample cannabinoid tx agreement. Agreement includes safe storage – especially important if kids nearby!¹⁶⁷
- Monitor for benefits & harms. **Exit Strategy:** stop (often taper) if trial unsuccessful.
Possible taper to prevent withdrawal: ↓ by 25% q1week.

Monitoring for Cannabis Use Disorder (CUD)

9% of adults who use cannabis non-medically may develop addiction (& up to 17% if started in adolescence).⁵¹

Prior to Tx: Screen for CUD	During Tx: Monitor for CUD	In primary care, ⁴⁷ watch for:
1) Options for screening: CUDIT-R specific to cannabis. ⁴⁵ CAGE-AID Questionnaire short & practical. ⁴⁶ 2) Diagnosing: use DSM-5 criteria. ⁵³	During Tx: Monitor for CUD <ul style="list-style-type: none"> • rapid or unsanctioned dose ↑ • frequent changes needed • wants dried cannabis only • wants high potency THC only • misuse of other substances • urine drug screen: aberrant • concerns from friends/family • poor functioning (school/work/social) • missed follow-up; reports of lost or stolen cannabis 	<ul style="list-style-type: none"> ♦ respiratory problems ♦ depression/anxiety/amotivation ♦ issues functioning/concentrating (e.g. in studies, work, relationships)
Symptoms of Cannabis Withdrawal (onset 1-2 days, peak 2-6 days) Anger, aggression, appetite change, weight loss, anxiety , irritability, restlessness, sleep disturbance, cannabis craving, physical discomfort.		Treating CUD: ⁴⁸⁻⁵⁰ <ol style="list-style-type: none"> Brief interventions Withdrawal management (e.g. sleep hygiene, brief symptomatic relief, ?nicotine replacement) Psychosocial interventions (e.g. motivational enhancement, CBT) <p>[Note: Pharmacologic tx, e.g. with naltrexone, appears ineffective]</p>

Choosing Between Products

note: currently Canada has a "two-stream" cannabis system: medically authorized cannabis, and cannabis through retail sale.

	Prescription Cannabinoids e.g. nabilone, nabiximols	Cannabis	
		via medical authorization	via retail sale
Quality Control	Regulated. Health Canada pharmaceutical production standards in place (has Drug Identification Number).	In Saskatchewan, sellers from both medical & retail streams use the same cannabis sources (a Health Canada licensed producer). Production standards exist, including testing for pesticides & THC/CBD concentrations. ⁴³ However, similar to non-Rx herbal supplements, cannabis may have less vigorous production standards than Rx drugs.	
Dosing & Guidance	<ul style="list-style-type: none"> • Standardized. • Some indications and dosing are Health Canada approved. • Will show up on the electronic medical record (e.g. PIP in Saskatchewan). 	<ul style="list-style-type: none"> • Challenging. e.g. THC in 1 puff of cannabis joint can range from 1 to >10mg. No "studied usual dose". • Prescriber may pick strain/ratio and max quantity allowed for patient. May limit duration, e.g. "one 60mL bottle of CBD oil, then see prescriber for further authorization." • Overall, less control than prescription products (e.g. "dosing interval" does not exist). 	Patient selects the product, dose, dosing interval, and route of administration. Difficult to provide monitoring, boundaries, or education.
	Note: despite prescriber attempts to guide product and dosing, patients may supplement with retail cannabis against medical advice.		
Access	Dispensed by community pharmacy.	Exclusively by mail/courier.	At cannabis retail store; online ordering possible too.
Paperwork	Written or electronic prescription.	See Paperwork Required for Medical Cannabis box, right.	None.
Coverage	<ul style="list-style-type: none"> • Occasional private insurance coverage. • SK EDS and prior approval criteria for specific indications. 	<ul style="list-style-type: none"> • Occasional private insurance coverage (e.g. Manulife and Sunlife on a case-by-case basis as of 2018). • Veteran's affairs coverage (max 3g/day dried cannabis) ~\$8/gram; May grow at home to ↓ costs. {Calculator for home production limit amount - link below}	No coverage by any drug plans or private insurance; can't be claimed on income tax. Average price still uncertain (Ranges from \$8-20/gram)

Paperwork Required for Medical Cannabis

1. Complete medical document form (link ①). In SK, complete treatment agreement form (link ②, or visit RxFiles.ca and search "agreement").⁵⁶
2. Submit medical document to Licensed Producer (link ③) who mails cannabis (dried, oil, buds, or leaves) to patient.
3. Or, patients may apply to grow their own product at home (e.g. 15 plants for 3g/day, see link ④).
4. Medical document must be re-authorized at least once per year.
5. In SK, prescribers required to keep list of pts.
6. No set daily limit; max possession is lesser of 150g or 30 times daily amount.

① www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/marihuana/info/med-eng.pdf
 ② <http://www.cps.sk.ca/IMIS/Documents/Programs%20and%20Services/Patient%20Agreement%20Template%20-%20Medical%20Cannabis.pdf>
 ③ www.hc-sc.gc.ca/dhp-mps/marihuana/info/list-eng.php
 ④ www.canada.ca/en/health-canada/topics/production-cannabis-for-your-own-medical-purposes.html

Calculator for the production of a limited amount of cannabis for medical purposes: <http://health.canada.ca/en/health-canada/services/drug-health-products/buying-using-drug-health-products-safely/cannabis-medical-purposes/accessing-cannabis-medical-purposes/production-cannabis-medical-purposes/calculator.html>
 Ⓜ=EDS in SK Ⓡ=prior approval NIHB ✕ =not covered SK Ⓢ=not covered NIHB Ⓛ=NIHB palliative care 2-AG=2-Arachidonoylglycerol AEA=Anandamide CBD=cannabidiol CB1=cannabinoid receptor type 1 CB2=cannabinoid receptor type 2 CBZ=carbamazepine
 CINV=chemotherapy-induced nausea and vomiting CUD=cannabis use disorder MS=multiple sclerosis PIP=pharmaceutical information program TCA=tricyclic antidepressant; SCI=spinal cord injury SJW=St. John's Wort THC=delta-9-tetrahydrocannabinol

