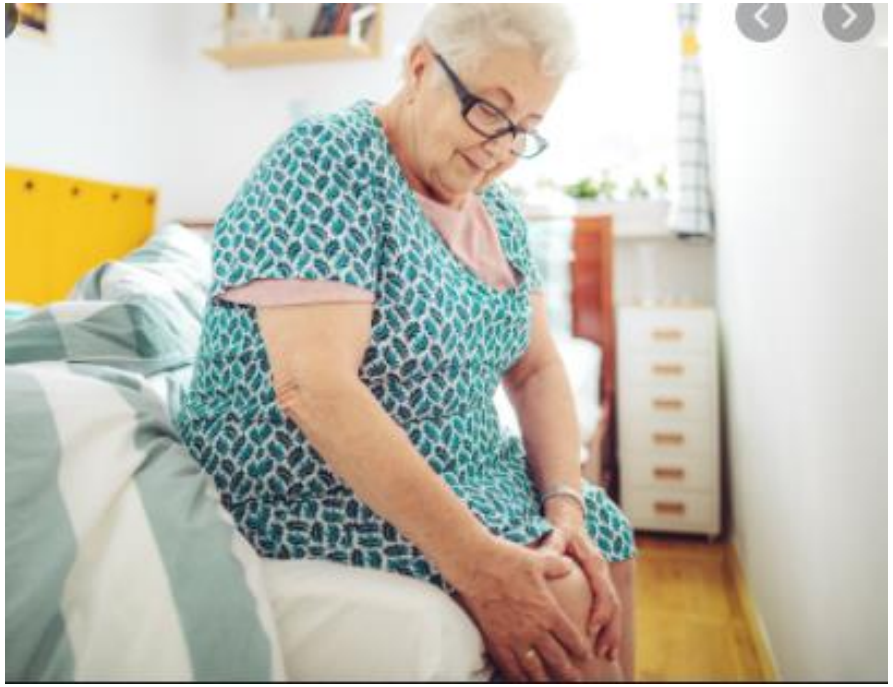
Cannabis for the elderly: pain and sleep



Mary-Ann Fitzcharles
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McGill Refresher course workshop, Nov 2020

McGill University Health Centre

Disclosure

Financial interests: Lilly (program moderator).

- **Health Canada**: Core member of Science Advisory Committee on Health Products Containing Cannabis (SAC-HPCC).
- **Australian** Centre for Cannabinoid Clinical and Research Excellence (ACRE): international advisory member
- **Arthritis Foundation US**: international advisor
- **Canadian Rheumatology Association**: lead for pragmatic approach to medical cannabis use for persons with rheumatic diseases

Objectives

- To understand the evidence for cannabis use in the elderly
- To have knowledge of the risks for use
- To be able to counsel patients effectively

Points to consider in the elderly

- Who is suggesting use
- What symptoms to be treated & severity
- Using a drug with psychoactive effects
  - Cognition
  - Balance
  - Drug-drug interaction
- Dosing & duration of action

Some key points from the previous lecture

- Poor evidence for pain and sleep
- Psychoactive effects for small amounts of THC (in young people)
- Psychomotor effects (in young people)
- Mental health concerns (Syst rev of syst rev 2020)
- Cardiovascular concerns
- Cannabis and cancer
- Artisanal products not regulated
  - Expect that all products will contain at least some THC

The elderly couple wishing to try cannabis

- Living independently
- Amy has anxiety, mild Parkinson’s &early dementia, difficulty sleeping
- Bill has angina, CHF (controlled) and inoperable OA knees. He enjoys a gin and tonic each evening

Amy has anxiety, mild dementia, mild Parkinson's and sleep problems

All studies av. Age 40-60 yrs (no age sub analyses)

