



University of California  
San Francisco

VA



U.S. Department  
of Veterans Affairs

# Modern Management of Pain: Current Strategies for Maximizing Results While Minimizing Opioids

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American College of Physicians Northern California Chapter

Scientific Meeting

October 2019

# Disclosures

- No financial relationships with commercial interests within the past year
- No discussion of investigational use of medications
- There will be discussion of 'off label' use of medications or products

# About Me

- Associate Professor of Clinical Medicine at the San Francisco VA, UCSF
- Deputy Chief: Primary Care SFVA
- Primary Care Clinician, Eureka, CA VA Clinic
- About 25% of my patients use prescription opioids to treat their chronic non-cancer pain



# Learning Objectives:

- At the end of this presentation you will be able to:
  1. Describe a framework for evaluating and managing chronic pain
  2. Assess your patient's pain (using PEG score)
  3. List 4 keys to non cancer pain management
  4. Discuss cannabis with your patients

# Case: Mrs. Healy



Mrs. Healy:

59F, transferring her care to you as she recently moved to the area.

PMHx: Hypertension, Depression

Social: drinks 1 glass wine per night. Never smoker

CC: left knee (OA), left hip (OA), low back pain (degenerative)

Rx: ibuprofen; APAP/Hydrocodone 1-2 tabs daily

Pain recently worse, wondering about an increase in Rx. She has also heard about CBD and is wondering if she should try this.

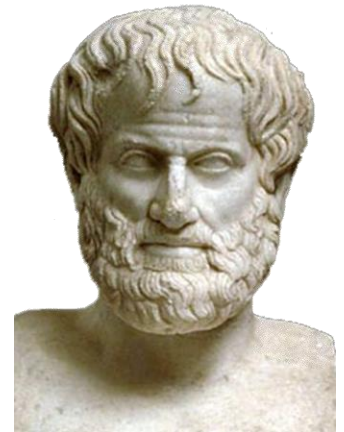
# Questions

- How to address chronic pain in a new (to you) patient?
- CBD? What is that?
- What if she were on a higher opioid dose?

# Philosophy Slide

- No single modality will successfully treat more than a minority of patients with a painful condition
- Pain relief ↔ improved: sleep, depression, fatigue, quality of life, function, and ability to work
- Failure with one modality does not necessarily mean failure with others, even within a class
- Success or failure can be determined within 2-4 weeks, and success, when achieved, tends to be long lasting
- Because success rates are low, a wide range of medications / modalities is needed to do the best for most patients, especially in complex chronic conditions

**Perhaps we are not always treating pain, but instead, suffering – Louis Kuritzky, MD**





# A Framework for Managing Chronic Pain

1. Establish the Diagnosis (management may differ)
2. Current State: functionality
3. Current and Past treatment
4. Evaluate Risks of treatment
5. Establish Goals
6. Set Expectations
7. Add a Therapy
8. Evaluate Efficacy
9. Repeat 2-8

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# Chronic Pain in Women

- Higher prevalence of joint pain
  - 1.6x low back pain, 1.12x knee pain, 1.64x hip pain
- Disparities in treatment
  - More likely to have delays in care
  - More likely to have pain attributed to psychological issue
- Differences in responses to analgesia
- In the VA, military sexual trauma (MST) is associated with increased rates of chronic pain

# Chronic Pain in Vulnerable Subpopulations

- Racial and Ethnic disparities
  - Pain is evaluated less frequently and undertreated more often in African Americans, Latinxs, Asian Americans, Native Americans, and English as Second Language populations
- Elderly
  - Higher prevalence of chronic conditions, decreased sensitivity to pain. Undertreatment of pain

# Case: Mrs. Healy, chronic knee, hip and back pain

## Establish the Diagnosis

- a. Exam: left knee bony medial compartment tenderness, small effusion. Straight leg raise positive, left. Pt reports mild radiculopathy in the lower extremities. Pain with extreme of ROM left hip.
- b. Prior knee, hip x-rays: moderate OA left >> right
- c. Prior MRI, lumbar spine: degenerative disease. No spinal stenosis. Mild foraminal narrowing.

# Case: Mrs. Healy, chronic knee, hip and back pain

## Current State

### a. Use a brief pain score: i.e. PEG

Over the past week...

