MEDICAL CANNABIS: WHAT YOU NEED TO KNOW

Kelay Trentham, MS, RDN, CSO
Oncology Dietitian
MultiCare Regional Cancer Center

What we'll talk about:

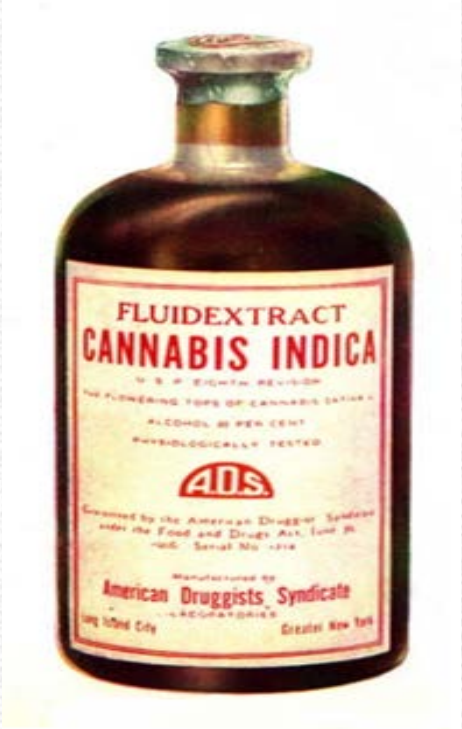
- History of medical use of cannabis
- Effectiveness for managing some issues
- Forms of use: pros and cons
- Contraindications and adverse effects
- WA law provisions

What is Cannabis…?

- **Dangerous Drug?**

OR

- **Natural Medicine?**



Cannabis is…

- **A plant From the *Cannabaceae* family:**
  - Hops
  - Hackberry

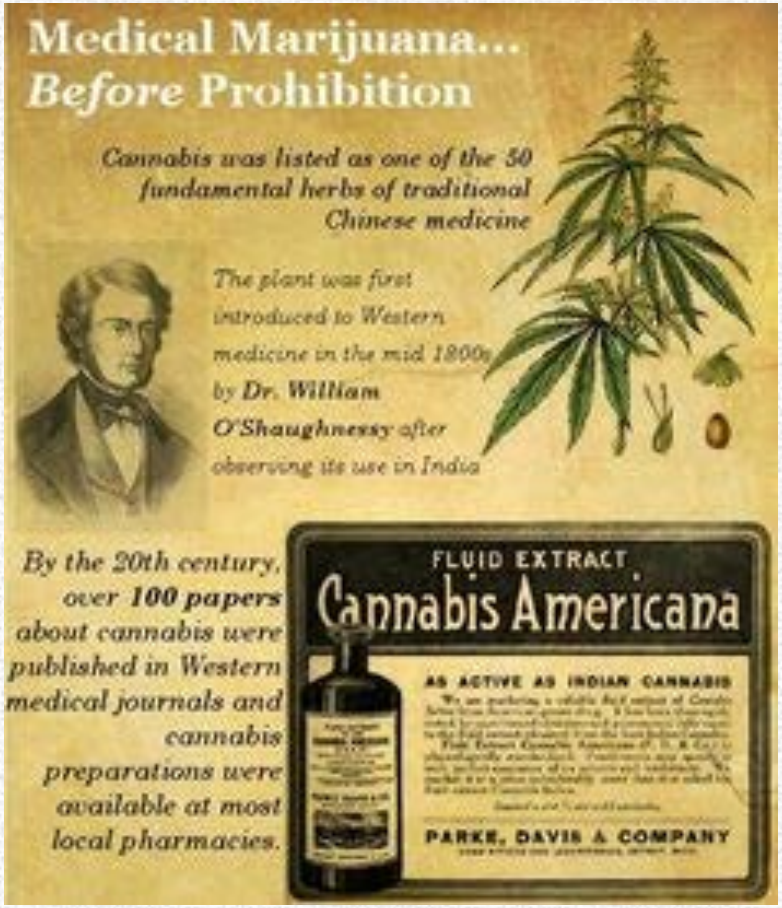
- **With many names:**

  AKA: “grass”, “weed”, “ganja”, “marijuana”, “hash”, “bhang”, etc.

(Russo 2007)

Its rise…

- **Long history of medicinal use**
  - >3,000 years ago: Egypt, China
  - 1st – 2nd century CE: Pen-ts'ao Ching
- **Intro to Western Medicine: 1839**



(Russo 2007; Backes 2014)

