Cannabis in Serious Illness Care

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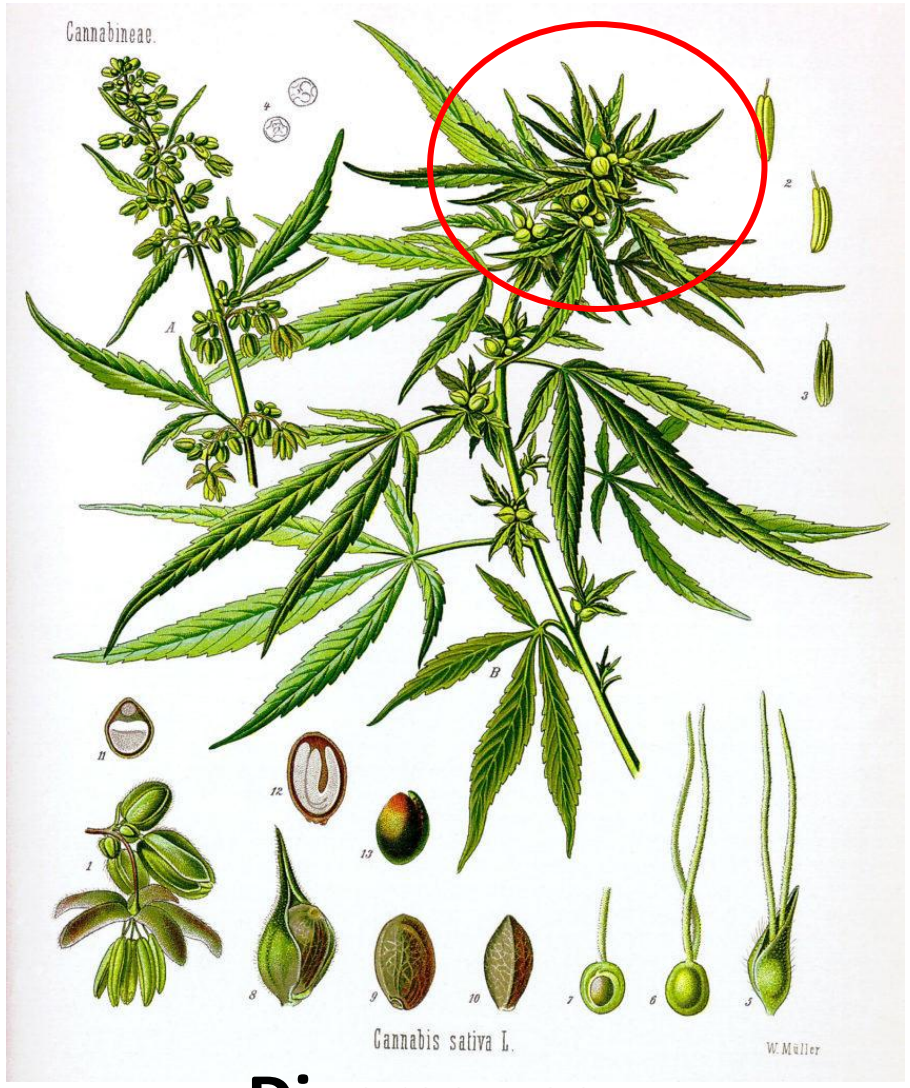
No disclosures or conflicts of interest

Learning objectives

- Review the biology and pharmacology of cannabinoids
- Describe patient and oncologist attitudes & practices around cannabis in serious illness
- Review evidence for cannabis in treating common symptoms in serious illness
- Discuss clinical implications and practical approach to use of cannabis in patients with serious illness

Humans & cannabis

Widely cultivated



Diverse use

Flower = pharmacopeia

Stalks/hemp = fiber (~8000 BCE)

