Pain and Substance Use Disorder

Mental Health Comorbidity

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Years Lived with Disability

Top 30 Diseases

(JAMA 2013;310:591-608)

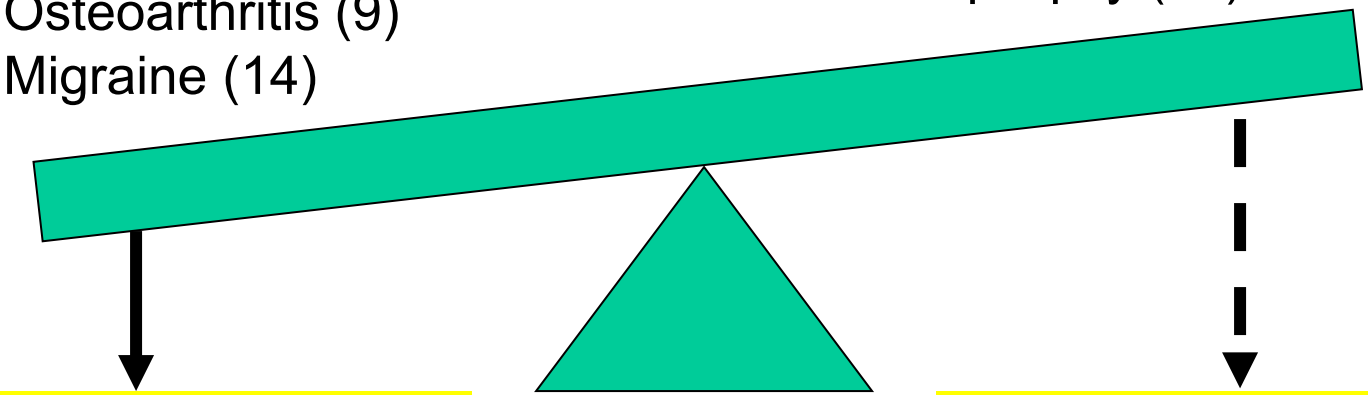
- COPD (6)
- Diabetes (8)
- Asthma (10)
- Alcoholism (12)
- Dementia (13)
- Ischemic heart disease (16)
- Stroke (17)
- Hearing loss (19)
- Chronic kidney disease (22)
- Vision loss (26)
- Road injury (27)
- Epilepsy (30)

Depression **(2)/Anxiety (5)**
5.6 million YLDs

Drugs (7) /Alcohol (13)
2.1 million YLDs

P A I N

- Low back pain (1)
- Neck pain (4)
- Other musculoskeletal (5)
- Osteoarthritis (9)
- Migraine (14)