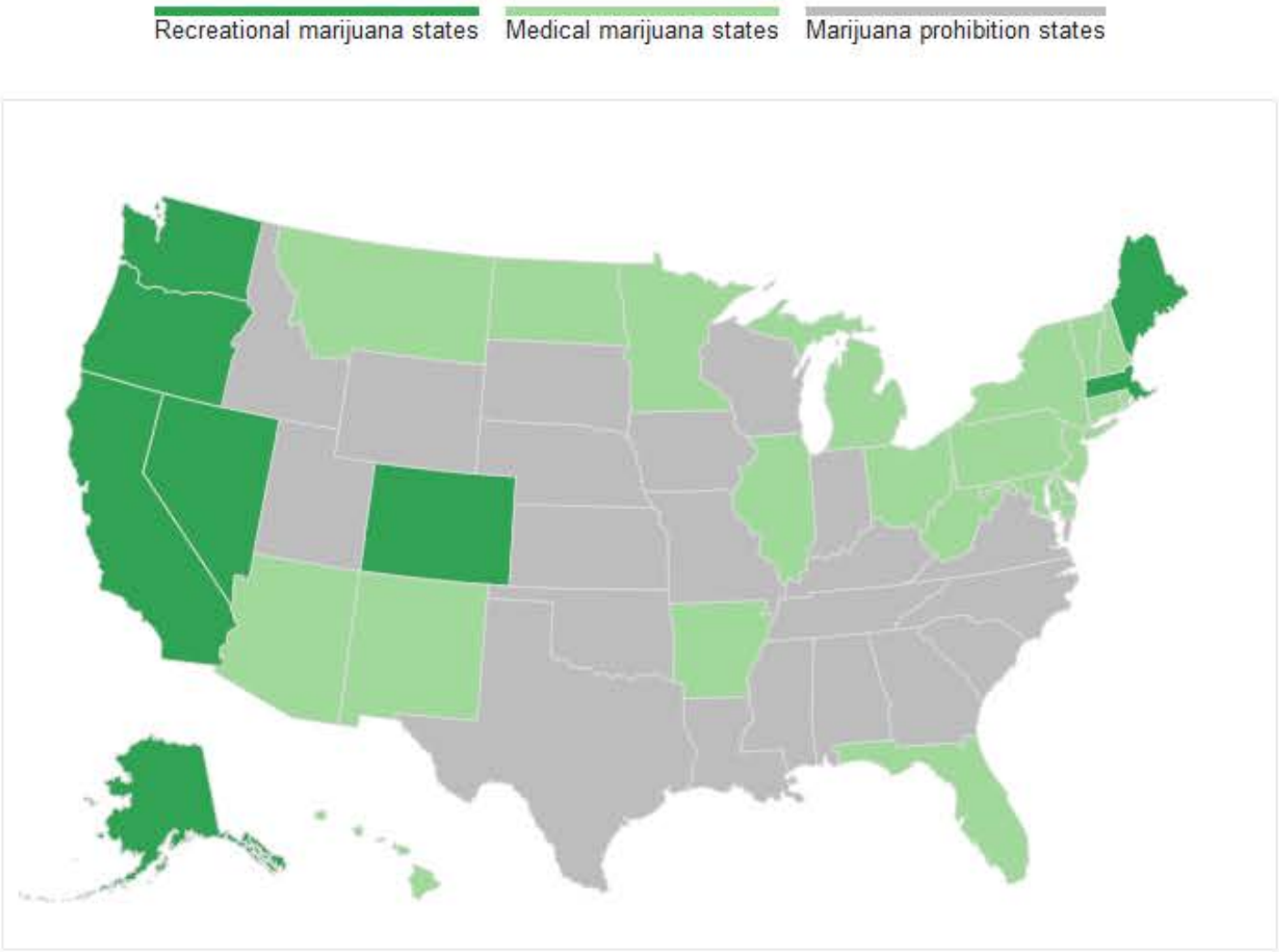
And its fall…

- **1937: banned in all US States**
- **1942: Removed from USP**
- **1970: Schedule 1 classification**

  "no accepted medical use"

(NIH-NCI; Backes 2014)

