Treatment of "PAIN" in OUD

- Dr. Joel Bordman
- OUDPC November, 2019

Faculty/Presenter Disclosure

- **Faculty:** *Dr. Bordman*
- **Relationships with commercial interests:**
  - Grants/Research Support: N/A
  - Speaker's Bureau: Invidior, Sea Courses, OCFP, CareToKnow.ca, LEAP
  - Consultant: Invidior, OCFP, CMPA, Knight,

Disclosure of Commercial Support

- **This program has received financial support from the following sponsors in the form of an educational grant:**
- **NA**

<u>Potential for conflict(s) of interest</u>:

  - Indivior produces and distributes a product that will be discussed in this program:
    - Suboxone ® (Buprenorphine/Naloxone)
    - Sublockade ® (monthly sc injection of Buprenorphine)
- Knight produces and distributes a product that will be discussed in this program:
  - Probuphine ® (q6month implant of Buprenorphine)

Mitigating Potential Bias

- Every effort will be made to point out and explain possible bias

OBJECTIVES

- To review the treatment of ACUTE pain in the opioid dependent patient
- To review the treatment of CHRONIC pain in the opioid dependent patient
- To review methadone and buprenorphine in the treatment of pain in the face of OUD
- To review a DDX of chronic Widespread pain

Case AP

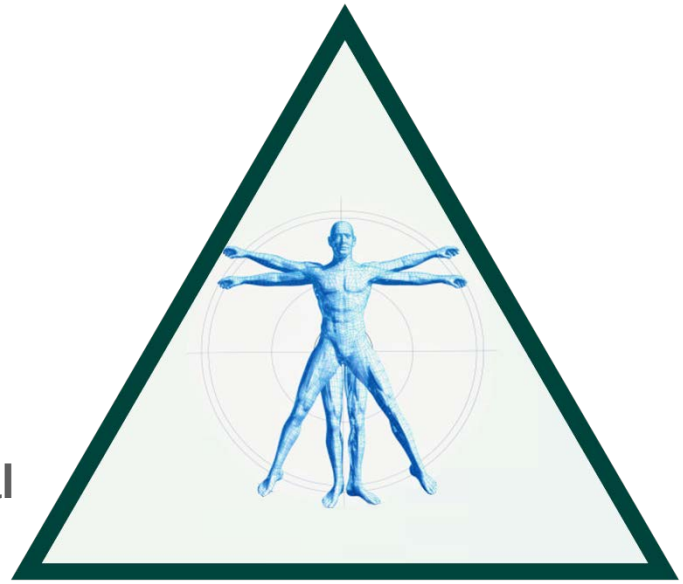
- Born 1968, seen 09/2013
- Referral from teaching hospital pain clinic
- Back pain, unable to work
- Was prescribed LA-Oxycocet, now buying 40mg, 4-6/day.
- Swallow
- Researched: went to addiction clinic, told not a candidate due to ‘pain’

Benzo scenario…..

- “new”azepam licensed as a substitution therapy for benzodiazepine dependence.
- “new”azepam clinics open up across Ontario
- “new”azepam clinics screen patients who have problematic benzodiazepine use or are physically dependent …
- And if they have an underlying anxiety disorder….
- they are turned away

TRIAD OF CHRONIC PAIN TREATMENT

Physical / Rehabilitative



Psychological

Medical

- Pharmacological
- Interventional

Pain in MAT...

- ACUTE pain treatment in MAT
  - Opioid
  - Non-opioid

- CHRONIC pain treatment in MAT
  - Opioid
  - Non opioid

PEARLS for Acute pain - opioid

- An acute pain condition is NOT the time to "*punish*" someone for opioid dependence
- Avoid opioid of past misuse
- Tie in dispensing to MAT dispensing
- Communicate with other HCPs, know the usual natural history of pain condition

