

Chronic pain and Mary Jane: Results from research

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Disclosures

I have nothing to disclose.

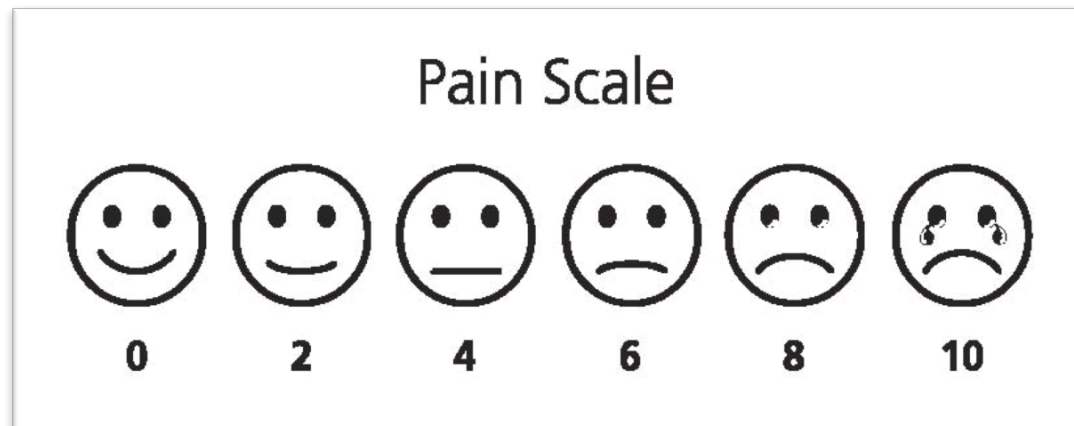
Learning objectives

1. Understand the definition and mechanisms of pain and its prevalence
2. Identify the pain conditions where medical marijuana is effective
3. Identify current and future directions for research surrounding the use of cannabinoids for the treatment of pain

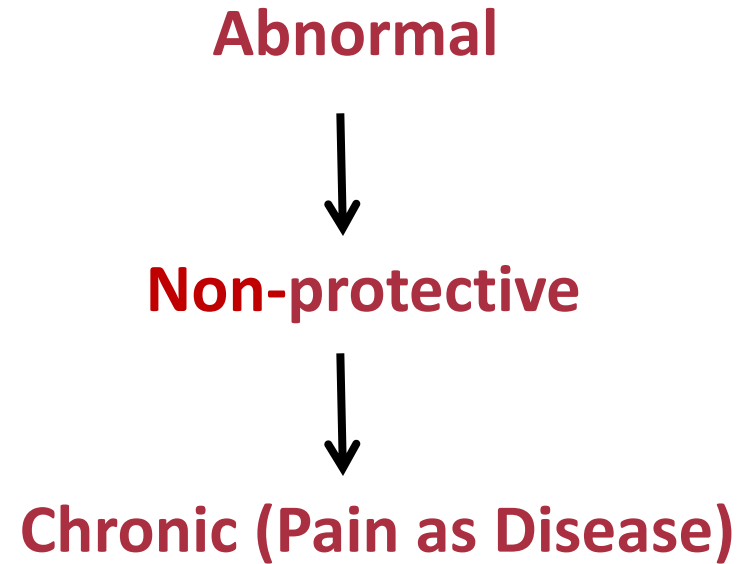
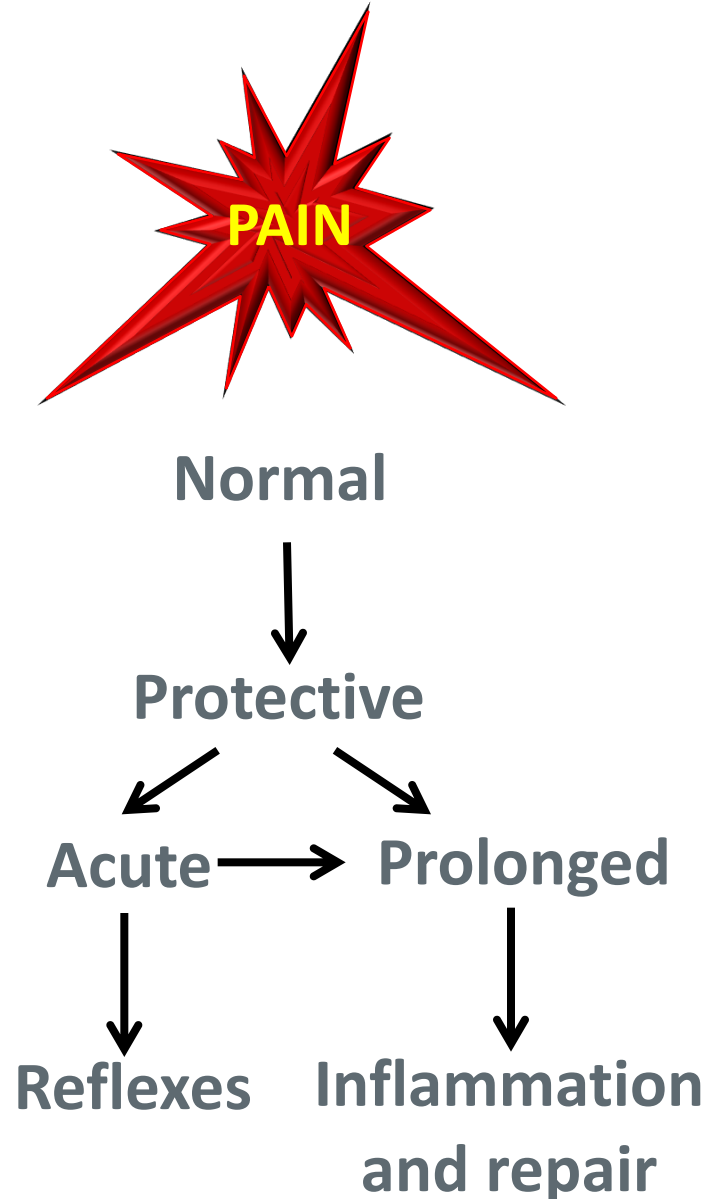
What is pain?

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”

-International Association for the Study of Pain (IASP)

