Opioid Prescribing: Current Considerations

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Faculty/Presenter Disclosure

- **Faculty: Launette Rieb**
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- Specifically, no pharmaceutical, medical device or communications company: **No bias**

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Learning Objectives

- Review the new evidence on risks associated with opioids for chronic non-cancer pain
- Consider pain induced by opioids
- List ways to mitigate the risk of overdose, addiction/diversion, sleep apnea
- Reflect on your practice and who may benefit from changes in opioid dose, monitoring, or dispensing

Opioids … for chronic low-back pain, Cochrane Review (Chaparro 2013)

- 15 trials which included 5540 participants
- More pain relief and fxn in short term
- No information from RCTs supporting the efficacy and safety of opioids used for more than four months
- The **current literature does not support that opioids are more effective than other groups of analgesics** for LBP such as anti-inflammatories or antidepressants

Analgesic Efficacy of Opioids

- Systematic review and meta-analysis
- Some evidence for opioid use acutely and under 6 mo, lack of studies on benefits > 1 yr
- Many studies show long term harms of LOT vs non opioid tx for CNCP:
  - Increased risk of overdose, substance abuse and dependence, fractures, myocardial infarction, and use of medication to treat erectile dysfunction.
- "Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports dose dependent risk for serious harms"

Chou R. Ann Intern Med. 2015;162(4):276-86

US CDC 2016 – Summary

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later
- Extensive evidence shows the possible harms of opioids
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm

CDC Guidelines for Prescribing Opioids for Chronic Pain (Dowell 2016)

- Establish tx goals and function
- Non-opioid therapies preferred
- Only use when benefit outweighs risk
- Lowest effective dose <50 MEDD<<90 mg
- Avoid concurrent benzodiazepines
- Re-evaluate every 3 months
- If an OUD develops – offer methadone or buprenorphine
- Used for many CPSBC standards/guidelines

Analgesic Efficacy of Opioids

(Ballantyne, 2006)

- Only 1 out of every 4 patients get some pain relief with opioids initially, the others should be taken off right away, not left on with other medications added
- Average just **20-30% analgesia**
- Fantasy that endless dose escalations will provide further reductions in pain, instead may produce opioid induced hyperalgesia (see appendix)

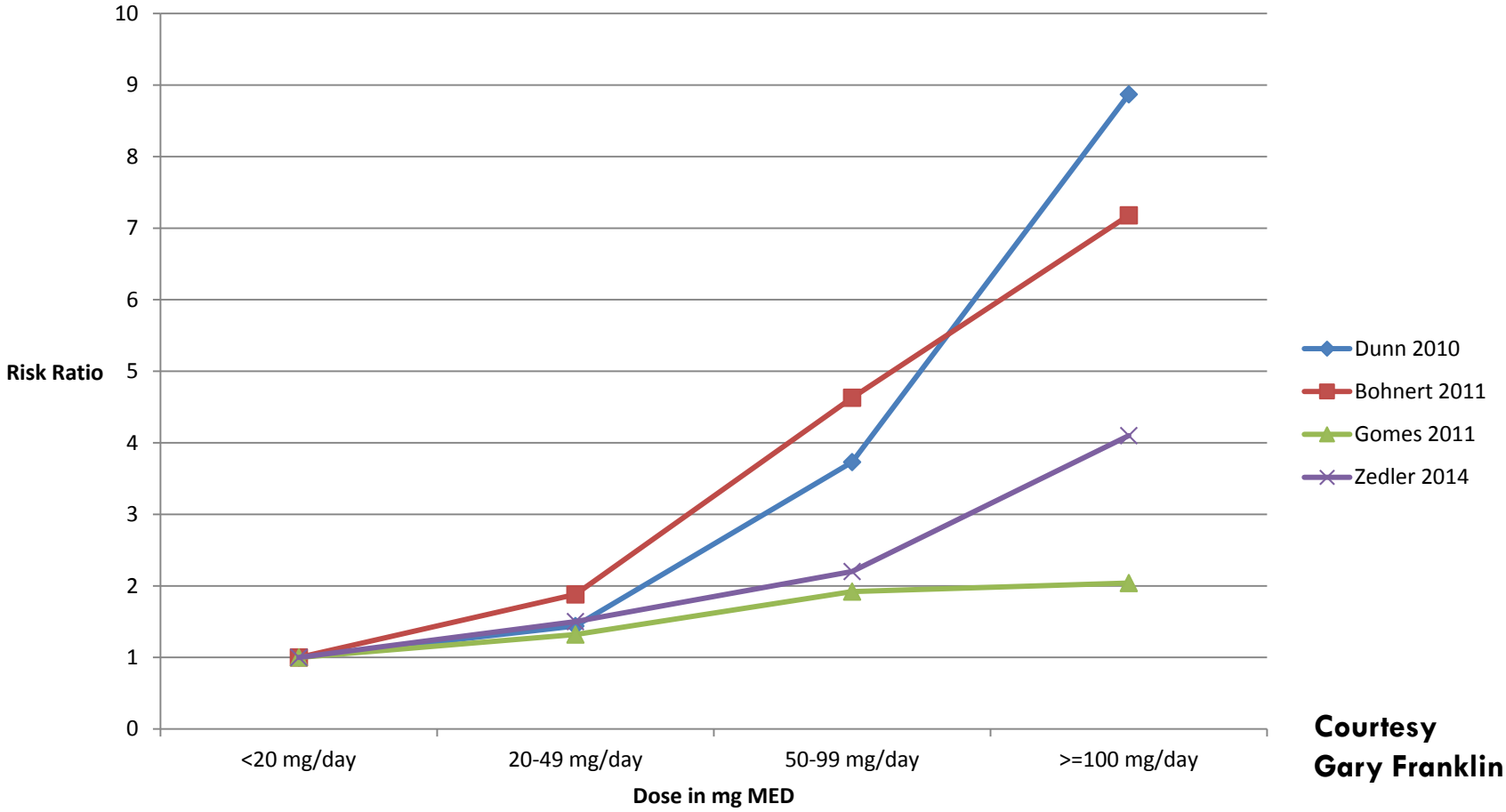
Opioid Harms

- Overdose
- Addiction
- Diversion
- Testosterone suppression
- Depression
- Sleep Apnea
- Cardiac events
- Motor vehicle accidents
- Increasing pain

Factors Associated with OD

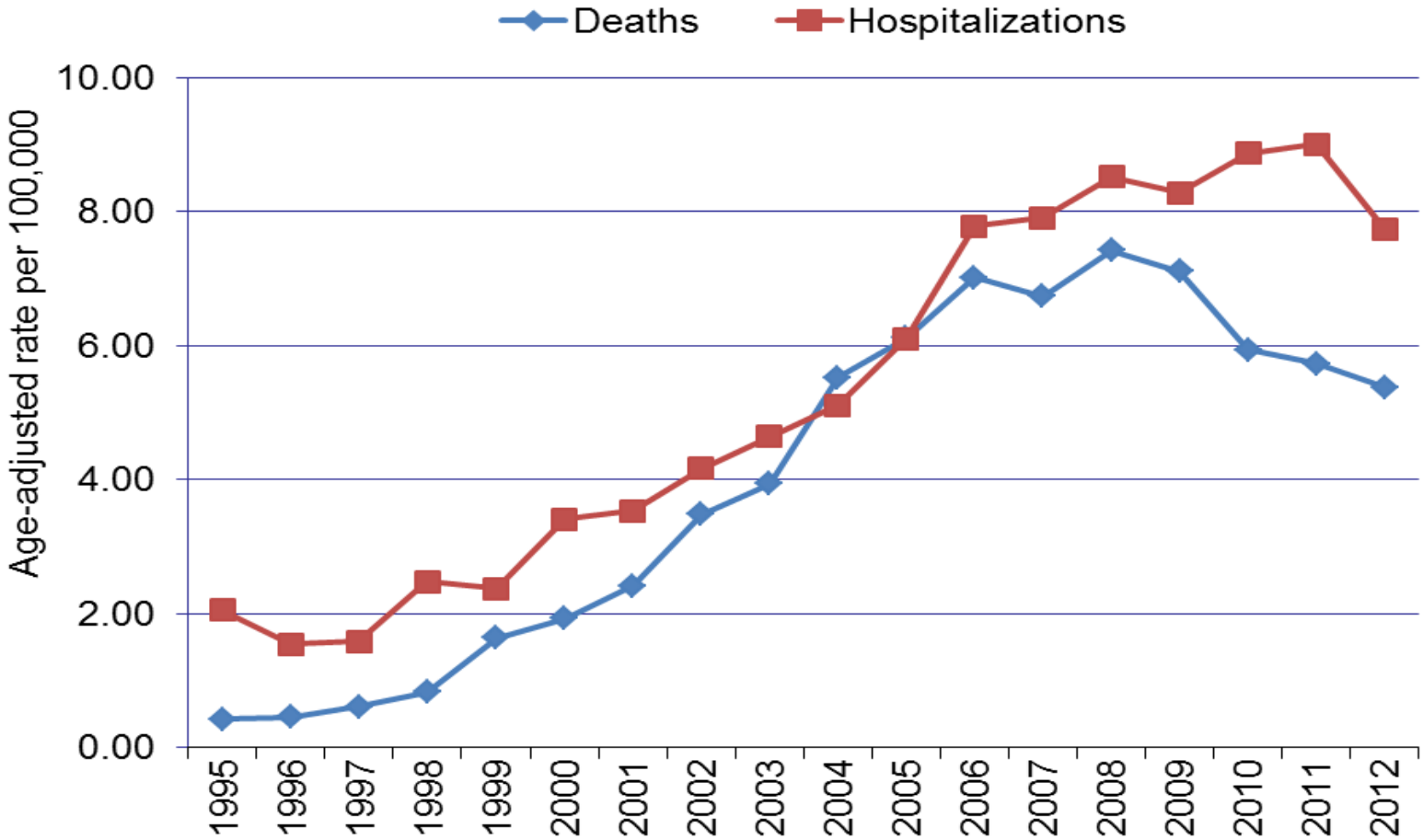
- Aberrant behaviors
- Recent initiation of opioids
- Methadone
- Concomitant use of benzodiazepines
- Obtaining opioid prescriptions from multiple providers
- Substance abuse and other psychological comorbidities
- **Higher dose**