Cannabinoids: Online Extras

College of Physicians & Surgeons of Saskatchewan: The College's bylaw

The College's bylaw which regulates physician authorization of medical marihuana is now in effect. The bylaw is numbered Bylaw 19.2 of the regulatory bylaws of the College and is available at the College's website. Visit: http://www.cps.sk.ca/imis/CPSS/CPSS/Programs_and_Services/Medical_Marijuana/Medical_Cannabis.aspx. A summary of the bylaw follows:

1. The bylaw begins with a statement that there has not been sufficient scientific or clinical assessment to provide evidence about the safety and efficacy of marihuana for medical purposes. The bylaw begins with an acknowledgement that federal government regulations have authorized the use of marihuana for medical purposes.
 2. A physician cannot authorize the use of marihuana for a patient unless the physician is also the treating physician for the condition for which the patient is authorized to use marihuana. For example, if a patient is to be authorized to use medical marihuana to deal with symptoms of MS, the physician must also be the treating physician for the patient's MS.
 3. A physician must review the patient's medical history, review relevant records pertaining to the condition for which the use of marihuana is authorized and conduct an appropriate physical examination before authorizing the patient's use of marihuana.
 4. The patient must sign a written treatment agreement which contains the following:
 - A) A statement from the patient that the patient will not seek a prescription for marihuana from any other physician during the period for which the marihuana is prescribed;
 - B) A statement by the patient that the patient will utilize the marihuana as prescribed, and will not use the marihuana in larger amounts or more frequently than is prescribed;
 - C) A statement by the patient that the patient will not give or sell the prescribed marihuana to anyone else, including family members;
 - D) A statement by the patient that the patient will store the marihuana in a safe place
- Sample treatment agreement: <http://www.cps.sk.ca/iMIS/Documents/Programs%20and%20Services/Patient%20Agreement%20Template%20-%20Medical%20Cannabis.pdf>
- Or visit www.RxFiles.ca and search "agreement".
5. The physician's record for the patient must include the requirements for all medical records and, in addition, contain the following:
 - A) The treatment agreement signed by the patient;
 - B) The diagnosis for which the patient was authorized to purchase marihuana;
 - C) A statement of what other treatments have been attempted for the condition for which the use of marihuana was prescribed and the effect of such treatments;
 - D) A statement of what, if anything, the patient has been advised about the risks of the use of marihuana;
 - E) A statement that in the physician's medical opinion the patient is likely to receive therapeutic or palliative benefit from the use of marihuana to treat the patient's condition.
 6. The physician must retain a single record, separate from other patient records, which can be inspected by the College, and which contains:
 - A) The patient's name, health services number and date of birth;
 - B) The quantity and duration for which marihuana was prescribed;
 - C) The medical condition for which marihuana was prescribed;
 - D) The name of the licensed producer from which the marihuana will be obtained, if known to the physician.
 7. Physicians who prescribe marihuana will be required to provide the College with the information referenced in paragraph 6:
 - A) Every twelve months if the physician has prescribed marihuana to fewer than 20 patients in the preceding 12 months;
 - B) Every six months if the physician has prescribed marihuana to 20 or more patients in the preceding 12 months.
 8. The bylaw prohibits physicians from diagnosing or treating patients at the premises of a licensed producer;
 9. The bylaw prohibits physicians who prescribe marihuana from having an economic or management interest in a licensed producer;
 10. The bylaw prohibits physicians from storing or dispensing marihuana from any location where the physician practices medicine.