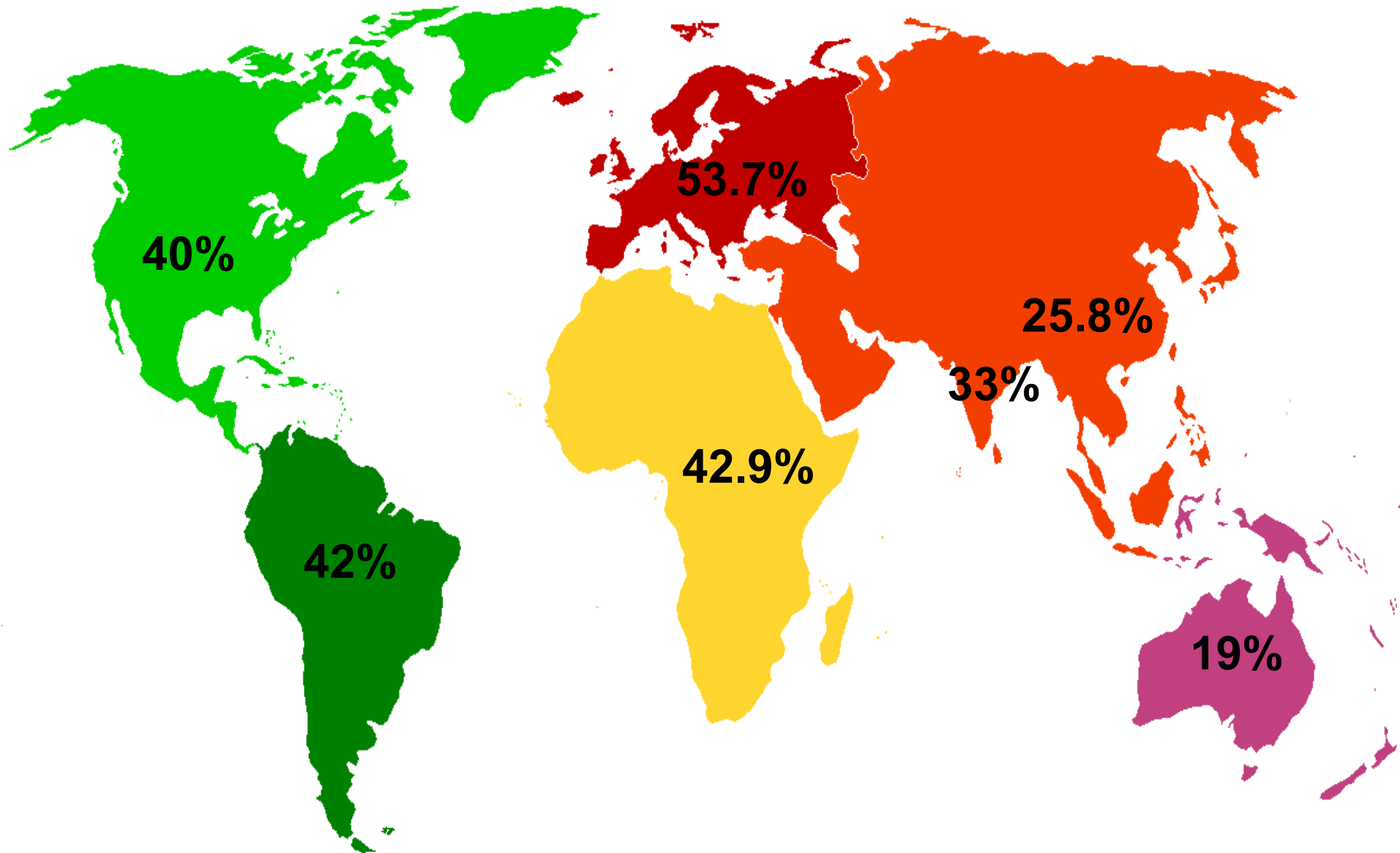


The two faces of pain: Protection and disease

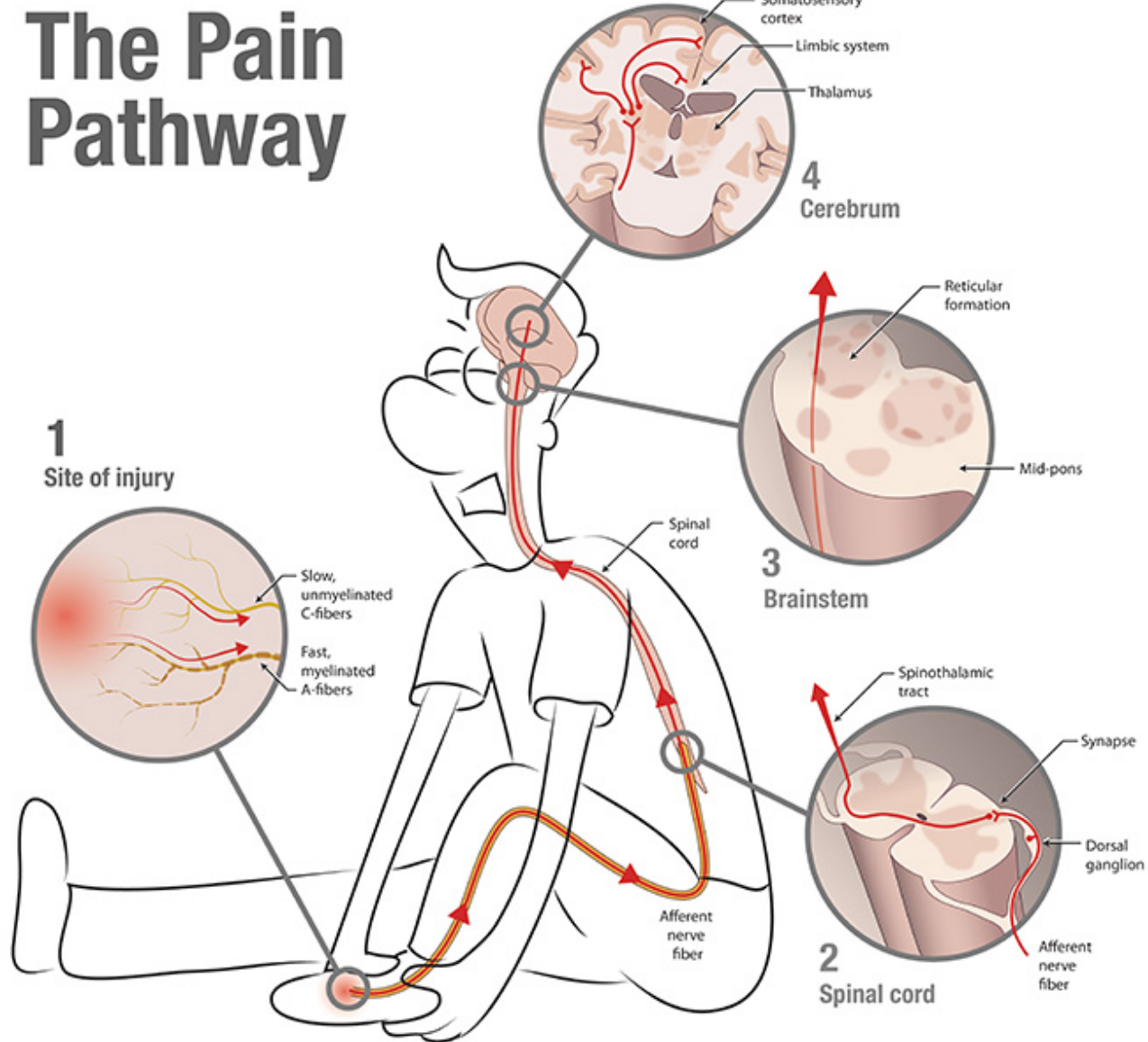


Therapeutic goal:
Eliminate abnormal pain
without interfering with normal,
protective pain

Chronic pain is a highly prevalent problem worldwide



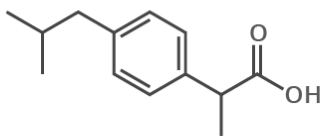
The body interprets pain using a simple neural pathway



Chronic pain is poorly treated

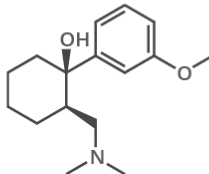
N IBUPROFEN

POTENTIAL FOR SERIOUS SIDE EFFECTS LESS THAN OTHER NSAIDS



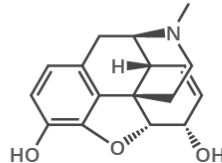
O TRAMADOL

METABOLISED IN THE BODY TO A MORE POTENT OPIOID



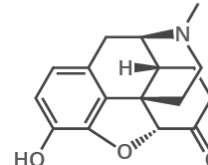
O MORPHINE

THE FIRST INDIVIDUAL PLANT ALKALOID EVER ISOLATED



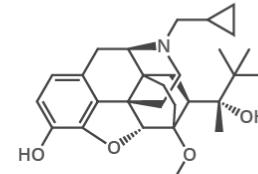
O HYDROMORPHONE

MOSTLY USED INTRAVENOUSLY IN A HOSPITAL SETTING



O BUPRENORPHINE

ALSO COMMONLY USED TO TREAT OPIOID DEPENDENCE



- 82% of chronic pain patients reported that their pain was “treated poorly” (National Pain Foundation, 2014).
- Over 50% of chronic pain patients complain that they have no control over managing their pain (National Pain Foundation, 2014).
- Females suffer disproportionately than males from chronic pain disorders— in some cases over 3x more (Mogil, 2012).