Acute pain – Non-opioid

- NSAIDS, COX II Inhibitors
- Acetaminophen

Acetaminophen

- Acute: dose maximum 4g/day (or 3.2g/day or 2.6g/day)
- Hepatic metabolism → hepatotoxicity
  - Alcohol
  - Toxicity with chronic users
  - Fasting/malnutrition
- No indication for treating inflammatory condition

NSAIDS and COXIBs

- RCT Evidence in acute nociceptive, post-op, inflammatory arthritis & dental pain
- Useful for mild-moderate nociceptive pain and inflammatory pain

NSAIDS

- Inflammatory pain, opioid sparing
- Adverse effects
  - GI (4-16%)
  - CV (thrombosis, MI, CVA)
  - Renal
- Caution
  - Bleeding risk
  - Renal impairment
  - Long term use
  - Drug interactions (caution with ASA for CV risks)

Pain in MAT...

- ACUTE pain treatment in MAT
  - Opioid
  - Non-opioid

- CHRONIC pain treatment in MAT
  - Opioid
  - Non opioid

Brief Pain Inventory - BPI

Pain Assessment Tool

Brief Pain Inventory (Short Form) - Modified

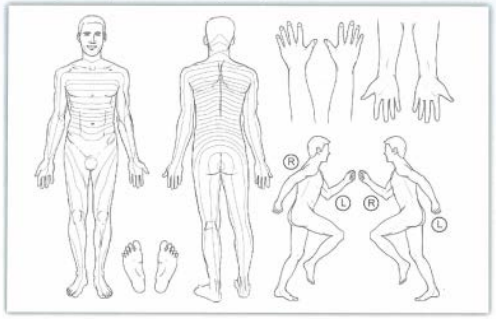
Date:____ /____ /____

Name:_____ , _____
Last First

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

☐ Yes ☐ No

On the diagram below, shade in the areas where you feel pain. Put an "X" on the areas where it hurts the most.



What things make your pain feel worse?

What things make your pain feel better?

What treatments or medications are you receiving for your pain?

Date:____ /____ /____

Name:_____ , _____
Last First

Please rate your pain by circling the one number that best describes your pain at its WORST in the past week.

No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

Please rate your pain by circling the one number that best describes your pain at its LEAST in the past week.

No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

Please rate your pain by circling the one number that best describes your pain on the AVERAGE.

No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

Please rate your pain by circling the one number that tells how much pain you have RIGHT NOW.

No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

In the last week, how much relief have your pain treatments or medications provided? Please circle the one percentage that shows how much RELIEF you have received.

No relief 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% Complete relief

Circle the one number that describes how, during the past week, pain has interfered with your:

A. General activity

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

B. Mood

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

C. Walking ability

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

D. Normal work (includes both work outside the home and housework)

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

E. Relations with other people

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

F. Sleep

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

G. Enjoyment of life

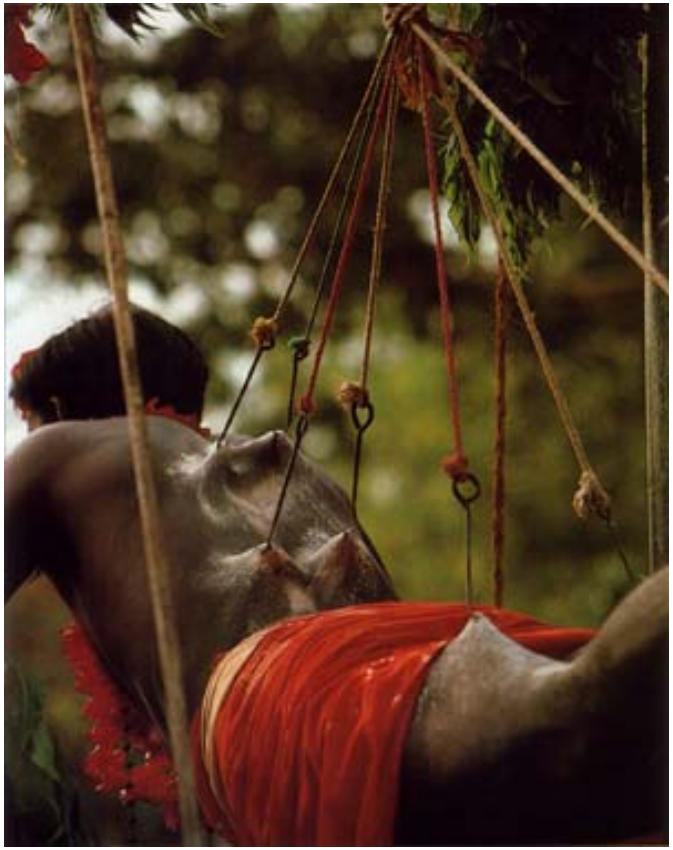
Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

