Medical Cannabis and Acute Care

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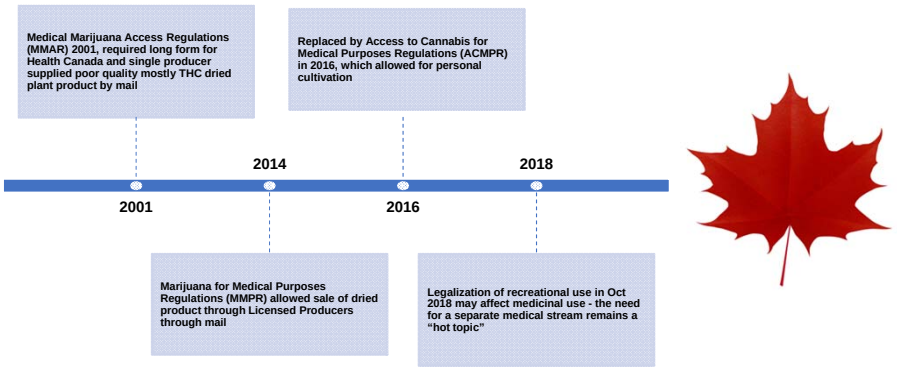
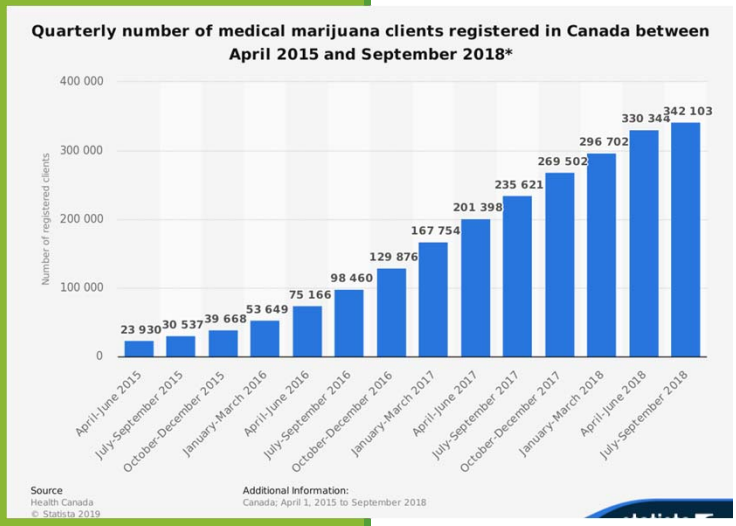
Medical Cannabis – a Timeline





Medical Cannabis Registrations

The latest data suggest that by the end of Sept 2018, almost 350K patients had registered with Health Canada through ACMPR, up from fewer than 100 in 2001

Source: Health Canada, 2019

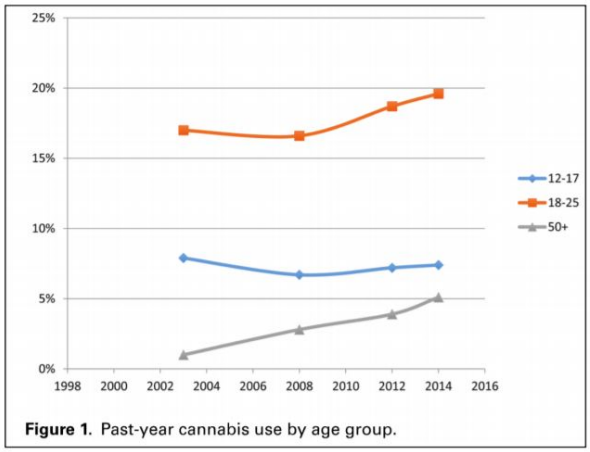


Figure 1. Past-year cannabis use by age group.