9.7 million YLDs

8.0 million YLDs

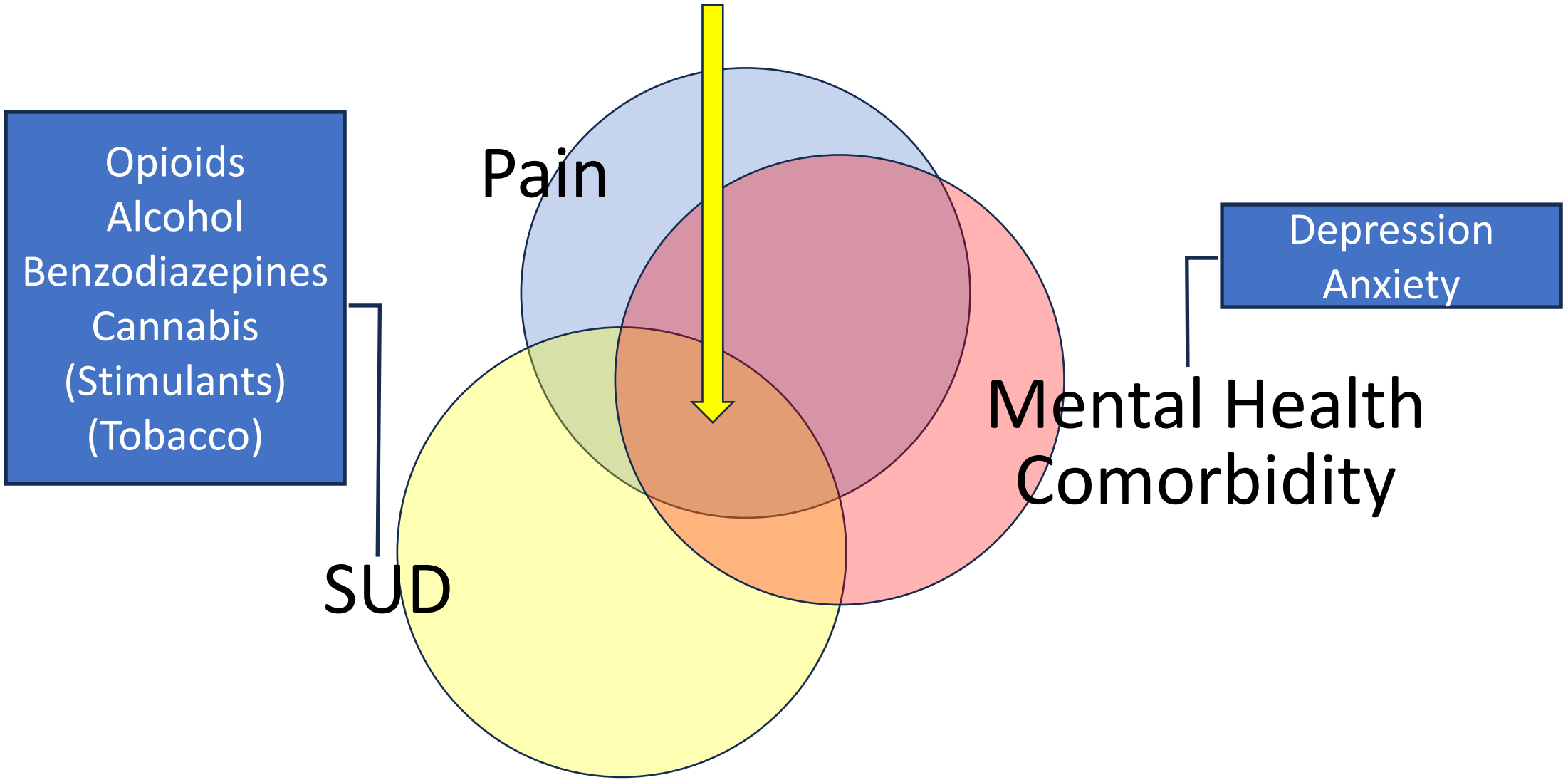
2 Principal Sources for My Presentation

- Trial experience in pain, depression, anxiety, opioids
  → *Collaborative care/Telecare/Stepped care*
- Rapid literature search (2010-2024)
  - Meta-analyses or reviews

    AND
  - Pain and Substance
  - Pain and Alcohol
  - Pain and Psychiatric
  - Pain and Mental
  - *[not Pain and Depression/Anxiety or Pain and Opioids → too broad]*