Interference Scale total score: / 70

Adapted from Cleeland and Ryan.

An assessment tool for pain adds one component to subjective and objective parameters for the evaluation of a patient. Among available assessment tools, preferences vary across clinicians. As such, the Brief Pain Inventory Tool may or may not be better than any other assessment tool.

Reference: 1. Cleeland CS and Ryan KM. Pain Assessment: Global Use of the Brief Pain Inventory. Ann Acad Med. 1994;23(2):129-38.



What are we really treating?

Chronic Pain
vs.
Suffering

2 possible reasons for scars:

- Tribal leader successfully meditates through annual ritual customs
- Man tortured while rebel forces take over village

WORD ORIGINS

- MORPHINE
  - Latin Morpheus, from Greek god of sleep

- NARCOTIC
  - from Greek *narko*, for 'numbness'

2 sentences to patients…

- You have chronic pain and I'm going to prescribe you pain killers
- You have ***chronic suffering*** and ….
  - I'm going to prescribe you a pill that will...
  - *Temporarily dissociate* you from your suffering...
  - And you will eventually develope tolerance ....
  - And you will get less and less benefit from these pills and you will require higher and higher doses....

- Lets look at some key points in the 2017 Pain Guidelines

Recommendation 3&4

- **For patients with chronic non-cancer pain with an active substance use disorder**
- We recommend against the use of opioids
- *Clinicians should facilitate treatment of the underlying substance use disorders, if not yet addressed.*

- **For patients with chronic non-cancer pain with an active psychiatric disorder whose non-opioid therapy has been optimized, and who have persistent problematic pain**
- We suggest stabilizing the the psychiatric disorder before a trial of opioids is considered

- A clever person solves a problem
- A wise person avoids it.

- Albert Einstein

Recommendation 9: Weak

- **For patients with chronic non-cancer pain who are currently using 90mg morphine equivalents of opioids per day or more**
- We suggest tapering opioids to the lowest effective dose, potentially including discontinuation, rather than making no change in opioid therapy.
- *Some patients are likely to experience significant increase in pain or decrease in function that persists for more than one month after a small dose reduction; tapering may be paused and potentially abandoned in such patients.*

What to do with the “legacy” patient?

- Provide updated informed consent
  - Complications : sleep apnea, hypogonadism, falls, early dementia with benzo’s, etc
- Review pain diagnosis
- Review risk factors
- Have a family member come in (?)
- A Naloxone kit (?)

PEARLS: Chronic pain – opioid therapy in MAT

- As a general rule adding another long term opioid should be avoided (especially the past opioid of choice)
- MAT as a split dose considered
- Very important to have well thought out goals and an exit strategy
- Can switch to “pain treatment paradigm” if your diagnosis was incorrect (document this!)

Methadone – mechanisms of action

- ***μ and delta opioid receptor agonist***
  - Analgesia and typical opioid SE profile; may have more diaphoresis and flushing
- ***NMDA receptor antagonist***
  - May help to prevent or reverse opioid tolerance and hyperalgesia
  - Theoretical advantage for neuropathic pain
- ***Inhibits re-uptake of norepinephrine & serotonin***
  - Evolving evidence for this mechanism-based analgesia via descending modulation in neuropathic pain

Lynch ME. Pain Res Manag 2005; 10(3):133-44.
Davis MP.Support Cancer Care 2001; 9;773-83.
Fishman SM.Pain Med 2002; 3:339-48.