(Schauer et al., *Am J Prev Med* 2016)

Medical vs Recreational

MEDICAL

Older, less experienced users (40+)

Prefer high CBD/low THC

Prefer oils/caps vs smoked

Interested in topicals, suppositories, SL sprays

Use cannabis as an alternative to Rx opioids or mood stabilizers

May have medical conditions which require guidance regarding choices of strains

RECREATIONAL

Young users

High THC (rosins, shatter, BHO, hash oil)

In search of euphoric effects

Tend to be resistant to non-inhaled routes of use

Table 4. Patient medical conditions

Medical Condition	n (%)
Anxiety Disorder	732 (31.7%)
Depression	729 (31.6%)
Pain	681 (29.5%)
Sleep disorder	589 (25.5%)
PTSD	502 (21.8%)
Migraines	336 (14.6%)
Degenerative Disc Disease	278 (12.1%)
Irritable bowel syndrome	247 (10.7%)
Fibromyalgia	214 (9.3%)
Spinal Disk Herniation	194 (8.4%)
ADHD	169 (7.3%)
Cancer	142 (6.2%)
Restless Leg Syndrome	137 (5.9%)
Asthma	128 (5.5%)
GERD	120 (5.2%)
Hypertension	116 (5.0%)
Diabetes	96 (4.2%)
Obsessive Compulsive Disorder	74 (3.2%)
Bipolar	71 (3.1%)
Diverticulitis	50 (2.2%)
Total Responses	2307

Patient Diagnoses

1. Mood > 85%
2. Pain > 65%
3. Sleep > 30%

(many co-morbid conditions)

Wan et al, J Pain Manage 2017;10(4)

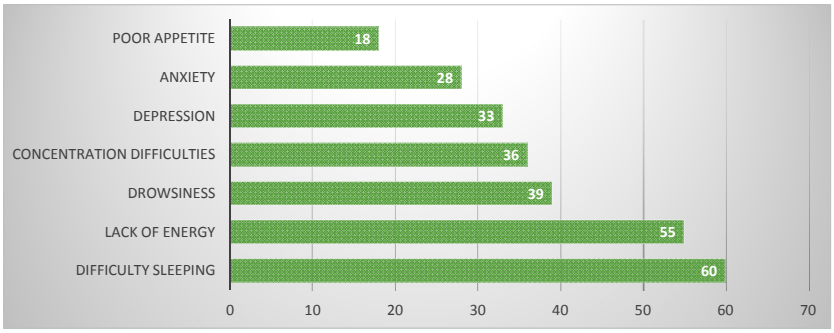
Green and Silver Report (October, 2018)

Primary Conditions:

1. Back pain (67%)
2. Anxiety (63%)
3. Arthritis (58%)

Co-Morbidities in Neuropathic Pain

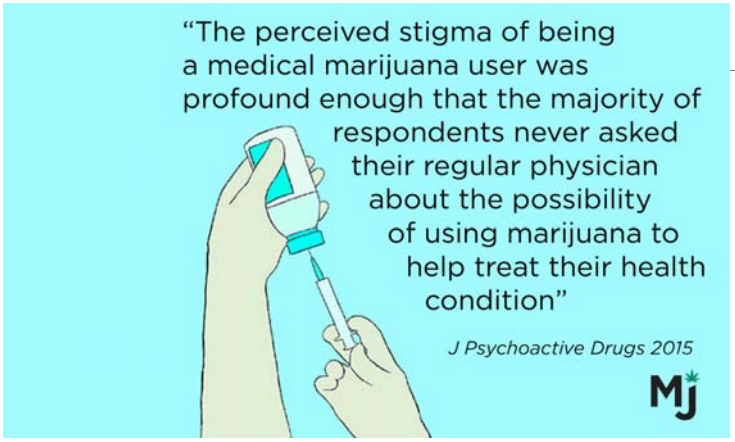
Percentage of patients with moderate-to-severe discomfort due to symptoms (n = 126)



Meyer-Rosberg K, et al. *Eur J Pain*. 2001;5(4):379-89.