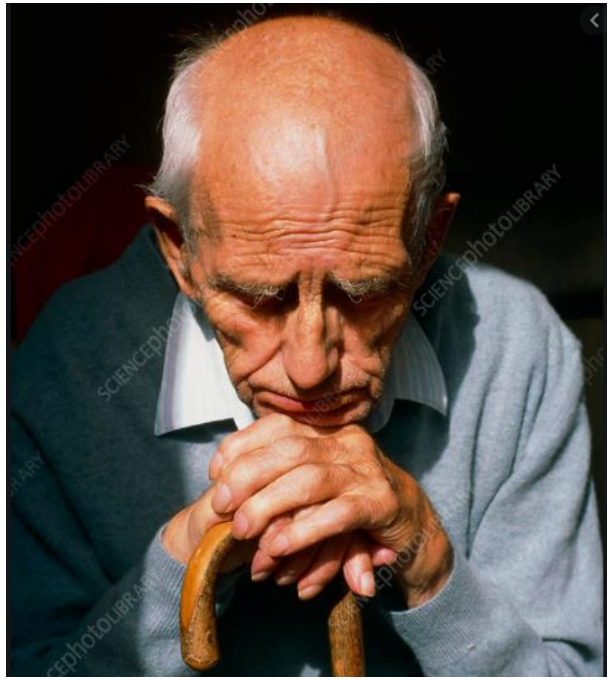
- Anxiety
  - very low quality evidence THC±CBD on anxiety with medical illness
- Sleep (Babson[4], Whiting[5])
  - CBD may help insomnia, REM sleep disorder, daytime sleepiness
  - Low quality evidence for help sleep disturbance

1. Minerbi. Drugs & Aging 2018. 2. Black N et al. Lancet Psychiatry Dec 2019 4. Babson K. Curr Psychitry Rep 2017; 5.Whiting et al. JAMA 2015

Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis

- Meta-analysis 83 studies, 3067subjects [1]
  - Anxiety, depression, PTSD, Tourette, psychosis

- Results
  - scarce evidence for effect depressive or anxiety disorders, ADHD, PTSD, Tourette syndrome, or psychosis.
  - very low quality evidence THC±CBD on anxiety + medical illness
  - insufficient evidence to provide guidance for cannabinoids in mental disorders.



1. Black N et al. Lancet Psychiatry Dec 2019

Cannabinoids: neurological disease, agitation & mood, palliative care [1]

- Neurological disease (Whiting, Am Academy Neur)
  - MS…tendency to help spasticity & pain in MS
  - Parkinson's..(10 studies, 181 pts)….± motor symptoms
- Agitation & mood (Noel, Lim)
  - Anxiety……CBD or nabilone (2 small studies)
  - Dementia agitation…(2 small studies)..mixed results
- Palliative care cancer patients (Mucke)
  - (9 studies, 1561 pts)
  - No clinically sig. effect on pain, N&V, appetite, sleep

1. Minerbi. Drugs & Aging 2018

What can we suggest for Amy

- Trial CBD at night 2.5 mg
- Do not make brownies or cookies
- Warnings
  - Risk of increased anxiety
  - All products will have little THC
  - Do not buy an artisanal product

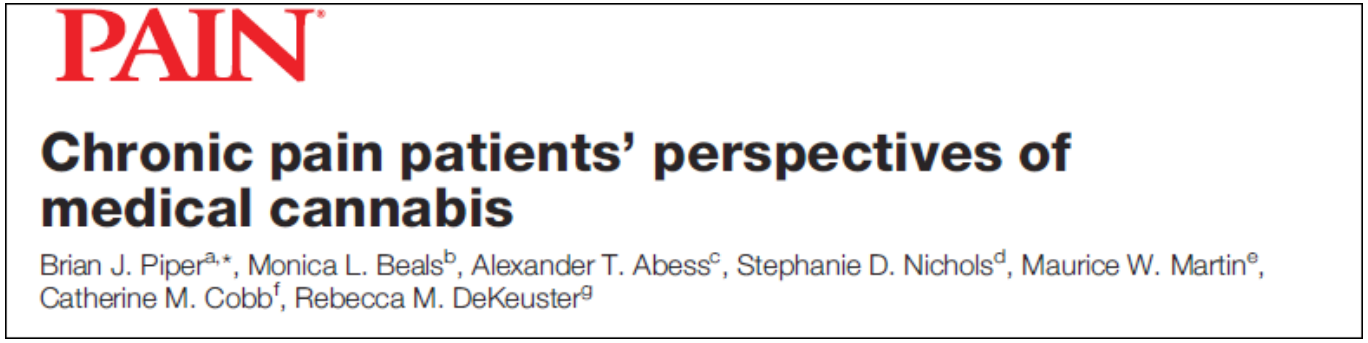
Bill has OA pain, angina and CHF

All studies av. Age 40-60 yrs (no age sub analyses)