Dose-related risk of opioid overdose

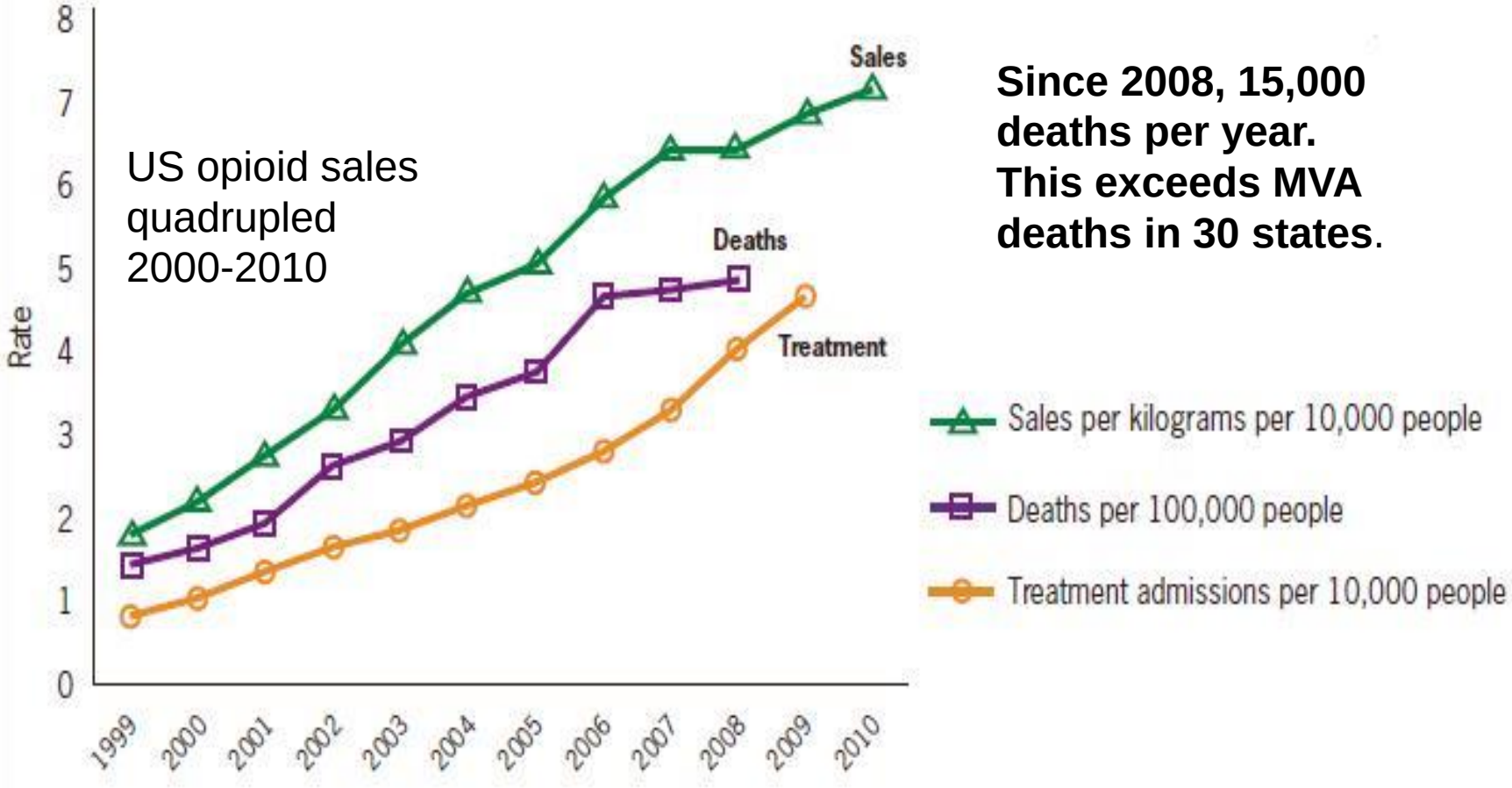


Courtesy Gary Franklin

Prescription Opioid Involved Overdoses Washington State



Rates of prescription painkiller sales, deaths and substance abuse treatment admissions (1999-2010)



US opioid sales quadrupled 2000-2010

Since 2008, 15,000 deaths per year. This exceeds MVA deaths in 30 states.

SOURCES: National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009

Slide courtesy Mark Sullivan

Dose Dependent Risk of Developing Opioid Addiction

- Long-term prescribed opioid use (>90 d) associated with a dose dependent increased risk of an opioid abuse or dependence
  - Low dose (1-36 mg MEDD): OR 15
  - Moderate dose (36-120 mg MEDD): OR 29
  - High dose (≥120 mg MEDD): **OR 122**

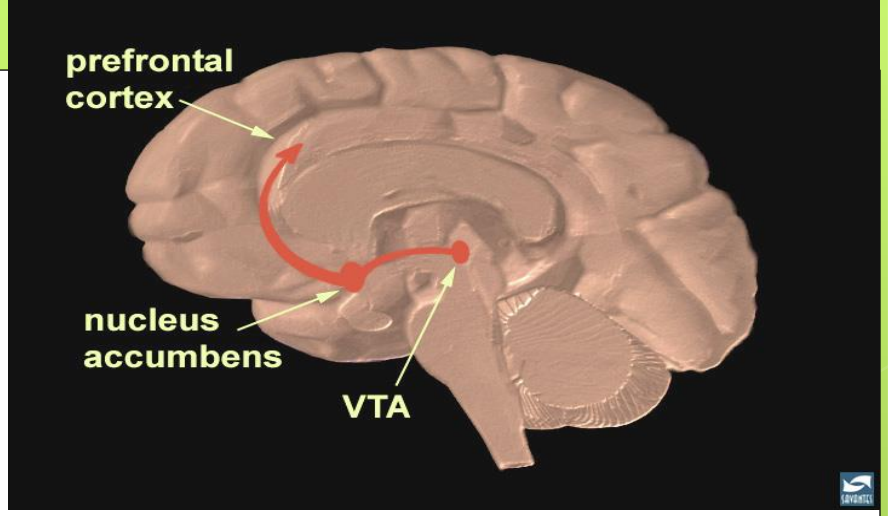
(Edlund 2014)

Prescription Opioid Misuse and Addiction

- Estimates vary from 4% to 26%, or higher
  - One study (n=801) of pts with CNCP based on standardized interviews[a]
    - 26% purposeful oversedation
    - 39% increased dose without prescription
    - 8% obtained extra opioids from other doctors
    - 18% used for purposes other than pain
    - 12% hoarded pain medications

(Fleming, J Pain 2007)

Remember



- All mood altering substances (prescribed or illicit) can reduce pain while intoxicated
- All substances (including pain medications) that cause dopamine release in the misolimbic system can be overvalued – even in the absence of true addiction – hence the emotional attachment around discussing opioids, cannabinoids, benzodiazepines and stimulants with patients

Risk of SUD

- Those at highest risk:
  - Active SUD
  - Past Hx of SUD
  - Family Hx of SUD
  - Active psychiatric illness
  - Childhood trauma, esp. sexual abuse in women
  - Youth

  Exposure:
  - Dose dependent rise in risk of SUD

Risk Assessment for SUD if Prescribed Opioid Medications

Opioid Risk Tool

By Lynn R. Webster MD

Item (circle all that apply)	Item score if female	Item score if male
1. Family History of Substance Abuse:		
Alcohol	1	3
Illegal Drugs	2	3
Prescription Drugs	4	4
2. Personal History of Substance Abuse:		
Alcohol	3	3
Illegal Drugs	4	4
Prescription Drugs	5	5
3. Age (mark box if 16-45)	1	1
4. History of Preadolescent Sexual Abuse	3	0
5. Psychological Disease Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar, Schizophrenia	2	2
Depression	1	1
Total		
Total Score Risk Category: Low Risk: 0 to 3, Moderate Risk: 4 to 7, High Risk: 8 and above		