References: Cannabinoid Chart – www.RxFiles.ca

1. Health Canada. Information for health care professionals: Cannabis (marihuana, marijuana) and the cannabinoids. 2013. Available from <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html>. Accessed August 17, 2018.
2. Allan GM, Ramji J, Perry D, Ton J, Beahm NP, Crisp N, Dockrill B, Dubin RE, Findlay T, Kirkwood J, Fleming M. Simplified guideline for prescribing medical cannabinoids in primary care. *Canadian Family Physician*. 2018 Feb 1;64(2):111-20.
3. Fischer B, Russell C, Sabioni P, van den Brink W, Le Foll B, Hall W, Rehm J, Room R. Lower-risk cannabis use guidelines: a comprehensive update of evidence and recommendations. *American journal of public health*. 2017 Aug;107(8):e1-2.
4. RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2018. CPS online: Cannabis [cited August 17, 2018]. Available from www.myrxtx.ca. Subscription required.
5. Canadian Pharmacists Association. Cannabis for Medical Purposes Guide. 2018. Available from https://www.pharmacists.ca/cpha-ca/assets/File/education-practice-resources/Cannabis_EvidenceGuide_2018.pdf. Accessed August 17, 2018.
6. College of Family Physicians of Canada. Authorizing dried cannabis for chronic pain or anxiety: preliminary guidance. 2014. Available from: <https://www.cfpc.ca/uploadedFiles/Resources/PDFs/Authorizing%20Dried%20Cannabis%20for%20Chronic%20Pain%20or%20Anxiety.pdf>. Accessed August 17, 2018.
7. Kahan M, Srivastava A, Spithoff S, Bromley L. Prescribing smoked cannabis for chronic noncancer pain. Preliminary recommendations. *Can Fam Physician* 2014;60:1083-90 (Eng), e562-70 (Fr).
8. Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *New England Journal of Medicine*. 2014 Jun 5;370(23):2219-27.
9. Nugent SM, Morasco BJ, O'neil ME, Freeman M, Low A, Kondo K, Elven C, Zakher B, Motu'apuaka M, Paynter R, Kansagara D. The effects of cannabis among adults with chronic pain and an overview of general harms: A systematic review. *Annals of internal medicine*. 2017 Sep 5;167(5):319-31.
10. Koppel BS, Brust JC, Fife T, Bronstein J, Youssof S, Gronseth G, Gloss D. Systematic review: Efficacy and safety of medical marijuana in selected neurologic disorders Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014 Apr 29;82(17):1556-63.
11. Allan GM, Finley CR, Ton J, Perry D, Ramji J, Crawford K, Lindblad AJ, Korownyk C, Kolber MR. Systematic review of systematic reviews for medical cannabinoids: Pain, nausea and vomiting, spasticity, and harms. *Canadian Family Physician*. 2018 Feb 1;64(2):e78-94.
12. Meng H, Johnston B, Englesakis M, Moulin DE, Bhatia A. Selective cannabinoids for chronic neuropathic pain: a systematic review and meta-analysis. *Anesthesia & Analgesia*. 2017 Nov 1;125(5):1638-52.
13. Whiting PF, Wolff RF, Deshpande S, Di Nisio M, Duffy S, Hernandez AV, Keurentjes JC, Lang S, Misso K, Ryder S, Schmidtkofer S. Cannabinoids for medical use: a systematic review and meta-analysis. *Jama*. 2015 Jun 23;313(24):2456-73.
14. Smith LA, Azariah F, Lavender VT, Stoner NS, Bettiol S. Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy. *Cochrane Database Syst Rev* 2015;(11):CD009464.
15. Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W. Cannabis-based medicines for chronic neuropathic pain in adults. *The Cochrane Library*. 2018 Jan 1.
16. Health Canada. Cannabis Market Data, 2018. Available from <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/licensed-producers/market-data.html>. Accessed August 17, 2018.
17. Casarett D. The achilles heel of medical cannabis research—inadequate blinding of placebo-controlled trials. *JAMA internal medicine*. 2018 Jan 1;178(1):9-10.
18. Beal JE, Olson R, Laubenstein L, Morales JO, Bellman P, Yangco B, Lefkowitz L, Plasse TF, Shepard KV. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *Journal of pain and symptom management*. 1995 Feb 1;10(2):89-97.
19. Devinsky O, Cross JH, Laux L, Marsh E, Miller I, Nabbout R, Scheffer IE, Thiele EA, Wright S. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *New England Journal of Medicine*. 2017 May 25;376(21):2011-20.
20. Devinsky O, Patel AD, Cross JH, Villanueva V, Wirrell EC, Privitera M, Greenwood SM, Roberts C, Checketts D, VanLandingham KE, Zuberi SM. Effect of Cannabidiol on Drop Seizures in the Lennox–Gastaut Syndrome. *New England Journal of Medicine*. 2018 May 17;378(20):1888-97.
21. Wilsey B, Marcotte T, Deutsch R, Gouaux B, Sakai S, Donaghe H. Low-dose vaporized cannabis significantly improves neuropathic pain. *J Pain* 2013;14(2):136-48.
22. Wilsey B, Marcotte T, Tsodikov A, Millman J, Bentley H, Gouaux B, et al. A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. *J Pain* 2008;9(6):506-21.
23. Elzinga S, Ortiz O, Raber J. The Conversion and Transfer of Cannabinoids from Cannabis to Smoke Stream in Cigarettes. Available from <http://cannabinetics.org/pdfs/thca-a.pdf>
24. Cannimed prices available from <https://www.cannimed.ca/collections/all>. Accessed August 17, 2018.
25. Busse JW, Craigie S, Juurlink DN, Buckley DN, Wang L, Couban RJ, et al. **Guideline for opioid therapy and chronic noncancer pain. CMAJ. 2017 May 8;189(18):E659-E666.** Also accessible in full online at: <http://nationalpaincentre.mcmaster.ca/guidelines.html>
26. Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend*. 2011 May 1;115(1-2):120-30.