Methadone Toxicity

- "Methadone was disproportionately involved in a third of opioid-related deaths nationwide during the 2000s, although representing less than 5% of total opioid prescriptions."
  - Webster, 2011 pain topics.org
- CDC March 31, 2017/ 66(12); 320-323:
- "Methadone accounted for approx. 1% of all opioids prescribed for pain but accounted for approx. 23% of a prescription opioid deaths in 2014".

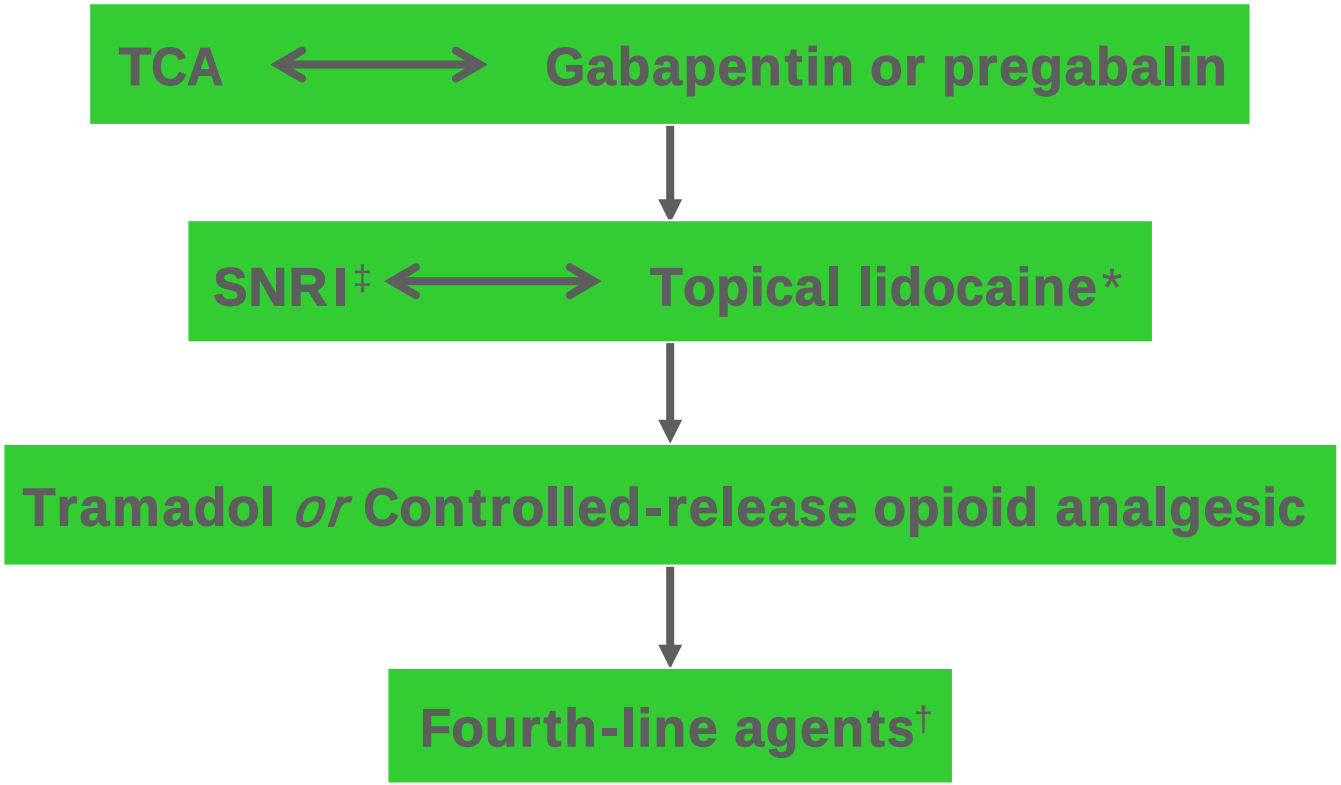
Pain treatment 2019

- *Primum non nocere*
- *First, do no harm*

Non- Opioid Chronic Pain "Tool Box"