    → *15 selected reviews/meta-analyses*

The Triple Threat



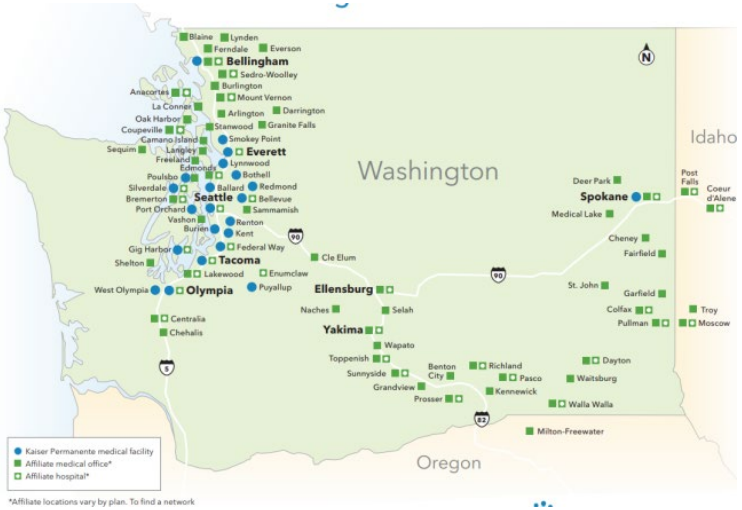
MI-CARE Trial

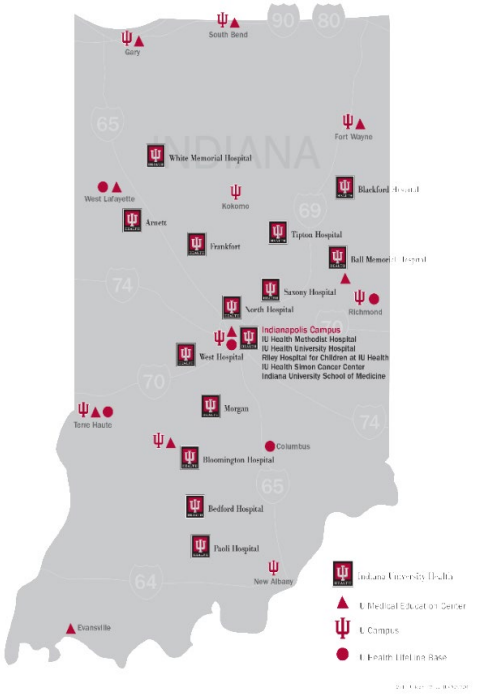
National Institute Of Mental Health of the National Institutes of Health under Award Number UF1MH121949 (Bradley and DeBar)

DESIGN: Encouragement (Zelen) pragmatic trial

SETTINGS: Kaiser Permanente Washington, Indiana University Health

ELIGIBILITY: ≥ 18 years of age with EHR diagnosis consistent with past year OUD (ICD-10 or on buprenorphine) and a PHQ-9 depression score ≥ 10 in the past we





MI-CARE Sample (n = 800)

Clinical Features

• Median age	46
• Female	62%
• Minoritized race/ethnicity	13%
• Rural residency	23%
• Medicaid enrolled	19%
• On buprenorphine	33%
• On long-term opioids	34%

Mental Health Diagnoses (ICD)

• Depression-related disorder	67%
• Anxiety-related disorder	77%
• Posttraumatic stress disorder	21%
• Alcohol use disorder	14%
• Stimulant use disorder	14%

Conditions (interview)

• Chronic pain	64%
• Sleep problems	57%
• Nonopioid substance issues	34%

Chronic Pain and Substance Use

10% rule of thumb

- Opioid use disorder (OUD) occurs in ~10% of chronic pain patients on long-term opioid therapy (LTOT). Also, 50-60% of patients using nonmedical prescription opioids jin substance use programs have pain.
- Alcohol: moderate to heavy drinking in 15-20% of patients with chronic pain, which also has 2-fold increased risk of alcohol use disorder (AUD).
  - Alcohol use may be associated with lower odds (OR = 0.76) of chronic pain (i.e., possible analgesic effect); moderate use may improve pain, whereas effects of heavy use are inconclusive in terms of making pain better vs. worse.
  - AUD and OUD increase risk and treatment response of one another as well as pain
- Benzodiazepines → ~10% of chronic pain patients may develop sedative use disorder
- Cannabis ~10% of chronic pain patients can develop cannabis use disorder

Martel 2018; Karimi 2022; Witkiewitz 2018; van Rijswijk 2019; Zale 2015; Morasco 2011; Lusted 2013

Managing Comorbidity (≥ 2 disorders)

- Screening: 1 condition should prompt screening for the others (pain/mental/substance)
- Treating sequentially
  - If one condition is “major” and the other is “minor” (severity & impairment)
  - If one condition is a greater treatment priority for the patient
- Treating simultaneously
  - If both conditions cause substantial distress or impairment.
  - If the untreated condition remains bothersome after treating the other condition
- Monitoring outcomes
  - Easier for symptoms (pain, depression, anxiety) where there are responsive scales
  - For substances, there are scales/criteria for screening and diagnosis but less clear for what are criteria for improvement (abstinence, less DSM criteria, days on MAT, …)

How much better than placebo?