Seed = food

Cannabis & cannabinoids

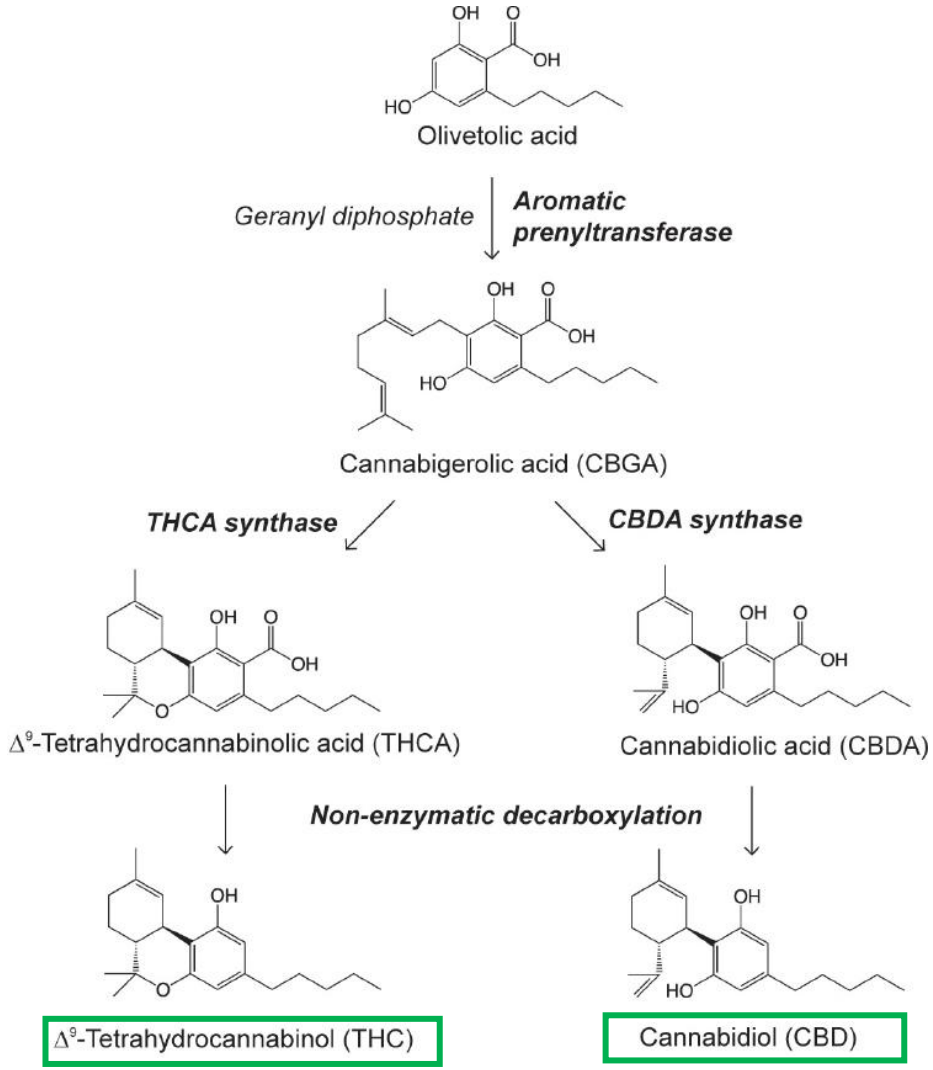
>104 different cannabinoids

Terpenes

Flavonoids

Other compounds

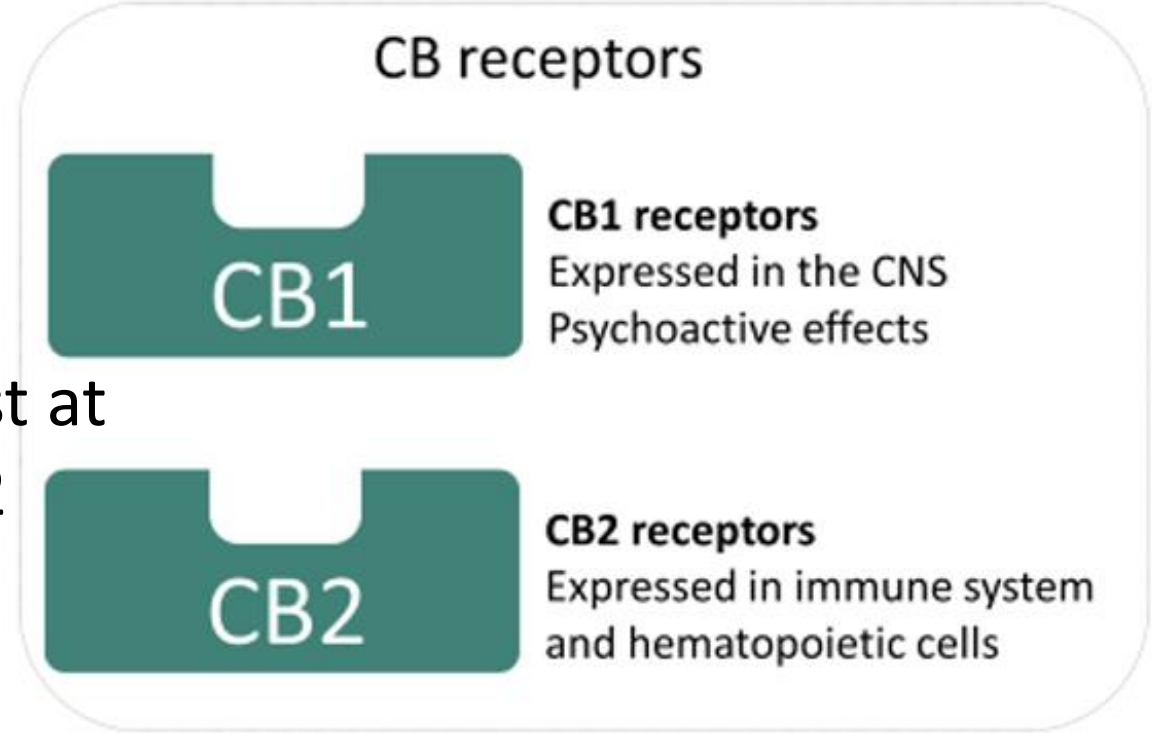
Entourage effect

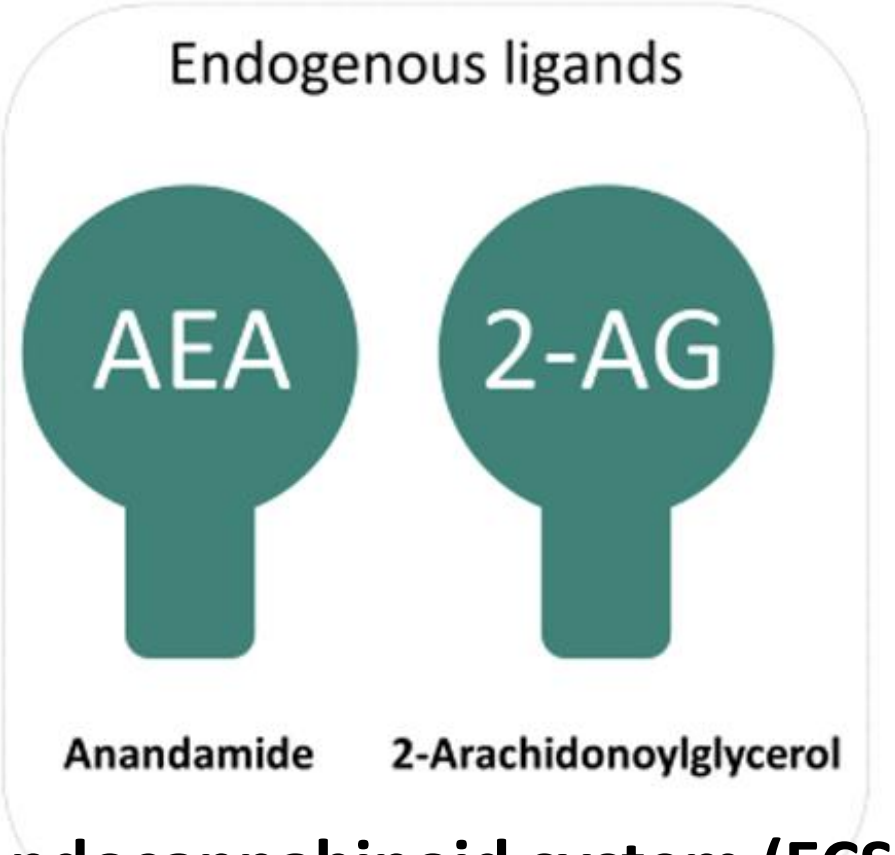


3 “chemotypes”: THC, CBD, hybrid

Cannabinoid pharmacology

G-protein coupled receptors





THC:
Partial agonist at
CB1 + CB2

CBD:
Low affinity for CB1 + CB2;
activity at 5-HT1A, TRPV1

The endocannabinoid system (ECS)