Current treatment options (e.g., opioids)
leave millions of people untreated.

Side effects of opioid analgesics limit their use

Miosis (pin point pupil)

Out of it (sedation)

Respiratory depression

Physical dependence

Histamine release (excessive itch)

Increased intracranial pressure

Nausea


Euphoria

Current opioid policies affect patients' qualities of life

Dialogue, Dialogue, Dialogue: Strategies to Facilitate Translation

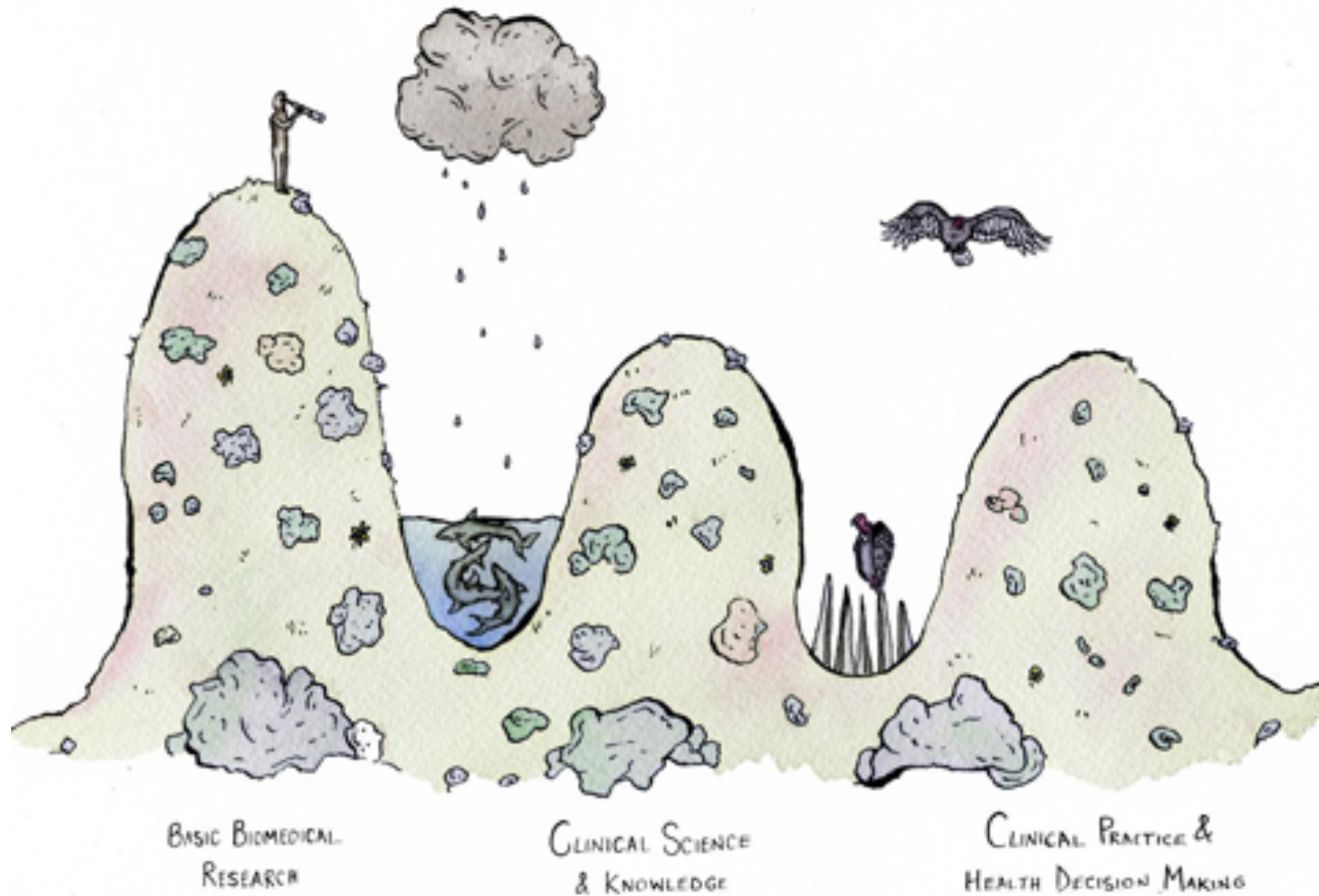
The development of new and effective analgesics requires ongoing, productive, back-and-forth communication between basic scientists and clinicians

by Ram Kandasamy on 30 Aug 2016

 Dialogue between clinicians, scientist & Please do NOT forget to include genuine Pain patients whos rights have've been stripped right now in the name of "addicts".there's NO other efficient pain treatment for them to be able to just make it through their day.

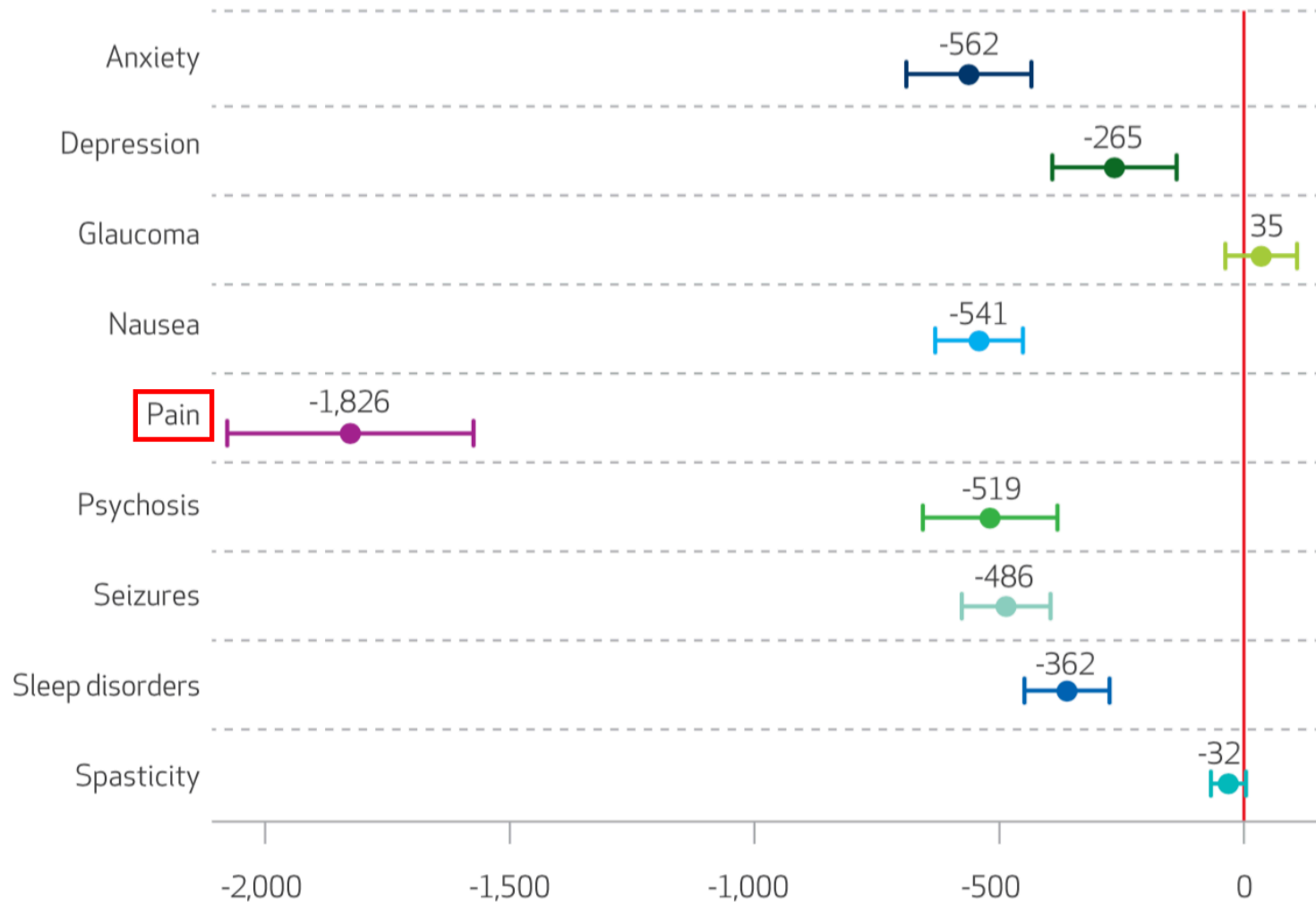
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Bench-to-bedside translation of analgesics is SLOW