Its resurgence…

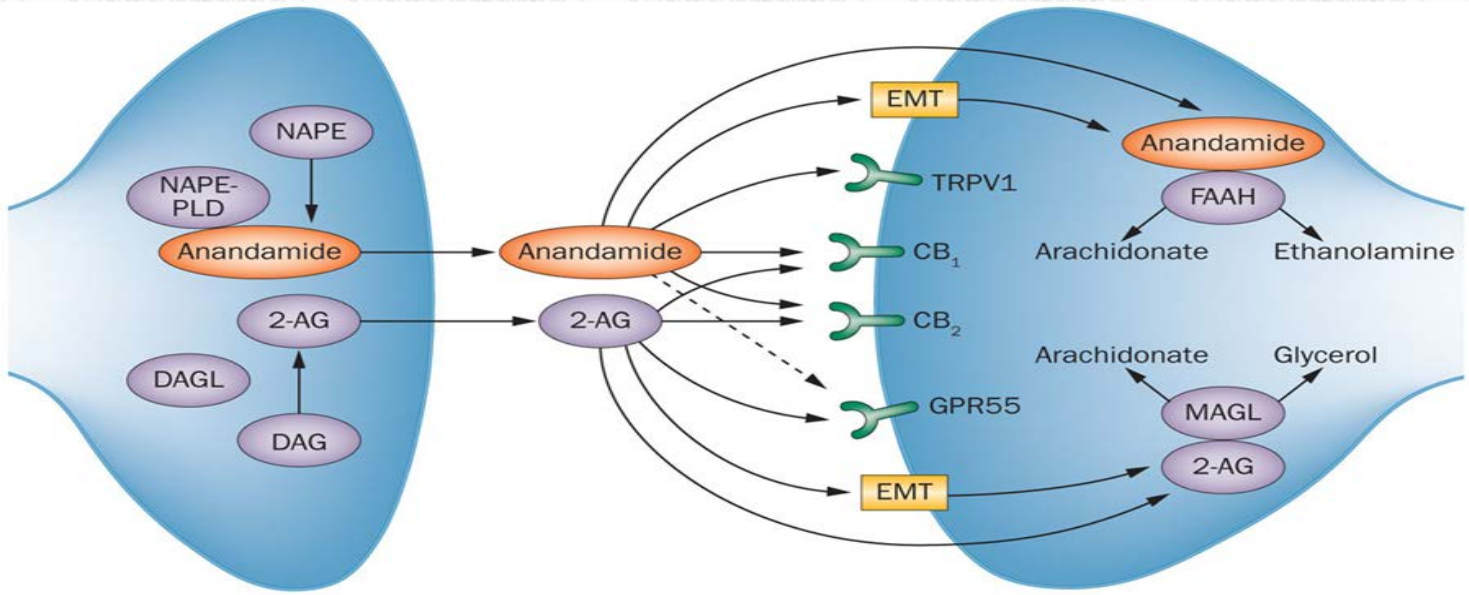


Not pictured: Guam, Puerto Rico

(Map source: *The Cannabist* website)

The Endocannabinoid System

- Receptors: CB1 (nervous system) & CB2 (immune cells)
- Endocannabinoids



Schicho, R. & Storr, M. (2013) Patients with IBD find symptom relief in the *Cannabis* field
Nat. Rev. Gastroenterol. Hepatol. doi:10.1038/nrgastro.2013.245

Battista 2012, Vemuri & Makriyannis 2015

What's so special about Cannabis?

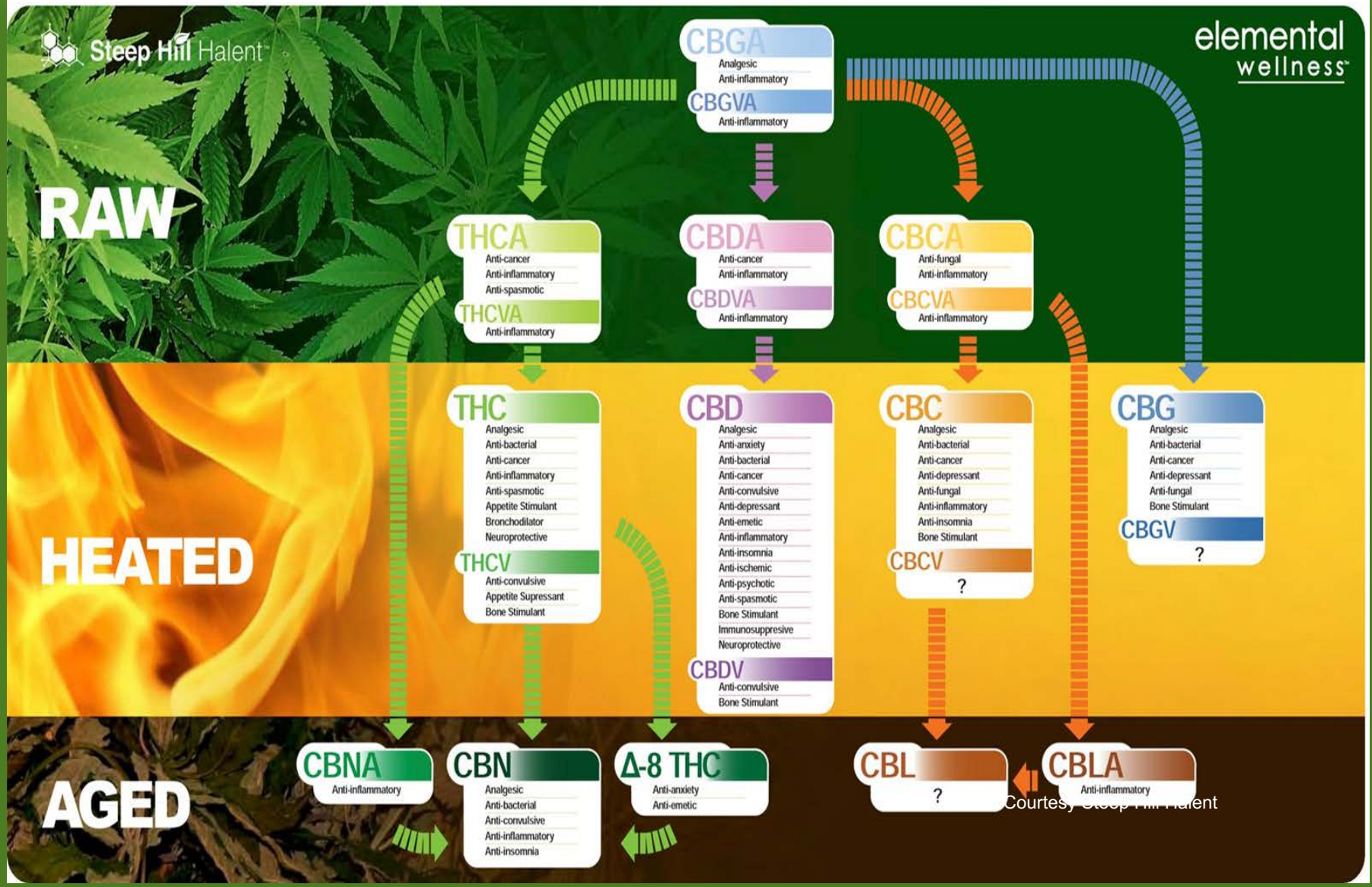
- **Phytocannabinoids:**
  - "…any plant-derived natural product capable of either directly interacting with cannabinoid receptors or sharing chemical similarity with cannabinoids, or both."
  - 110+ in cannabis