Why patient request medical cannabis

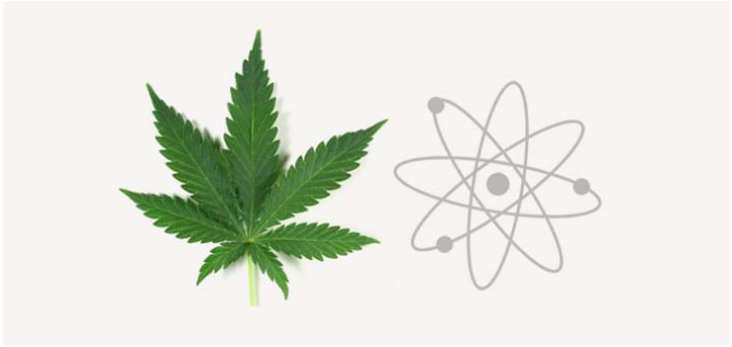
1. They do not feel that their current medication is working well enough
2. They are experiencing side effects from their current medication and wish to discontinue it
3. They have been recommended a specific medication (ex. opioid for pain) which they do not wish to take (ex. due to the risk of addiction)
4. A friend told them cannabis could help them manage their condition and "it's safer"
5. They are currently self-medicating using cannabis
6. They have complex health issues and wish to have a formal medical assessment and recommendations for which products to take (and how)
7. They have read that high dose cannabis may help treat their condition (ex. cancer)



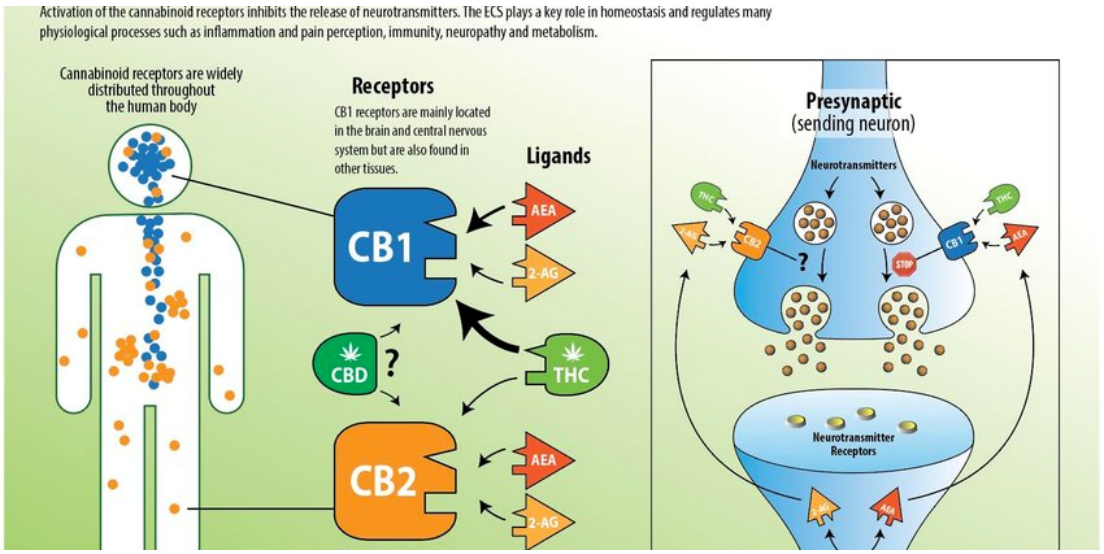
Sources of Information (or not)

Cannabis Use - A Cautionary Tale

- Unstable heart disease (chest pain, recent history of heart attack, poorly controlled atrial fibrillation, heart failure)
- History of stroke (CVA) or "mini" stroke (TIA)
- Serious lung or liver disease (asthma, COPD, cirrhosis, chronic Hep C)
- History of schizophrenia, bipolar disorder or psychosis
- History of drug or alcohol abuse or dependency
- Currently taking high doses of opioids, sedatives or benzodiazepines (ex. Ativan)
- Because cannabis crosses into the placenta and is excreted in breast milk, women who are pregnant or breastfeeding should *not* use cannabis.