(Furlan 2010)

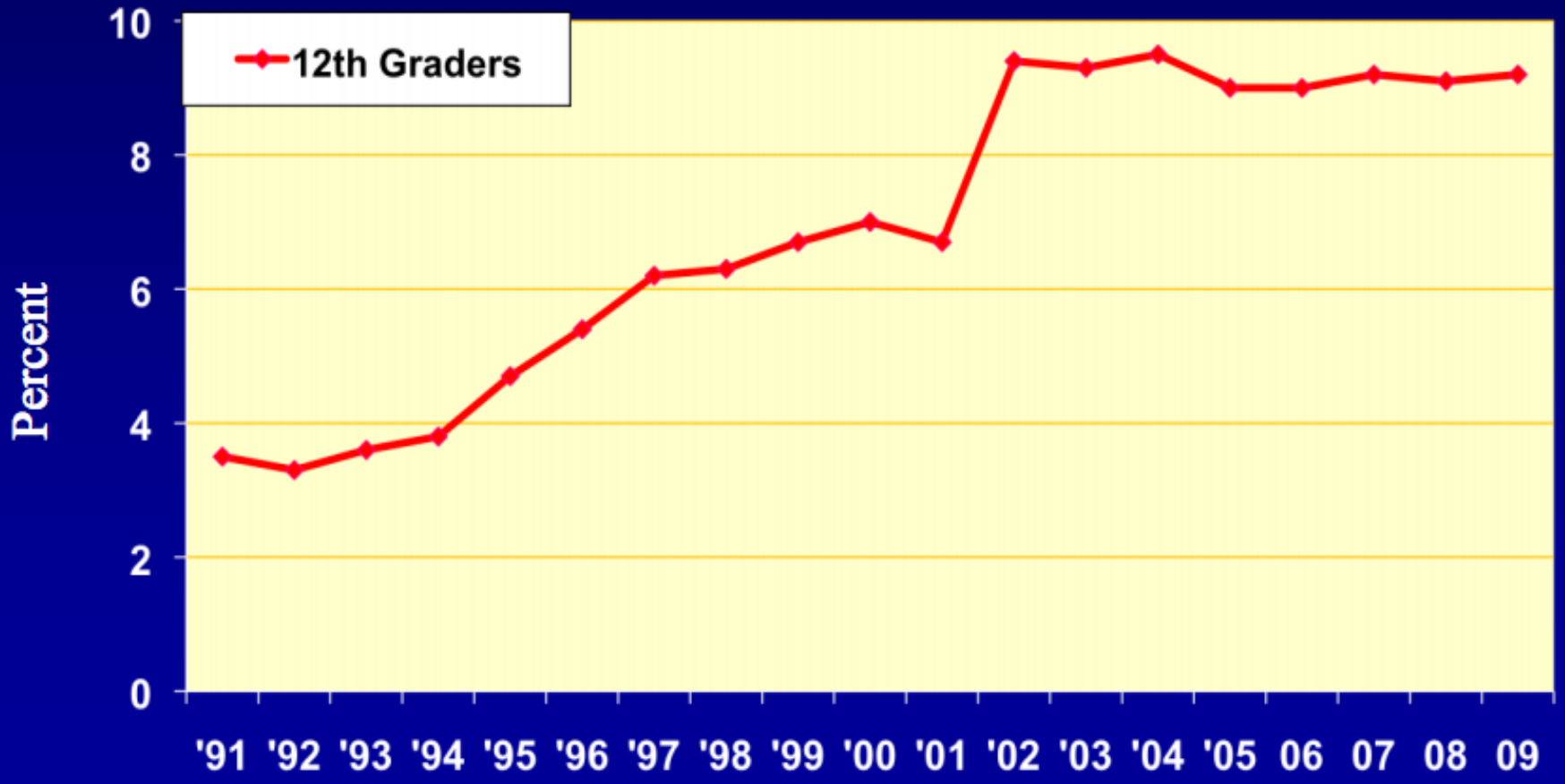
Opioid Tx Agreement & UDS

(Starrels, 2010)

- Systematic review
- Misuse was reduced between 7 and 23% (addiction, diversion, aberrant drug related behaviors)
- Supports the effectiveness of treatment agreements and UDS to reduce substance misuse

Non-Medical Prescription Opioid Use

MTF: Annual Use Prevalence 12th Graders



http://www.monitoringthefuture.org/pubs/monographs/overview2009.pdf

Testosterone Suppression

- Opioids can suppress testosterone levels
- Males only
- Dose dependent
- Opioid lowering or elimination may remedy
- Testosterone replacement available
- Consider screening all men on opioids

Bawor M. Drug Alcohol Depend. 2015 Apr 1;149:1-9

Also Consider…

- Sleep apnea risk – do overnight oximetry
- Cardiac risk – do ECG in those at risk?
- MVAs – advise not to drive during initiation or dose increase, and anytime if sedated
- Depression/anxiety/PTSD – screen at intake and at visits

Opioid Use Can Cause Pain

Opioids Causing Pain

Opium use causes "*internal rheumatism*"

(Quincey TD, 1821)

"Morphine "*tends to encourage the very pain it pretends to relieve*"

(Albutt, 1870)

PAIN

Pain 100 (2002) 213–217

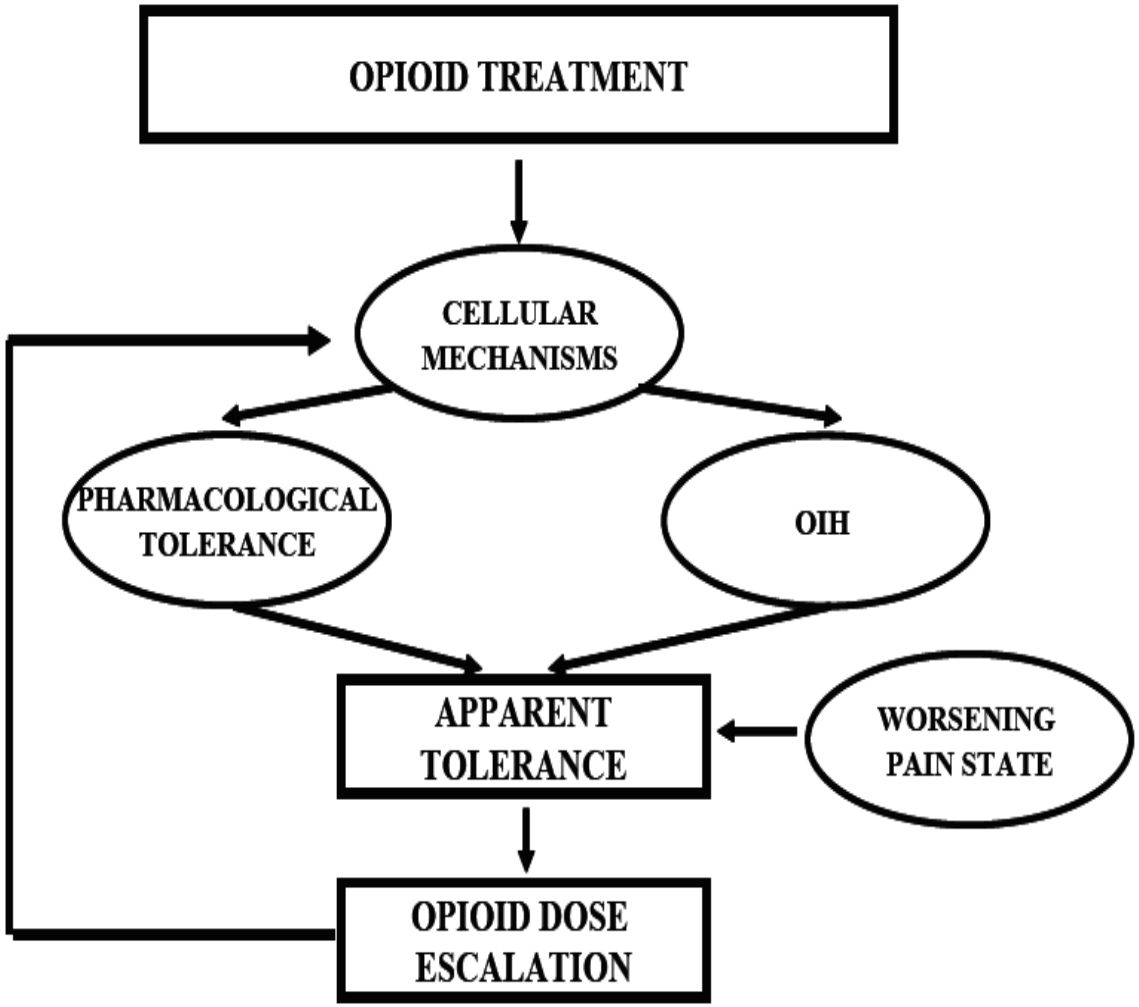
www.elsevier.com/locate/pain

Topical review

Opioid-induced abnormal pain sensitivity: implications in clinical opioid therapy