- **Properties:**
  - Pain-relieving
  - Anti-anxiety
  - Anti-seizure
  - Anti-nausea
  - Anti-inflammatory
  - Anti-oxidant
  - Anti-tumor
  - Neuroprotective

And the list goes on!

(Gertsch et al. 2010; Pacher et al. 2006; Ahmed et al. 2015; Russo 2011)

Cannabinoids and Their Therapeutic Effects



Courtesy Steep Hill Halent

The "Most Studied" Cannabinoids

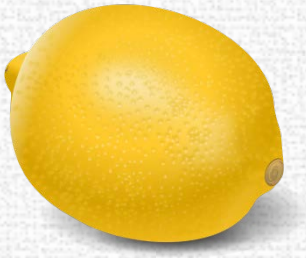
Cannabinoid:	Receptor Activity:	Major Effects:	Associated Rx drug:
THC:	CB1: nervous system (strong) CB2: immune cells (weak)	Psychoactive Anti-nausea Pain relief Anti-spasmodic Anti-inflammatory	Marinol (dronabinol) Cesamet (nabilone) Sativex (nabiximols) Levonantradol
CBD:	CB1: nervous system (weak) CB2: immune cells (weak)	Pain relief Neuroprotective Anti-seizure Anti-anxiety Anti-nausea	Sativex (nabiximols) Epidiolex (cannabidiol)

(Russo 2011)

Terpenoids:

- Essential oil components
- Characteristic aroma
- Pharma effects

- Limonene
- Myrcene
- Pinene
- Linalool
- Caryophyllene(s)
- Nerolidol
- Phytol



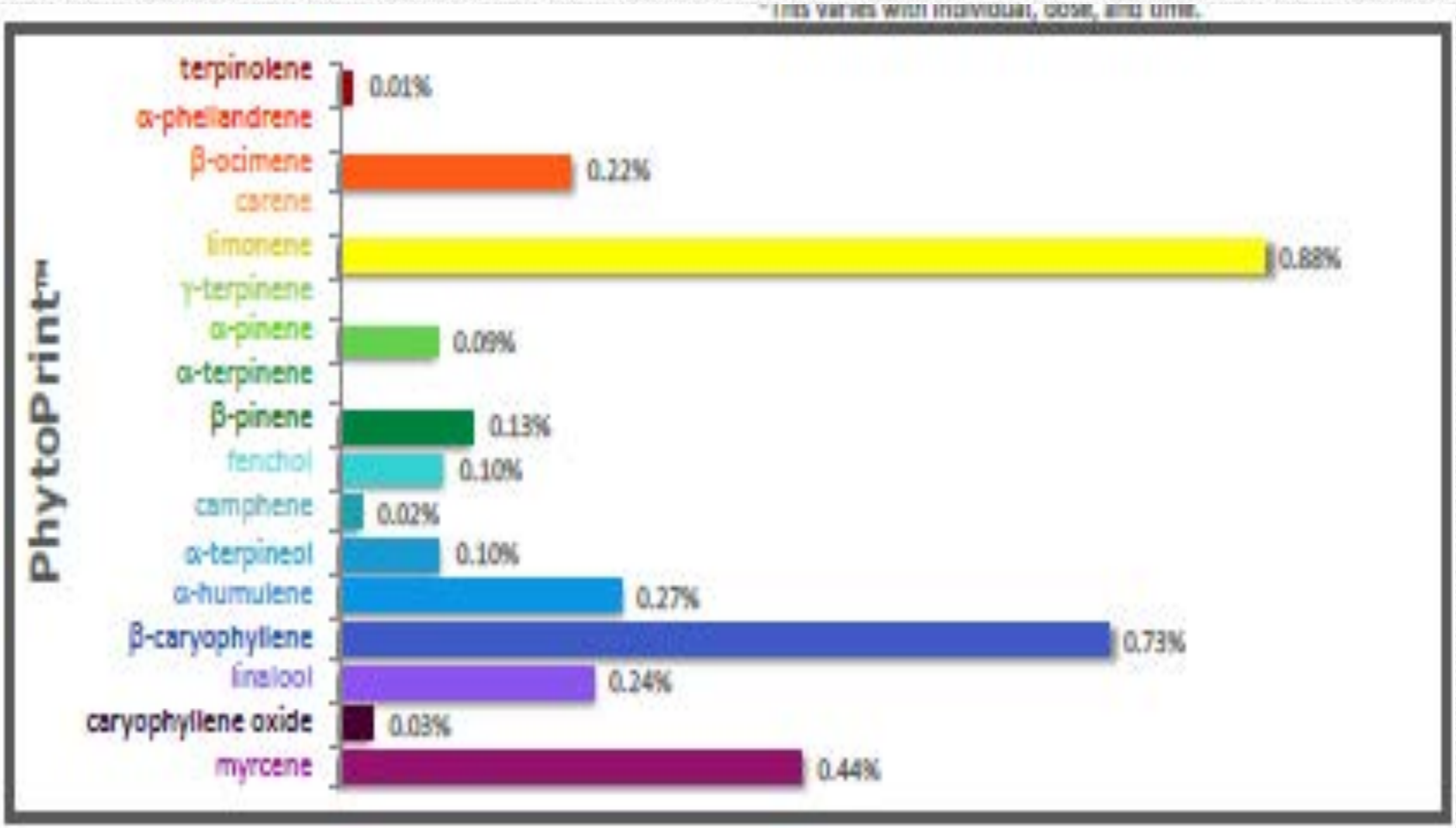
(Russo 2011)