- Retrograde signaling
- Homeostatic function

Effects of cannabinoids

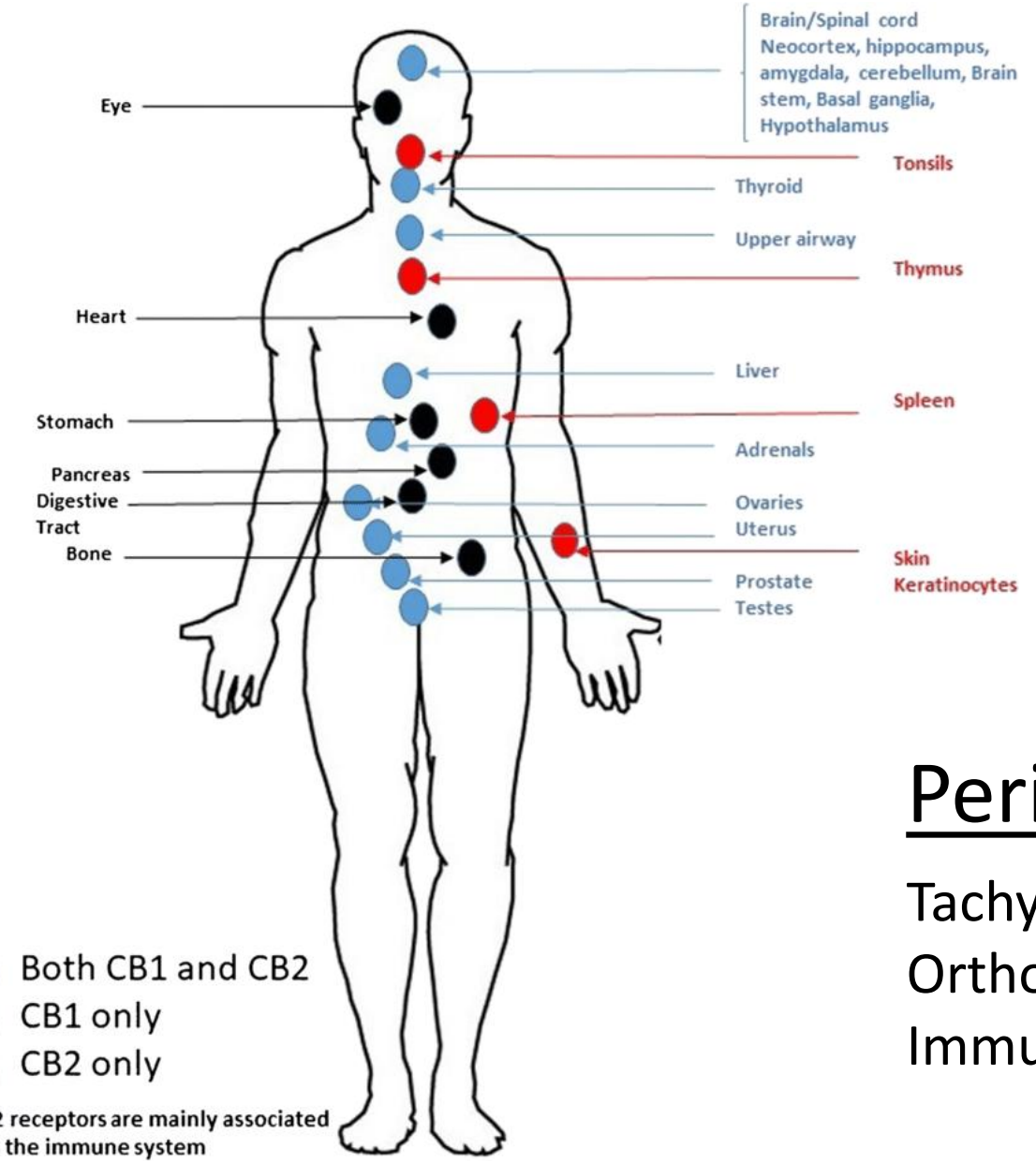
Central

Anti-nociceptive

Anti-convulsant

Psychoactive

- Relaxation, euphoria
- Inc sensory perception
- Impaired cognition
  - STM
  - reaction speed
  - Motor coordination
  - attention



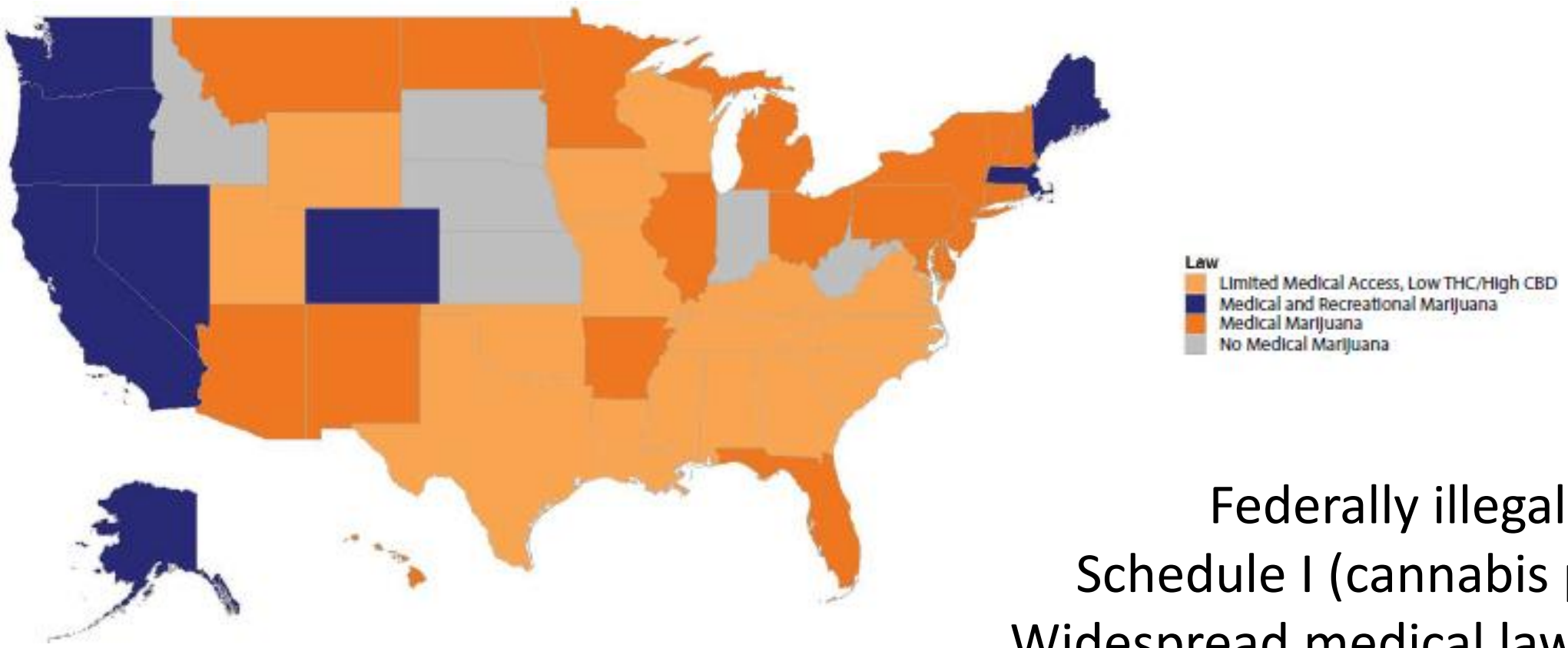
Peripheral

Tachycardia

Orthostasis

Immune modulation

Cannabis in the US



Federally illegal
Schedule I (cannabis plant)
Widespread medical laws (1996)
Recreational use
Dispensaries
Research restrictions

Cannabinoids in medicine

ABLE 2-2 Cannabinoid-Based Medications

	CANNABINOID-BASED MEDICATIONS		
	Substance	**Route of Administration**	**Description**
latural Product Derived Compounds	Cannabidiol (CBD)	Oral capsule Oromucosal spray	Cannabinoid extracted from *Cannabis* plant
	Cannabis	Multiple	Multiple active cannabinoids
	Cannador	Oral capsule	THC and CBD from *Cannabis* extract
	Epidiolex® (FDA Fast Track)	Oil	Concentrated CBD from *Cannabis* extract
	Nabiximol (Sativex®) (FDA Fast Track)	Oromucosal spray	THC and CBD extract from two *Cannabis* plant varieties
	Tetrahydrocannabinol (THC)	Oral capsule Smoked Oromucosal spray	Active cannabinoid of *Cannabis* plant
	THC/CBD	Oral capsule	Combination of cannabinoids
ynthetic Compounds	Ajulemic acid (AjA) (FDA PHASE II Active)	Oral capsule	Synthetic nonpsychoactive cannabinoid
	Dronabinol (Marinol®; Syndros®) (FDA approved)	Oral capsule	Synthetic THC
	Nabilone (Cesamet®) (FDA approved)	Oral capsule	Synthetic cannabinoid—THC analogue