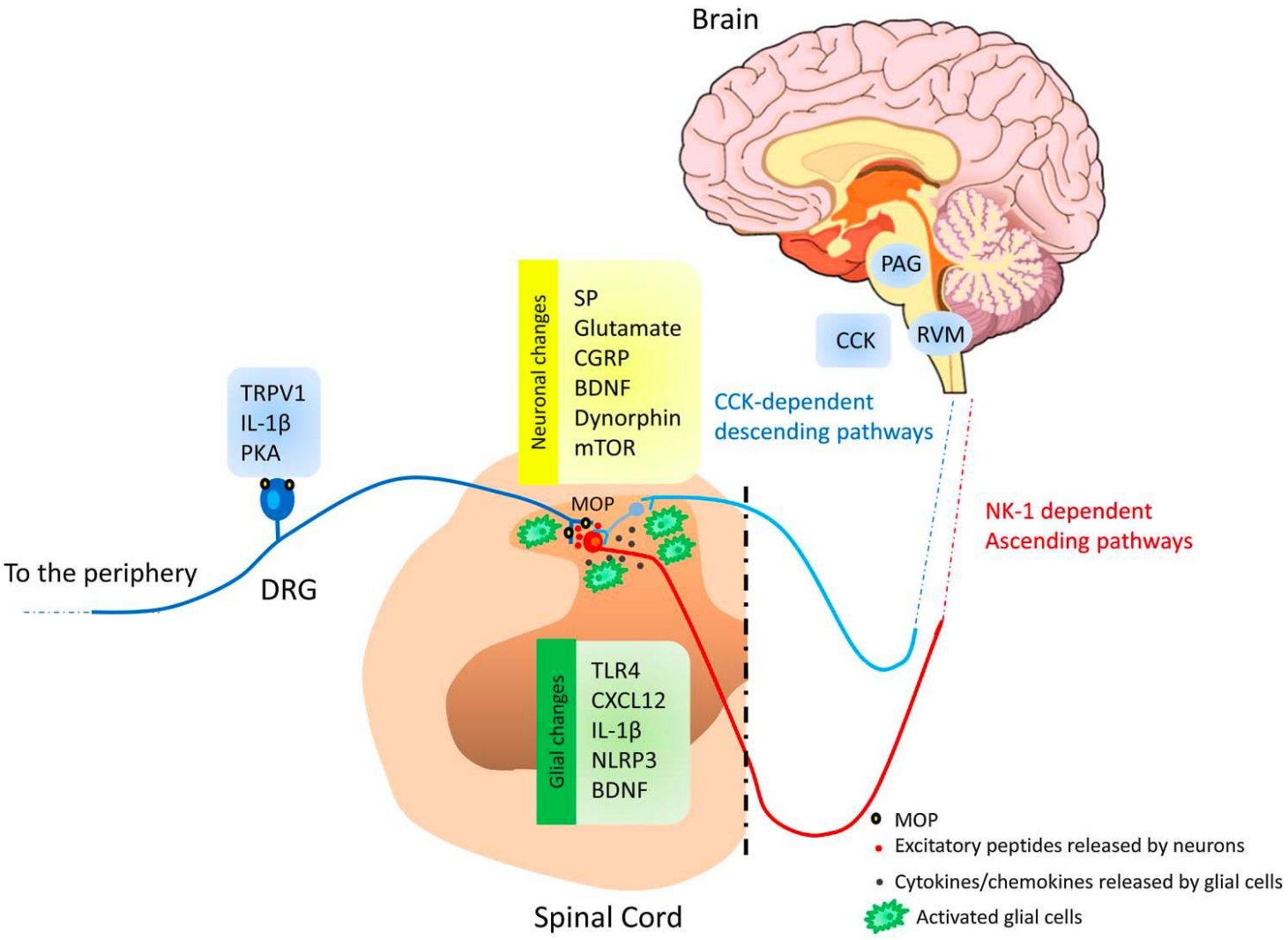
Jianren Mao*

MGH Pain Center, Department of Anesthesia and Critical Care, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA


OPIOID TREATMENT
CELLULAR MECHANISMS
PHARMACOLOGICAL TOLERANCE
OIH
APPARENT TOLERANCE
WORSENING PAIN STATE
OPIOID DOSE ESCALATION

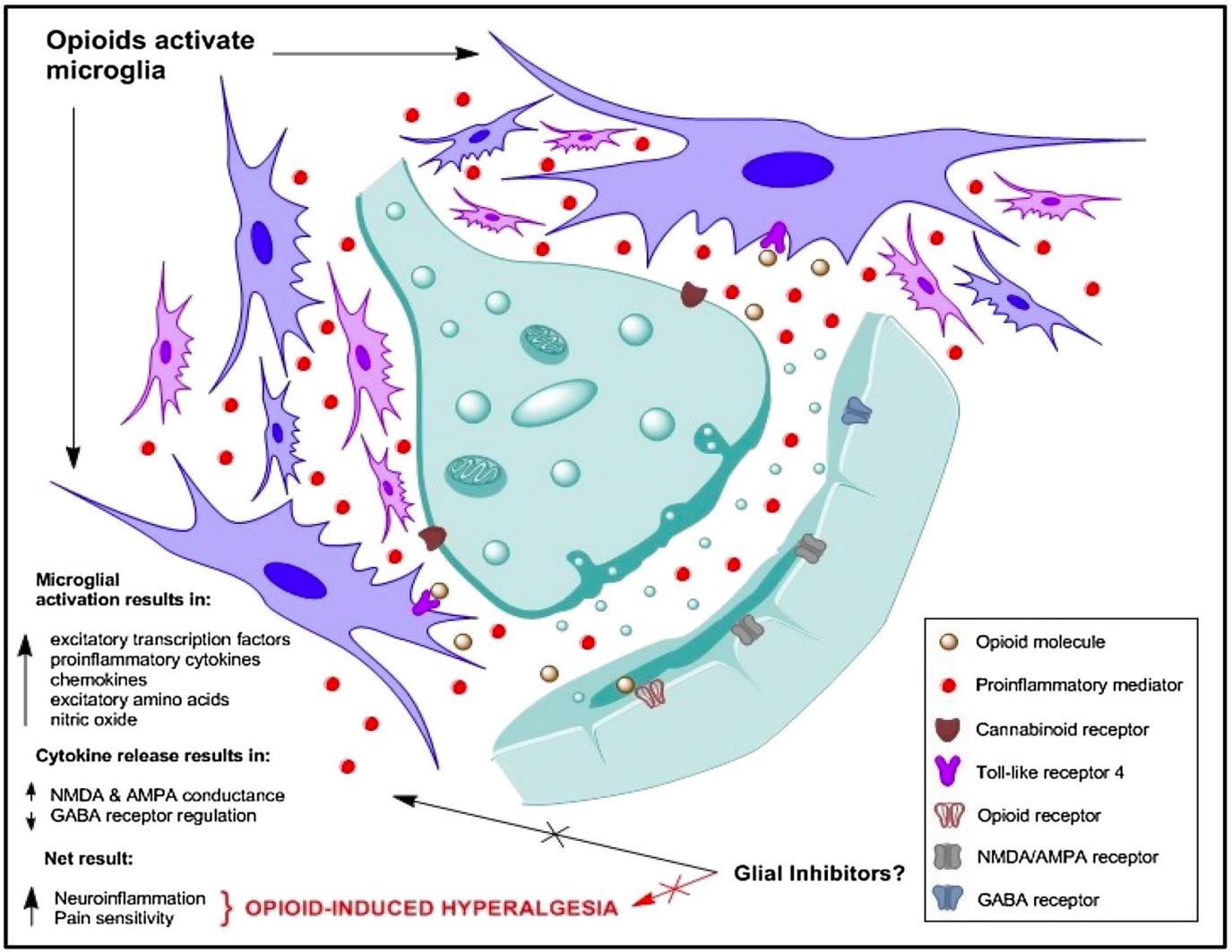
(Mao, 2008)

Opioid-induced Pain Sensitization



(Ravat and Ballantyne, 2016)

OIH Mechanisms - Microglia



(Arout, 2015)

Significant Pain Reduction in Chronic Pain Patients after Detoxification from High Dose Opioids

- Baron and MacDonald, 2006
- Retrospective study of opioid detoxification
- 21/23 patients had significant decrease in pain after detoxification

Withdrawal-induced hyperalgesia (WIH)

- Unmasking OIH with opioid cessation
  - PAIN
- AND release of catecholamines due to withdrawal
  - Causes neuroinflammatory and neuroimmune response
  - PAIN

Pain Med. 2008 November ; 9(8): 1158–1163. doi:10.1111/j.1526-4637.2008.00475.x.

Reduced Cold Pain Tolerance in Chronic Pain Patients Following Opioid Detoxification

Jarred Younger, PhD, **Peter Barelka, MD**, **Ian Carroll, MD, MA**, **Kim Kaplan, MD**, **Larry Chu, MD**, **Ravi Prasad, PhD**, **Ray Gaeta, MD**, and **Sean Mackey, MD, PhD**
Stanford University School of Medicine, Department of Anesthesia, Division of Pain Management, Palo Alto, California, USA

Conclusions—These findings suggest that the withdrawal of opioids in a chronic pain sample leads to an acute increase in pain sensitivity.