Some Terpenoid Activities:

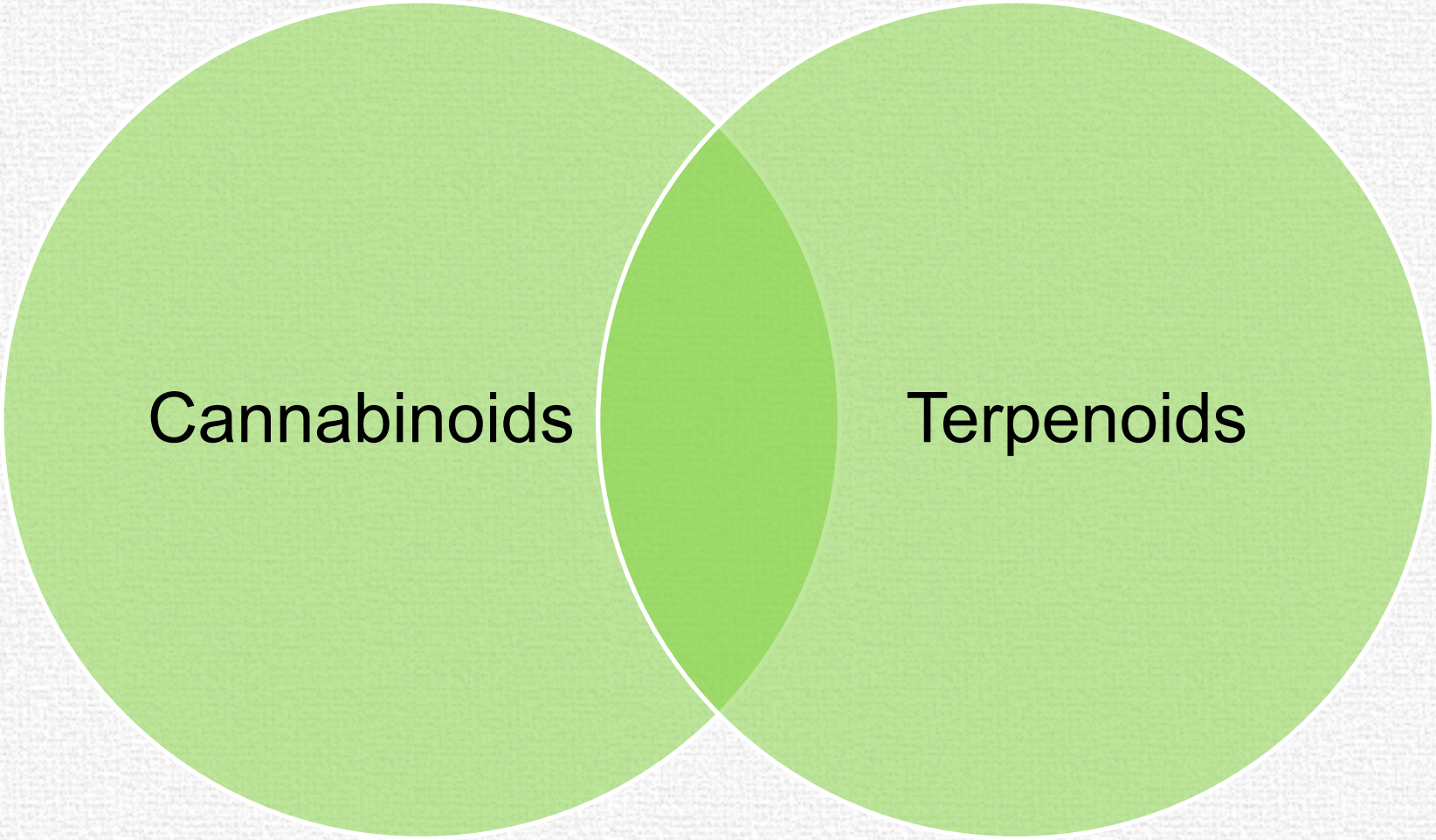
Terpenoid:	**Noted Effects:**
• Limonene	anti-anxiety, anti-depressant
• Myrcene	anti-inflammatory, sedative
• Pinene	anti-inflammatory, bronchodilator
• Linalool	anti-anxiety, anti-convulsant
• Caryophyllenes	anti-inflammatory, anti-fungal
• Nerodilol	sedative, anti-protozoal