- Non opioids
  - Acetaminophen
  - NSAIDS
  - COX-2 Inhibitors
- Adjuncts
  - Antidepressants
  - Anti epileptics
  - Topical agents

Pharmacological Management of Chronic Neuropathic Pain: 2007 Canadian Pain Society Guidelines



Add additional agents sequentially if partial but inadequate pain relief

TCA: Tricylic antidepressant; SNRI: Serotonin-norepinephrine reuptake inhibitor
*5% gel or cream; useful for focal neuropathy such as postherpetic neuralgia.
†Lamotrigine, methadone, clonazepam, topiramate, valproic acid. ‡Do not add SNRIs to TCAs.

Moulin DE, et al. *Pain Res Manage*. 2007;12(#):###-###.

Tricyclic Antidepressants (TCAs)

- Mechanism:
  - Reduction in action potential firing of sodium channel activity
  - Inhibition of reuptake of norepinephrine and serotonin
- Common adverse events
  - Dry mouth, constipation, daytime drowsiness, urinary retention, orthostatic hypotension, arrythmias, weight gain
- Caution:
  - CVD
  - Urinary retention
  - Glaucoma
  - Risk of OD

Gabapentin

- Blocks a2d receptor of N-Type Ca channels
- Neuropathic pain, migraine, mood stabilizer,,
- Synergistic effect with opioids (Gilron, 2005)
- 100mg hs test dose then titrate by 300mg q3 days up to 3600mg+ (tid dosing)
- Adjust dosing in renal insufficiency

Gabapentin and Opioids

- Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case–control study

- In this study we found that among patients receiving prescription opioids, concomitant treatment with gabapentin was associated with a substantial increase in the risk of opioid-related death (49%).

- PLoS Med. 2017 Oct; 14(10): e1002396. Published online 2017 Oct 3. doi: 10.1371/journal.pmed.1002396 PMCID: PMC5626029 PMID: 28972983. Gomes, Tara, et al