Cannabinoids in medicine: therapeutic uses & risks

- Substantial evidence :

chronic pain, chemotherapy-induced NV, patient-reported spasticity in MS, sleep disturbances

- Limited evidence: Tourette's syndrome, anxiety, PTSD, appetite stimulation in AIDS

Risks:

- Cannabinoid hyperemesis syndrome (CHS)
- Cognition
- Falls
- Anxiety, psychosis

Cannabis in serious illness care

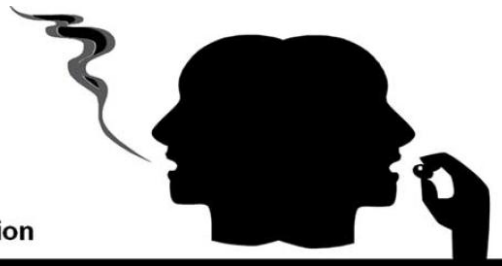
- How are patients with cancer using cannabis?

- What are oncologists' beliefs, knowledge, and practice around cannabis?

- Where are the conversations happening?

Cannabis use among patients at a comprehensive cancer center in a state with legalized medicinal and recreational use

926 patients
24% use in last year
21% in last month



Methods of Inhalation

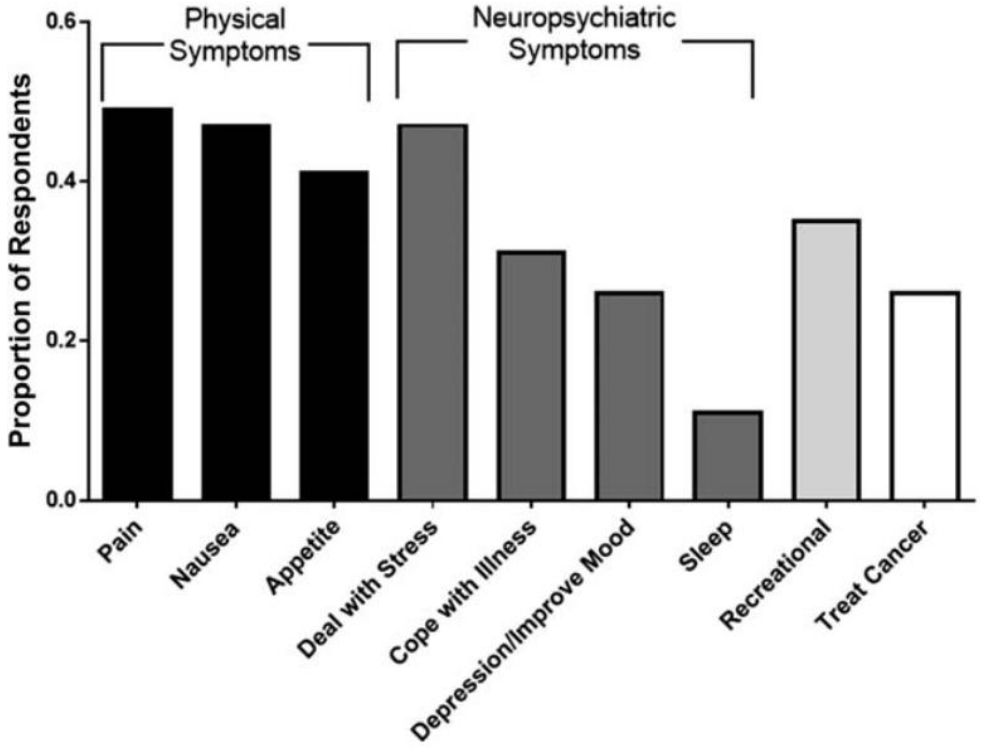
Method n=153*	n(%)
Pipe	95 (62)
Vaporizer	77 (50)
Joint	47 (31)
Water pipe/Bong	44 (29)
Other	5 (3)

Methods n=220*	n(%)
Both inhalation & ingestion	89 (40)
Ingestion only	65 (30)
Inhale/Smoke only	64 (29)
Topical	6 (3)
Other	2 (1)

Methods of Ingestion

Method n=154*	n(%)
Purchased candy/edibles	72 (47)
Butters/oils	64 (42)
Homemade baked goods	52 (34)
Purchased baked goods	40 (26)
Purchased beverages	21 (14)

Figure 2. Patterns of cannabis use among active users. *Total percentages may be greater than 100%, because respondents select more than one option.