Russo 2011

Terpenoid Analysis



The “Entourage Effect”



Reviewing the Evidence

- **Available studies will include:**
  - Synthetic THC (dronabinol, nabilone)
  - Extracted THC +/- CBD
  - Less often: “whole cannabis”

Cancer: Nausea/Vomiting

Cannabinoid	Control	Results	Reference
Dronabinol Levonantradol Nabilone	Anti-nausea meds & Placebo	➢ More effective ➢ Preferred	Tramer et al. 2001
Dronabinol Nabilone Levonantradol	Anti-nausea meds	Dronabinol: decreased nausea, was preferred NS NS	Rocha et al. 2008
Nabilone	Anti-nausea meds	80%: ↓ nausea 78%: people: preferred	Ware et al. 2008
Dronabinol	Ondansetron & Placebo	Dronabinol: 71% Ondansetron: 64% Placebo: 15%	Parker et al. 2011

Appetite

- **Dronabinol vs. Megestrol acetate** (Jatoi et al. 2002)
  - Improved appetite:

    Megace 75% vs. Dronabinol 49%

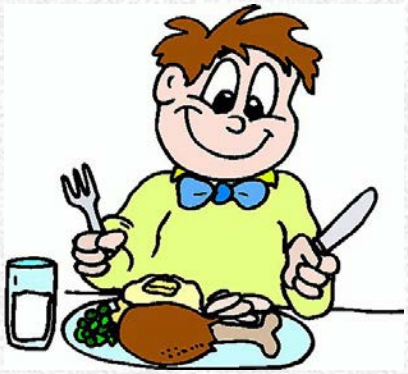
  - Advanced cancer patients

Appetite

- **THC+CBD vs. THC vs. Placebo** (Strasser et al. 2006)
  - No Difference

*Very low dose studied (2.5 mg THC)

Smoked Cannabis



- P>0.001 for trend

Symptom	Grade	Change
Nausea	None Mod Severe	+37% -38% +1%
Vomiting	None Mod	+23% -23%
Anorexia	None Mod Severe	+36% -38% +2%
Weight loss	None Mod Severe	+35% -32% -5%

(Bar-Sela et al. 2013)

Taste and Smell

- **THC vs. placebo** (Brisbois et al. 2011)
  - Chemosensory response:
    - Significant improvement: 36% THC vs. 15% placebo
  - "Food tastes better":
    - 55% THC, 10% placebo ($p = 0.04$)
  - Pre-meal Appetite score:

    THC > placebo
  - Pilot study: n= 11 (THC), 10 placebo

Pain/neuropathy:

Cannabinoid	Pain	Results	Notes	Ref
Mixed	CA, other	Canna > effective placebo	Significant Adverse effects	1
Mixed	Neuro, other	15/18 trials: sig, modest effect	No severe AEs, no dropouts; placebo or active control	2
Mixed	CA, other	27/38 RCTs: sig relief	Placebo or active control	3
Cannabis	Neuro	6 RCTs: All = sig relief	3 studies: clinically meaningful relief 45, 53, 61% C vs. 18, 24, 26% p	4

(1: Martin-Sanchez 2009; 2: Lynch & Campbell 2011; 3: Aggarwal 2013; 4: Deshpande 2015)