Pain Medicine

Pain Medicine 2010; 11: 1587–1598
Wiley Periodicals, Inc.

ORIGINAL RESEARCH ARTICLES

Associations between Heat Pain Perception and Opioid Dose among Patients with Chronic Pain Undergoing Opioid Tapering

W. Michael Hooten, MD,*† Carlos B. Mantilla, MD, PhD,* Paola Sandroni, MD, PhD,‡ and Cynthia O. Townsend, PhD†

Departments of *Anesthesiology,

†Psychiatry and Psychology and

‡Neurology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA

Higher starting dose = more hyperalgesia, AND
Tapering from higher doses was associated with lower values of Heat Pain (i.e. more hyperalgesia) in a dose dependent manner N= 109

Possible OIH/WIH Mitigators – pre/clinical

- NMDA antagonists (ketamine, etc.)
- NSAIDs (ketorolac, ibuprofen, etc.)
- Gabapentinoids (gabapentin, pregabalin)
- Alpha and beta blockers
- Cannabinoids?
- Melatonin
- Microglia TLR-4 antagonists, e.g. (+)-naloxone, (+)-naltrexone, ibudilast
- Opioid tapering, or rotation then tapering, instead of abrupt stop

(Arout, 2015; Chu, 2012; Mao, 2006; Grace, 2014; Xin 2012; Hutchinson. 2012)

Clinical Note

PAIN

OPEN

Withdrawal-associated injury site pain (WISP): a descriptive case series of an opioid cessation phenomenon

Launette Marie Rieb[a,b,*], Wendy V. Norman[a], Ruth Elwood Martin[c], Jonathan Berkowitz[d], Evan Wood[b,e], Ryan McNeil[b,e], M.-J. Milloy[b,e]

December 2016, 157(12) 2865–2874

Open access:

http://journals.lww.com/pain/pages/articleviewer.aspx?year=2016&issue=12000&article=00028&type=abstract

WISP – descriptive case series

Mixed methods study of patients on opioids for CNCP or addiction

- 5 screening Q – optional full survey of 35 Qs
- 58 screened, 47 confirmed WISP, of these
- 34 completed the full surveys (21 by interview)
- WISP median pain intensity 8/10 (original injury 10/10), more painful than general withdrawal
- WISP median duration 2 wks, but 18% > 1 mo.
- WISP can be a risk factor for opioid reinitiation
- Mitigators included gabapentin and NSAIDS

WISP VS original injury & w/d pain

"God, it felt just like it did when it was healing when it was broken, yeah. I don't know how—any other way to describe it."

- Participant #2, 53 year-old white male, original injury - fractured arm at age 12

"I was pounding my legs…old injury sites are horrendous. So, like it's more severe in those spots. The other part you can like go, get through with a hot cloth, or whatever, with Gravol and stuff, but old injury sites come back with like, severe severity."

- Participant #17, 58 year old Indigenous female, original injury—foot fractures requiring plating and lower leg injuries requiring fasciotomies after a home invasion, capture, and repeated assault with a hammer

WISP - Emotional Aspects

"There's also not just physical pain…I was run over by a semi so I suffered some physical injuries that come up in withdrawal, but also there's anxiety from it too…It's like PTSD from that big time"

- Participant #8, 38 year old white male with previous multiple bilateral lower leg and foot fractures after being struck and pulled underneath a semi-trailer

WISP Theories

- *"all part of the drug withdrawal"*
- *"I don't think it healed right"*
- *"might be psychological"*
- *"I thought, okay, it's such a strong pull to do the drugs that my brain figured out that because I started taking opiates when I sprained my ankle, it's going to start kicking the pain out at the ankle to get more opiates..."*
  - Participant # 5, 35 year old white male, original injury—right ankle tendon tear requiring casting

WISP Discussion

Severe

OI > WISP > W/D

2 weeks ++

Aversive

Relapse

Theories

MNY.ca

Central sensitization

High opioid dose

Multiple w/d

Abrupt cessation

Noradrenaline

Neuroinflammatory

Neuroimmune

(Woolf, 1983; Barron et al., 2013; Hooten, et al. 2015; Prosser, et al., 2008; Wang et al., 2011; Celerier et al., 2001; DeLeo et al 2004; Raghavendra et al. 2002; Bie et al., 2003; Treister et al, 2012; Karasz et al., 2004)


1887
Mrs. Winslow's
SOOTHING
SYRUP
FOR CHILDREN TEETHING

Best Practice for Opioid Therapy (NOUGG-2010)

- Complete history, physical, differential Dx
- Risk assessment SUD, psychiatric issues
- Medication review + urine drug screen
- Appropriate trial of non-opioid alternatives
- Pre/post-opioid pain and function questions
- Treatment agreement -1 MD, visits, scripts
- "Trial" of opioid – if no response to low dose then likely will not respond to high dose
- Taper off benzodiazepines first if possible
- Use Opioid Manger and PharmaNet
- http://nationalpaincentre.mcmaster.ca/opioid/

Reduce Risk when Prescribing

- Random UDS, PharmaNet, opioid agreement
- Random call backs for pill counts to pharmacy
- Bubble pack medications
- Patch return to pharmacy for next dispense
- Shorten dispensing frequency/amount
- Change to OD formulation with daily witnessed ingestion
- Taper off – or send to detox/treatment facility if continued alcohol, benzo or illicit substance use

CPSBC standards and guidelines – key points for LTOT – informed consent

Non-opioid treatments for pain preferred

Standards for LTOT:

- Discuss: risks in light of poor evidence of benefit, must abstain from alcohol
- Not with benzo, stimulant, sedative/hypnotic
- Random UDS or pill counts at least annually
- Use only short acting meds for acute pain
- Short dispense on hospital discharge – few d.
- Primary prescriber - max 3 months or 250 tabs
- Review hx and px every 3 months
- Offer take home naloxone to all on LTOT

CPSBC standards and guidelines – key points cont'd

Standards:

- Doses >50 morphine milligram equivalents (MME) per day warrant careful reassessment and documentation
- Doses >90 MME per day warrant substantive evidence of exceptional need and benefit. (This advice excludes treatment with methadone)

Guidelines:

- PharmaNet required, other meds discussed

Functional Assessment

Universal Precautions – The 5 As (Gourley, 2005)

1. Activities of daily living
   - Work, self care, mobility, leisure, sport, sleep
2. Analgesia
3. Adverse effects
4. Affect
5. Aberrant drug-related behaviors

Screening tools

- Substance Use Disorders
  - AUDIT – alcohol (free from WHO)
  - DAST – drugs, or CAGE-AID
  - COMM – current opioid misuse measure
- Mood
  - BDI - Beck Depression Inventory
  - PHQ9
  - Various sleep, anxiety, bipolar, and PTSD screens
- Pain and function
  - PDI – Pain Disability Index
  - AREBRO – catastrophizing and predictor of return to work

Patients at High Risk for SUD (NOUGG - 2010)

- Prescribe only for well-defined somatic or neuropathic pain conditions
- Relatively contraindicated in headache and fibromyalgia
- Start with lower doses and titrate in small dose increments
- Monitor closely for signs of aberrant drug related behaviors

No Benzos

- For patients with chronic non-cancer pain (CNCP) and/or SUDs on/off opioid therapy -

benzodiazepines are contraindicated

  - No help with pain
  - Helps with sleep initiation but not maintenance
  - Rebound insomnia
  - Withdrawal anxiety
  - Increased risk of unintentional OD, MVA, falls
  - Opioids + benzos + alcohol especially lethal
  - Advisable to taper off benzos prior to opioid start

When to Suggest Opioid Taper?

- Patient on opioid for a condition not indicated for opioid use
- Patient on opioids without significant improvement in pain and function
- Safety sensitive position
- Sleep apnea, or other relevant medical issues
- Pain sensitization – suspected OIH, WIH, or WISP
- Active substance abuse/dependence where harm reduction not viable
- Patient requests to come off

Opioid Withdrawal

Withdrawal is not life threatening

- Unless patient has a history of seizures, is dehydrated, suicidal or pregnant

- Warn patients of OD risk post detox

Opioid Withdrawal

- DSM-5…3+ within minutes to days of stopping:
  - Dysphoria
  - N or V
  - muscle aches
  - lacrimation or rhinorrhea
  - diarrhea
  - yawning
  - fever
  - insomnia
  - Pupillary dilitation, piloerection or sweating

Where to start?

- First make a diagnosis
  - Use? Substance Use Disorder?
- Is there physiologic dependence?
  - Is a withdrawal syndrome present?
  - How severe? Life threatening?
- What is the patient's circumstance?
  - Support setting? Mental/physical health? Do they need residential detoxification?

Helping with Opioid Tapering

Education:

- Go over what opioids DO in the body
- Explain WITHDRAWAL symptoms, incl. pain
- Normalize and temporalize – go slow in legacy pts

Medication adjuvants:

- Decrease catecholamines: a-blockers, breathing exercises, mindfulness, etc.
- Regulate sleep: TCAs, tetracyclics, melatonin
- Treat pain and w/d: NSAIDS, gabapentinoids, etc.
- Opioid rotate then taper (eg. to bup/nx or methadone if you have experience doing this)

Typically…opioid tapering is not an emergency!