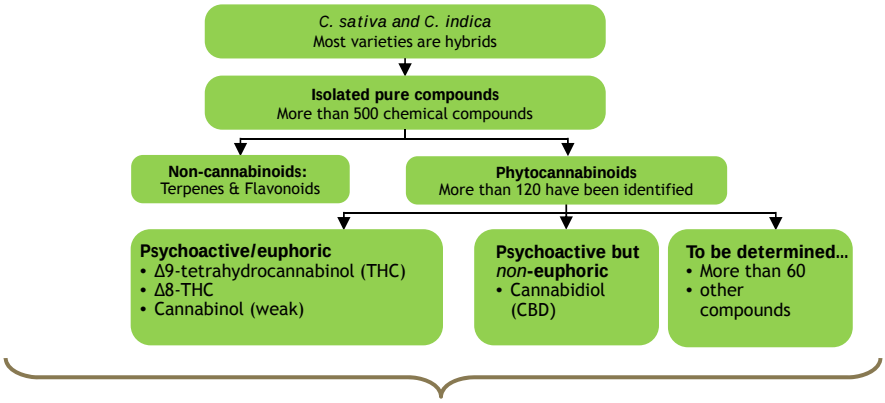
Cannabinoids and the Endocannabinoid System



"There is strong evidence that dysregulation of the ECS contributes to many human diseases including pain, inflammation, psychiatric disorders and neurodegenerative diseases"

HEALTH CANADA, 2018

What Is in Cannabis?



1. ElSohly MA, et al. *Life Sci.* 2005;78(5):539-48; 2. Wang M, et al. *J Forensic Sci.* 2017;62(3):602-11; 3. Russo EB. *Br J Pharmacol.* 2011;163(7):1344-64; 4. Kalant H. *Pain Res Manag* 2001;6(2):80-91.

Cannabis: Two Main Active Compounds

1. Responsible for many of the pharmacological effects of cannabis, including its psychoactive effect or "high"

THC

2. Varieties with high concentrations of THC can cause anxiety, disorientation, and intoxication in some patients.

Interacts with cannabinoid receptors (mostly CB1) to induce:

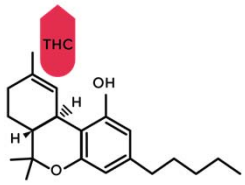
Analgesia (low dose)

Antispasmodic activity

Reduction of chemotherapy-induced nausea and vomiting

Appetite stimulation

Decreased intestinal motility



THC
(Delta-9-tetrahydrocannabinol)

Cannabis: Two Main Active Compounds

CBD

1. Indirect effects on CB1 and CB2 (i.e. does NOT bind)
2. Affects the activity of a significant number of other targets including ion channels, receptors, and enzymes

Research has indicated CBD has the following effects:

Anti-inflammatory

Analgesic

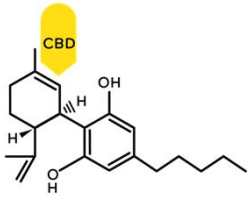
Antiemetic

Antipsychotic

Anxiolytic

Anti-convulsant

CBD (Cannabidiol)



Entourage Effect

Refers to the combined effect of the cannabinoids, terpenes, and other active ingredients work together to produce an effect that is greater than the sum of their parts

A 1981 study found that whole plant extracts produced 330% more activity than THC alone. The researchers hypothesized that cannabis contains “synergist” and “inhibitor” compounds (now known to be cannabinoids and terpenes) – “plant-based medicine”

CBD has a well-documented synergy with THC, reducing its negative effects (ex. paranoia) and amplifying its benefits (lower doses required)

Hemp CBD
vs
Cannabis CBD

CBD IS CBD….EXCEPT….