(0-100 scale → 5-10 points is clinically important)

Drug (# trials for LBP/OA)	LBP	OA
NSAID (n=13/9+)[1,2]	4	5-8
Opioids (n=13/12)[2,6]	8-10	6
Acetaminophen (n=3/10)[3,4]	0	4
Gabapentin (n=3)[5]	0	--

1) Enthoven, Cochrane Review 2016. 2) Smith, Osteoarthritis & Cartilege 2016.
3) Machado, BMJ 2015. 4) Roberts, Ann Rheum Dis 2015 .
5) Shanthanna, PLOS Medicine 2017. 6) Shaheed, JAMA Int Med 2016.

Risk of Chronic Use & Opioid Use Disorder (OUD) after Opioid Prescription

Author	Sample	Patients	Chronic (> 3 mo)	OUD
			1 in 20	1 in 200
Quinn	Population	10,300,000	2.1%	- -
Hwang	Population	177,000,000	7.7%	- -
Quinn	Adolescents	1,000,453	0.3%	- -
Edlund	Chronic Pain	197,269	5.5%	0.2%
Brat	Postop	1,015,116	- -	0.6%
Brummett	Postop	36,177	6.0%	- -

Quinn, Pain 2017, Hwang, Am J Prev Med 2016, Quinn, JAMA Pediatrics, Edlund Clin J Pain 2014, Brat, BMJ 2018, Brummett, JAMA Surgery 2017

Fatal Opioid Overdose Risk in Patients on LTOT

compared to 1 to < 20 mg morphine per day

Daily Dose & Risk	NNH for Fatal Overdose
Medium dose (mg) - ≥ 50 MME	667
Higher dose (mg) - ≥ 100 MME	400

Dowell, CDC Opioid Guidelines, JAMA 2016

	Evidence-based Nonpharmacological Therapy for LBP (Chou, Ann Intern Med 2016)	# trials
A	Exercise	122
	Chiropractic/manipulation	61
	Acupuncture	49
	Multidisciplinary rehabilitation	44
A	Psychological therapy (CBT, …)	32
	Massage	26
A	Yoga	14
A	Mindfulness-based stress reduction	3
A	Tai chi	2

A = Active Therapy (requires patient work)

Nonpharmacological Treatments for Chronic Pain: 7 Caveats

1. Evidence standards: not as strict as FDA is for medications
2. Imperfect placebo: active vs. control cannot be as completely matched (masked) as drug trials
3. Usually requires multiple sessions and, more importantly, patient motivation and “work”
4. Superior efficacy to analgesics is not established
5. Evidence for long-term efficacy (> 1 yr.) is limited
6. Shortage of trained & interested providers
7. Variable reimbursement