- As out patients most can drop 5-10% every 1-2 weeks, sometimes slowing to every 2-4 weeks for the last 20-30% of the opioid
- For patients on LOT for many years who have failed more rapid tapering, just slow it down to drop every 1-3 months
- Even if you drop the dose 5% every 3 months, in a year they will be down 20%, and by 2 years 40%. But this is ridiculously slow if they are on extremely high doses or have only been on a couple of years or less

Opioid Lowering Options

1. Convert to long acting opioid – taper
2. Taper with short acting opioid
3. Withdrawal symptom management
4. Opioid substitution/rotation - taper

Opioid Tapering - Long

- Conventional wisdom is to convert short acting opioids to long acting then taper Sometimes short is needed to add back in at the end due to dose strength
- Convert to long acting (same drug less 25% - 50%, rest is given as short acting PRN 1st wk – convert rest wk 2)
- Once on just long acting: Taper ~5-10% per wk
- If the patient has lots of social support can try tapering 10% q 4d
- If rotating opioids beware of conversion
- Lack of cross tolerance with some opiates

Opioid Tapering – Example

- Pt taking hydromorphone (short) 200 mg/d
- 1st conversion: Hydromorphone (long) 75 mg q12 h plus hydromorphone (short) 4 mg 1-2 q4h prn – warn about driving, sedation
- 2nd week: see if prn doses needed – if so add in as long acting, e.g. 100 mg q12h
- 3rd week on…taper 5-10%, typically faster at first and slower at the end of the taper
- Taper until on lowest dose strength long 3q12h
- Then re-introduce short to complete weekly taper, e.g. hydromorphone (short) 2mg q8h; 1mg q6h; 1mg q8h; 1mg am and hs;1mg hs;off

Opioid Tapering – Short

- Sometimes easiest to simply taper what the patient is currently using
  - E.g. Percocet 16-20/d, taken 6 tid +/- 2/d
- If it is a dual agent first switch to eliminate the ASA or acetaminophen (bloodwork?)
  - E.g. Oxycodone 5 mg 18/d
- Next spread out the daily dose evenly based on the ½ life of the medication
  - E.g. Oxycodone 5 mg 5/4/4/5 spread q6h

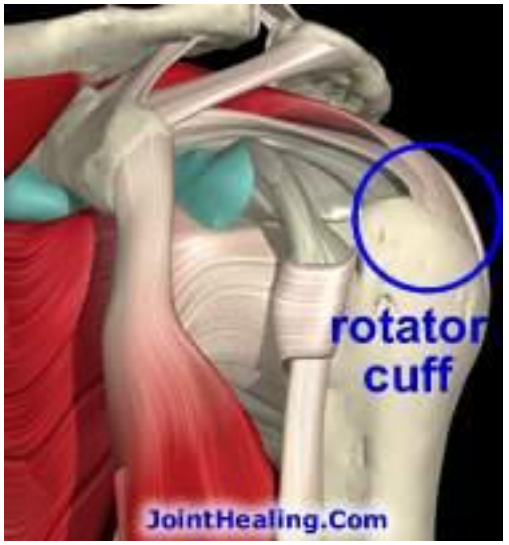
Opioid Tapering – Example

- Next taper the medication – depending on the patient's symptoms the drop can be ever 4 -14 days, always dropping nighttime dose last
- Oxycodone 5 mg 4/4/4/5 spread q6h
- Oxycodone 5 mg 4/4/4/4 spread q6h
- Oxycodone 5 mg 4/3/4/4 spread q6h
- Oxycodone 5 mg 4/3/3/4 spread q6h
- Oxycodone 5 mg 3/3/3/4 spread q6h
- Oxycodone 5 mg 3/3/3/3 spread q6h
- Continue this pattern until 0/0/0/1, then off

Opioid Tapering – Combo

- If patient using a combination of short and long acting – conventional wisdom is to taper short first, but since often this is what patients "feel" and are attached to you can taper it last
- Oxycodone ER 80 mg q12 h plus oxycodone 10mg 1-2 prn 4/d max
- Taper Oxycodone ER first by 10 mg every 4-14 days dropping morning dose, then evening dose
- Hold the oxycodone short 10 mg at q6h until off the Oxycodone ER then taper by 5 mg as per previous schedule leaving the hs to be last off

Ms. Z



- 55 yr. old care aid injured
- Rt. Shoulder pain, sleep and mood changes
- MRI – full thickness tear and atrophy in supraspinatus, a possible tear in subscapularis, tendonopathy in infraspinatus, fluid in the subacromial bursa and deltoid bursa
- Ortho suggested conservative management

Ms. Z. – cont'd

- Tx – cortisone injections some help
- Mood – 2h sleep/night, anxious, tired
- PMH
  - Previous shoulder injury, resolved
  - Asthma
  - HTN
  - Hyperlipidemia
  - Obesity
  - Depression – "treated" for 12 years

Ms. Z, cont'd

Meds:

- T#3 – 2 q3h up to12/d, runs out early nb 50 pills given q2 wk = 3-4 pills a day allowed by perscription
- T#1 – 3 q3h up to 18/d when out of T#3s
- Clonazepam 0.25mg qam, 0.5mg noon, 0.25mg qpm, 1.5mg hs (dosing x 12 yrs)
- Oxazepam 45mg hs (x 12 yrs)
- Methylphenidate (Ritalin) 20mg tid when working, 10mg bid when off work (x 12yrs)

Ms. Z – cont.

- Meds – cont.
  - Trazadone 300mg hs
  - Chloral hydrate 500mg hs
  - Risperidone 1.5 mg hs
  - Rabeprazole (Pariet) 20 mg od
  - Montelukast (Singulair) 10mg hs
  - Salbutamol prn
  - Advair 1 puff bid

Ms. Z. – cont.

- Meds, cont.
  - Diltiazem CD 180mg od
  - Fosinopril 10mg od
  - Hydrochlorothiazide 25mg od
  - "Failed" + antidepressants, TCAs, neuromod.
  - So stimulant to wake, opiate and anxiolytic in day, and sedative-hypnotics and antipsychotic to sleep

Ms. Z – substance use Hx

- Caffeine: 1c coffee q3d
- Tobacco: ½ ppd (from 1ppd), enjoyment
- Alcohol: current - 1drink q 1/2 - 2 wks (understands it is contraindicated), around 30 had 4-5 yrs of problems - once weekly 1 bottle of wine, kids taken in by cousins. Finally divorced, church, cut back on ETOH and got kids back
- Drugs: no reported use

Ms. Z – Px

Pleasant caucasian woman, slightly sedated

- Ht = 5'0" , wt = 230 lbs
- BP elevated
- Cradling right arm, head tilted to right
- Limited shoulder flex, abd., int. rotation
- Shoulder/arm strength reduced - pain limited
- Diffusely tender whole shoulder girdle

Ms. Z. - Dx

- Rt rotator cuff tear, tendonopathy, atrophy
- Mood changes & meds began when drinking and divorcing, still low, anxious, sleep disturbed
- Chronic pain disorder – physical and psych
- Overmedicated
- Substance use disorder – ETOH abuse/dep in remission with intermittent use

Ms. Z. – Dx – cont'd

- Tobacco dependence
- Current opioid dependence vs pseudo-add.
- Asthma
- Hypertension
- Hyperlipidemia
- Obesity
- Positive work environment – social support

Ms. Z. – Recommendations

- Chronic pain program – guarded prognosis
- Taper methylphenidate to elimination
- Taper chloral hydrate, T#3, T#1
- Consolidate benzos and begin slow taper

Ms. Z. - Recommendations, cont'd

- Discontinue alcohol,
- Hold or decrease cigarettes
- Physio + general conditioning & wt loss
- Psych support, self regulation training

- Call family MD and Psychiatrist

Ms. Z. – After 6 weeks

- Was able to completely come off methylphenidate, codeine (T#3, T#1), and chloral hydrate
- Clonazepam reduced to 1.5 mg hs
- Oxazepam reduced to 30 mg hs
- Same dose of trazadone 300mg hs
- Same dose of risperidone 1.5mg hs
- Off alcohol, nicotine <1/2ppd, +caffeine

Ms. Z. – 6 wks, cont'd

- Lost 15 lbs
- BP normalized 125/76
- Sleep still 2-3 hrs/night, plus 4 hrs rest
- Activity increased – cardio: 45min from 10
- Improved head, neck & arm posture
- Improved shoulder ROM & strength
- Learned relaxation, breathing, mindfulness

Ms. Z. – 6 wks, cont'd

- Pain "a little bit better, easier to deal with"
- Beck depression scale went from severe range on intake to mild
- Mood: "Gosh, a lot better and much clearer. I am much, much better than before… I am alive! I have more energy."