Smoked Cannabis

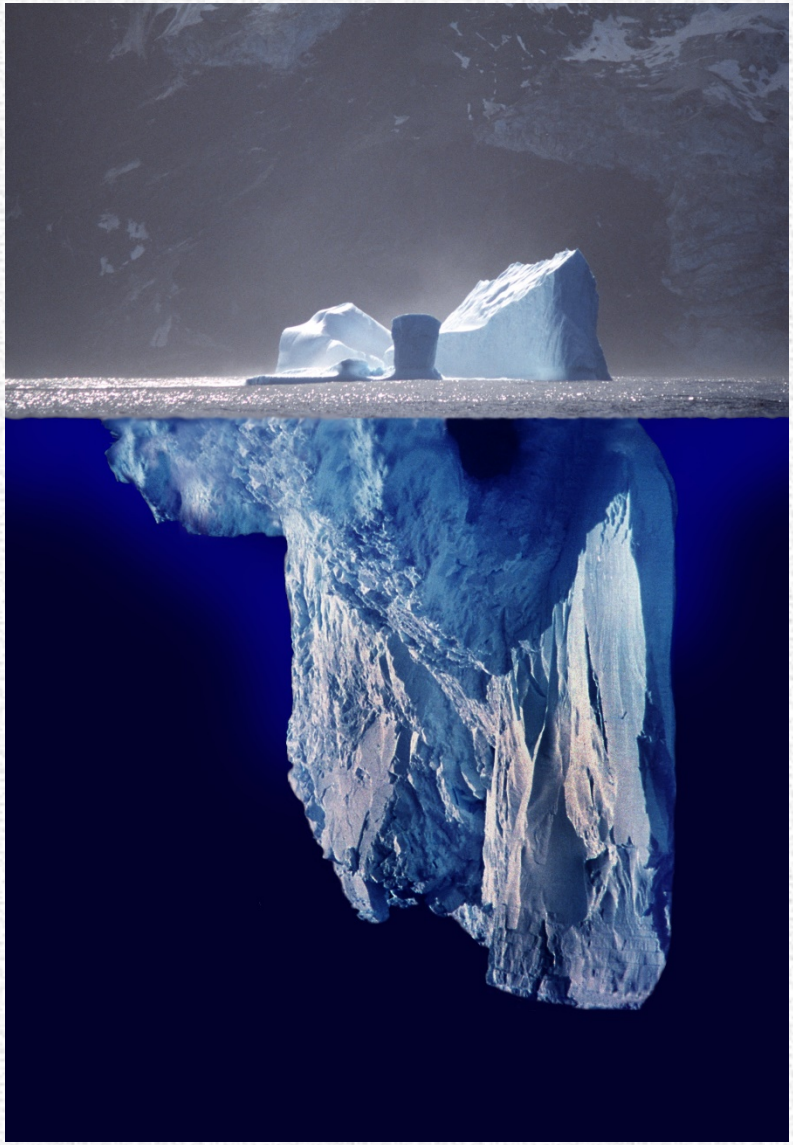
Symptom	Grade	Change
Pain	None Mod Sev	+23% +3% -26%

(Bar-Sela et al. 2013)

Cannabis a “Cancer Cure”?

- Limited Preclinical Evidence:
  - *In vitro, In vivo*
  - 1 small study: GBM
- Potential? *maybe*
- Certainty? No

What we know:



Cannabis Administration Routes:

Inhalation (Smoking & Vaping)

- Onset: seconds to minutes
- Duration: 2-3 hours
- Bioavailability: 10-35%

- Vaping: less toxic byproduct

(Grotenhermen 2003; Huestis 2007; Aggarwal 2013)

Caution…

- What is a “dab”?
  - Inhalation of volatile “concentrate”
  - Extracted via solvents, liquid gas, CO2
- Safety concerns:
  - Residual solvents: >80% samples
  - Pesticides: 33% samples
    - Paclobutrazol: not listed with EPA for use on food crops

(Raber et al. 2015)

Caution…

- Risk to the severely immunocompromised patient…
  - Bacteria, molds on green bud
  - Few case reports: aspergillus via inhaled cannabis

    *can be fatal

- Sterilization?

(Ruchlemer 2015)

Oromucosal: Sprays, Tinctures

- Onset: ~15 – 30 minutes (average)
- Duration: 45 min – 2 hours
- Bioavailability:
  - Highly variable
  - Inhaled > OM >/= oral
  - *Less first-pass metabolism
  - Increases with food

(Guy & Robson, 2003)

Oral Ingestion: Edibles, Capsules

- Onset: 30 min – 2 hours
- Duration: 5 - 8 hours
- Bioavailability: variable, 4-20%

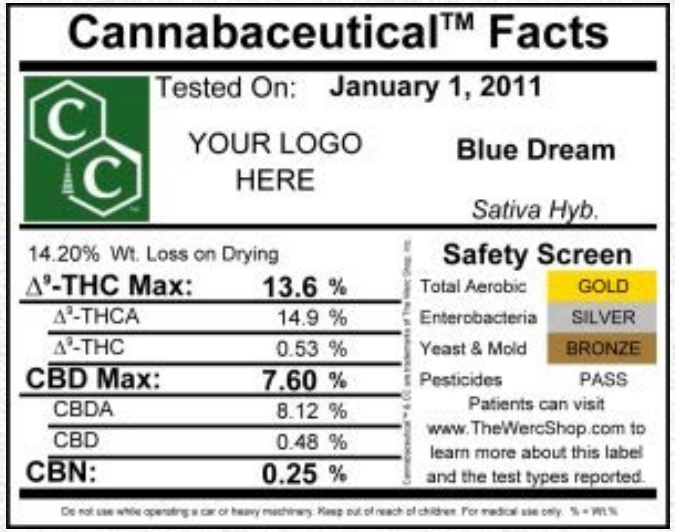
- *First-pass metabolism: 11-OH-THC
  - *Potent psychoactive*
  - *Reduces bioavailability THC*

- **More difficult to determine dose**

(Grotenhermen 2003; Huestis 2007; Aggarwal 2013)

A word of Caution…

- Labeling inaccuracies…
- Content analysis:
  - 17% accurately labeled
  - 23% under-labeled (had >THC content!)
  - 60% over-labeled
- Contributes to:
  - Overdosing
  - Difficulty dosing



Cannabaceutical™ Facts

Tested On: **January 1, 2011**

YOUR LOGO HERE

Blue Dream

Sativa Hyb.