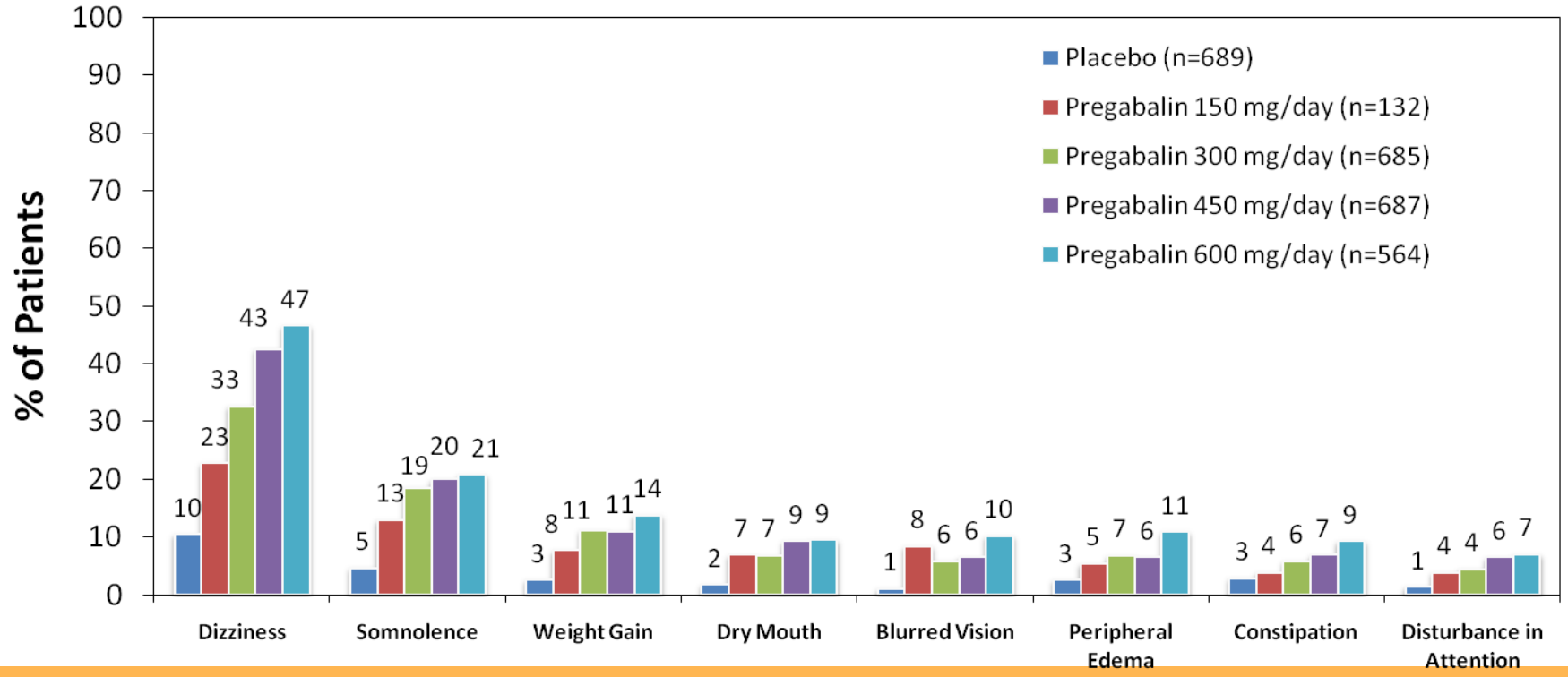
Pregabalin

- Action same as GPN
- Officially indicated for neuropathic pain (PHN, DN, Central NeP), fibromyalgia
- Linear absorption kinetics – BID dosing
- Side effects similar to GPN
- Start 25-75mg qhs then bid x7; 150mg bid x7→ 300 bid x 7
- Effects seen within 1 week of adequate dosing
- Adjust dosing in renal insufficiency

Pregabalin Treatment-Emergent Adverse Events

Fibromyalgia Placebo-controlled Studies[1]

Most common events which occurred in ≥ 5% of pregabalin patients and statistically significantly more frequent and greater than placebo.