Medical marijuana laws reduce opioid prescriptions

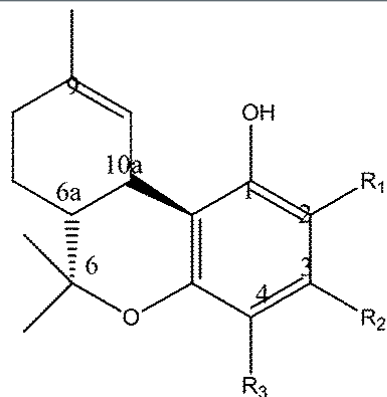
Average numbers of daily doses filled for prescription drugs annually per physician in states with a medical marijuana law, by condition categories studied, compared to the average numbers in states without a law



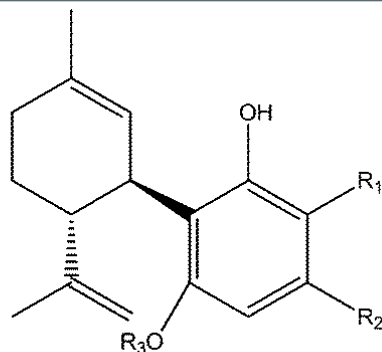
Many arguments oppose the clinical use of *Cannabis*

- Chemical composition of *Cannabis* is complex, variable, unknown; thus, predicting effects are not possible
- *Cannabis* is harmful to individual and public health
- The push for medical cannabis is part of a well-structured and funded strategy to legalize *Cannabis* for general use
- Smoking *Cannabis* may be harmful because of products of combustion

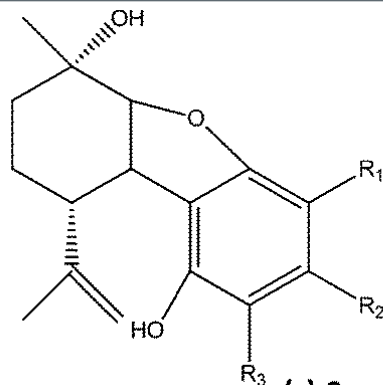
Cannabis contains 100+ cannabinoids (537 constituents total)