- i. P = average **P**ain intensity, 0 = no pain, 10 = worst pain
- ii. E = interference with **E**njoyment of life, 0 = none, 10 = completely
- iii. G = interference with **G**eneral activity, 0 = none, 10 = completely

### b. Mrs. Healy reports: P = 5, E = 6, G = 5, total 16.

**30% improvement is considered meaningful**

# Case: Mrs. Healy, chronic knee, hip and back pain

## Goals:

- Hike
- Improve tolerance of standing
- Avoid surgery



## Function:

- Can walk, but painful after 500 ft., worse in afternoon.
- Can't stand for long to cook, do dishes.
- Ibuprofen improves pain to about a '4'.
- APAP/Hydrocodone improves pain to about a '3'.



# Case: Mrs. Healy, chronic knee, hip and back pain

## Current and Past Treatment

- Acetaminophen: “didn’t work”
- NSAIDs: ibuprofen 200mg 1-2 tabs BID PRN
- Acetaminophen/Hydrocodone 5mg/325mg 1 tab PO BID PRN
- Acupuncture: hasn’t tried
- Physical Therapy: hasn’t tried
- Topical creams: hasn’t tried
- SNRI: no, currently on Zoloft for depression
- Gabapentin: hasn’t tried
- TCA: hasn’t tried

# Standard Therapies

Consider for all patients:

- Weight loss –  
5-10% loss can lead to improved pain scores
- Exercise
- Physical Therapy: modest improvement in pain scores
- Smoking, alcohol cessation/minimization
- Mental Health screening
- Substance use disorder screening

# Add a therapy

Alternative /  
Complementary

Medications

Cannabis

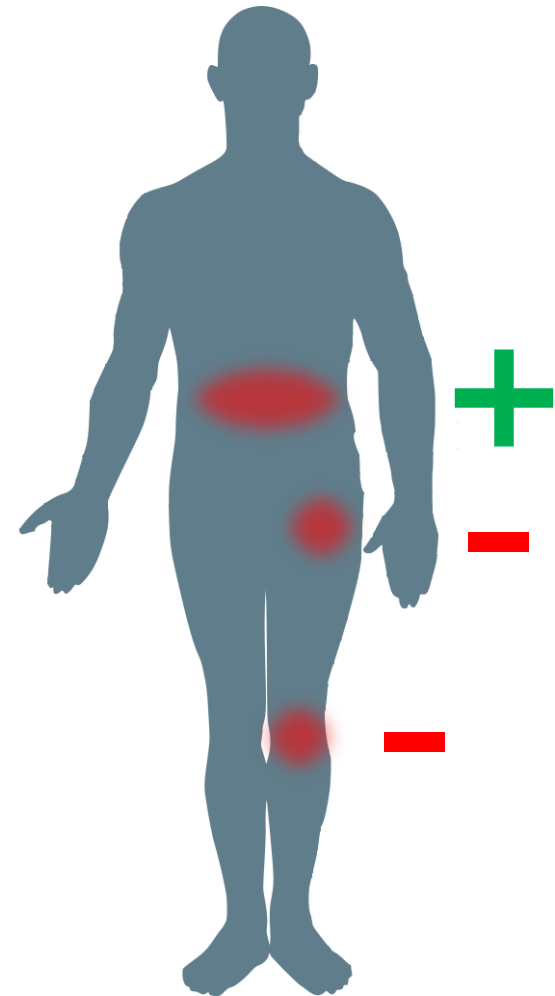
# Alternative and Complementary Practices

# Selected Alternative and Complementary Practices

- Acupuncture
  - back: small effect on pain, function
  - knee: not clinically significant
- Yoga
  - back: mod effect on pain and function
- Tai Chi
  - back: mod effect on pain and function
- Mindfulness
  - back: small effect on pain and function