Pegram et al. *Cancer* 2017

Pegram et al. *Cancer* 2017

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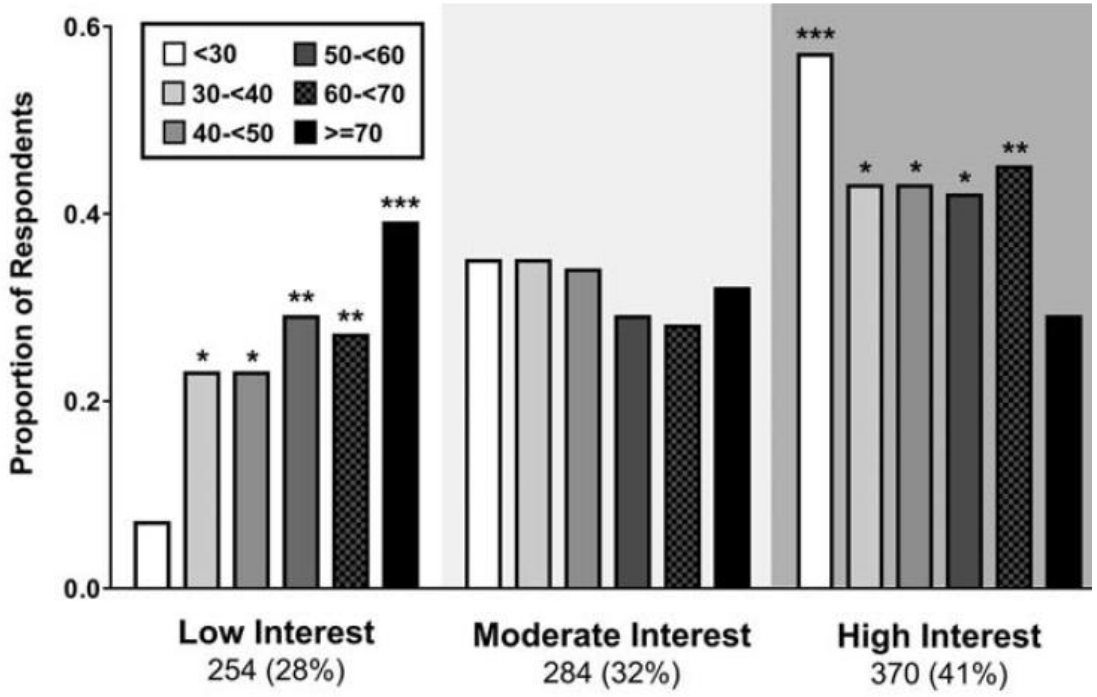
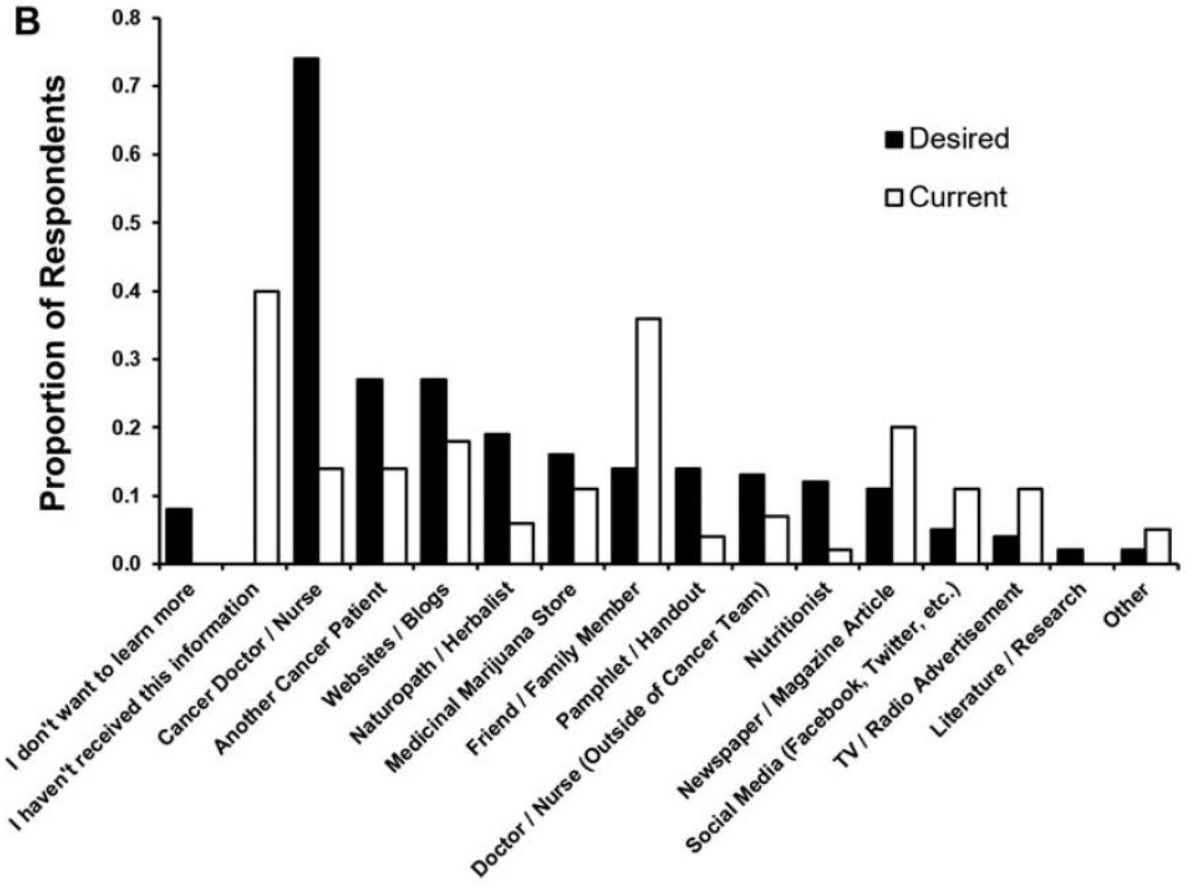
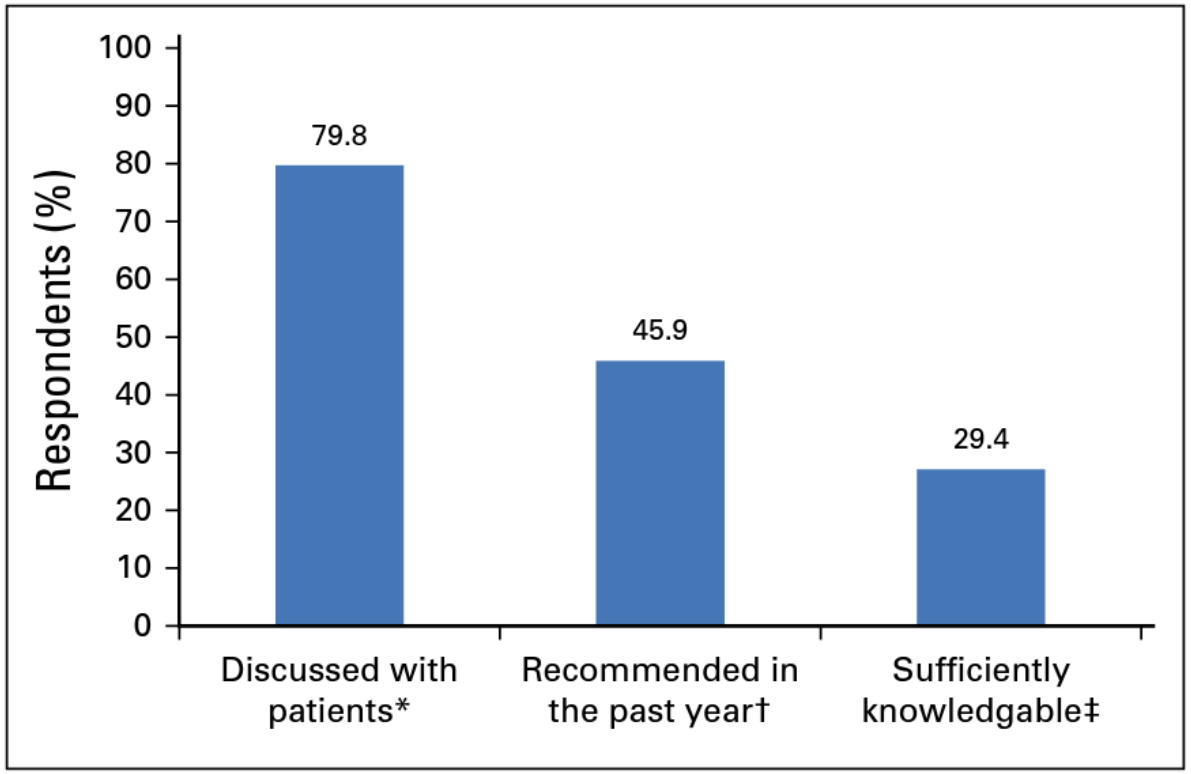
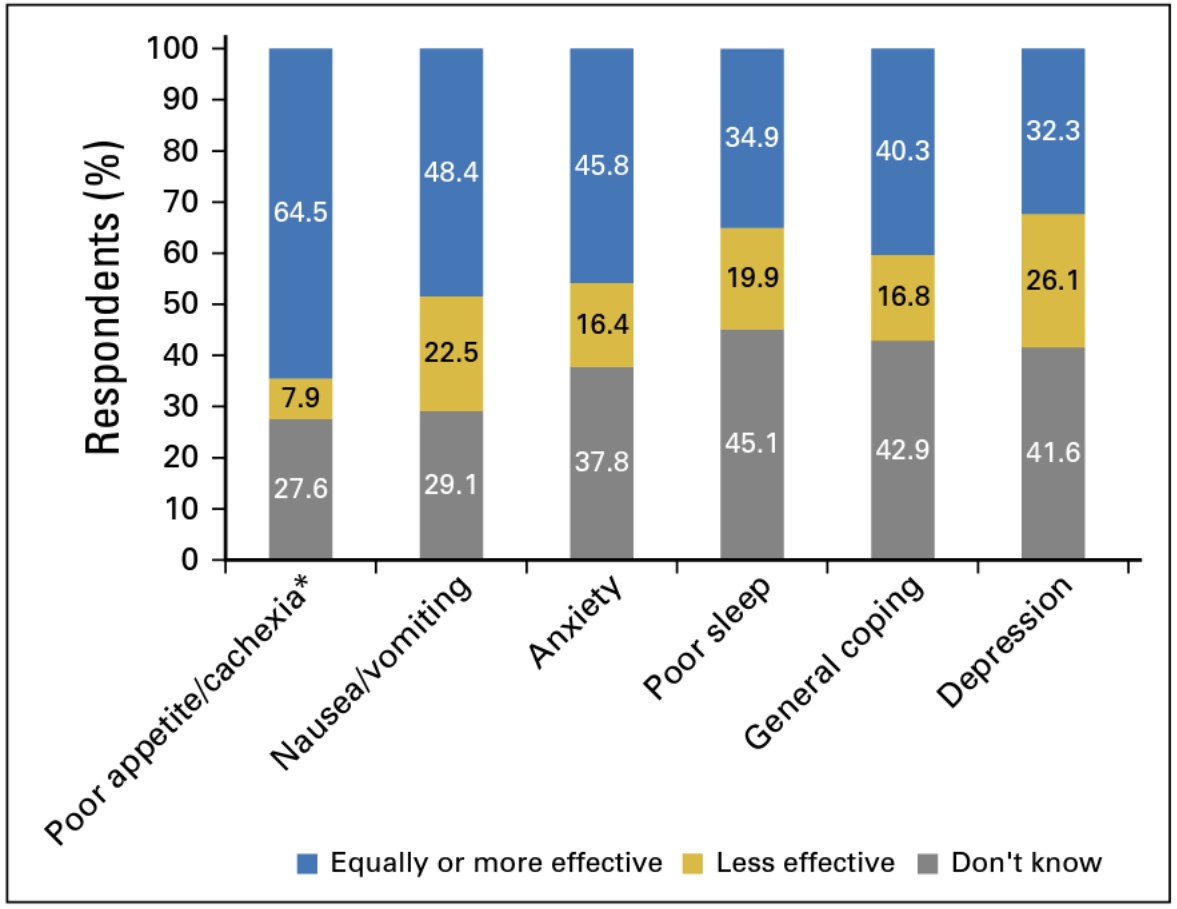