14.20% Wt. Loss on Drying

Δ^9-THC Max:	**13.6 %**
Δ^9-THCA	14.9 %
Δ^9-THC	0.53 %
CBD Max:	**7.60 %**
CBDA	8.12 %
CBD	0.48 %
CBN:	**0.25 %**

Safety Screen

Total Aerobic	GOLD
Enterobacteria	SILVER
Yeast & Mold	BRONZE
Pesticides	PASS

Patients can visit www.TheWercShop.com to learn more about this label and the test types reported.

Do not use while operating a car or heavy machinery. Keep out of reach of children. For medical use only. % = Wt.%

(Vandrey et al. 2015)

Rectal: Suppositories

- Favored for absorption, no first-pass metabolism
  - Peak concentration: 1-8 hours
  - Bioavailability : ~2 X that of oral

(Huestis 2007; Grotenhermen 2003)

Skin

- **Creams, Ointments**
  - No Studies
- **Transdermal Patch**

  Preclinical research
  - Animal model → plasma for 48 hrs
  - CBD, CBN → 10 fold higher

  - ***More research needed***

www.hc-sc.gc.ca/dhp-mps/marihuana

Contraindications:

- Allergy
- Pregnancy & breastfeeding
- CVD, Respiratory
- Hepatic, Renal
- Mental health hx
  - schizophrenia, bipolar d/o, depression

(Kahan 2014, Sachs 2015, Health Canada)

Precautions:

- Hx CVD, Angina
- HTN
- Asthma, COPD

(Kahan 2014, Sachs 2015, Health Canada)

Adverse Effects:

- Elevated/rapid Heart Rate
- Sedation, Somnolence
- Dizziness, loss of balance
- Impaired memory
- Confusion, disorientation, hallucination
- Headaches
- Anxiety

(Deshpande 2015; Whiting et al. 2015)

Lessening the Side Effects:

- When THC:CBD @ ~ 1:1
  - ↓ anxiety, memory issues

- Terpenoids
  - Pinene: ↓ memory issues
  - Limonene, linalool: ↓ anxiety

(Russo & Guy 2006; Morgan et al. 2010; Russo 2011)

Cannabis-Drug Interactions:

- *Oral* cannabis effects increased by:
  - Cardiac: amiodarone, dilitiazem, verapamil
  - Antibiotic: clarithromycin, erythromycin
  - Anti-fungal: fluconazole, isoniazid, itraconazole, ketoconazole, miconazole
  - HIV Protease Inhibitor: ritonavir

- Drug effects increased by cannabis:
  - Alcohol
  - Benzodiazepines (Ativan, Valium, Xanax, Restoril, etc.)
  - Opiates: codeine, fentanyl, morphine

(Backes 2014)

WA Medical Law:

- Medical authorization from:
  - MD, DO, ARNP, PA, ND

- Over 18: good for 1 year
- Under 18: good for 6 months

- Qualified 18-20 yrs old: only enter medical endorsed store

- DOES NOT PROTECT:
  - federal law violation; employer policies; landlord policies; DUI

Common Qualifying Conditions: WA

- **Cancer**
- **Muscle spasms/spasticity disorders, including MS**
- **Glaucoma**
- **HIV/AIDS**
- **Cachexia**
- **Epilepsy, Seizure disorders**
- **Pain, unrelieved by standard treatments, meds**
- **Nausea**
- **IBD, including Crohn's**

(procon.org)

Why get a medical “card”?

- Can designate a provider to purchase and/or grow
  - Up to 4 plants
- *<u>However</u>*, only purchase per rules for non-patients
- Affirmative Defense:

  *If possess not more than 4 plants, 6 usable ounces
- Access Medical Product:
  - Tested for: potency, foreign matter, bacteria, residual solvents, mycotoxins

Why be in the database?

- Allows purchase:
  - 3x the recreational limit
  - High THC product (if available)
  - Immature plants, clones, seeds from licensed grower
  - Minus sales/use tax
- Allows possession of:
  - 6 to 15 plants
- Participation in cooperative

Why be in the database?

- WA state arrest protection
  - Card must be
    - presented if questioned
    - kept with supply
  - Must be in compliance with law

- Info NOT shared with federal government
  - unless convicted for violating WA law

- www.doh.wa.gov/youandyourfamily/marijuana/medicalmarijuana

In Summary:

- Cannabis
  - has a long history of medical use
  - may be effective for some conditions
- There are pros/cons:
  - to use of various forms, due to adverse effects
- Research, talk with your medical team
- Awareness of WA law is important

Resources:

- WA State Dept of Health
  - “You and Your Family, Medical Marijuana”
- International Association for Cannabis as Medicine
  - cannabis-med.org
- Americans for Safe Access
  - Safeaccessnow.org
- Health Canada: Medical Use of Marijuana
- “Cannabis Pharmacy” *by* Michael Backes