27. **COMPASS**. Ware MA, Wang T, Shapiro S, Collet JP; COMPASS study team. Cannabis for the Management of Pain: Assessment of Safety Study (COMPASS). *J Pain*. 2015 Dec;16(12):1233-1242.
28. Laumon, B., Gadegbeku, B., Martin, J. L., and Biecheler, M. B. (2005). Cannabis intoxication and fatal road crashes in France: population based case-control study. *BMJ*. 331: 1371
29. Alberta College of Family Physicians. Tools for Practice #210: **Blazing Through the Evidence on THC Versus CBD Combinations in Medical Cannabinoids**. Danielle Perry, Joey Ton, G. Michael Allan. Available from https://www.acfp.ca/wp-content/uploads/tools-for-practice/1524259665_tfp210thc-cbd.pdf. Accessed August 17, 2018.
30. Health Canada. **National Cannabis Survey, first quarter 2018**. Available from <https://www150.statcan.gc.ca/n1/daily-quotidien/180418/dq180418b-eng.htm>. Accessed August 17, 2018.
31. FDA drug product monograph. Epidiolex (cannabidiol) oral solution. Available from https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210365lbl.pdf. Accessed August 17, 2018.
32. Moon AM, Buckley SA, Mark NM. Successful Treatment of Cannabinoid Hyperemesis Syndrome with Topical Capsaicin. *ACG Case Reports Journal*. 2018;5:e3. doi:10.14309/crj.2018.3.
33. Thiele EA, Marsh ED, French JA, Mazurkiewicz-Beldzinska M, Benbadis SR, Joshi C, et al. Cannabidiol in patients with seizures associated with Lennox–Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2018; 391: 1085–96.
34. Health Canada. Cannabis Stats Hub. Available from <https://www150.statcan.gc.ca/n1/pub/13-610-x/cannabis-eng.htm>. Accessed August 17, 2018.
35. Aldington S, Williams M, Nowitz M, Weatherall M, Pritchard A, McNaughton A, Robinson G, Beasley R. THE EFFECTS OF CANNABIS ON PULMONARY STRUCTURE, FUNCTION AND SYMPTOMS. *Thorax*. 2007 Jul 31; [Epub ahead of print] Smoking cannabis was associated with a dose-related impairment of large airways function resulting in airflow obstruction and hyperinflation. In contrast, cannabis smoking was seldom associated with macroscopic emphysema. The 1:**2.5 to 5 dose equivalence between cannabis joints and tobacco cigarettes** for adverse effects on lung function is of major public health significance.
36. Jouanous E, Lapeyre-Mestre M, Micallef J; French Association of the Regional Abuse and Dependence Monitoring Centres (CEIP-A) Working Group on Cannabis Complications. Cannabis use: signal of increasing risk of **serious cardiovascular disorders**. *J Am Heart Assoc*. 2014;3:e000638
37. Reis JP, Auer R, Bancks MP, et al. **Cumulative Lifetime Marijuana Use and Incident Cardiovascular Disease** in Middle Age: The Coronary Artery Risk Development in Young Adults (**CARDIA**) Study. *Am J Public Health*. 2017 Apr;107(4):601-606.
38. Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of **marijuana** inhalation: what cardiologists need to know. *Am J Cardiol*. 2014 Jan 1;113(1):187-90.
39. Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. *Circulation*. 2001 Jun 12;103(23):2805-9.
40. **WHO** data. World Health Organization (WHO). Cannabis: a health perspective and research agenda. 1997. Available from: <http://apps.who.int/iris/bitstream/handle/10665/63691/WHO?sequence=1>
41. Bonn-Miller MO, Loflin MJE, Thomas BF, Marcu JP, Hyke T, Vandrey R. Labeling Accuracy of Cannabidiol Extracts Sold Online. *JAMA*. 2017 Nov 7;318(17):1708-1709.
42. Vandrey R, Raber JC, Raber ME, Douglass B, Miller C, Bonn-Miller MO. Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products. *JAMA*. 2015 Jun 23-30;313(24):2491-3.
43. Health Canada. Additional Information for Licensed Producers under the Access to Cannabis for Medical Purposes Regulations. Available from <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/licensed-producers/additional-information-licensed-producers-under-access-cannabis-medical-purposes-regulations.html>. Accessed September 7, 2018.
44. Haney M, Malcolm RJ, Babalonis S, Nuzzo PA, Cooper ZD, Bedi G, Gray KM, McRae-Clark A, Lofwall MR, Sparenborg S, Walsh SL. Oral Cannabidiol does not Alter the Subjective, Reinforcing or Cardiovascular Effects of Smoked Cannabis. *Neuropsychopharmacology*. 2016 Jul;41(8):1974-82.
45. bpac.org.nz; The Cannabis Use Disorder Identification Test – Revised. Accessed online 21Sep18 at https://bpac.org.nz/BPJ/2010/June/docs/addiction_CUDIT-R.pdf
46. Canadian Guideline for Safe and Effective Use of Opioids for CNCP – Part B. CAGE Questionnaire. Accessed online 21Sep18 at http://nationalpaincentre.mcmaster.ca/documents/cage_questionnaire.pdf
47. Winstock AR, Ford C, Witton J. Assessment and management of cannabis use disorders in primary care. *BMJ*. 2010 Apr 1;340:c1571.
48. Spithoff S, Kahan M. Cannabis and Canadian youth: evidence, not ideology. *Can Fam Physician*. 2014 Sep;60(9):785-7, 793-5.
49. Sabioni P, Le Foll B. Psychosocial and pharmacological interventions for the treatment of cannabis use disorder. *F1000Res*. 2018 Feb 12;7:173.
50. De Aquino JP, Sherif M, Radhakrishnan R, Cahill JD, Ranganathan M, D'Souza DC. The Psychiatric Consequences of Cannabinoids. *Clin Ther*. 2018 Apr 17. pii: S0149-2918(18)30106-1.
51. Canadian Centre on Substance Use and Addiction. Cannabis – Canadian Drug Summary. 2018 Jun. Accessed online 04 Sept 2018 at <http://www.ccsa.ca/Resource%20Library/CCSA-Canadian-Drug-Summary-Cannabis-2018-en.pdf>
52. Kalk NJ, Boyd A, Strang J, Finch E. Spice and all things nasty: the challenge of synthetic cannabinoids. *BMJ (Clinical research ed.)*. 2016 Oct 24;355:i5639.
53. Miller et al. Marijuana Addictive Disorders and DSM-5 Substance-Related Disorders. *J Addict Res Ther*. January 2017 S11 013. Available from https://www.researchgate.net/publication/315959756_Marijuana_Addictive_Disorders_and_DSM-5_Substance-Related_Disorders

54. ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC. Changes in cannabis potency over the last 2 decades (1995–2014): analysis of current data in the United States. *Biological psychiatry*. 2016 Apr 1;79(7):613-9.
55. Hels T, Lyckegaard A, Simonsen KW, Steentoft A, Bernhoft IM. Risk of severe driver injury by driving with psychoactive substances. *Accident Analysis & Prevention*. 2013 Oct 1;59:346-56.
56. College of Physician and Surgeons of Saskatchewan. Medical Cannabids. Accessed from http://www.cps.sk.ca/imis/CPSS/CPSS/Programs_and_Services/Medical_Marijuana/Medical_Cannabis.aspx on October 10, 2018.
57. Frank B, Serpell MG, Hughes J, Matthews JN, Kapur D. Comparison of analgesic effects and patient tolerability of nabilone and dihydrocodeine for chronic neuropathic pain: randomised, crossover, double blind study. *BMJ*. 2008 Jan 26;336(7637):199-201.
58. Nielsen S, Sabioni P, Trigo JM, Ware MA, Betz-Stablein BD, Murnion B, Lintzeris N, Khor KE, Farrell M, Smith A, Le Foll B. Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis. *Neuropsychopharmacology*. 2017 Aug;42(9):1752-1765.
59. Campbell G, Hall WD, Peacock A, Lintzeris N, Bruno R, Larance B, Nielsen S, Cohen M, Chan G, Mattick RP, Blyth F, Shanahan M, Dobbins T, Farrell M, Degenhardt L. 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 Jul;3(7):e341-e350.
60. Corroon JM Jr, Mischley LK, Sexton M. Cannabis as a substitute for prescription drugs - a cross-sectional study. *J Pain Res*. 2017 May 2;10:989-998.
61. Lucas P et al. Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. *Int J Drug Policy*. 2017;42:30-35.
62. Boehnke, K. F., E. Litinas, and D. J. Clauw. 2016. Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. *Journal of Pain* 17(6):739–744.
63. <https://www.theglobeandmail.com/canada/british-columbia/article-number-of-veterans-using-opioids-declines-significantly-as-cannabis/>
64. Bradford AC. et al. Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D. *Health Aff (Millwood)*. 2016 Jul 1;35(7):1230-6. doi: 10.1377/hlthaff.2015.1661
65. Ashley C et al. Association between US state medical cannabis laws and opioid prescribing in the Medicare Part D population. *JAMA Intern Med*. 2018;178(5):667-672.
66. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999–2010. *JAMA internal medicine*. 2014;174(10):1668-1673. doi:10.1001/jamainternmed.2014.4005.
67. Wang GS, Roosevelt G, Heard K. Pediatric marijuana exposures in a medical marijuana state. *JAMA Pediatr*. 2013 Jul;167(7):630-3.
68. Wade DT, Collin C, Stott C, Duncombe P. Meta-analysis of the efficacy and safety of Sativex (nabiximols), on spasticity in people with multiple sclerosis. *Mult Scler* 2010;16(6):707-14.
- 69.

Additional references for Cannabinoids:

- Adashi EY. Brief Commentary: Marijuana Use During Gestation and Lactation-Harmful Until Proved Safe. *Ann Intern Med*. 2019 Jan 8.
- Agar M. Medicinal Cannabinoids in **Palliative Care**. *Br J Clin Pharmacol*. 2018 Jun 20.
- Agrawal A, Rogers CE, Lessov-Schlaggar CN, et al. Alcohol, Cigarette, and Cannabis Use Between 2002 and 2016 in **Pregnant Women** From a Nationally Representative Sample. *JAMA Pediatr*. 2018 Nov 5.
- Akturk HK et al. Association between cannabis use and **risk for diabetic ketoacidosis** in adults with type 1 diabetes. *JAMA Intern Med* 2018 Nov 5.
- Akturk HK, Taylor DD, Camsari UM, et al. Association Between Cannabis Use and Risk for **Diabetic Ketoacidosis** in Adults With Type 1 Diabetes. *JAMA Intern Med*. 2018 Nov 5.
- Allan GM, Finley CR, Ton J, et al. Systematic review of systematic reviews for **medical cannabinoids: Pain, nausea and vomiting, spasticity, and harms**. *Can Fam Physician*. 2018 Feb;64(2):e78-e94.
- Allan GM, Ramji J, Perry D, et al. **Simplified guideline** for prescribing **medical cannabinoids** in primary care. *Can Fam Physician*. 2018 Feb;64(2):111-120.
- Ananth P, Ma C, Al-Sayegh H, et al. Provider Perspectives on Use of **Medical Marijuana in Children With Cancer**. *Pediatrics*. 2017 Dec 12.
- Arterberry BJ, Treloar Padovano H, Foster KT, et al. Higher average potency across the United States is associated with progression to **first cannabis use disorder symptom**. *Drug Alcohol Depend*. 2018 Dec 6.
- Baker T, Datta P, Rewers-Felkins K, Thompson H, Kalleem RR, Hale TW. Transfer of **inhaled cannabis into human breast milk**. *Obstet Gynecol*. 2018;131:783-788.
- Barnes MP. The case for **medical cannabis**-an essay by M P Barnes. *BMJ*. 2018 Jul 25;362:k3230.
- Bertrand KA, Hanan NJ, Honerkamp-Smith G, et al. Marijuana Use by **Breastfeeding** Mothers and Cannabinoid Concentrations in Breast Milk. *Pediatrics*. 2018 Sep;142(3). pii: e20181076.
- Bhattacharyya S, Wilson R, et al. Effect of **Cannabidiol** on Medial Temporal, Midbrain, and Striatal Dysfunction in People at Clinical **High Risk of Psychosis**: A Randomized Clinical Trial. *JAMA Psychiatry*. 2018 Aug 29.
- Boehnke KF, Clauw DJ. Brief Commentary: Cannabinoid **Dosing for Chronic Pain** Management. *Ann Intern Med*. 2019 Jan 8.
- Bonomo Y, Souza JD, Jackson A, et al. Clinical issues in **cannabis** use. *Br J Clin Pharmacol*. 2018 Jul 2.
- Bourque J, Afzali MH, Conrod PJ. Association of **Cannabis Use With Adolescent Psychotic Symptoms**. *JAMA Psychiatry*. 2018 Jun 6.
- Bradford AC, Bradford WD, Abraham A, et al. Association between US **state medical cannabis** laws and opioid prescribing in the Medicare Part D population. *JAMA Intern Med*. Published online April 2, 2018
- Braun I, Tulsy J. Reconciling the Discrepancies in Medicine's **Relationship to Medical Marijuana**. *Ann Intern Med*. 2018 Oct 2.
- Braun IM, Wright A, Peteeet J, et al. Medical **Oncologists'** Beliefs, Practices, and Knowledge Regarding **Marijuana** Used Therapeutically: A Nationally Representative Survey Study. *J Clin Oncol*. 2018 May 10;JCO2017761221.
- Briscoe J, Casarett D. **Medical Marijuana Use in Older Adults**. *J Am Geriatr Soc*. 2018 Apr 18.
- Bryan AD, et al. Effect of Including Alcohol and Cannabis Content in a **Sexual Risk-Reduction Intervention** on the Incidence of **Sexually Transmitted Infections** in Adolescents: A Cluster Randomized Clinical Trial.