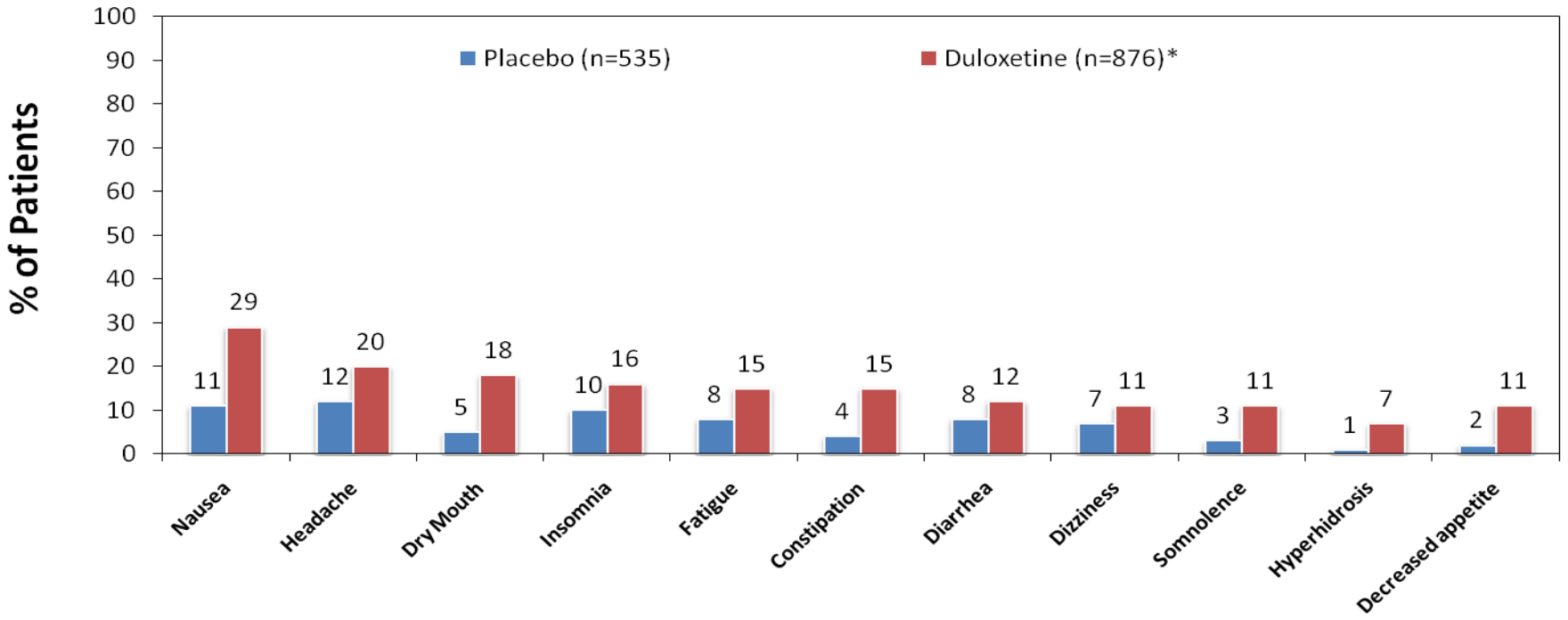
1. Lyrica Product Monograph. Pfizer Canada ULC. Last revised: June 21, 2010.

Duloxetine

- Independent analgesic effect (significant pain relief) has been demonstrated within the first week
- Starting dose: 60 mg/day[3]
- (A starting dose of 30 mg may be considered for tolerability reasons, with a target dose of 60 mg/day within 1-2 weeks[1])
- Usual maintenance dose: 60-120 mg/day (maximum 120 mg/day)[2,3]

Duloxetine Treatment-Emergent Adverse Events Fibromyalgia Placebo-controlled Studies[1]

Most common events which occurred in ≥ 5% of duloxetine patients and statistically significantly more frequent than placebo.



* Pooled data from all patients receiving duloxetine 60 mg/day, 120 mg/day and 60 mg/twice per day in randomized placebo – controlled clinical trials

1. Cymbalta Product Monograph. Eli Lilly Canada Inc. Last revised: October 6, 2010.

Cannabinoids

Legalization and Opioid Overdose Mortality

- Three states (California, Oregon, and Washington) had medical cannabis laws effective prior to 1999. Ten states (Alaska, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Mexico, Rhode Island, and Vermont) enacted medical cannabis laws between 1999 and 2010
- States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate (95%CI, −37.5%to −9.5%; *P* = .003) compared with states without medical cannabis laws
- The lower rate of overdose mortality strengthened over time
  - ✓ Year 1 (−19.9%; 95%CI −30.6%to −7.7%; *P* = .002)
  - ✓ Year 6 (−33.3%; 95%C, −44.7%to −19.6%; *P* < .001)

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010, Marcus A. et al. JAMA Intern Med. 2014;174(10):1668-1673, Aug 25, 2014

June 10, 2019

- Association between medical cannabis laws and opioid overdose mortality has reversed over time.
- From -21% to +23%

- Chelsea L. Shover, PNAS 1903434116


SAY NO
TO POT

Pharmaceutical Cannabinoids

- Nabilone (Cesamet)
  - 0.5, 1.0mg BID
  - cancer chemo nausea and vomiting

- THC / CBD spray (Sativex)
  - MS neuropathic pain
  - severe cancer pain on opioids

Topicals

- Lidocaine (USA)
- Capsaicin cream
- Diclofenac diethylamine gel 1.16%

Vitamin D for Chronic MSK pain

- "According to a comprehensive review of the clinical research evidence, helping certain patients overcome chronic musculoskeletal pain and fatigue syndromes may be as simple, well tolerated, and inexpensive as a daily supplement of vitamin D."