- Pain (Cochrane, Nugent[2], Petze[3], Stockings) [1]
  - low strength evidence for neuropathic pain
  - Small effect on pain overall
  - NNT 20, NNH 3

1. Minerbi. Drugs & Aging 2018. 2.Nugent S et al Annals Int Med 2017. 3. Petze F et al..Schmerz 2016;

Patients universally attest to positive effects cannabinoids


PAIN

Chronic pain patients' perspectives of medical cannabis

Brian J. Piper[a,*], Monica L. Beals[b], Alexander T. Abess[c], Stephanie D. Nichols[d], Maurice W. Martin[e], Catherine M. Cobb[f], Rebecca M. DeKeuster[g]

- 984 pts, medical cannabis dispensaries NE USA[1]
  - >70% effective for all pains
- 1300 FM pts, US survey..National Pain Foundation[2]
  - 62% very effective

1. Piper, Pain 2017, 2 US National Pain Foundation survey 2014

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THE ONLY ARTHRITIS STUDY
Transdermal CBD in OA [1]

- Bid application: CBD total 250 mg/day, 500 mg/day, placebo
- 320 patients, mean age 62 yrs, 12 weeks, worst pain 6.9

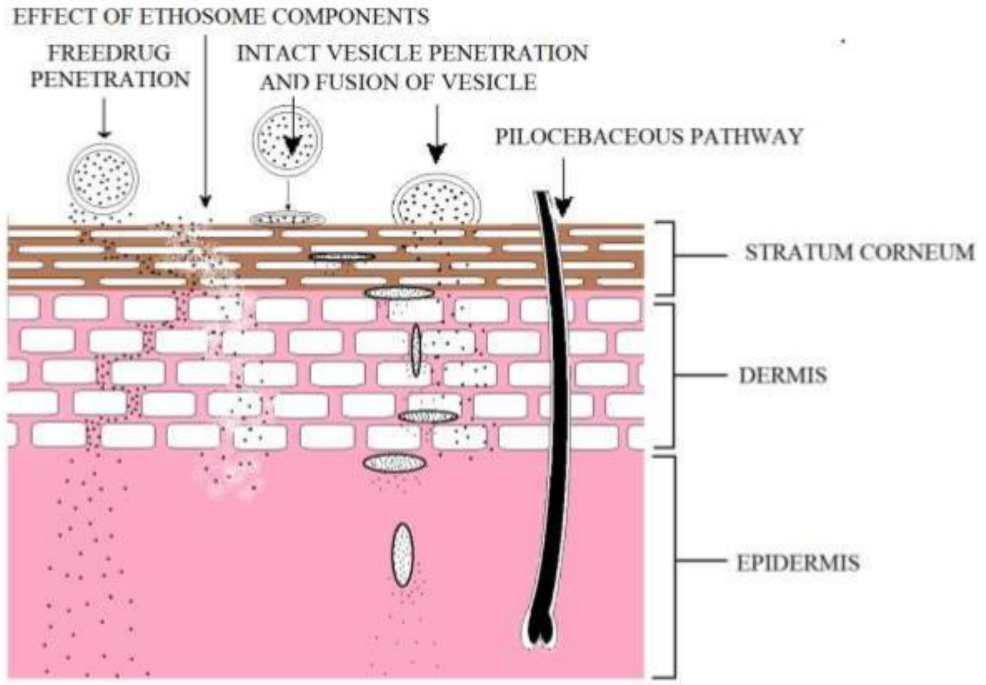
Results

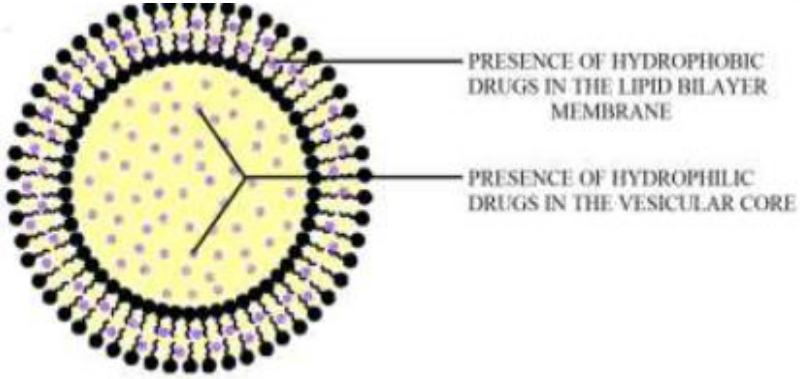
- Pain reduction not significant between groups -2.6, -2.8, -2.4
- Responder 250 mg CBD vs placebo, 53% vs 34% (p=0.016)
- Men responded better than women

1. Hunter D et al. Osteoarthritis Cartilage 2018

A perfect rubbing compound

- CBD is lipophilic
- Conc. In stratum corneu
- Ethosomal transport

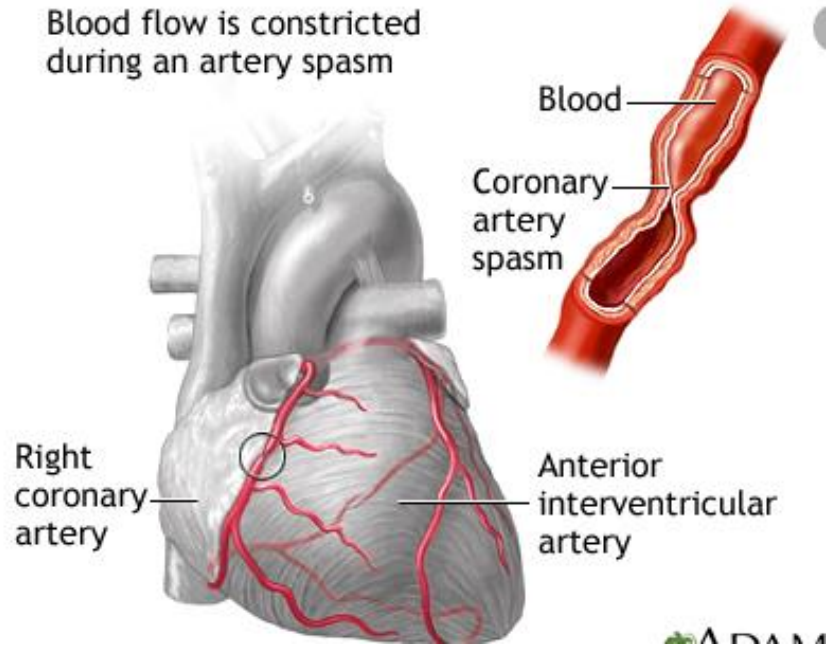




1. Lodzki M et al. J Control Release 2003.

Cannabis cardiovascular physiological effects 2020

- Activates sympathetic & parasympathetic nervous system
  - Low dose: vasodilatation, tachycardia, ↑myocardial oxygen demand
  - High dose: hypotension, bradycardia, ↓ cerebral blood flow
- Procoagulant effect…CB1 & CB2 platelets
- Vasoconstriction in coronary, cerebral and peripheral arteries
- Increased plasma volume..aldosterone effect
- Tolerance to CV effects lost rapidly