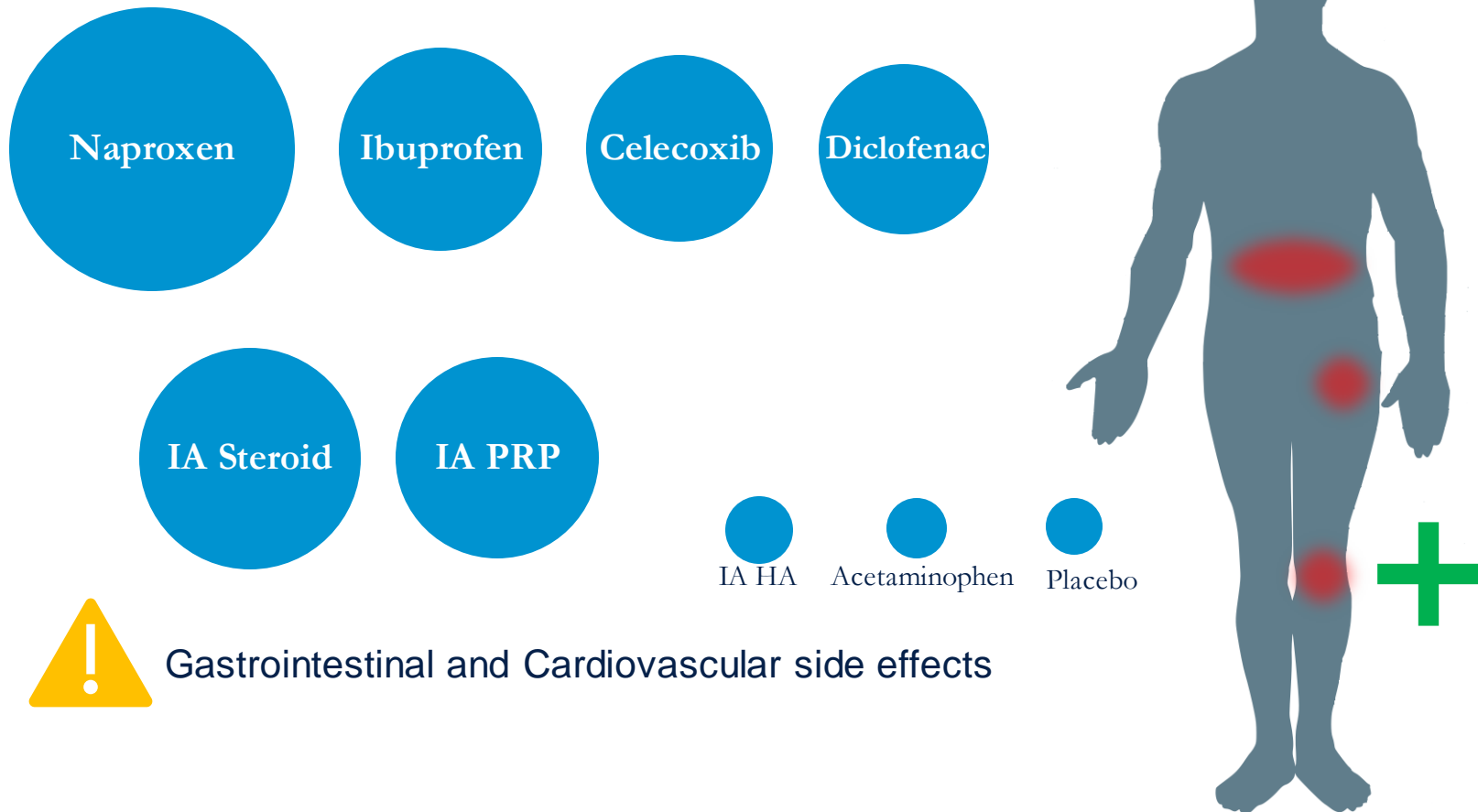
\$\$ (not covered by insurance)  
Minimal side effects



# Medications

# 2018 JAAOS Network Meta-analysis: Knee OA

## Treatment Rank, Combined Pain and Function



Gastrointestinal and Cardiovascular side effects

IA = intra-articular; PRP = platelet-rich plasma; HA = hyaluronic acid

# 2018 JAAOS Network Meta-analysis: Knee OA

- RCTs, minimum 30 patients, followed > 4 weeks
- Ranked effectiveness probabilities for pain and function
- Naproxen had largest effect on function and overall ranked #1 for pain + function effect, followed by IA steroid, PRP, and then ibuprofen
- IA Steroid had large effect on pain, no sig on function
- Acetaminophen, IA HA, no different than placebo
- Drawbacks: heterogeneous, direct comparisons could be lacking, did not include PT, exercise



# 2015 Annals of Int Med Network Meta-analysis: Knee OA

- Utilized RCTs
- Evaluated pain, function, stiffness
- IA HA with greatest effect on pain and function, followed by diclofenac
- Acetaminophen: no different than placebo
- Drawbacks: lower-quality studies. IA HA compared to oral placebo