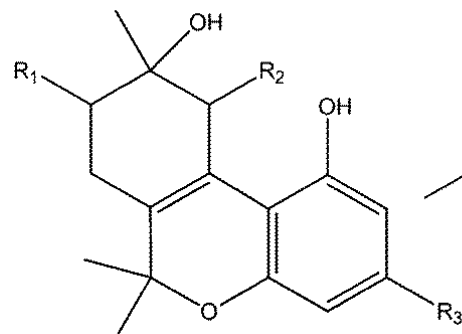
(a) Δ^9 -Tetrahydrocannabinol



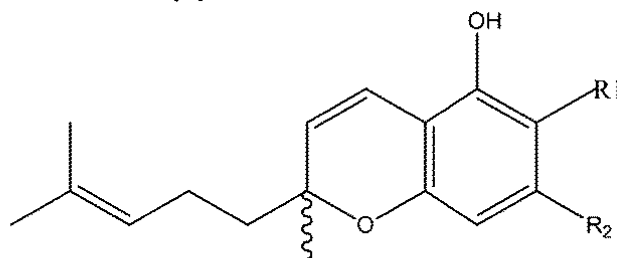
(b) Cannabidiol



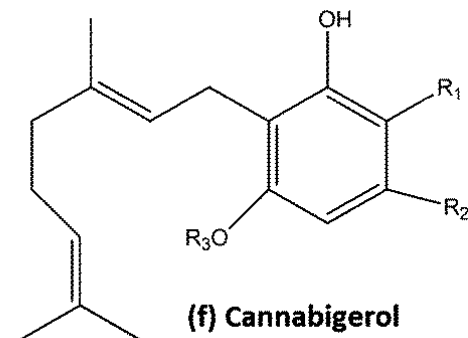
(c) Cannabielsoin



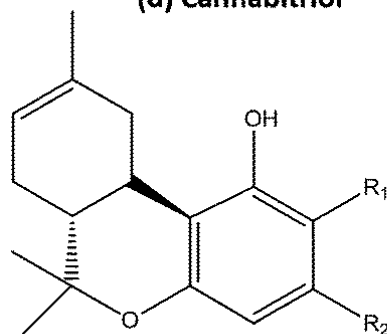
(d) Cannabitrinol



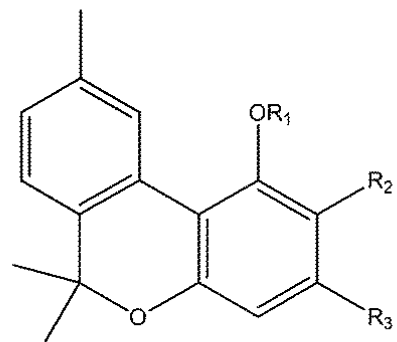
(e) Cannabichromene



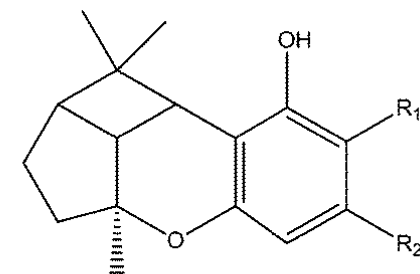
(f) Cannabigerol



(g) Δ^8 -Tetrahydrocannabinol



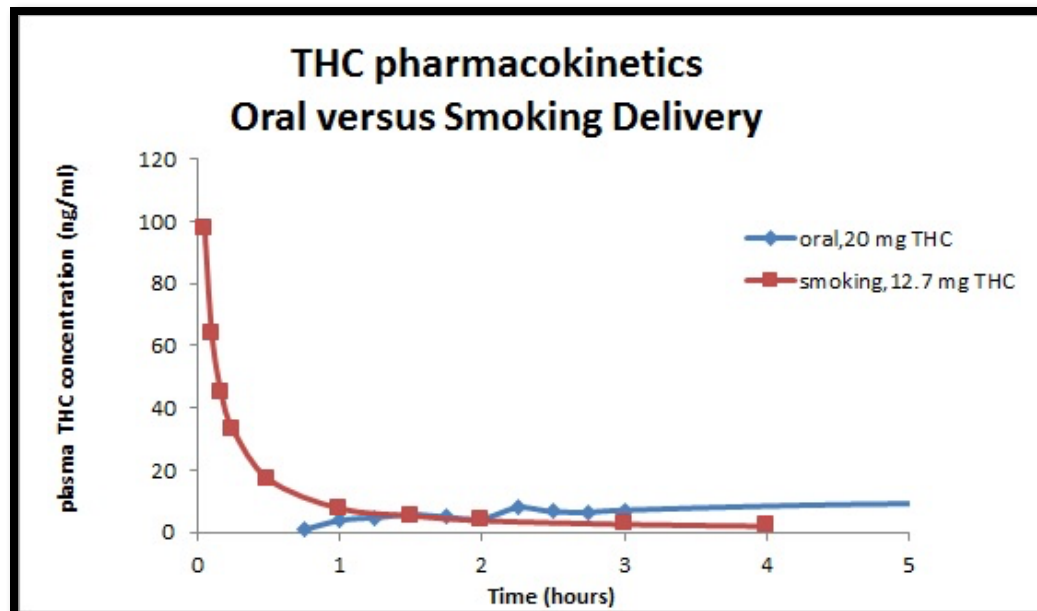
(h) Cannabinol and Cannabinodiol



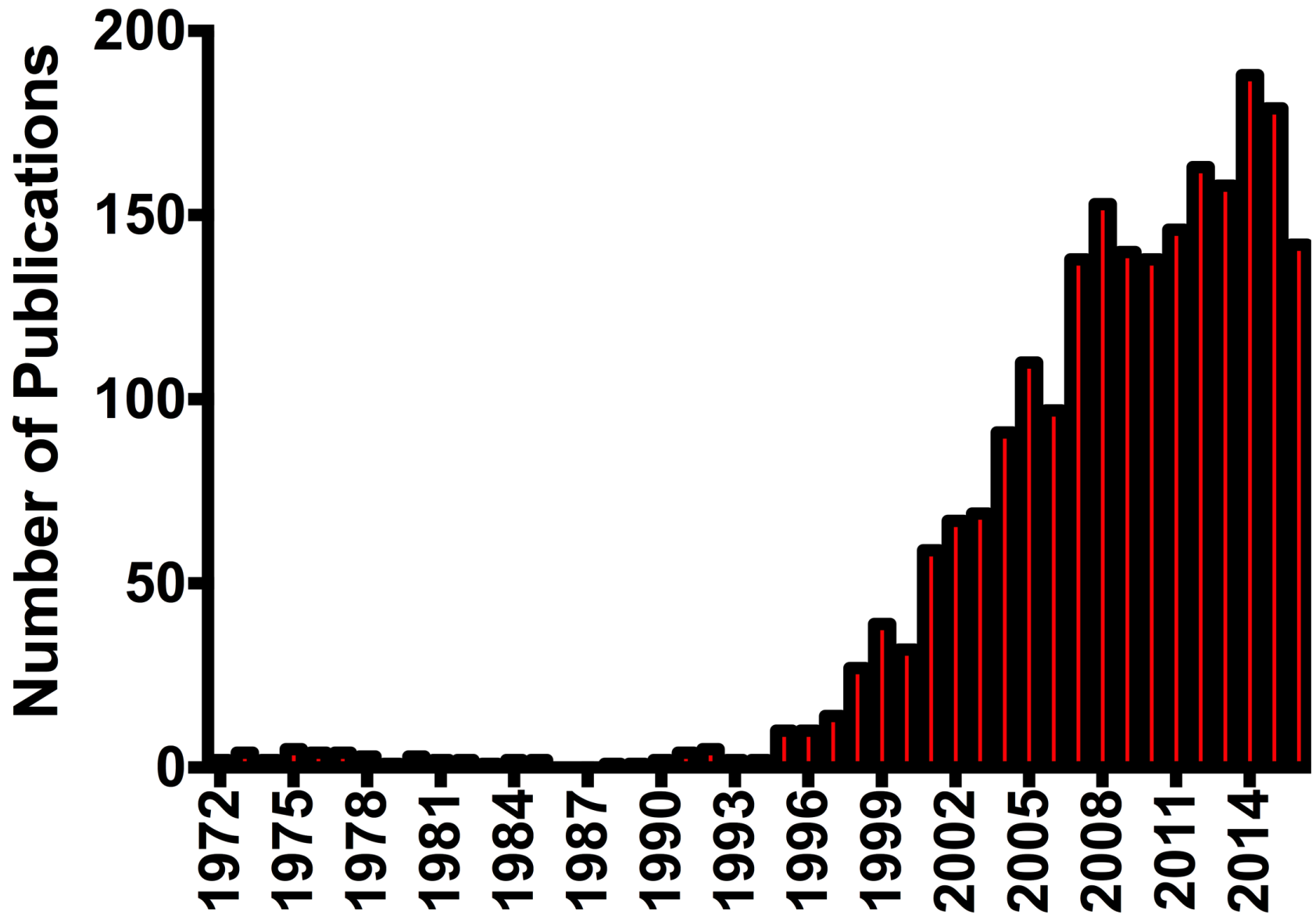
(i) Cannabicyclol

Clinical pharmacology of *Cannabis* is complex

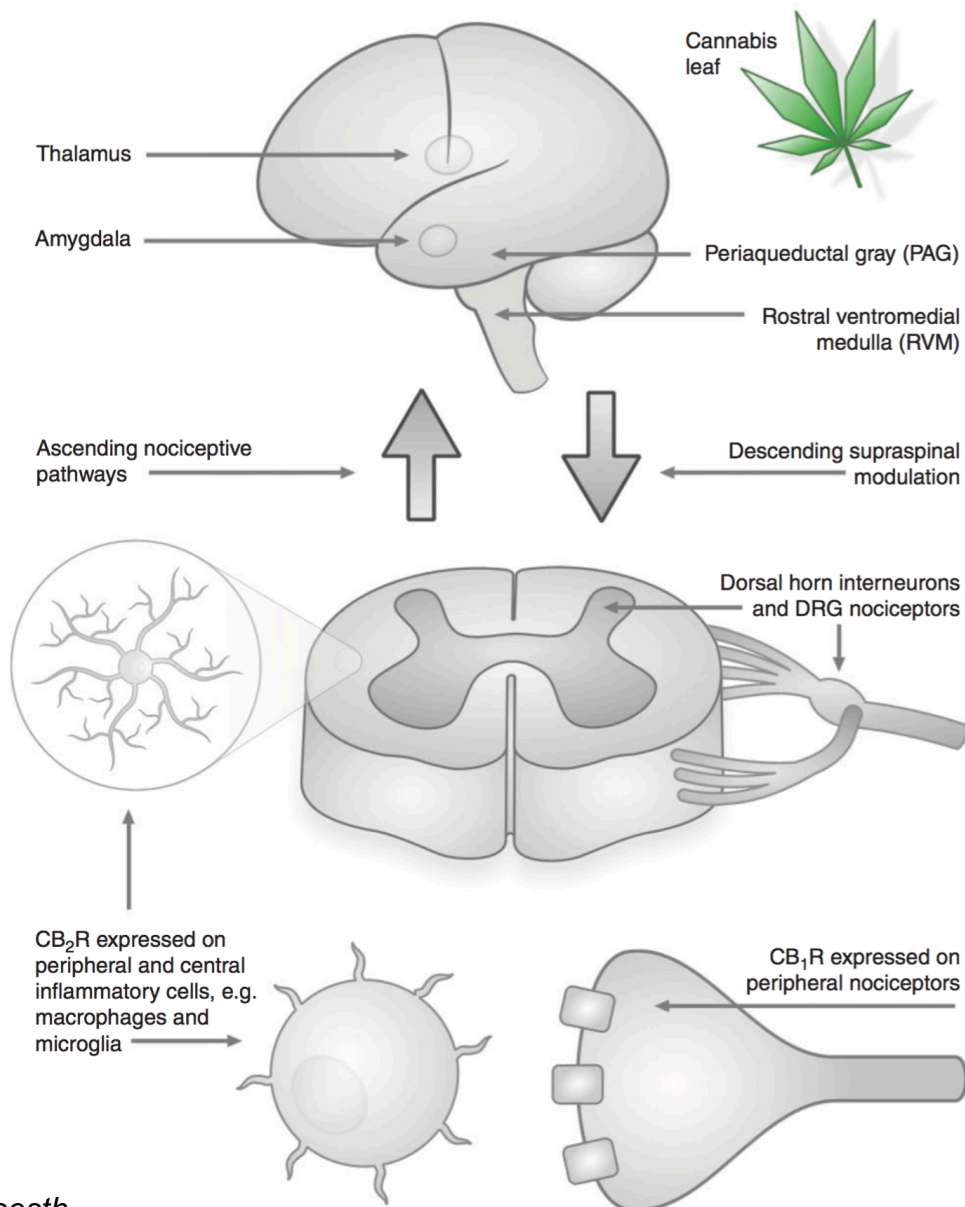
- Elimination is slow: days to weeks; 20-35% found in urine; 80% found in feces; stored in adipose
- Fast absorption if vaporized, slower if ingested or topical
- ✓ No constipation or respiratory suppression
- ✓ No LD₅₀



Cannabinoid/pain research is very new



How do cannabinoids provide pain relief?