Leavitt, 2008. Pain topics.org

Chronic Widespread Pain - DDx

- Endocrine conditions
  - Hypothyroidism, Hyperparathyroidism
- Inflammatory conditions
  - Early stages of inflammatory arthritis (when joint swelling is minimal)
  - Polymyalgia rheumatica (older patients)
  - SLE, Seronegative spondyloarthropathies

Hwang E, Barkhuizen A. Update on rheumatologic mimics of fibromyalgia. Curr Pain Headache Rep. 2006 Oct;10(5):327-32. Review.

Chronic Widespread Pain - DDx

- Neurological conditions
  - Multiple sclerosis , Peripheral neuropathy
- Drug-related causes
  - Statin induced body pain
  - Aromatase inhibitor body pain
  - Chemotherapy-related neuropathy

Chronic Widespread Pain - Labwork

- CBC, ESR, Uric Acid
- CRP, ANA, RF
- TSH
- Serum Calcium and phosphate
- CK
- B_{12}

Buprenorphine in Chronic pain

- Sublingual burprenorphine is effective in the treatment of chronic pain syndrome. Herbert L. Malinoff, et al. American Journal of Therapeutics 12, 379-384 (2005)

- Conversion from High-DoseFull Opioid Agonists to Sublingual Buprenorphine reduces Pain Scores and Improves QoL for Chronic Pain Patients. Daitch, et al, Pain Medicine 2014

- Buprenorphine – an attractive opioid with underutilized potential in treatment of chronic pain. Khanna, J of Pain Research 2015:8 859-870

Options with acute pain and Bup/Nx

- Increase Bup/Nx dose (split?)
- Decrease Bup/Nx dose and add a ‘conventional’ opioid
- Same Bup/Nx dose and add a ‘conventional’ opioid or adjunct

- Despite some literature, it is preferable to not discontinue Bup/Nx
- Communicate with the other health care providers

OBJECTIVES

- To review the treatment of ACUTE pain in the opioid dependent patient
- To review the treatment of CHRONIC pain in the opioid dependent patient
- To review methadone and buprenorphine in the treatment of pain in the face of OUD
- To review a DDX of chronic Widespread pain

- The good physician treats the disease;
- the great physician treats the patient who has the disease.

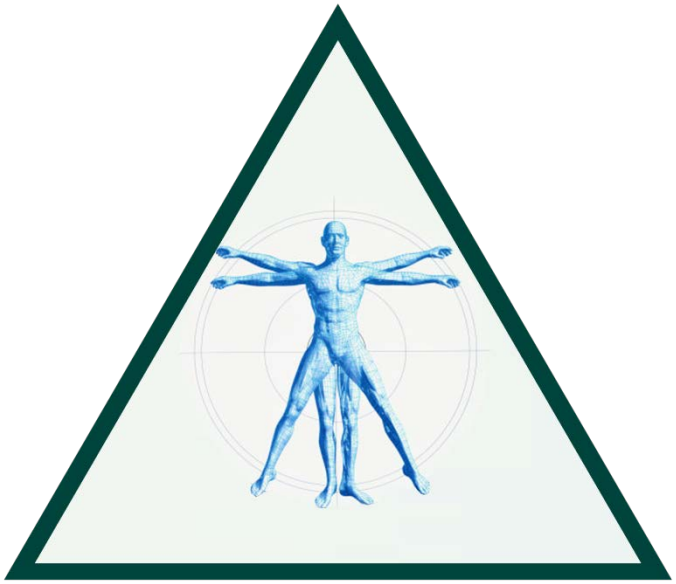
Sir William Osler

- Be kind, for everyone you meet is fighting a harder battle.

Plato

TRIAD OF CHRONIC PAIN TREATMENT

Physical / Rehabilitative



Psychological

Medical

- Pharmacological
- Interventional

Thank you!