# 2017 Lancet Network Meta-analysis: Knee and Hip OA

- Utilized RCTs, 100+patients, knee/hip OA, comparing NSAIDs or acetaminophen with placebo
- Evaluated pain, function
- All interventions except for acetaminophen were superior to placebo
- Diclofenac 150mg / day was most effective in improving pain and function

# NSAIDs, oral: selected classes

## Salicylates

- ASA
- Salsalate

## Propionic Acids

- Naproxen
- Ibuprofen
- Ketoprofen

## Acetic Acids

- Diclofenac
- Etodolac
- Indomethacin
- Ketorolac

## Oxicams

- Meloxicam
- Piroxicam

## COX-2

- Celecoxib

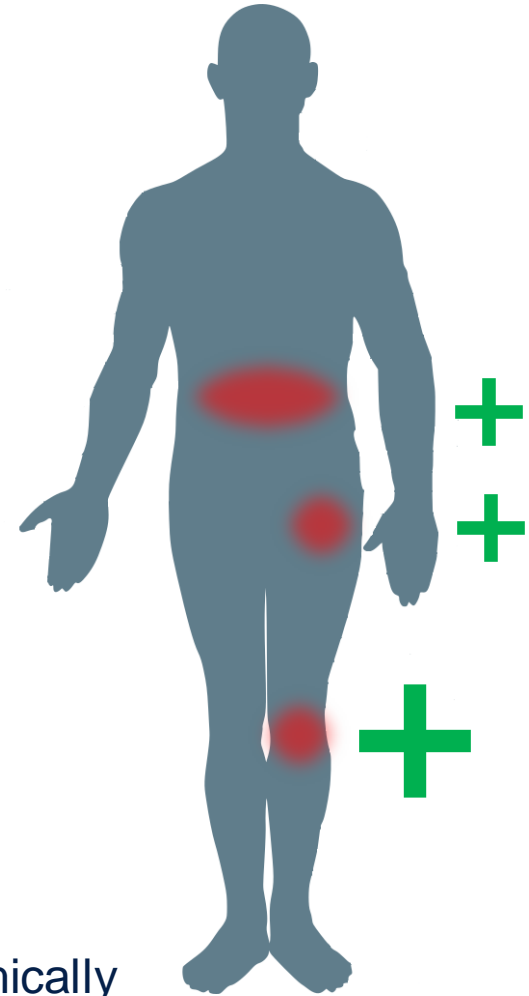
Some patients may respond better to NSAIDs in a different class, and sometimes even within a class

# NSAIDs: Caution

- 4-fold increase in GI bleed risk, 3-fold in COX-2
- Risk increases with age
- Use PPI in patients with elevated GI risk
- Choose naproxen in patients with CV risk
- Avoid in patients with recent CV event
- Avoid in patients with HF

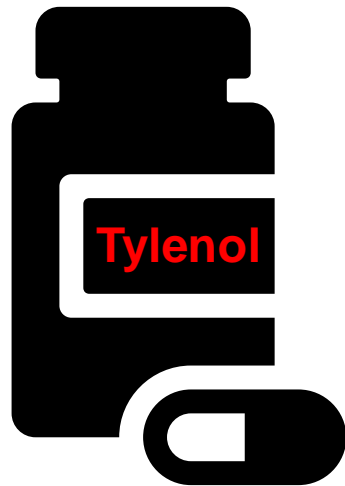
# Topical Treatments

- Cochrane Review, 2017
  - Topical Diclofenac and ketoprofen had modest effect on OA, mostly knee
  - Smaller effect, less evidence for
    - topical lidocaine (back pain, neuropathic)
    - capsaicin (post-herpetic neuralgia)