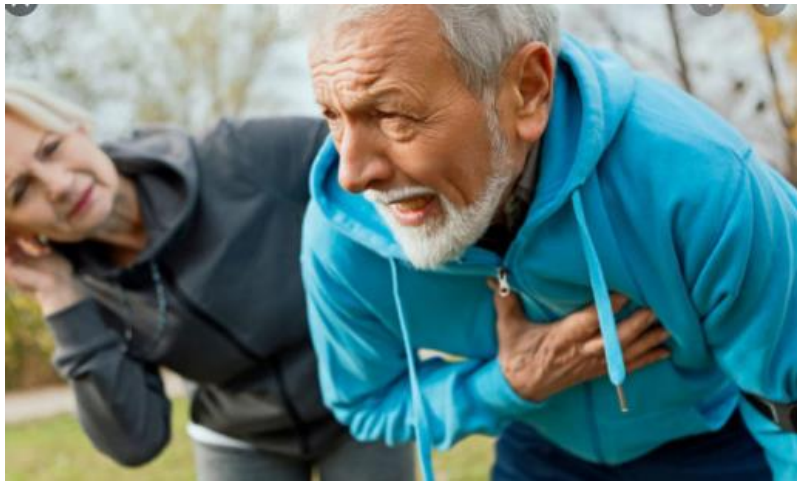
1. *Latif Z et al. J of Clin Med 2020*

Cardiovascular risks of cannabis [1]

- Myocardial infarction
  - Pediatric reports of MI, cardiac arrest, vasospasm
  - Adults 3800 MI cases, risk ↑4.8-fold after smoking cannabis [2]
  - MI mortality ↑3-fold
  - More frequent use, greater risk of cardiac events
  - Thrombus formation, endothelial dysfunction (STEMI)

- Angina
  - ↓Threshold after cannabis…time to onset symptoms ↓by 50%

- Arrythmias
  - ↑ 2-fold
  - Atrial fib (26%), ventricular fib(22%)



1. *Latif Z et al. J of Clin Med 2020. 2 Mittleman M et al. Circulation 2001*

Cannabis and driving[1-2]

- ↑ Lane weaving
- Impaired reaction times
- Drive more slowly
- *Additive effects alcohol, other drugs + cannabis

1. Hartman. *Clin Chem 2013., 2.*Bondallaz. *Forensic Science International 2016.*

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Risk of MVA when driving + cannabis

McGill study (2018)[1]

- Complex driving-related performance was affected at all time points after cannabis use
- 2x ↑ in crash risk at post-cannabis time points
- effects up to 5 hours after use

Motor Vehicle accidents

- Transport Canada (2013): Cannabis use 5x risk MVA crash[2]
- Meta-analysis 9 studies, 49,000 (fatalities or serious injuries)[3]
  - cannabis 2x risk fatal or serious MVA

1. Ogourtsova T. CMAJ 2018; 2 Beirness et al 2013.; 3. Asbridge M et al BMJ. 2012

Drug-drug interactions

Theoretical considerations only

- Cannabinoids metabolized via cytochrome P450[1]
  - Limited info in clinical practice…mostly theoretical
  - THC and CBD inhibit CYP2D6

- CBD is substrate for CYP2C19 and CYP3A4
  - CBD potential ↑antidepressants, ↑gabapentin, ↑tofacitinib, ↓clopidogrel
  - CBD can boost plasma levels of THC
  - Cannabis & tobacco induce CYP1A2..↓ TCA, ↓warfarin

1. Foster BC, et al. Cannabis and Cannabinoids: Kinetics and Interactions. Am J Med. 2019.

What can we suggest for Bill

- Do not smoke cannabis
- Consider a topical
- Not sure that a small dose THC will have ay effect
- Psychomotor effects, driving

Medical cannabis in the elderly: the concerns [1]

- Cognition
  - Effects of THC last up to 24hrs (Mensigna 2006)
  - 5* risk of MVA (Beirness 2013)

- CV risks
  - ↑HR, ↑BP
  - ↑MI, sudden death, TIA, stroke, arrhythmia
  - Recreational marijuana risk for MI, 2 million US MI pts (adjusted OR 1.031)

1. Minerbi. Drugs & Aging 2018

Medical cannabis in the elderly the concerns [1]