Medical Oncologists' Beliefs, Practices, and Knowledge Regarding Marijuana Used Therapeutically





Braun et al *Journal of Clinical Oncology* 2018

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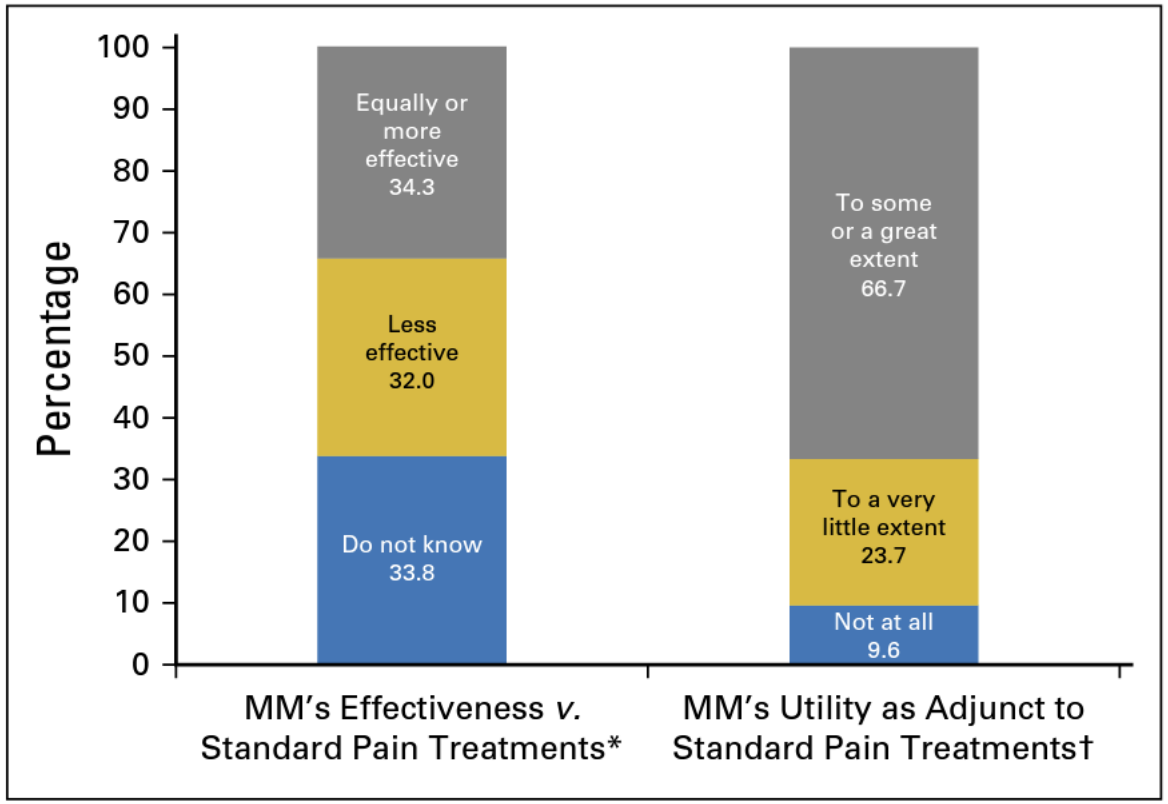