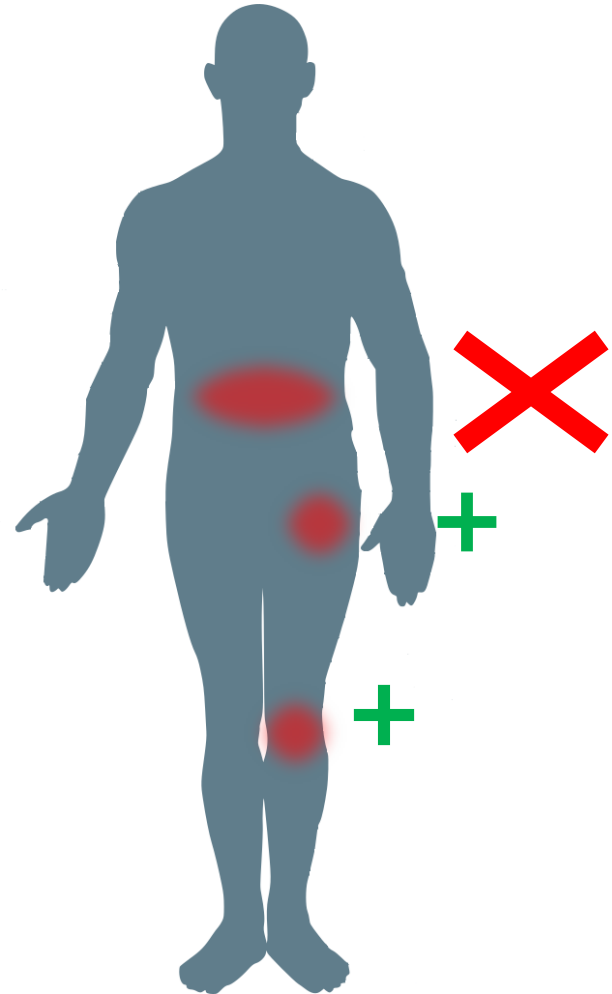


Some of the topical NSAID is absorbed systemically

# Acetaminophen: Update



Increase in liver enzymes



# Acetaminophen: Update

- ACP Review 2017, low back pain (10 trials, 1 large, placebo-controlled)
  - No effect on pain or function for acetaminophen vs. placebo or NSAIDs for acute pain (up to 4 weeks)
  - No study evaluated for chronic or radicular pain
- BMJ Review 2015, low back pain, OA of hip/knee (13 trials, acute and chronic pain)
  - Back Pain: no effect on pain or function for acetaminophen vs. placebo
  - OA: significant but small reduction in pain score and disability
  - Noted increase in liver enzymes



## Mrs. Healy: update

BMI: 27 – nutrition evaluation, weight loss, exercise program.

Referred to acupuncture for back. Starting yoga class.

Referred to physical therapy for knee pain

Continuing Mental Health Program

Switched ibuprofen to diclofenac, add diclofenac cream for knee, lidocaine for back

Perform IA corticosteroid injection to knee at next visit

Discussed risk / benefits of opioids, side effects. “not ready” to consider dropping dose

Review in 3 months





Mrs. Healy: update, 3 months

PEG: 4 / 5 / 4 = 13!

Prior:

5 / 6 / 5 = 16

Lost 5 lbs! Did not like acupuncture. Staying with yoga class

PT: some improvement

Tolerating oral diclofenac.

Steroid injection helped for about 2 months.

Did not think topical diclofenac helped for knee

Lidocaine cream helping a little for her back

Review opioids: "I would consider decrease". F/u 3 months.

# Neuropathic Pain

Evidence for neuropathic pain treatment for:

- SNRIs (duloxetine, venlafaxine)
- Gabapentin – caution!
- Pregabalin
- Tricyclic Antidepressants

# Opioids vs. Non-Opioids, JAMA 2018



**Opioids to 100 MEDD**

 more side effects

**No difference in functional status**

**Improved pain scores in non-opioid group**



**Acetaminophen / NSAIDs  
then add...  
TCA / Gabapentin  
then add...  
Pregabalin / Duloxetine**

# Opioids vs. Non-Opioids, JAMA 2018

- 12-month randomized trial comparing opioids to non-opioids for mod-severe chronic back or knee/hip OA in 240 patients of the Veterans Health Administration
  - Avg age upper 50s, men > women
  - Intervention: titrated opioids to 100 MEDD vs. [acetaminophen/NSAIDs, then +TCA/Gabapentin, then +pregabalin/duloxetine]
  - Outcome measures: pain related function, pain intensity
  - Results: no significant difference in pain-related function (about 60% of patients had response in both groups). Pain intensity score improved in non-opioid group (54% of pts vs 41%). Opioids had more side effects.