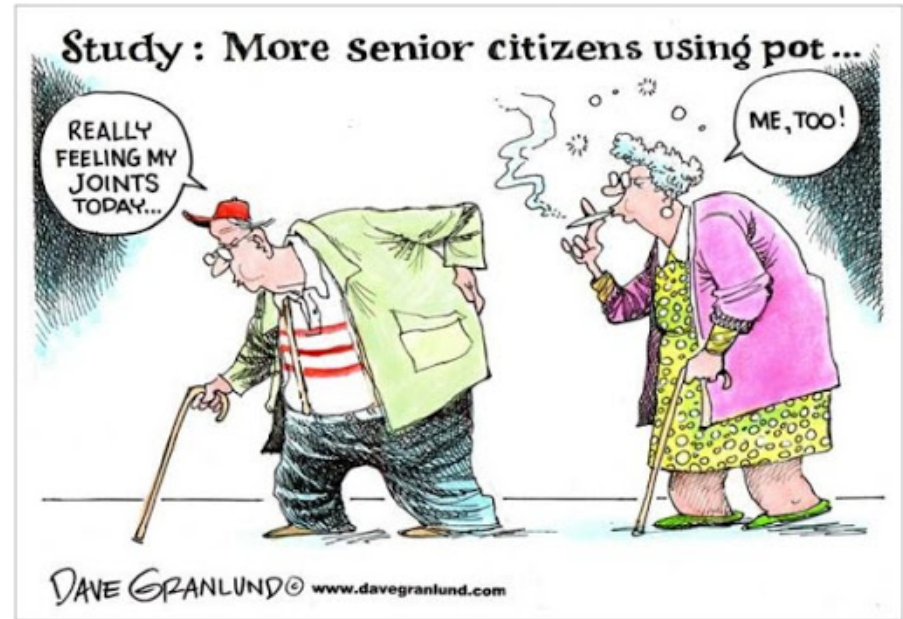
Cannabinoid-based therapies are currently on the market

- Dronabinol (Marinol): Δ^9 -tetrahydrocannabinol (Schedule III)
- Nabilone (Cesamet): Synthetic Δ^9 -tetrahydrocannabinol (Schedule II)
- Nabiximols (Sativex): Δ^9 -tetrahydrocannabinol/cannabidiol (Schedule IV)
- Medical marijuana: Δ^9 -tetrahydrocannabinol/cannabidiol/others (Schedule I)



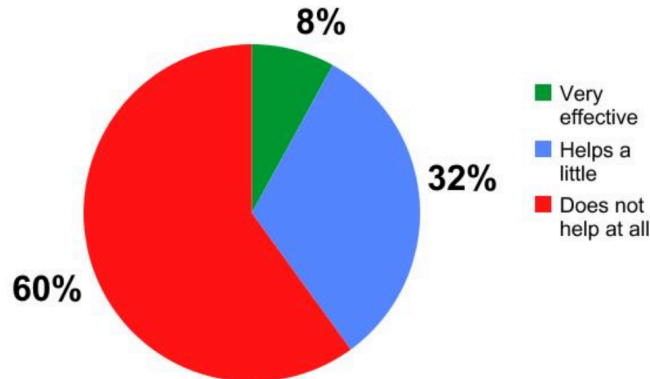
Cannabinoids provide relief against multiple types of pain

- Myofascial pain syndrome
- Diabetic neuropathy
- **Neuropathic pain** syndrome
- Central pain syndrome
- Phantom pain
- Spinal cord injury
- **Fibromyalgia**
- Osteoarthritis
- Rheumatoid arthritis
- Discogenic back pain
- HIV-associated neuropathy
- Malignant pain
- Cancer pain
- **Headaches/Migraine**
- Muscle cramps



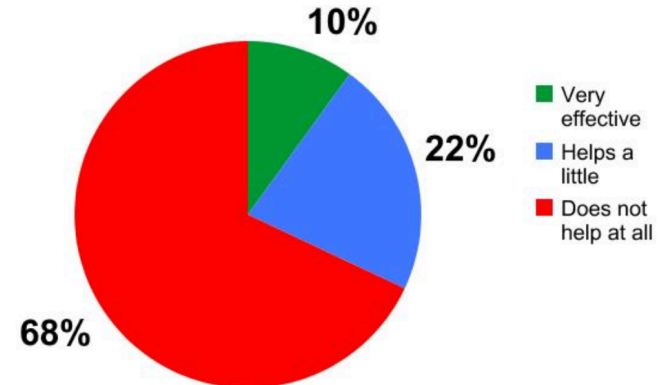
Cannabis is more effective against fibromyalgia pain

How would you rate the effectiveness of Cymbalta (Duloxetine) in treating your fibromyalgia symptoms?



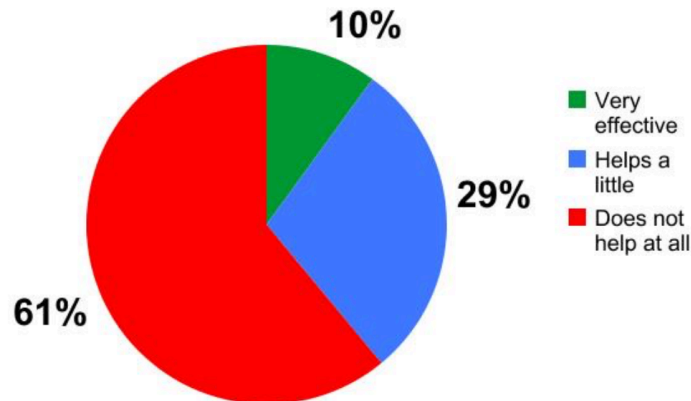
National Pain Foundation survey

How would you rate the effectiveness of Savella (Milnacipran) in treating your fibromyalgia symptoms?



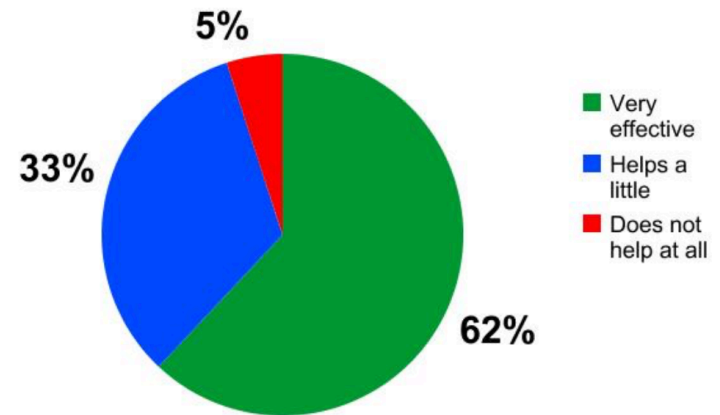
National Pain Foundation survey

How would you rate the effectiveness of Lyrica (Pregabalin) in treating your fibromyalgia symptoms?