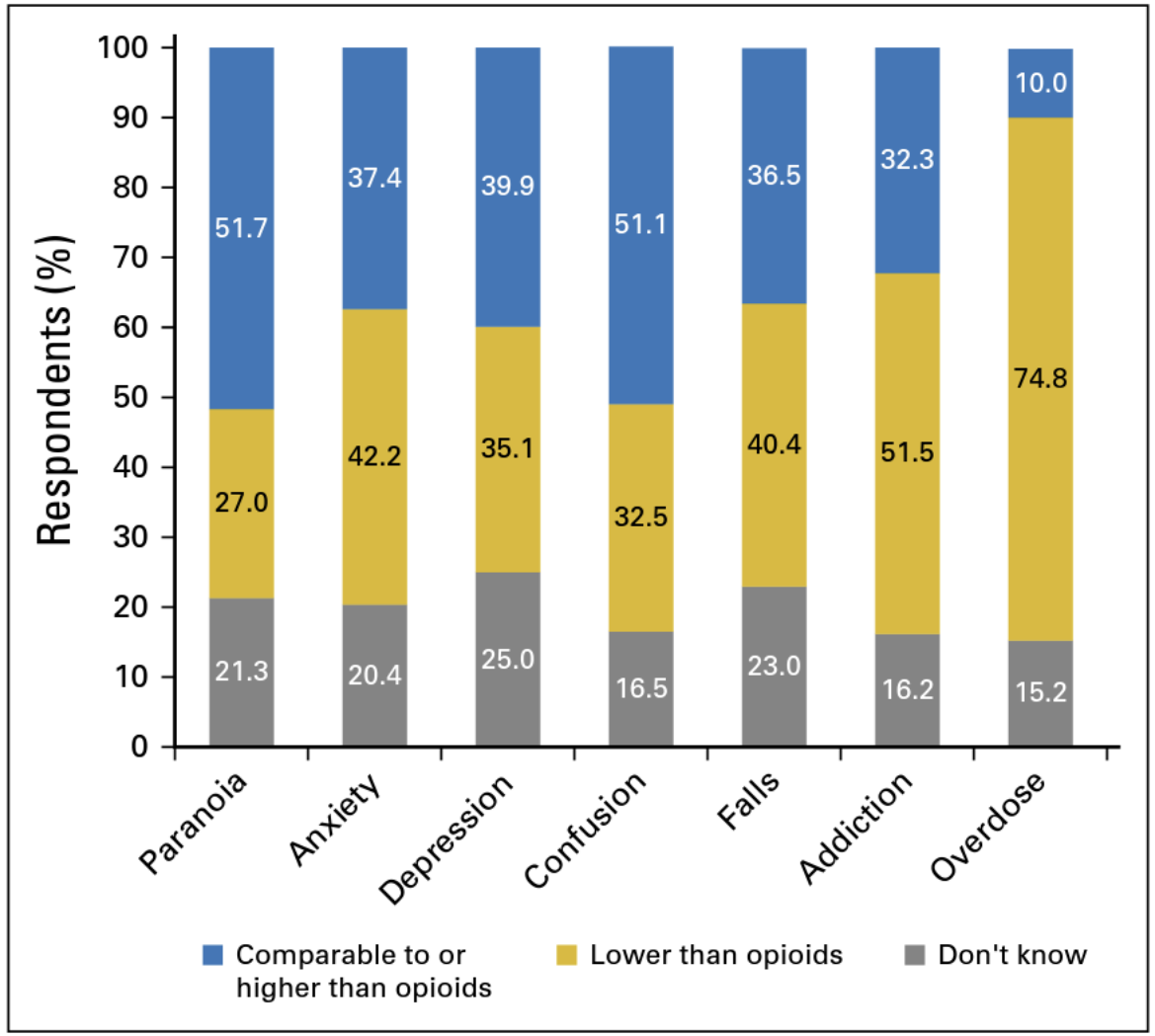

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Cannabis use in serious illness care: evidence base

- Pain
- Chemotherapy-induced nausea & vomiting
- Anorexia, cachexia
- Neuropsychiatric symptoms (sleep, mood, anxiety)
- Cancer-directed therapy

Cannabis use for pain

- The most cited reason for use in patients with cancer
- Systematic review of 28 RCTs of cannabis products & mixed chronic pain (Whiting et al 2015 *JAMA*)

    17/28 neuropathic pain (also MS, MSK, RA, chemo-induced pain)

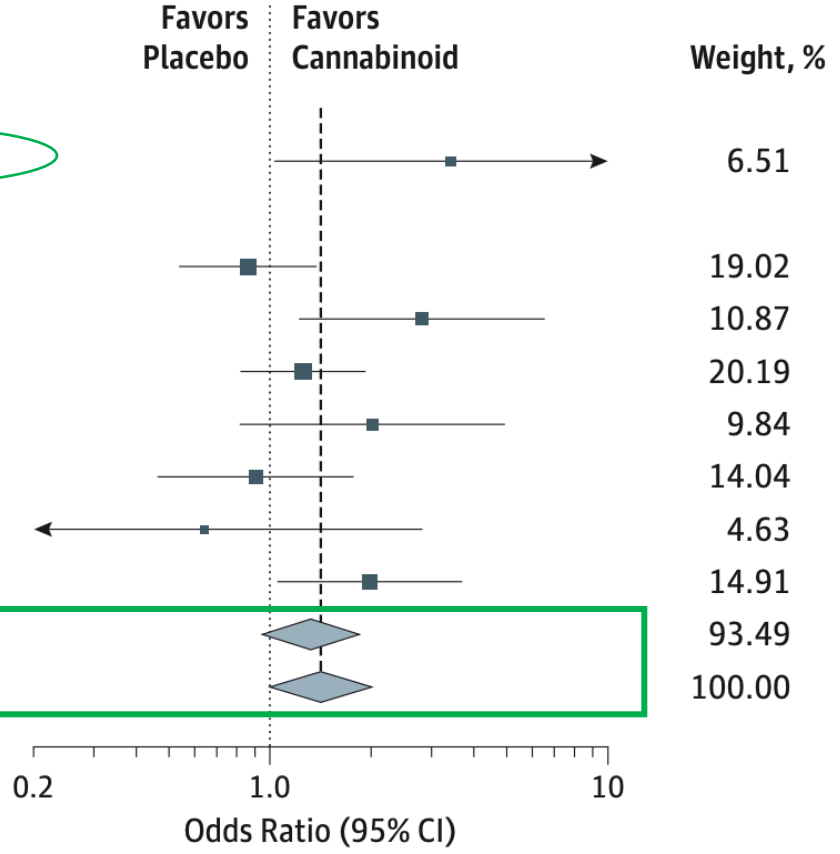
    22/28 plant-derived products (nabiximols, flower, THC oral spray)

    27/28 placebo (1 active comparator amitriptyline)

Whiting et al 2015

Figure 2. Improvement in Pain

Improvement in Pain With Cannabinoid vs Placebo by Study	Cannabinoid Events No.	Cannabinoid Events Total No.	Placebo Events No.	Placebo Events Total No.	Odds Ratio (95% CI)	Weight, %
Tetrahydrocannabinol (smoked)						
Abrams et al,[77] 2007	13	25	6	25	3.43 (1.03-11.48)	6.51
Nabiximols						
GW Pharmaceuticals,[22] 2005	54	149	59	148	0.86 (0.54-1.37)	19.02
Johnson et al,[69] 2010	23	53	12	56	2.81 (1.22-6.50)	10.87
Langford et al,[65] 2013	84	167	77	172	1.25 (0.81-1.91)	20.19
Nurmikko et al,[76] 2007	16	63	9	62	2.00 (0.81-4.96)	9.84
Portenoy et al,[67] 2012	22	90	24	91	0.90 (0.46-1.76)	14.04
Selvarajah et al,[70] 2010	8	15	9	14	0.63 (0.14-2.82)	4.63
Serpell et al,[88] 2014	34	123	19	117	1.97 (1.05-3.70)	14.91
Subtotal $I^2 = 44.5\%$, ($P = .0.94$)	241	660	209	660	1.32 (0.94-1.86)	93.49
Overall $I^2 = 47.6\%$, ($P = .0.64$)	254	685	215	685	1.41 (0.99-2.00)	100.00



**Effect size consistent with another review in 2015 of effect of inhaled cannabis on neuropathic pain (5 RCTs)*

Cannabis use for pain

<u>There is evidence in adults with chronic pain that patients treated with cannabinoids are more likely to experience a clinically significant reduction in pain symptoms</u>