JAMA Pediatr. 2018 Feb 12:e175621.

Carley DW, Prasad B, Reid KJ, et al. Pharmacotherapy of Apnea by Cannabimimetic Enhancement, the **PACE** Clinical Trial: Effects of **Dronabinol** in **Obstructive Sleep Apnea**. *Sleep*. 2017 Nov 7.

Caulley L, Caplan B, Ross E. **Medical Marijuana for Chronic Pain**. *N Engl J Med*. 2018 Oct 18;379(16):1575-1577.

Crume TL, Juhl AL, Brooks-Russell A, et al. Cannabis Use During the Perinatal Period in a State With Legalized Recreational and Medical Marijuana: The Association Between Maternal Characteristics, **Breastfeeding** Patterns, and Neonatal Outcomes. *J Pediatr*. 2018 Jun;197:90-96.

Colizzi M, Murray R. **Cannabis and psychosis**: what do we know and what should we do? *Br J Psychiatry*. 2018 Apr;212(4):195-196.

Dai H, Catley D, Richter KP, et al. **Electronic Cigarettes and Future Marijuana Use**: A Longitudinal Study. *Pediatrics*. 2018 Apr 23.

De Aquino JP, Sherif M, Radhakrishnan R, et al. The **Psychiatric Consequences of Cannabinoids**. *Clin Ther*. 2018 Apr 17.

DeFilippis EM, Singh A, Divakaran S, et al. **Cocaine and Marijuana Use Among Young Adults With Myocardial Infarction**. *J Am Coll Cardiol*. 2018 Jun 5;71(22):2540-2551.

Devinsky O, Patel AD, Cross JH, et al. Effect of **Cannabidiol** on Drop Seizures in the **Lennox-Gastaut Syndrome**. *N Engl J Med*. 2018 May 17;378(20):1888-1897.

Devinsky O, Patel AD, Thiele EA, et al. Randomized, dose-ranging safety trial of **cannabidiol in Dravet syndrome**. *Neurology*. 2018 Apr 3;90(14):e1204-e1211.

Dickson B, Mansfield C, Guiahi M, et al. **Recommendations From Cannabis Dispensaries About First-Trimester Cannabis Use**. *Obstet Gynecol*. 2018 May 7.

Dilley JA, Richardson SM, Kilmer B, et al. **Prevalence of Cannabis Use in Youths After Legalization** in Washington State. *JAMA Pediatr*. 2018 Dec 19.

Doss MK et al. **Δ9-Tetrahydrocannabinol** at retrieval drives false recollection of neutral and emotional memories. *Biol Psychiatry* 2018 May 9.

Dryburgh LM, Bolan NS, Grof CPL, et al. **Cannabis Contaminants** - sources, distribution, human toxicity and pharmacologic effects. *Br J Clin Pharmacol*. 2018 Jun 28.

Duvall SW, Lindly O, Zuckerman K, et al. Ethical Implications for Providers Regarding Cannabis **Use in Children With Autism Spectrum Disorders**. *Pediatrics*. 2019 Jan 4.

Ghasemiesfe M, Ravi D, Vali M, et al. **Marijuana Use, Respiratory Symptoms, and Pulmonary Function**: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2018 Jul 3.

Good CB, Parekh N, Fischer K, et al. Brief Commentary: **Treating Pain-The Cannabis Conundrum**. *Ann Intern Med*. 2019 Jan 8.

Goodwin RD, Cheslack-Postava K, Santoscoy S, et al. **Trends in Cannabis and Cigarette Use Among Parents With Children at Home: 2002 to 2015**. *Pediatrics*. 2018 Jun;141(6).

Gostin LO, Hodge JG Jr, Wetter SA. Enforcing **Federal Drug Laws** in States Where Medical Marijuana Is Lawful. *JAMA*. 2018 Apr 10;319(14):1435-1436.

Grof CPL. **Cannabis, from plant to pill**. *Br J Clin Pharmacol*. 2018 Apr 27.

Gulland A. Sixty seconds on . . . **marijuana smoke**. *BMJ*. 2018 Jan 9;360:k72.

Haffajee RL, MacCoun RJ, Mello MM. Behind Schedule - Reconciling **Federal and State Marijuana Policy**. *N Engl J Med*. 2018 Jul 11.

Heard K, Monte AA, Hoyte CO. Brief Commentary: Consequences of Marijuana: **Observations From the Emergency Department**. *Ann Intern Med*. 2019 Jan 8.

Hill KP, Saxon AJ. The role of **cannabis legalization** in the opioid crisis. Invited commentary. *JAMA Intern Med*. Published online April 2, 2018.

Ishida JH, Auer R, Vittinghoff E, et al. **Marijuana Use and Estimated Glomerular Filtration Rate** in Young Adults. *Clin J Am Soc Nephrol*. 2017 Oct 6;12(10):1578-1587.

Jansson LM, Jordan CJ, Velez ML. **Perinatal Marijuana Use and the Developing Child**. *JAMA*. 2018 Jul 16.