National Pain Foundation survey

How would you rate the effectiveness of medical marijuana in treating your fibromyalgia symptoms?



National Pain Foundation survey

Migraine impairs physical and psychological well-being

“Throbbing, pulsating, stabbing. On a bad day, I have difficulty leaving my bed, let alone my home. I cannot go to work on almost half of a month, cannot enjoy playing with my children or even meeting friends for a coffee. There are weeks during which I barely manage to keep my place in order. Darkness and silence are my friends of late. I basically don’t recognize myself anymore.”

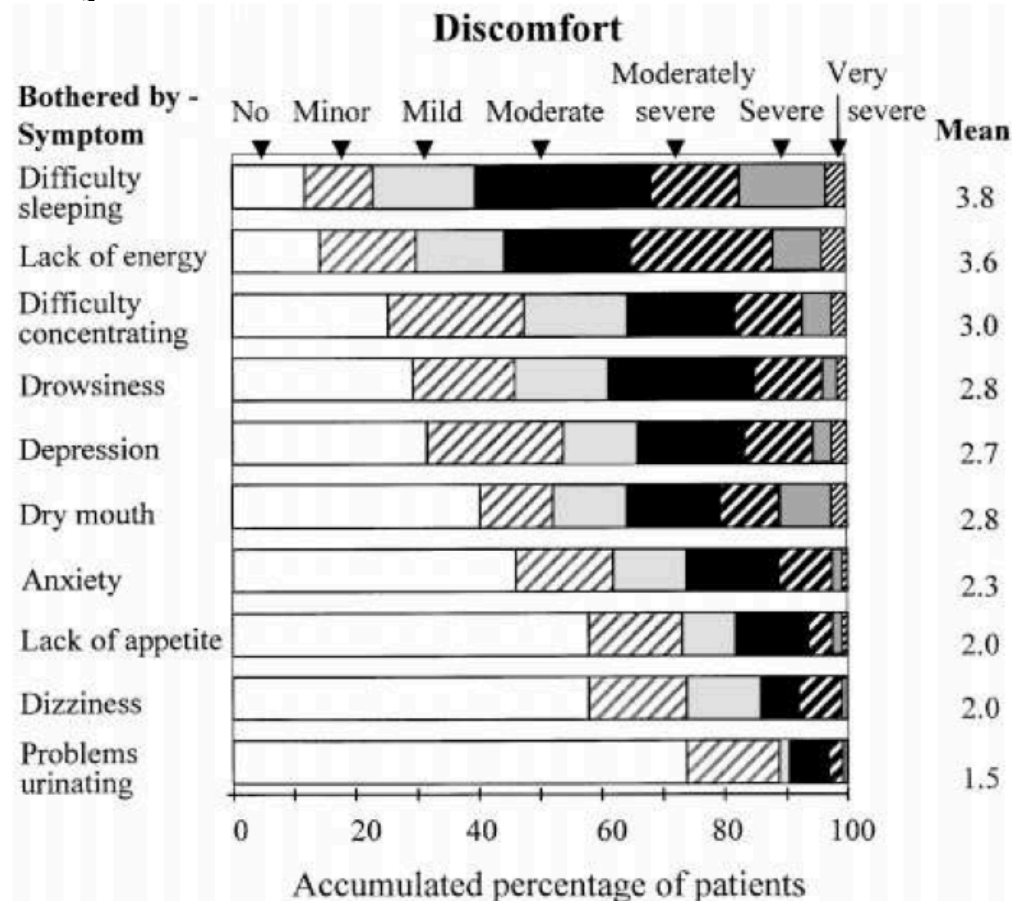
-Anonymous migraine patient, describing her illness

Cannabis and migraine: Anecdotes vs. research

- Dr. Cledinning in London first prescribed cannabis for migraine in the 1840's.
- Dr. Farlow described marijuana as having “few equals in its power over headaches” in 1889.
- Cannabis preparations were taken off the *US Pharmacopoeia* in 1941; however, Dr. Fishbein recommended oral cannabis for menstrual migraine in 1942.
- Smoked cannabis terminates migraine attacks within 5 min of inhalation and restore complete function within 15 min.
- Frequency of migraine headache was decreased with medical marijuana use.

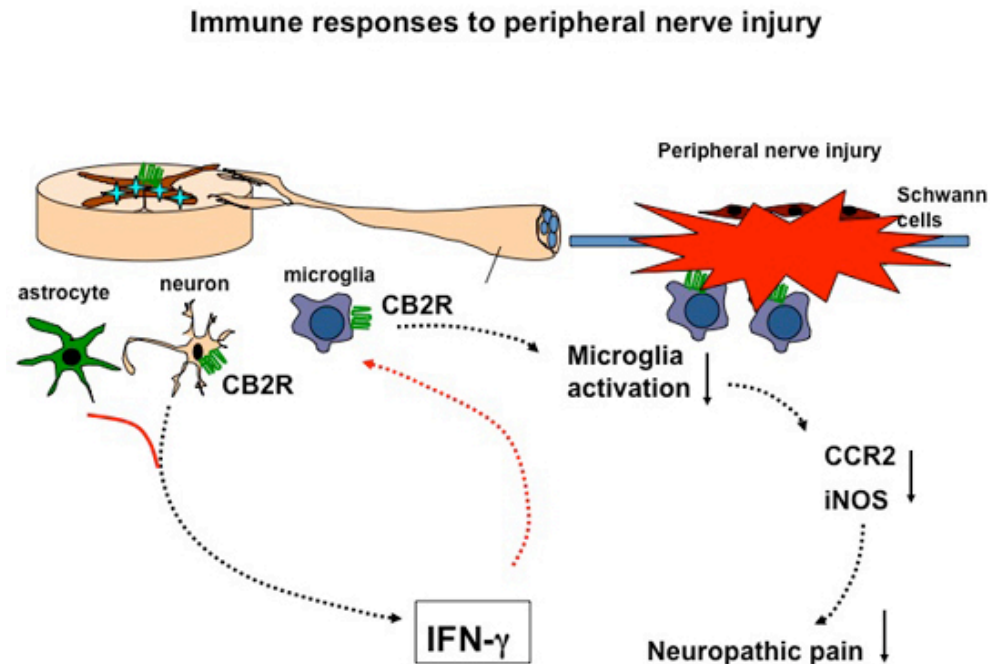
What is neuropathic pain?

- Neuropathic pain is caused by a problem with one or more nerves such that the nerve sends pain messages to the brain in the absence of any stimulus.