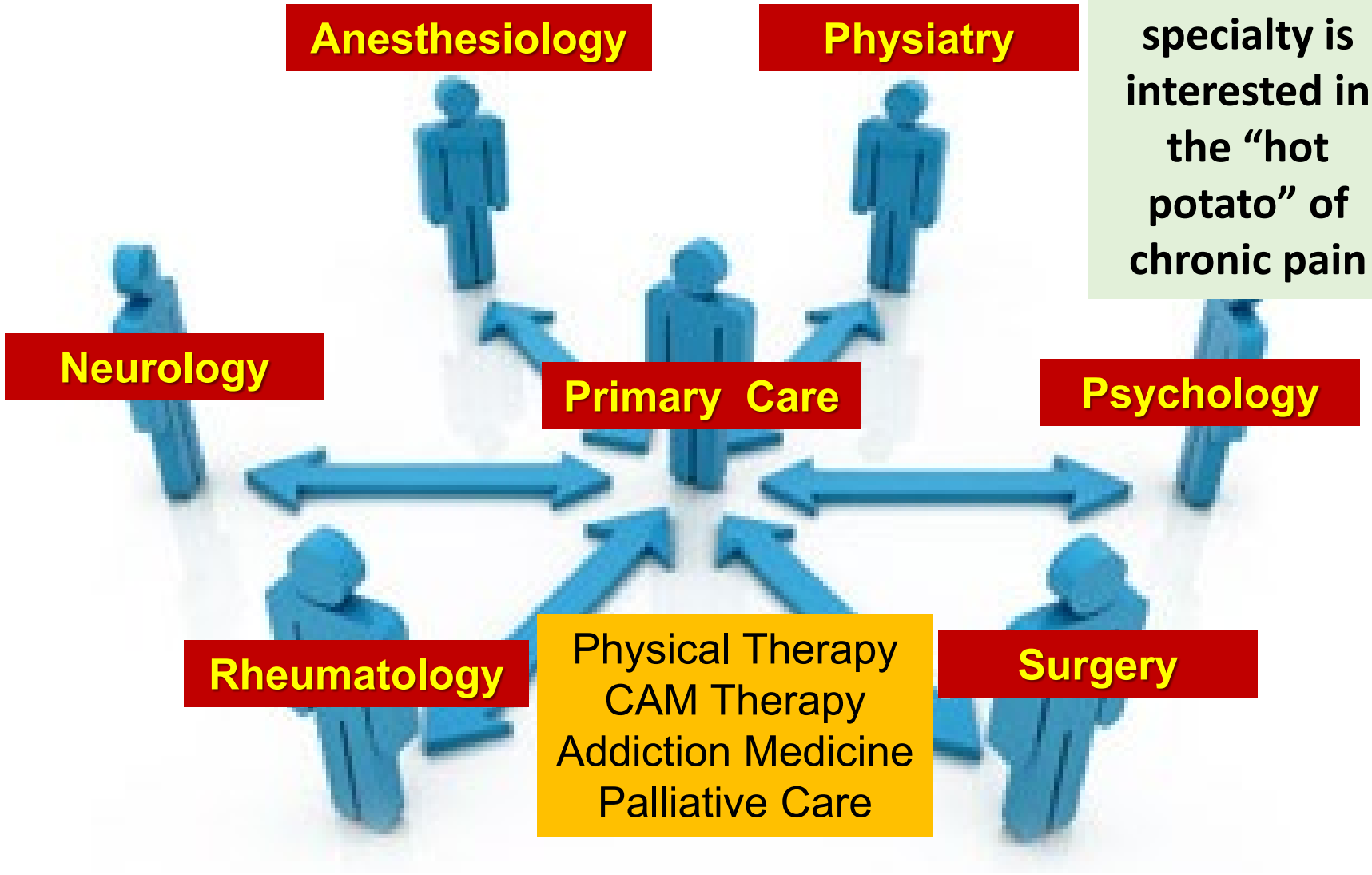
Kroenke & Cheville, JAMA 2017

Cannabis for Chronic Pain

- 2 systematic reviews (27 chronic pain trials[1]; 18 trials and 7 cohort studies[2])→ effective in neuropathic pain, but insufficient evidence for other types of pain. Similar findings in another review.[3]
- Harms (11 reviews in population studies) → motor vehicle accidents, psychotic symptoms, short-term cognitive impairment, sedation/dizziness.
- Most trials were short duration (2-15 weeks) and used synthetic FDA-approved cannabinoids rather than more complex marijuana products
- Other data suggests that pain effects of cannabis probably similar to other analgesics

1) Nugent, Ann IM 2017; 2) McDonagh, Ann IM 2020; 3) Hill, JAMA 2015

Perplexity of Pain Referrals



Only a minority of those in each specialty is interested in the "hot potato" of chronic pain

Research Gaps

- Cohort studies (3-5 years)
- EHR-based studies (trials or observational)
- SMART trial designs

1. **Opioids**
   - What is the role of opioid therapy in acute, severe, short-term pain (e.g., postop, trauma-related, dental)?
   - Is there any residual role for opioids as "last resort" in chronic pain?
2. **Cannabis** → What is the niche (as well as pros and cons) of increased cannabis use for treatment of chronic pain?
3. **Measure-based care (MBC)** → validate scales to monitor SUD treatment (like we have for pain, anxiety, depression)
4. **Site of care**: Which patients should be treated principally in primary care vs. principally in specialty care vs. co-managed (including collaborative/integrated care)?
5. **Sustaining pain control long-term** (few studies are > 12 months)

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