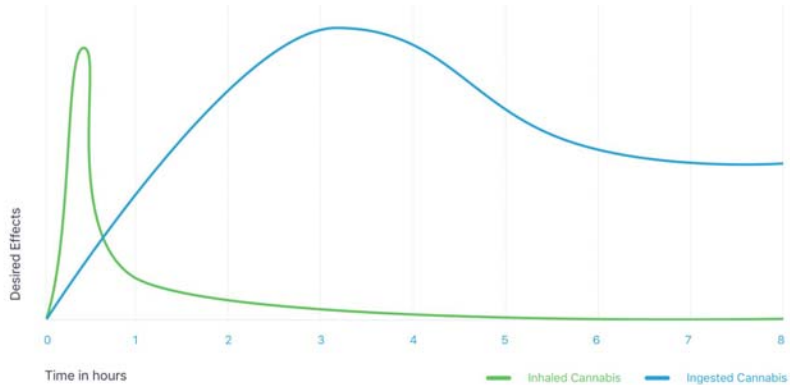
Hemp CBD vs Cannabis CBD

- Hemp is mainly grown for industrial purposes (growing conditions not regulated)
- Hemp = 3-5% CBD, require a large amount of plant to produce a small amount of hemp CBD oil (increased risk of contaminants)
- CBD oil created by licensed producers = 18-20% CBD (or higher)
- Hemp CBD oil is extracted from seeds, has little medicinal value
- Cannabis CBD oil is extracted from flowers, leaves, and the stalk of the plant
- By law, hemp oil can't contain more than 0.3% THC (0.3%) or *zero* % CBD and can only being used for non-medicinal purposes

How Patients use Medical Cannabis

Modes of Administration

		INHALED	INGESTED
ONSET		5-10 minutes	1-3 hours
DURATION		2-4 hours	6-8 hours
STARTING DOSE		1/2 teaspoon (0.1 g) of dried flowers	2.5 mg of THC and equal amount CBD
HOW IT'S ABSORBED		through the lungs directly into the bloodstream	from the GI tract, metabolized in liver before entering bloodstream



Inhalation (smoking, vaping) vs oral (oils, softgels/capsules)

Cannabis Oils & Capsules

- Taken by mouth
- Variable concentrations of THC and CBD
- 50% of THC content is metabolized to
- 11-hydroxy THC (4x more potent!)
- Onset of effect = 90 min
- Peak: 2-6hrs
- Duration of effect= 4-12 hrs

Typical Cannabis Regime for Chronic Pain

(Product Authorization: 1gm/day)

CBD

- Starting dose: 5mg OD (Spectrum Yellow oil = 0.4mL)
- May increase dose to BID-TID PRN
- No max dose per se but if no relief at doses > 30mg per dose then reconsider regime

THC:CBD

- Dosing based on THC content
- Starting dose: 1.25mg-2.5mg HS (Spectrum Blue oil = ~0.1-0.2 mL)
- Typical dose 0.3-0.4mL (3-4mg THC, 4.5-6mg CBD)
- Typical THC dose to experience euphoria = 10mg