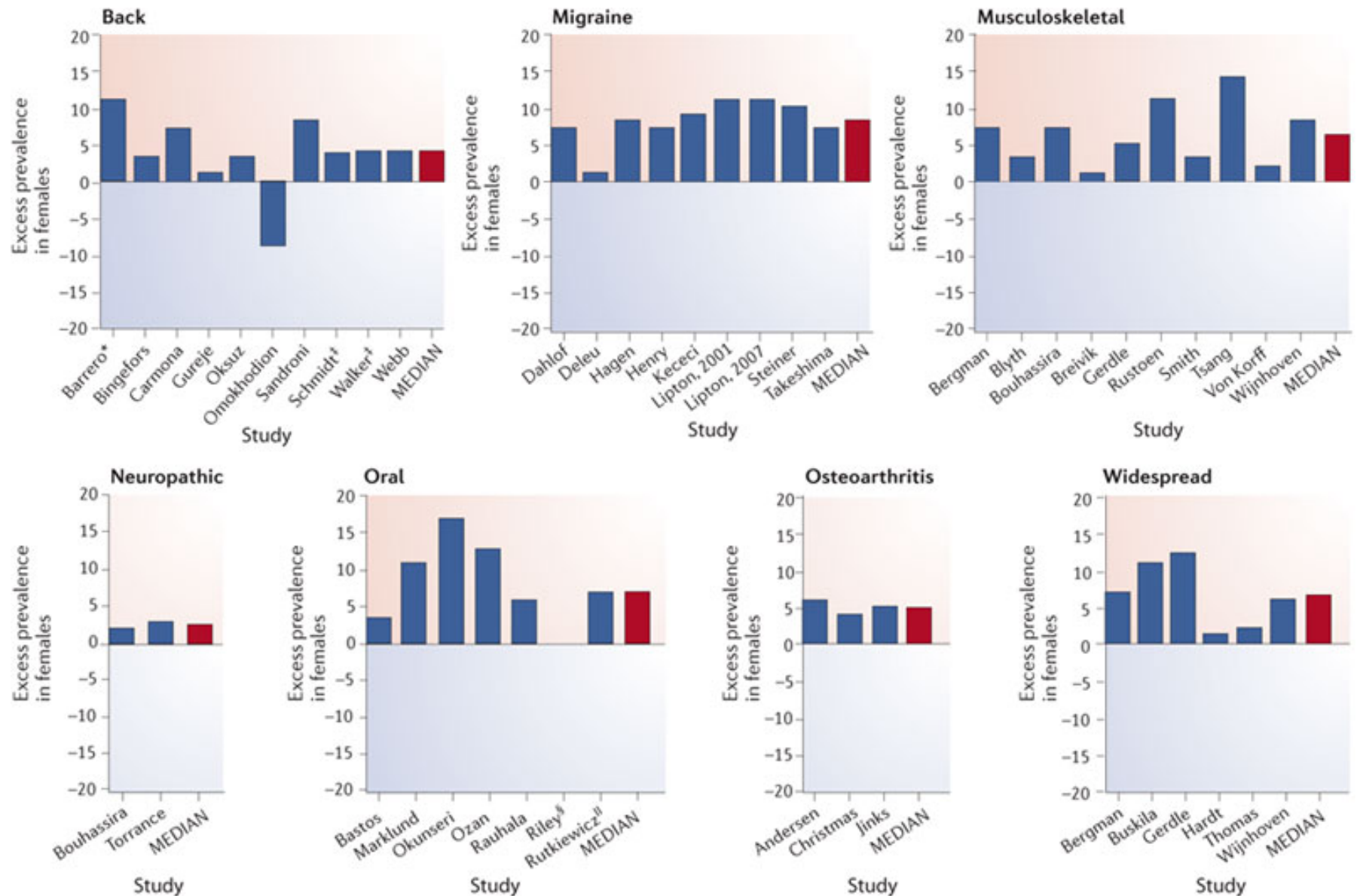


Cannabinoids may be effective for neuropathic pain

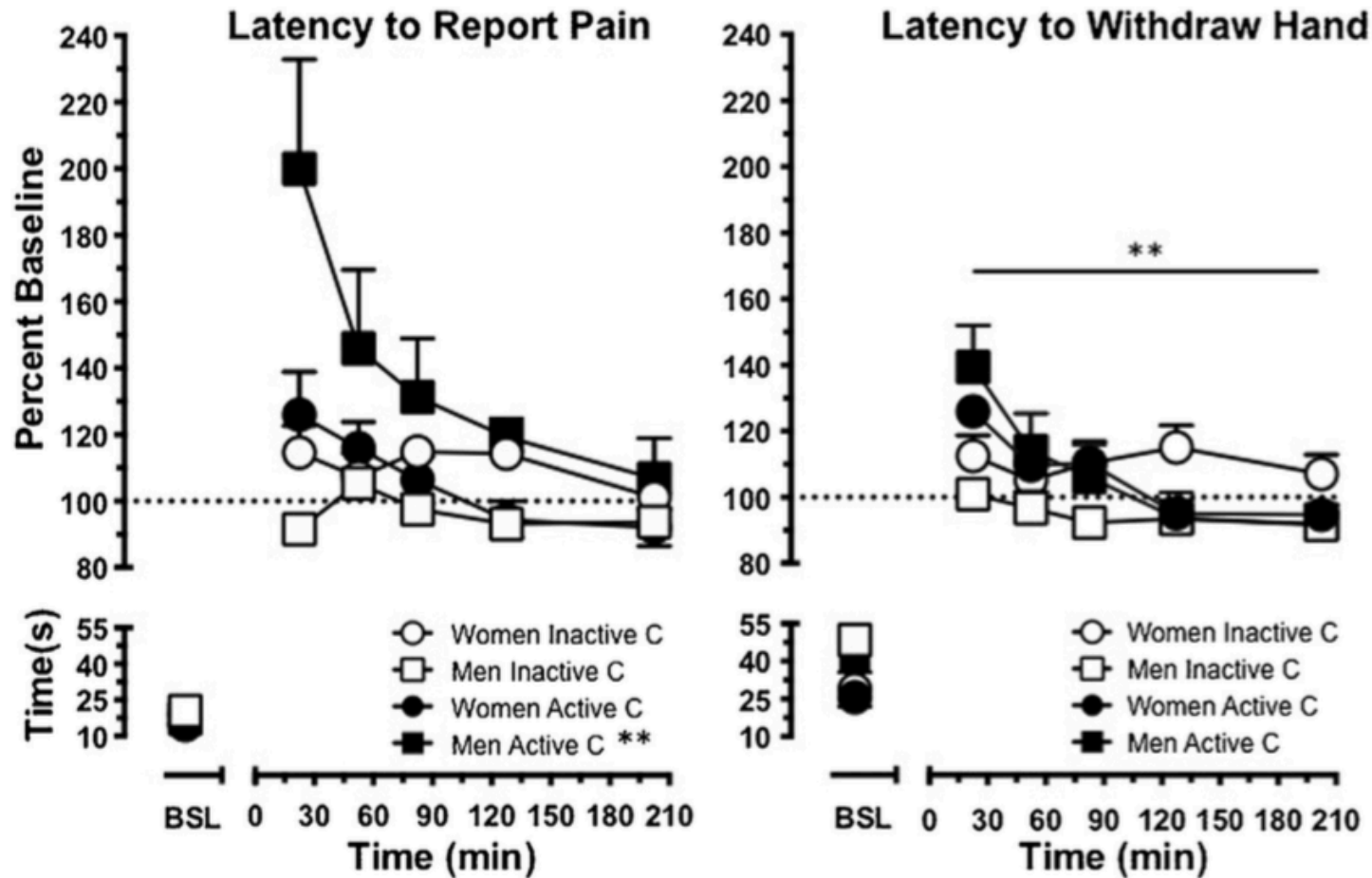
- Opioid analgesics are ineffective due to depletion of opioid receptors in the spinal cord following nerve injury.
- However, there is an upregulation of CB₁ receptors in the thalamus which may increase analgesic efficacy.



Females suffer disproportionately from chronic pain



Males are more sensitive to *Cannabis* analgesia



Advantages of cannabinoids over traditional analgesics

- Minimal side effects (no constipation or respiratory depression)
- Chronic use (1 year min.) is not associated with long-term negative consequences in adults
- No LD₅₀
- *Cannabis* use for pain is not associated with increased vascular, metabolic, blood, renal, musculoskeletal, gastrointestinal, pulmonary, or immune system disorders

Unanswered questions surrounding CB analgesia

- Limit psychoactivity?
- Peripherally-restricted CB agents?
- Cannabinoid x opioid synergy?
- Legal status?
- **Is marijuana a magic bullet for chronic pain patients?**