# What happens after tapering opioids?

- Low-quality evidence suggests improvement in function and quality of life
- Slight improvement to no change in pain

# Buprenorphine

- High affinity, partial agonist mu receptor
- Long acting
- Transdermal, SL tablet, injection (IM)
- Less respiratory depression?
- Lower abuse potential
- Decreased side effects
- Consider if pt having side effects with other opioids
- QTc prolongation at  $> 20\text{mcg/hr}$

# Buprenorphine/Naloxone (Suboxone)

- For opioid use disorder
- SL tablet/film
- Need DEA-X waiver/training
- Addition of Naloxone discourages abuse

# Buprenorphine

If current morphine equivalent daily dose (MEDD):

- ≤30 mg: initiate TD 5 mcg/h weekly at next dosing interval of around-the-clock opioids
- 30-80 mg: taper opioids to ≤30 mg MEDD, then initiate 10 mcg/h weekly at next dosing interval of around-the-clock opioids
  - May use short-acting analgesics as needed until analgesic efficacy attained with 10 mcg/h patch, or with titration to 20 mcg/h patch
- >80 mg: the maximum dose of buprenorphine patch (20 mcg/h) may not provide adequate analgesia for patients requiring high doses; consider alternatives unless the plan is to taper and maintain on lower MEDD



# Buprenorphine

## Inpatient/procedure:

- Continue buprenorphine or Suboxone at current dose
- Optimize non-opioid analgesia
- May use additional short-acting opioids

## Key points

- Minimum titration period 72 hrs
- Advise pt to keep tab/film in mouth to allow absorption



Mrs. Healy: update, 6 months

PEG (Current): 3 / 4 / 3 = 10!

Prior:

4 / 5 / 4 = 13

5 / 6 / 5 = 16

Wt stable. Continuing home exercise program. Able to tolerate standing more. Went on short hike. No neuropathy

Repeat steroid injection today for left knee

Review opioids: interested in starting a taper.

Continue PRN diclofenac (sparingly), topical lidocaine, yoga

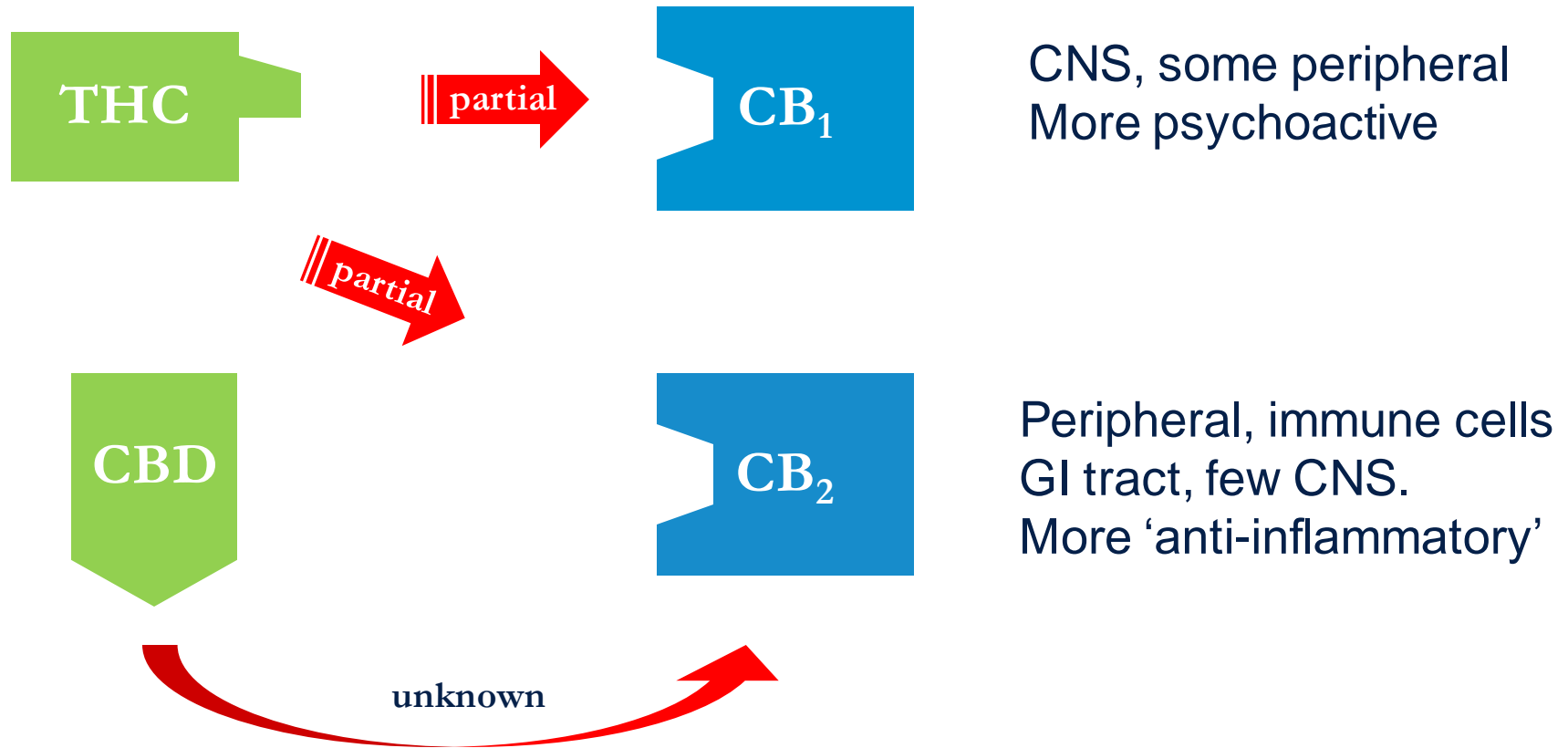
CBD?