- No trials in cancer populations or comparing cannabinoids to standard of care
- Little known about effect size, doses, formulations, ROA, or side effects

<u>Consistent with oncologists' beliefs & practices:</u>

- Lack of consensus for efficacy as a primary agent
- Supporting use as adjunctive treatment, lower risk than opioids

Chemotherapy-induced nausea/vomiting (CINV)

Synthetic cannabinoids (nabilone, dronabinol) FDA-approved for CINV in mid-1980s

Whiting et al 2015: 28 RCTs using mixed cannabinoids for CINV

- 14/28 used nabilone
- 20/28 used active comparators (15 used prochlorperazine)
- Greater benefit for cannabinoids > placebo or active agents (not significant)

Cochrane review 2015: 23 RCTs; nabilone or dronabinol for CINV

- Mix of placebo & active comparator
- Cannabinoids highly effective, preferred by patients, but concluded no evidence to support 1st line tx

Substantial evidence; low quality trials, no evidence using CBD

Cancer-Associated Anorexia-Cachexia Syndrome

- Cannabis-In-Cachexia-Study-Group (Phase 3 multicenter RCT) 2006
  - Intent-to-treat analysis yielded no difference (appetite, QoL, toxicity)
- Dronabinol vs megestrol in advanced CA patients 2002
  - Megestrol superior for both appetite & weight gain
  - Matches AIDS-wasting study
- There is insufficient evidence to support or refute the conclusion that cannabinoids are an effective treatment for cancer-associated anorexia-cachexia syndrome

Neuropsychiatric symptoms: sleep, anxiety, mood

- Moderate evidence for short-term sleep outcomes (cannabinoids, primarily nabiximols) in disturbance associated w/ OSA, fibromyalgia, chronic pain, MS

- Limited evidence for anxiety symptoms (only in public speaking r/t social anxiety)

- Limited evidence for depression symptoms (mixed cannabinoids) in mood associated w/ chronic pain or MS

Cancer-directed therapy

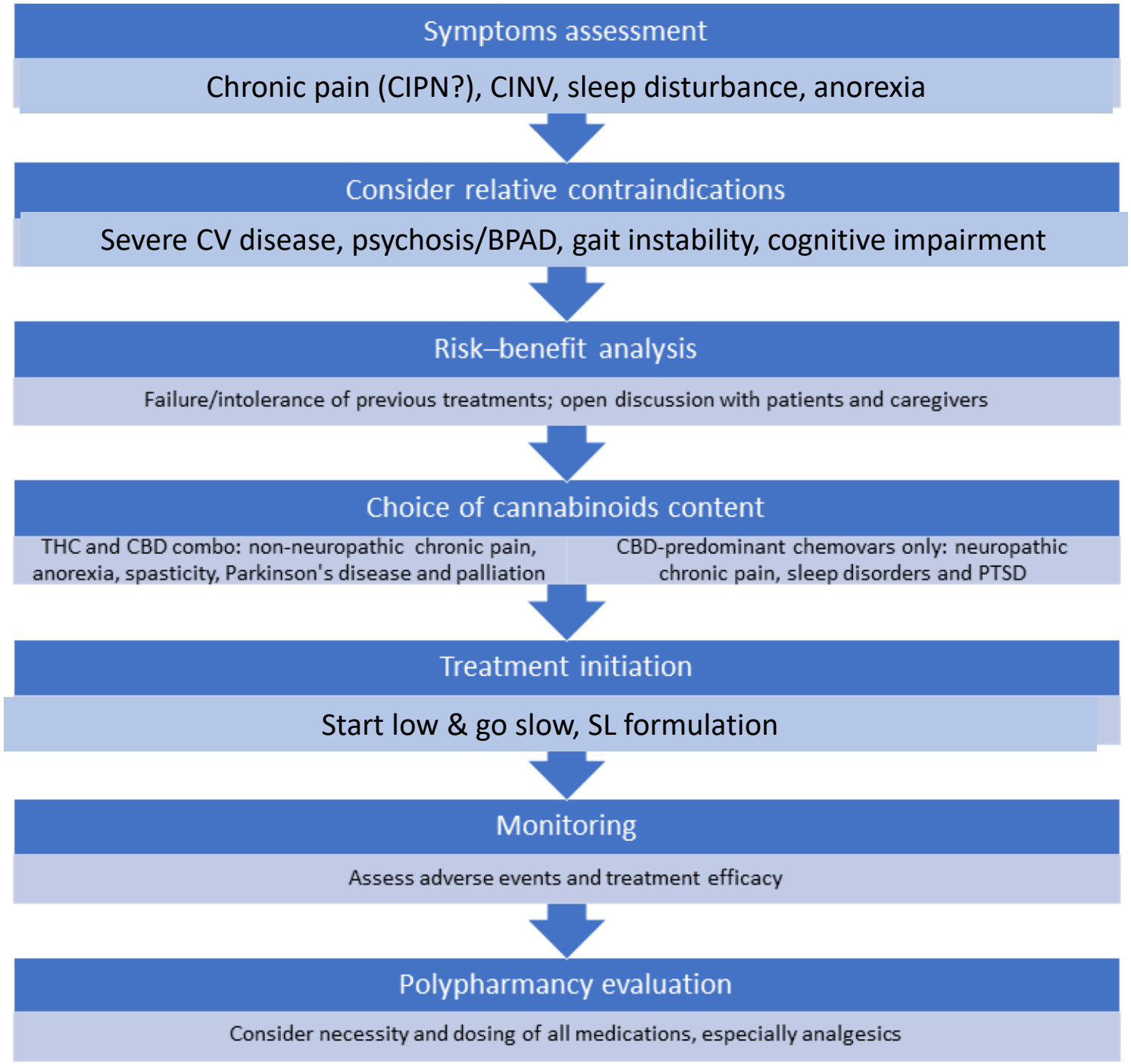
- 30% of patients who reported using cannabis cited treating the cancer itself as a reason

- One good-quality review of anti-tumor effects of cannabinoids on gliomas
    - 35 studies, 1 small clinical trial
    - All 16 in vivo studies found anti-tumor effect

- No clinical evidence; ++ preclinical signal

Rick Simpson Oil- Canadian engineer who used high-potency THC oil to treat his tinnitus & basal cell carcinoma

Practical approach to cannabis use in serious illness care



Adapted from Abuhasira et al 2019

Case examples

- 80yo male with metastatic gastric adenocarcinoma with severe pain is offered a 5mg THC cannabis gummy by son. He felt no relief one hour later so ate two more gummies. Three hours later he was obtunded and lay on the wooden floor so long that he suffered radial nerve compression.

- 57yo woman with ovarian cancer has significant chemotherapy-induced nausea. She beings smoking cannabis and despite initial relief, her nausea worsens. She begins using higher doses of cannabis and is up to smoking 6 joints a day. Her oncologist convinces her to ween off the cannabis and her nausea improves.

Conclusions

The science behind cannabis use in patients with serious illness continues to lag far behind what our patients are using in real life

There is evidence of variable quality in for pain, CINV, and sleep (mostly not cancer specific)

Patients are getting most of their information from non-medical sources (family and friends, popular media) but they want information from their healthcare providers

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