Jones HJ, Gage SH, Heron Jet al. Association of Combined Patterns of **Tobacco and Cannabis Use in Adolescence With Psychotic Experiences**. *JAMA Psychiatry*. 2018 Jan 17.

Karcher NR, Barch DM, Demers CH, et al. Genetic Predisposition vs Individual-Specific Processes in the Association Between **Psychotic-like Experiences** and Cannabis Use. *JAMA Psychiatry*. 2018 Oct 17.

Kaufman TM, Fazio S, Shapiro MD. Brief Commentary: Marijuana and **Cardiovascular Disease**-What Should We Tell Patients? *Ann Intern Med*. 2019 Jan 8.

Kelkar AH, Smith NA, Martal A, et al. An Outbreak of Synthetic **Cannabinoid-Associated Coagulopathy** in Illinois. *N Engl J Med*. 2018 Sep 27;379(13):1216-1223.

Kelsall D. Watching **Canada's experiment with legal cannabis**. *CMAJ*. 2018 Oct 15;190(41):E1218.

Kelly LE, Junker A. Considerations for clinical trials to study **cannabinoids in Canadian children with neurologic disorders**. *CMAJ*. 2018 Aug 27;190(34):E1002-E1003.

Knutzen KE, Moran MB, Soneji S. Combustible and Electronic **Tobacco and Marijuana Products in Hip-Hop Music Videos**, 2013-2017. *JAMA Intern Med*. 2018 Oct 15.

Keyhani S, Steigerwald S, Ishida J, et al. **Risks and Benefits of Marijuana Use**: A National Survey of U.S. Adults. *Ann Intern Med*. 2018 Jul 24.

Lawson JA, Scheffer IE. Therapeutic use of medicinal cannabis in difficult to manage **epilepsy**. *Br J Clin Pharmacol*. 2018 Aug 7.

Lee JD, Schatz D, Hochman J. **Cannabis and Heart Disease**: Forward Into the Great Unknown? *J Am Coll Cardiol*. 2018 Jun 5;71(22):2552-2554.

Levy S, Weitzman ER. **Acute Mental Health Symptoms in Adolescent Marijuana Users**. *JAMA Pediatr*. 2018 Dec 17.

Lucas CJ, Galettis P, Schneider J. The Pharmacokinetics and the Pharmacodynamics of **Cannabinoids**. *Br J Clin Pharmacol*. 2018 Jul 12.

Lucas CJ, Galettis P, Song S, et al. **Cannabinoid Disposition After Human Intraperitoneal Use**: An Insight Into Intraperitoneal Pharmacokinetic Properties in Metastatic Cancer. *Clin Ther*. 2018 Jan 6.

Martin JH, Cranswick N. **Care and concern with cannabinoids used therapeutically**. *Br J Clin Pharmacol*. 2018 Aug 22.

McGuire P, Robson P, Cubala WJ, et al. **Cannabidiol (CBD)** as an Adjunctive Therapy in **Schizophrenia**: A Multicenter Randomized Controlled Trial. *Am J Psychiatry*. 2018 Mar 1;175(3):225-231.

Meng H, Johnston B, Englesakis M, et al. Selective **Cannabinoids** for Chronic **Neuropathic Pain**: A Systematic Review and Meta-analysis. *Anesth Analg*. 2017 Nov;125(5):1638-1652.

Minerbi A, Häuser W, Fitzcharles MA. **Medical Cannabis for Older Patients**. *Drugs Aging*. 2018 Nov 29.

Moreno MA, Gower AD, Jenkins MC, et al. **Social Media Posts by Recreational Marijuana Companies and Administrative Code Regulations** in Washington State. *JAMA Netw Open*. 2018;1(7):e182242.

Mucke M, Phillips T, Radbruch L, et al. **Cannabis-based medicines for chronic neuropathic pain in adults**. *Cochrane Database Syst Rev*. 2018 Mar 7;3:CD012182. The potential benefits of cannabis-based medicine (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) in chronic neuropathic pain might be outweighed by their potential harms. The quality of evidence for pain relief outcomes reflects the exclusion of participants with a history of substance abuse and other significant comorbidities from the studies, together with their small sample sizes.

Newton-Howes G. The challenges of **'medical cannabis' and mental health**: a clinical perspective. *Br J Clin Pharmacol*. 2018 Jun 20.

Pergam SA et al. Cannabis use among patients at a comprehensive **cancer center** in a state with legalized medicinal and recreational use. *Cancer* 2017 Nov 15; 123:4488.

Peters EN, Bae D, Barrington-Trimis JL, et al. **Prevalence and Sociodemographic Correlates of Adolescent Use and Polyuse of Combustible, Vaporized, and Edible Cannabis Products**. *JAMA Netw Open*. 2018;1(5):e182765.

Peters J, Chien J. Contemporary **Routes of Cannabis Consumption**: A Primer for Clinicians. *J Am Osteopath Assoc*. 2018 Feb 1;118(2):67-70.

Ramaekers JG. **Driving Under the Influence of Cannabis**: An Increasing Public Health Concern. *JAMA*. 2018 Apr 10;319(14):1433-1434.

Ramar K, Rosen IM, Kirsch DB, et al. Medical Cannabis and the Treatment of **Obstructive Sleep Apnea**: An American Academy of Sleep Medicine Position Statement. *J Clin Sleep Med*. 2018 Mar 30.

Ravi D, Ghasemiesfe M, Korenstein D, et al. Associations Between Marijuana Use and **Cardiovascular Risk Factors** and Outcomes: A Systematic Review. *Ann Intern Med*. 2018 Jan 23.