# Cannabis

# Cannabis

- 34 states, DC, Guam, Puerto Rico, U.S. V.I. have a medical marijuana program (as of June 2019).
- A subset of these have also authorized recreational use
- Some states have a CBD (low THC) program
- Federally, cannabis remains a schedule I drug
- The State of Hawaii: medical marijuana program only

# Cannabis: delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)



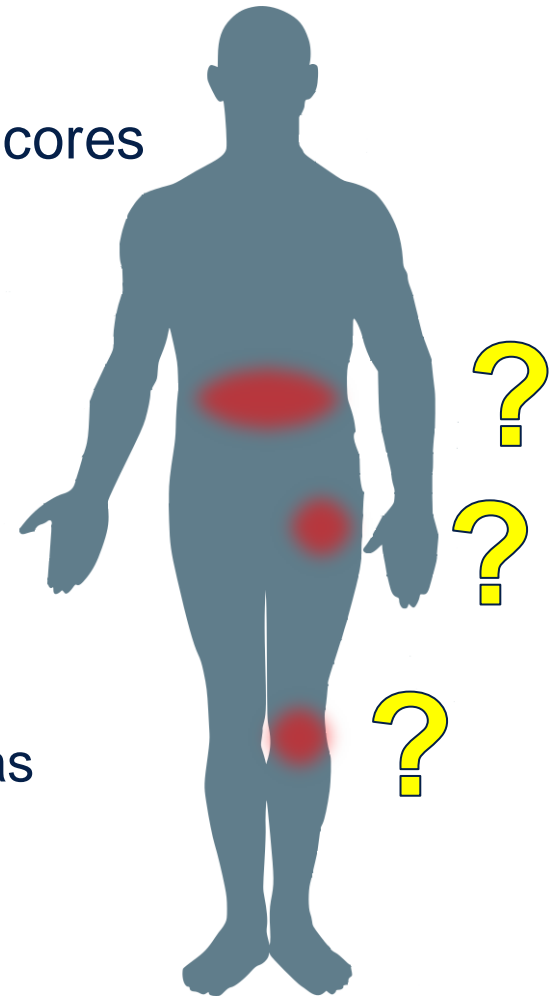
Serotonin, adenosine, glycine, opioid, cyclo-oxygenase  
May antagonize THC effects

# Cannabis: CBD

- Due to lack of psychoactive effects, toxic effects, and abuse potential, CBD has been focus for medical effects
- Formulation: from indica, sativa, or hemp (industrial)
- Usually a capsule, SL liquid, edible, or inhaled (not water soluble)
- Understanding of mechanism is incomplete
- Low oral bioavailability
- Optimal dose is unknown
- Research is mixed for pain
- Most patients using medical marijuana do so for chronic pain
- Approved for epilepsy (Epidiolex)

# Cannabis: Pain

- Some evidence for reduction in pain scores in neuropathic pain
- Reduction in opioid use?
- Rat models suggest OA/inflammatory benefit
  
- Research Caveats:
  - Most studies heterogeneous, risk of bias
  - Limited studies on back, knee, hip pain
  - Predominance of THC formulations



# Cannabis Reviews

- National Academy of Science 2017
  - “There is substantial evidence that cannabis is an effective treatment for chronic pain in adults”
- JAMA Review 2015
  - “There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity”
- Annals of Int Med Review 2017
  - “Limited evidence suggests that cannabis may alleviate neuropathic pain in some patients, but insufficient evidence exists for other types of chronic pain”