Typical consumption: 1-3gm/day

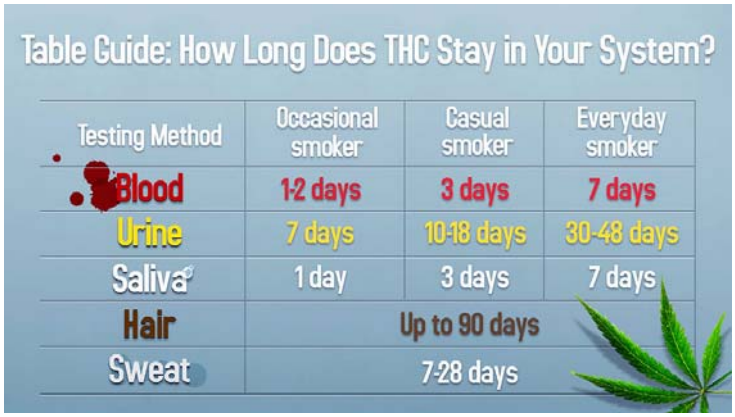
Source: MacCallum and Russo, 2018

Managing Medical Cannabis Patients in the Acute Care Setting

THC Pharmacokinetics

- ABSORPTION
  - Bioavailablity affected by route of use
    - Inhaled = 15-50%
    - Ingested – 6-20%
- DISTRIBUTION
  - THC readily distributes into fatty tissues as well as tissues with high perfusion (heart, lung, brain, liver)
  - Volume of distribution 10L/kg
  - Protein binding 97%
- METABOLISM
  - THC is metabolized by the liver via CYP450 (2C9, 2C19 and 3A4)
  - Oral ingestion results in higher concentrations of active metabolite than smoking
- EXCRETION
  - Feces 85%
  - Urine 20%
    - may remain present up to 13 days post consumption
    - positive UDS is NOT a reliable indicator of recent use

Source: RxTx, 2018 (CPS Online)



THC metabolism is highly variable may be affected by genetic polymorphisms

CBD Pharmacokinetics

- ABSORPTION
  - Bioavailablity affected by route of use
    - Inhaled = 11-45%
    - Ingested – 13-19%
- DISTRIBUTION

"No information is available for tissue distribution of CBD or its metabolites in living humans and relevant animal studies are scarce"

- METABOLISM
  - CBD is metabolized by the liver and intestines via CYP450 (2C19 and P3A4)
- EXCRETION
  - Feces 85%
  - Urine 20%
  - Half-life 18-32hrs

" The pharmacokinetics of CBD are complex and the bioavailability of oral CBD is low"

Source: Ujváry, I., & Hanuš, L. (2016

Possible Medication Interactions

- Opioids (ex. morphine, hydromorphone, codeine)
- Benzodiazepines (ex. lorazepam, clonazepam)
- Hypnotics (ex. zopiclone, sublinox)
- SSRIs (especially fluoxetine – Prozac)
- Warfarin (Coumadin) – newer blood thinners are safe (Xarelto, Eliquis)
- NSAIDs (ex. Celebrex, Diclofenac) **
- Azole antibiotics
- Statins (atorvastatin, rosuvastatin)
- St. John's Wort, 5-HTP
- Clobazam (if taken with high dose CBD)
- Valproic acid medications (ex. Divalproex)

!

Cannabis and Opiates

High doses of CBD have a *potential* interaction with opiates via CYP3A4 pathway however, adverse effects have not been documented clinically

- Oral CBD 400-800mg administered with IV fentanyl did not increase adverse effects

Lack of CB1 receptors in brainstem suggests possibility to potentiate opiate analgesia – i.e. THC (CB1 agonist) may widen therapeutic window for opiates

Important risk reduction strategy:

- CBD appears to REDUCE heroin-seeking behaviours, likely due to modulation of serotonin and dopamine
- Both CBD and THC are known to reduce opiate withdrawal symptoms

Cannabis users may require up to twice as much anesthesia when undergoing medical procedures

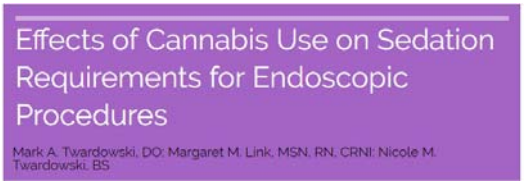
SOCIAL MEDIA HEADLINE : APRIL 2019

o

oSetting: outpatient endoscopy practice

o Methods: Retrospective chart review

o N = 250 (2015-2017)