Ryan SA, Ammerman SD, O'Connor ME, et al. Marijuana Use During **Pregnancy and Breastfeeding**: Implications for Neonatal and Childhood Outcomes. *Pediatrics*. 2018 Sep;142(3).pii: e20181889.

Ryan SA. A Modern Conundrum for the Pediatrician: The Safety of **Breast Milk** and the Cannabis-Using Mother. *Pediatrics*. 2018 Sep;142(3). pii: e20181921.

Schleider LB, Abuhassira R, Novack V. **Medical cannabis**: aligning use to evidence-based medicine approach. *Br J Clin Pharmacol*. 2018 Jun 2.

Schuster RM, Gilman J, Schoenfeld D, et al. One Month of **Cannabis Abstinence** in Adolescents and Young Adults Is Associated With **Improved Memory**. *J Clin Psychiatry*. 2018 Oct 30;79(6).

Scott JC, Slomiak ST, Jones JD, et al. Association of Cannabis With **Cognitive Functioning** in Adolescents and Young Adults: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2018 Apr 18.

Sharma U. **Cannabis hyperemesis syndrome**. *BMJ Case Rep*. 2018 Oct 14;2018.

Spindle TR, Cone EJ, Schlienz NJ, et al. **Acute effects of smoked and vaporized cannabis in healthy adults who infrequently use cannabis**: a crossover trial. *JAMA Netw Open*. 2018;1(7):e184841.

Staples JA, Redelmeier DA. The April 20 Cannabis Celebration and **Fatal Traffic Crashes** in the United States. *JAMA Intern Med*. 2018 Feb 12.

Starzer MSK, Nordentoft M, et al. Rates and Predictors of Conversion to **Schizophrenia or Bipolar Disorder** Following Substance-Induced Psychosis. *Am J Psychiatry*. 2017 Nov 28;appiajp201717020223. (Cannabis etc...)

Steigerwald S, Wong PO, Cohen BE, et al. Smoking, Vaping, and Use of **Edibles and Other Forms of Marijuana** Among U.S. Adults. *Ann Intern Med*. 2018 Aug 28.

Steigerwald S, Wong PO, Cohen BE, et al. Smoking, Vaping, and Use of **Edibles and Other Forms of Marijuana** Among U.S. Adults. *Ann Intern Med*. 2018 Dec 18;169(12):890-892.

Stockings E, 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 Oct;159(10):1932-1954.

Stockings E, Zagic D, Campbell G, et al. Evidence for **cannabis and cannabinoids** for **epilepsy**: a systematic review of controlled and observational evidence. *J Neurol Neurosurg Psychiatry*. 2018 Mar 6.

Subbaraman MS, Metrik J, Patterson D, et al. **Cannabis use during treatment for alcohol use disorders** predicts alcohol treatment outcomes. *Addiction*. 2017 Apr;112(4):685-694.

Sun AJ, Eisenberg ML. Association Between **Marijuana Use and Sexual Frequency** in the United States: A Population-Based Study. *J Sex Med*. 2017 Nov;14(11):1342-1347.

Tan WC, Sin DD. What are the long-term effects of smoked marijuana on **lung health**? *CMAJ*. 2018 Oct 22;190(42):E1243-E1244.

Tashkin DP. **Marijuana and Lung Disease**. *Chest*. 2018 May 17.

The Lancet Neurology. Clearing the haze around **medicinal cannabis**. *Lancet Neurol*. 2018 Mar;17(3):193.

Torres-Moreno MC, Papaseit E, Torrens M, et al. **Assessment of Efficacy and Tolerability of Medicinal Cannabinoids in Patients With Multiple Sclerosis** A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2018;1(6):e183485.

Trigo JM, et al. Nabiximols combined with motivational enhancement/cognitive behavioral therapy for the treatment of cannabis dependence: A pilot randomized clinical trial. *PLoS One*. 2018 Jan 31;13(1):e0190768.

Trivers KF, Phillips E, Gentzke AS, et al. **Prevalence** of Cannabis Use in Electronic Cigarettes **Among US Youth**. *JAMA Pediatr*. 2018 Sep 17.

Udow SJ, Freitas ME, Fox SH, et al. Exacerbation of **psychosis triggered by a synthetic cannabinoid** in a 70-year-old woman with Parkinson disease. *CMAJ*. 2018 Jan 15;190(2):E50-E52.

Weizman L, Dayan L, Brill S, et al. **Cannabis analgesia in chronic neuropathic pain** is associated with altered brain connectivity. *Neurology*. 2018 Oct 2 ; 91(14):e1285-e1294.

Wen H, Hockenberry JM. Association of medical and adult-use **marijuana laws with opioid prescribing** for Medicaid enrollees. *JAMA Intern Med*. Published online April 2, 2018.

Whitehill JM, et al. **Marijuana-using drivers, alcohol-using drivers, and their passengers**: prevalence and risk factors among underage college students [online May 12, 2014]. *JAMA Pediatr*.

Wilson KM, Torok MR, Wei B, Wang L, Lowary M, Blount BC. Marijuana and **Tobacco Coexposure in Hospitalized Children**. *Pediatrics*. 2018 Nov 19.

Yang YT, Szaflarski JP. The US Food and Drug Administration's Authorization of the **First Cannabis-Derived Pharmaceutical**: Are We Out of the Haze? *JAMA Neurol*. 2018 Nov 19.

Young-Wolff KC, Tucker LY, Alexeeff S, et al. Trends in Self-reported and Biochemically Tested **Marijuana Use Among Pregnant Females** in California From 2009-2016. *JAMA*. 2017 Dec 26;318(24):2490-2491.

Zhang H, Xie M, Archibald SD, et al. Association of **Marijuana Use** With Psychosocial and Quality of Life Outcomes Among Patients With **Head and Neck Cancer**. *JAMA Otolaryngol Head Neck Surg*. 2018 Aug 2.