# Cannabis: what is the optimal dose/preparation, what are the side effects?

- Unknown!
- Suggest...
  - CBD oil preparation (capsule or tincture) 5-10mg twice a day
  - Titrate slowly
  - Caution patient on slow onset (30 min) – don't repeat dose



- Dizziness, lightheadedness
- Psychosis
- Cyclic vomiting
- Inhalation: respiratory effects (bronchitis)

Most side effects related to THC, inhaled route

# Cannabis: Conclusion

- Inform patients that cannabis is not an alternative to standard pain treatment and that evidence for efficacy is lacking
- Not first line but consider prior to opioids
- Best evidence for use in neuropathic pain
- Use CBD-predominant preparation, orally
- Caution patient on side effects
- Caution patient about drug-drug interactions (unknown!)
- Avoid in pregnancy / lactation
- Avoid in adolescents



Mrs. Healy: update, 9 months

PEG (Current):  $2 / 3 / 2 = 7!$

Prior:

$3 / 4 / 3 = 10$

$4 / 5 / 4 = 13$

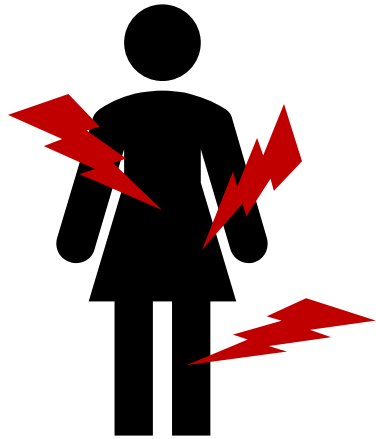
$5 / 6 / 5 = 16$

Hiking more. Tapered off APAP/Hydrocodone,  
no increase in pain.

Using occasional CBD

Continue PRN diclofenac (sparingly), topical lidocaine, yoga

Will continue to review every 6 months or so,  
sooner if pain increases



## Mrs. Healy: checklist

Dx: OA left knee, hip. Degenerative disease lumbar spine

Current PEG: 2 / 3 / 2

Current Function: hiking, walking, IADLs

Goals: continue hiking, do IADLs, avoid surgery

Current Rx: Diclofenac, topical lidocaine, CBD (occ)

Current non-Pharm: yoga, home exercise

Prior Rx: APAP / Hydrocodone (tapered off), acetaminophen (no effect), ibuprofen (better on oral diclofenac), topical diclofenac (no effect)

Prior non-pharm: acupuncture (no effect), PT (completed)

Mental Health: mild depression, on SSRI. Continuing treatment

Opioid Risk: none, tapered off.

# Recent Update, low back pain VA/DOD

Category	Intervention	Low back pain duration	
		< 4 weeks	chronic > 4 weeks
Self-care	Advice to remain active	X	X
	Books, handout	X	X
	Application of superficial heat	X	
Non-pharmacologic therapy	Spinal manipulation		X
	Clinician-guided exercise		X
	Acupuncture		X
	CBT and/or mindfulness-based stress reduction		X
	Progressive relaxation		X
	Exercise which may include Pilates, tai chi, and/or yoga		X
Pharmacologic therapy	NSAIDs	X	X
	Non-benzodiazepine skeletal muscle relaxants	X	
	Antidepressants (duloxetine)		X
Other therapies	Intensive interdisciplinary rehabilitation		X

# Recent Update, low back pain VA/DOD

- Recommend AGAINST:
  - Benzodiazepine
  - Long-term opioid therapy
  - Acetaminophen
  - Spinal epidural steroid injection (chronic)

# Take home points

- Framework: eval-measure-try-repeat
- **PEG**: in the last week average (0-10)
  1. **P**ain
  2. Interferes w/ **E**njoyment of life
  3. Interferes w/ **G**eneral activity
- 4 keys to non cancer pain management
  1. Oral NSAIDs are most effective for OA
  2. Topical NSAIDs have small effect for OA
  3. Acetaminophen minimal effect in OA
  4. Opioids: not first line
- Cannabis: data scarce, not first line, may be effective

# Recent Additional Resources

- NEJM – “Nonnarcotic Methods of Pain Management”
  - N Engl J Med 2019; 380:2440-2448
- Curbsiders Podcast:
  - <https://thecurbsiders.com/podcast/156-chronic-pain>



# Questions?