Cannabis User group (n=25)

o 19 colonoscopies

o 2 esophagogastroduodenoscopies (EGDs)

o 4 colonoscopy/EGDs

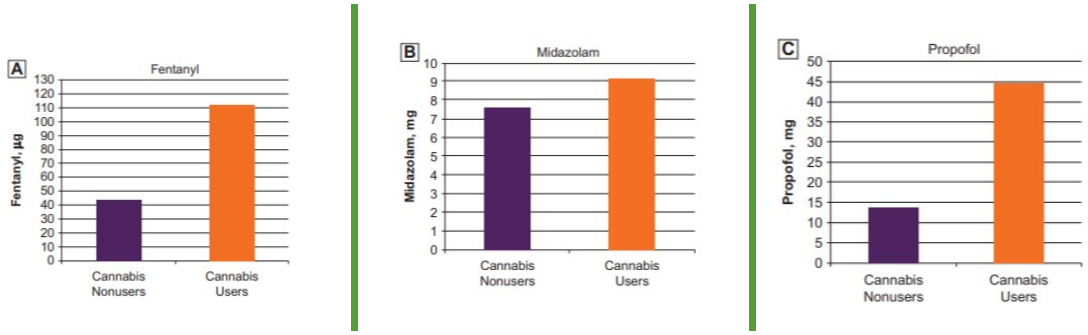
Cannabis Nonuser group (n=225)

- o 180 colonoscopies
- o 27 EGDs
- o 18 colonoscopy/EGDs

Amount of Required Sedation in Regular Cannabis Users Compared With Nonusers

	Amount of Sedation Required		
Sedative	**Cannabis Nonusers (n=225)**	**Cannabis Users (n=25)**	**Greate**
Fentanyl, µg	109.91	125.93	14
Midazolam, mg	7.61	9.15	19.6
Propofol, mg	13.83	44.81	220.5

"The statistical significance persisted when adjusted for age, sex, and use of alcohol, benzodiazepines, and opiates" (Twardorksi, et al., 2019)



Relative analgesic doses

Study Conclusions

- Regular cannabis use has a significant effect on the amount of sedation required to perform an endoscopic procedure
- The exact mechanism of the interaction is unknown
- The effect of regular cannabis use was consistent across different drug classes

"The standard practice of the endoscopist was to use no more than 10 mg of midazolam. We found that cannabis users tended to require closer to the maximum amount of the medication that is typically used, so they may have been more likely to need a higher dose for sedation and, therefore, were switched to propofol earlier than the standard patient. Nonusers required, on average, less midazolam for sedation"

"Determining cannabis use before procedural sedation can be an important tool for planning patient care"

SOURCE: J AM OSTEOPATH ASSOC. PUBLISHED ONLINE APRIL 15, 2019

Inhaled cannabis use – implications for GA

1. Inhaled cannabis increased cardiac workload, myocardial infarctions and strokes in young, chronic users

2. Chronic inhaled cannabis use caused similar pulmonary complications to those of a tobacco smoker – i.e. airway obstruction and increased anesthetic dosages needed to place laryngeal airways

3. Use within 72 hours of general anesthesia was advised against

4. *In vitro* and *in vivo* studies were contradictory regarding prothrombic or antithrombotic effects

5. The American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery recommend that cannabis use be treated an exclusionary criterion in the case of bariatric surgery (unclear if this refers only to inhaled cannabis)

Source: Huson, H. B., Granados, T. M., & Rasko, Y. (2018)

Educational Resources for Professionals

1. Spectrum e-Learning

https://spectrumcannabis.canopygrowthlearning.com

2. TMCI Global

https://themedicalcannabisinstitute.org/

3. Advancing Practice Medical Cannabis Certificate

http://www.advancingpractice.com/p-81-medical-cannabis-certificate-program.aspx

4. The Canadian Consortium for the Investigation of Cannabinoids

http://www.ccic.net

5. Monthly webinars

https://cannabiseducation.com/#webinar

QUESTIONS ?????