- Mental health
  - Aggravation of depression
  - Increased anxiety

- Elder abuse
  - Access of product by another for misuse or diversion

1. Minerbi. Drugs & Aging 2018

…in summary…cannabis in the elderly [1]

Studies to date on patients <60 yrs

Risks compounded in elderly

- Cognition
- Cardiovascular
- Gait and stability (surrogate is driving)

Cardiovascular [2,3]

↑ HR, ↑BP, ↑Myocardial oxygen demand

↑ MI, sudden cardiac death, arrhythmia, stroke & TIA

1. Minerbi. *Drugs & Aging* 2018; 2. ThomasG. *American Journal Card 2014; 3. Volkow ND. NEJM 2014.*

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2700 Israeli elderly patients

"Our study finds that the therapeutic use of cannabis is safe and efficacious in the elderly population"

- 901/2736 Israeli pts, 75 yrs, 6 mths months
  - Pain 67%, Cancer 61%
  - ↓ pain 8/10 to 4/10
  - ↓ of d/c opioid in 18%

- BUT……
  - 33% followed
  - 8/10 Pain score is very unusual
  - Designated Medical Cannabis clinic

Abuhasira. Eu J Int Med 2018

The CBD products

- CBD : OTC, wellness, dietary supplements, hemp oils
- Artisanal products
  - enriched with added cinnamon, cloves, turmeric etc
  - “pure” or boosted CBD up to 20%
  - “full-spectrum” with terpenes, flavonoids (entourage effect)

- **Inaccuracy labelling in US, Europe, Canada** [1,2,3]
  - 84 CBD commercial products analyzed [2]
  - 30% accurate
  - 21% contained THC
  - Mislabeling: vaping products 88%, oils 55%

1. Hazekamp A. Med canna & cannabinoids 2018. 2. Bonn-miller MO et al. JAMA, 2017.
3. Pavlovic R et al. Molecules 2018

FDA warnings to vendors [1]

- Medical claims not allowed for non FDA approved products
- Mislabelling of products re CBD and THC content
- Marketing as a nutraceutical or dietary supplement(not allowed when product is under study as a pharmaceutical)

1. FDA Warning letters and test results for Cannabidiol-Related products 2019

The blind men and the elephant: Systematic review of systematic reviews of cannabis use related health harms

The evidence for harms

- 44 systematic reviews, 1,053 studies
- Evidence shows a **clear association** between cannabis use and
  - Psychosis, affective disorders, sleep problems, anxiety, cognitive failures, respiratory events, CVS & GI disorders
  - Risk factor for MVA's, suicidal behaviour, partner and child violence
- Little info on dose dependency

Campeny E. et al. Eur. Neuropsychopharmacol April 2020.

Acute psychotomimetic effects cannabis 2020

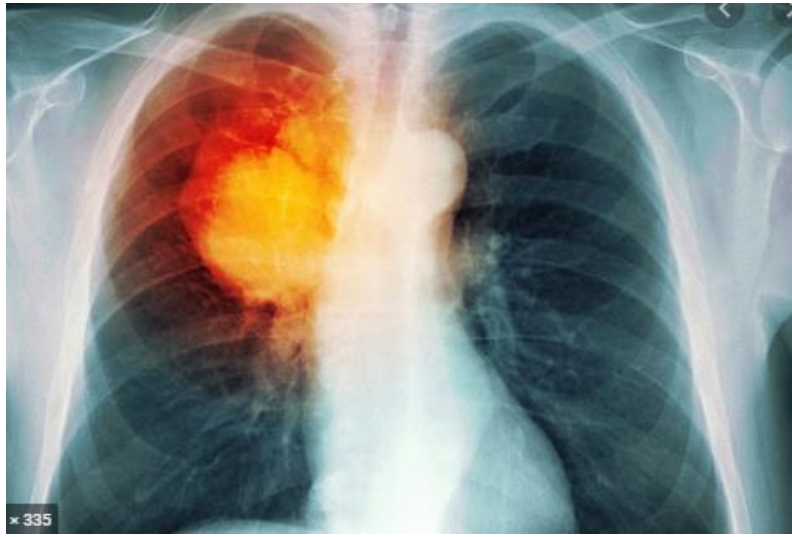
- Meta-analysis 15 studies, low risk of bias, 331 healthy subjects (mostly male, 20's) [1]
  - Acute cannabis administration…oral, inhaled IVI…tested over 1-2 hrs
  - 1.25-10mg (equivalent of a joint)

- Results
  - Single use induces acute psychotic (positive), negative symptoms and other psychiatric symptoms with large effect sizes
  - Symptoms not moderated by dose or previous cannabis use
  - CBD did not moderate these effects for 3 of 4 studies
  - Less effect in smokers…..?metabolism or ↓CB1 receptors in brain

1. *Hindley et al. Lancet Psychiatry April 2020*

Can cannabis influence treatments for cancer? Checkpoint inhibitors, cancer and cannabis

- 102 patients advanced cancers (lung, melanoma) starting immunotherapy
- 34 with cannabis, 68 no cannabis
- Mostly 20 gram/month, 28/34 inhaled



Results were significant for tumor progression and survival

users vs. non-users			
• Time to tumor progression:	3.4	vs.	13.1 months
• Overall survival:	6.4	vs.	28.5 months

"Collectively, cannabis consumption has considerable immunomodulatory effects, and its use among cancer patients needs to be carefully considered due to its potential effects on the immune system, especially during treatment with immunotherapy."

1. Bar-Sela et al. Cancers 2020

Contraindications and cautions

Contraindicated	Caution advised
• <25 years • Allergy • Pregnancy and breastfeeding • History psychosis, substance abuse, suicide ideation/attempts	• Elderly • Unstable mental health • CVS or pulmonary disease • Working in setting requiring concentration, executive function and alertness • Concomitant sedative or psychoactive drugs

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Stability of preparations, oils & teas

- Oils …better extraction, more stable than water

- Tea-15 mins boiling
  - ↓by 50% THC & CBD over 3-7 days ambient temp or fridge

- Oil- flowering tops heat to 145°C 30mins
  - 80-85% stable over 14 days, ambient temp

Standardized protocols needed for therapeutic continuity

Pacifici R. et al. Clin Chem Lab Med 2017

Cannabis dosing….limited info

- Literature identifies grams/day, (%THC , %CBD)
- Nabiximols (Sativex) CBD 2.5mg + THC 2.7mg/puff (up to 8 puffs/day)
- Most patients use 1–3 g/day (a joint 500 mg - 1 g)
- Doses > THC 20–30 mg/day may increase adverse events or induce tolerance

CBD

- ~50-2000 mg/day (children Dravet up to CBD 50mg/kg)
- Google begin with CBD 10mg, microdosing sometimes used

THC

- Most studies - 9% THC (COMPASS used 12.5% THC).
- inhalation - start with 1 inhalation , wait 15 min, then may ↑ by 1 inhalation every 15–30 min until desired symptom control
- For oils/oral - 2.5 mg THC at bedtime., then ↑ by 1.25-2.5 mg THC every 2 days.

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Cannabis administration

	Vaporization / Smoking	Oral	Oral mucosal
Onset (min)	5-10	60-180	15-45
Duration (h)	2-4	6-8	6-8
Pro	Rapid onset for acute or episodic symptoms	No odor convenient, discrete, advantage for chronic disease symptoms	Pharmaceutical form (nabiximols) documented efficacy and safety.
Con	Dexterity required, expensive, not all are portable Known hazards of smoking Unknown hazards of vaporizing	Slow onset of action Prolonged effect	Expensive

MacCallum CA, Russo EB. Eur J Int Med, 2018 .

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..and today's reality

- Patients experimenting with use
- Patients accessing cannabis via recreational route
- Medical cannabis
  - Often promoted by storefront non-medical experts, pseudoscience, offer individualized tailored treatment
  - Illegal access is cheaper
- Cannabis may have medical effects, but most not evidence-based