- She felt she had her "life back"

Ms. Z. –Recommend on d/c

- Return to work (GRTW)
- Continue slow taper of clonazepam by 0.125 mg to 0.25 mg q 1-2 wks
- Then taper oxazepam by 15 mg q1-2 wks
- Then taper risperidone by 0.5mg q1-2 wks
- Leave trazadone 300mg hs for 6-12 months
- May have life long sleep disturbance – so temper the need to treat with meds
  - That said, tryptophan & melatonin yet to try

Ms. Z. – Follow up

- Successful completion of a GRTW – fit without limitations
- Happy to be back in the workplace with friends
- Continued to do well at home and work upon review 6 mo. post discharge

Ms. Z. - Reflections

- Addiction?
- Pseudo-addiction?
- Opioid induced pain sensitivity?
- Mood induced pain and disability?
- Or instead iatrogenic cause of dysfunction
  - Layering meds to offset side effects of the last one prescribed, and time pressure in office – trying to fix symptoms


FARBENFABRIKEN
vorm.
FRIEDR. BAYER & Co
ELBERFELD.
Heroin
Name gesetzlich
Si Nom déposé

Opioid Tx if OUD

- For use when you cannot (or will not) prescribe opioids, e.g. opioid use disorder, street opioid use
- Protocol for short acting opioids like **heroin, codeine, morphine, oxycodone, etc.**
- A caregiver should accompany patient to appointments, agree to attend & dispense - then you can give 1 week's worth of meds
  - If no reliable caregiver daily dispensed from the pharmacy

Opioid w/d Management

- Environment: Reliable support person, safe, no caffeine, mild food, min exercise, avoid hot bath/shower/sauna
- Clonidine 0.1mg qid x4d, tid x1d, bid x1d, hs x1d all prn
  - Test dose 0.1mg, BP pre & 1-4h post in the office can be done (eg. For young women)
  - BP >90/60, if lower - give clonidine 0.05 mg tabs
  - Decreases temperature dys-regulation (hot/cold flashes) and NOR (insomnia & anxiety)
  - Warn pts of postural hypotension, driving

Opioid w/d Management,

- Gabapentin 300 – 600 mg tid, prn for anxiety, insomnia, and pain * Can be used for taper too
- +/- Trazodone 50 mg 1-2 tabs hs for insomnia
- Loperamide 2 mg after loose stool, 8/d max
- Dimenhydrinate 25mg 1-2 tid N+V
- Ibuprofen 400 mg q 6-8h for pain
- Acetaminophen 500mg q6h for pain
- * Substitutions:
  - Pregabalin 75-150 mg bid (start 25-50 mg hs)
  - quetiapine 25 mg ½ -1 bid - tid and 1-2 hs
  - diazepam 5 mg qid x 4d, tid x1d, bid x1d (classic, but more dangerous if opioids continue, diversion)

Opioid w/d Management,

- Try to start on a Monday (not Friday)
- Try to start medicines after 1d off heroin/morph
- Try to see or call in frequently
- Adjust medications according to symptoms
- If patient relapses, review symptoms (ask what was the worst part of the w/d) and try again – adjusting meds.
- Make a backup plan in the beginning – eg. if home detox fails x2 then residential detox or methadone (often more effective than detox)

Non-opioid SUDs

- All substances of abuse can produce pain relief during euphoria or sedation
- Patients confuse this momentary relief with pain control which it is not, but can drive pain
- Stabilization of the SUD is needed to treat the pain – e.g. alcohol, benzos, cocaine
- Even tobacco and caffeine can play a role in pain modulation, and should be addressed

Precautions if Any Active SUD

- Bubble pack medications
- Random call backs for pill counts
- RANDOM urine drug screens
  - Look for illicit substances, ensure taking prescription
  - Include ethyl glucoronide (ETG): 3-5d past alcohol use
- Put onto once daily formulations with daily witnessed ingestion at the pharmacy (no carries)
- Taper off opioids if drinking alcohol or on benzos

SUD in patients on LOT

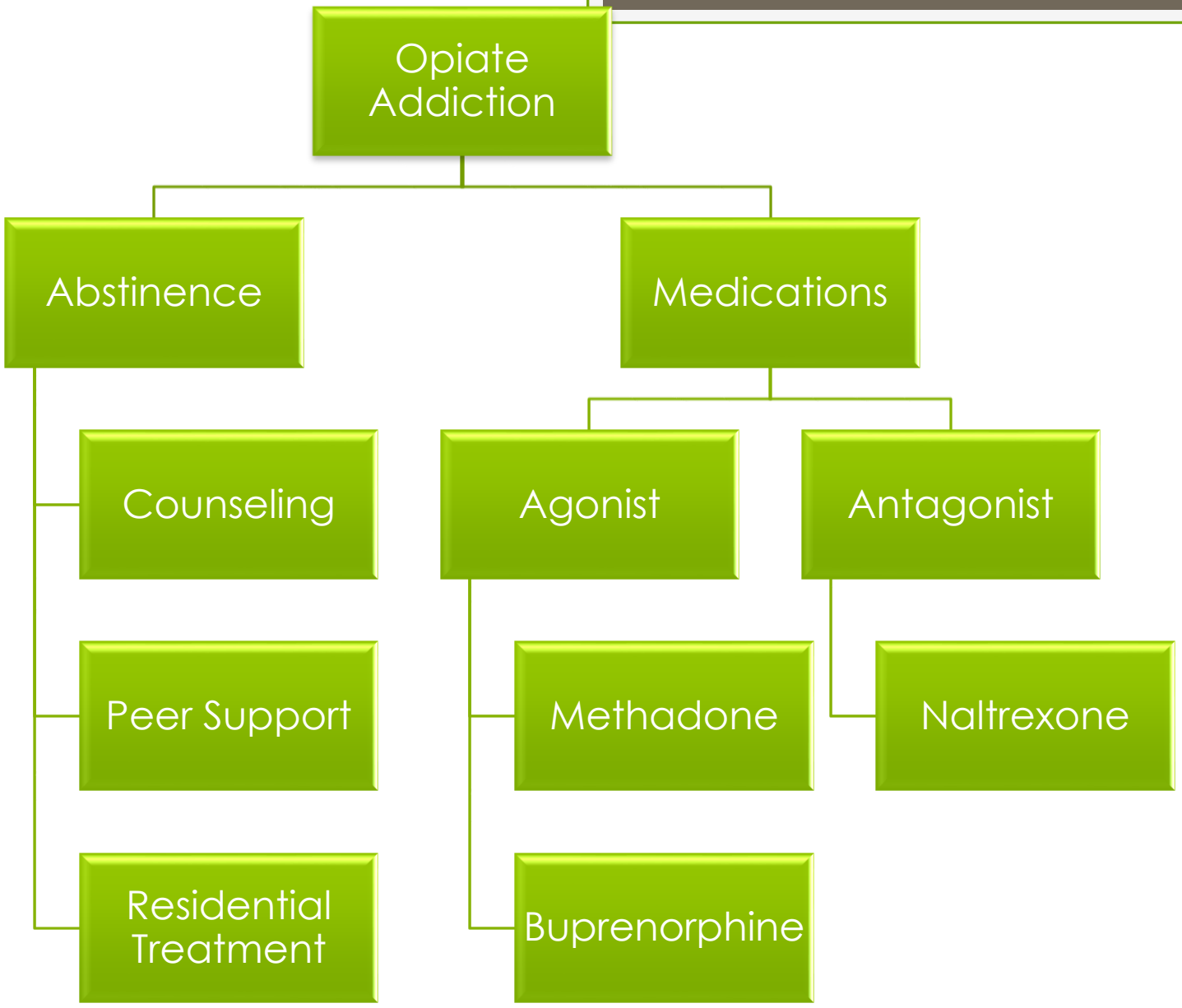
- Systematic review and meta analysis
  - Based on history and physician suspicion alone rates of substance dependence with opioid therapy was under 5%, under 1% if no past hx SUD
- However 5 studies did UDS as well:

  21% of patients had either no prescribed opioid and/or a non-prescribed opioid in their UDS

  15% had illicit drugs (Fishbain 2008)

Common Tx Goals for Pain & SUD

- Correct sleep disturbance
- Stabilize mood
- Eliminate unnecessary medications
- **Restore function**


Opiate Addiction
Abstinence
Medications
Counseling
Peer Support
Residential Treatment
Agonist
Antagonist
Methadone
Buprenorphine
Naltrexone

Opioid Substitution Therapy

- Methadone and buprenorphine/naloxone (bup/nx) can be used for pts with an opioid use disorders and pain
  - Dose once daily to eliminate withdrawal and block other opioids – may be sufficient
- **Methadone or bup/nx used for pain** +/- SUD can be dosed **q6-8h**
- Bup/nx currently off label for pain alone though can argue physiologic dependence, tolerance
- Methadone and bup/nx are used for detox

METHADONE

Morphine to Methadone

24 hour total oral morphine	Oral morphine to methadone conversion ratio
<30 mg	2:1
31-99 mg	4:1
100-299 mg	8:1
300-499 mg	12:1
500-999 mg	15:1
>1000 mg	20:1

Managing Cancer Pain in Skeel ed. Handbook of Cancer Chemotherapy. 6th ed., Phil, Lippincott, 2003, p 663

Methadone for Pain – without addiction

Advantages of methadone for CNCP:

- Theoretically good for neuropathic pain: binds to NMDA receptor, blocks glutamate (**one** of the pathways of tolerance and opioid induced hyperalgesia)
- Long half life (24-36 hrs) so it can lower withdrawal induced pain if dosed daily, may need q6-8h dosing for analgesia

Disadvantages of methadone for CNCP:

- Methadone vs morphine 43% increased risk of death, even methadone 20mg or less HR = 1.5 (Ray, 2015)

- Review, 3 studies - limited info, efficacy (Haroutiunian 2012)

Methadone should NOT be first line for CNCP (unless OUD)

Methadone for detox

- Course needed, and authorization
- Clinical judgment required for starting dose
- One example:
- Stop other opioids
- Methadone 10-30 mg on day 1 as per physician orders
- If 30 mg then taper by 5 mg per day until off
- If 10 mg taper by 2mg per day until off

Addiction

RESEARCH REPORT

doi:10.1111/j.1360-0443.2012.03870.x

Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study

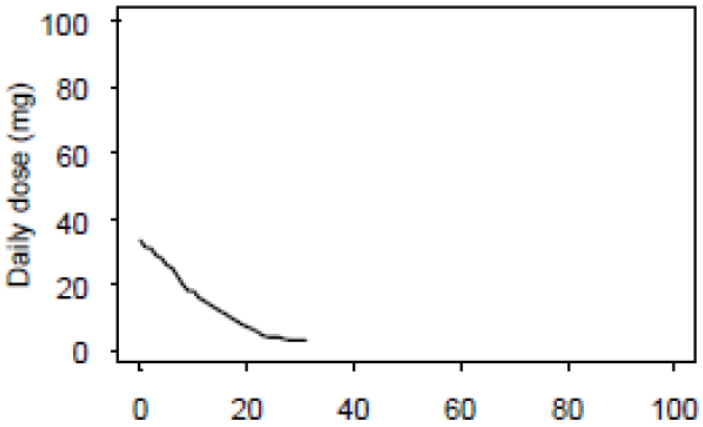
Bohdan Nosyk[1,2], Huiying Sun[3], Elizabeth Evans[2], David C. Marsh[4], M. Douglas Anglin[2], Yih-Ing Hser[2] & Aslam H. Anis[3,5]

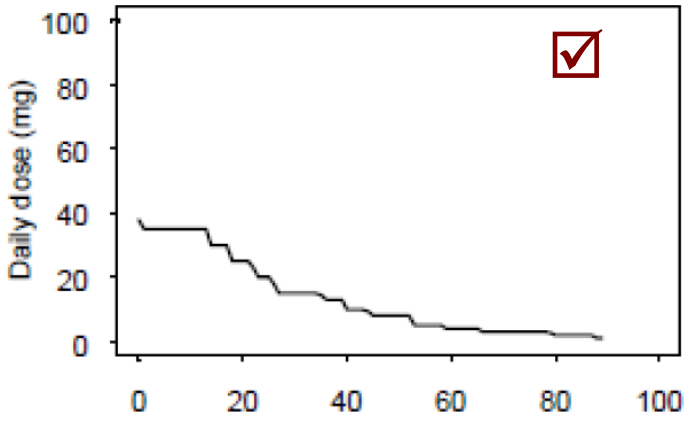
BC Centre for Excellence in HIV/AIDS, Vancouver, British Columbia, Canada,[1] UCLA Integrated Substance Abuse Programs, Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, Los Angeles, CA, USA,[2] Centre for Health Evaluation and Outcome Sciences, Vancouver, British Columbia, Canada,[3] Northern Ontario School of Medicine, Sudbury, Sudbury, British Columbia, Canada[4] and School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada[5]

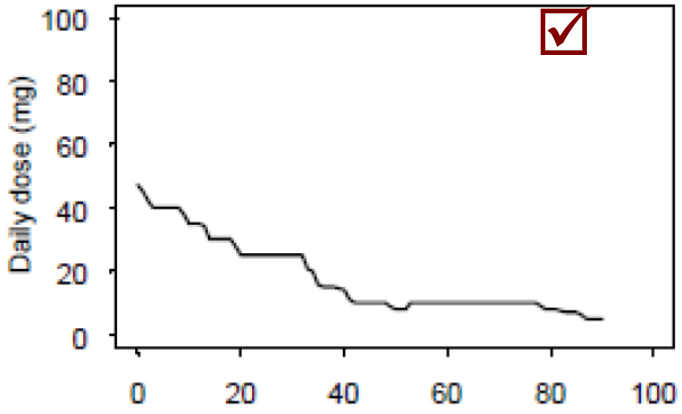
Results

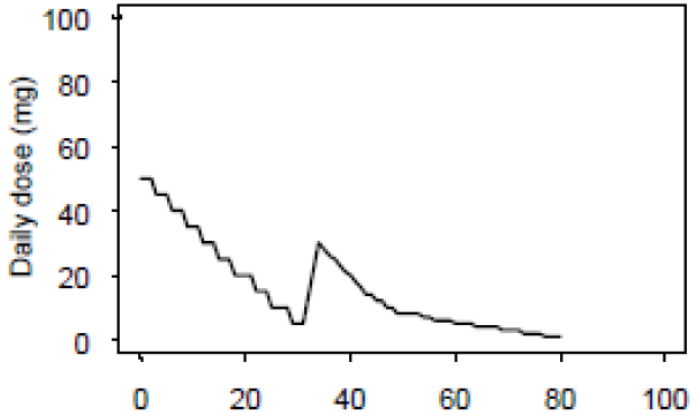
- 646/4183 sustained successful tapers = **13%**
- Younger, males, better tx adherence, lower mean max weekly doses
- Longer tapers better
  - 12-52 weeks vs <12 weeks OR 3.58
  - >52 weeks vs <12 weeks OR 6.68
- More gradual, stepped tapering schedule
  - 25-50% vs <25% of taper weeks OR 1.61

Patterns of Methadone Dose Tapering (Most successful checked)









Modified from Nosyk et al, Addiction 2012; 107(9):1621-9.

Ms. J.

- 19 year old street entrenched female youth
- Pierced, tattooed, black clothes torn
- Presents asking for methadone
- **Past Medical History**
  - Severe ankle sprain a year prior, air cast
  - X-ray negative
  - Ongoing pain, ER visits – “drug seeking”
  - Friends helped out with pills then heroin
  - No mood issues, sleep broken

Ms. J., cont'd

- **Medications**
  - Ibuprofen 400mg 1-2 prn
  - Acetaminophen ineffective
- **Substance Use History**
  - Tobacco started age 12, currently 1ppd
  - Marijuana started age 13, currently 2-3 jnts/d
  - Alcohol started age 13, 2 beer/wk, rare binges
  - Heroin – started 6 months prior with smoked heroin escalating to ¾ gm/d iv divided tid

Ms. J., cont' d

Social history

- On the street since age 17
- Father alcoholic, violent, she left home
- Recent breakup with boyfriend
- Has a dog which makes housing a challenge

- **Exam** – bony tenderness right ankle
- **What are the next steps?**

Ms. J., cont'd

- **Management**
  - Converted to methadone 85 mg/d
  - Referred to community counselor for housing
  - X-ray, CT, bone scan – occult fracture and low grade osteomyelitis
  - Antibiotics
  - Surgical intervention – internal fixation
  - Temporary oxycodone for several weeks following surgery

Ms. J., cont'd

- **Management, cont'd**
  - Physiotherapy
  - Tapered off methadone
  - Decreased tobacco and marijuana
- **Social follow-up**
  - Grade 12 equivalent study and exam
  - Applied and accepted to be a youth counselor

Ms. J., Case Highlights

- What can begin as pseudo-addiction (seeking pain relief but labeled as drug seeking) can become full blown addiction
- People who fall outside the average (due to class, race, sexual orientation, body ornamentation, age, lifestyle, etc.) can be misdiagnosed or not fully seen
- Treat the underlying condition
- Challenge yourself to see whole the person


Buprenorphine HCL
Sublingual Tablets
8 mg*
Midlothian

Buprenorphine/nx detox

Example:

- Stop other opioids, COWS score > 10
- Buprenorphine/nx 1-2 mg test dose
- If no precipitated withdrawal give 2mg q2-4 h until withdrawal subsides up to 8 mg on day 1, hold if sedated
- Day 2 give full dose from day 1, and 1-2 mg q4h up to 16 mg if needed to supress withdrawal (often just 8 needed total)
- Day 3 on: Taper 1-2 mg q1-2d, e.g…
  - Sub 8/8/6/6/4/4/2/2/1/1/bup patch 20/10/5

Buprenorphine - Induction Tips

- The day you stop other opioids put on a buprenorphine patch 20 mcg/h, which kicks in and slowly displaces other opioids
  - Less precipitated withdrawal when oral bup then starts the next day- just use 1mg test dose (if not patches use 1/8-1/4 bup/nx tab)
- In hospital can bridge other opioids with fentanyl (patch or iv) for 2 days prior to initiating buprenorphine
  - Stop fentanyl and add oral buprenorphine since fentanyl has a higher receptor affinity – so theoretically less precipitated withdrawal

Pain Medicine

Pain Medicine 2014; **: **–**
Wiley Periodicals, Inc.

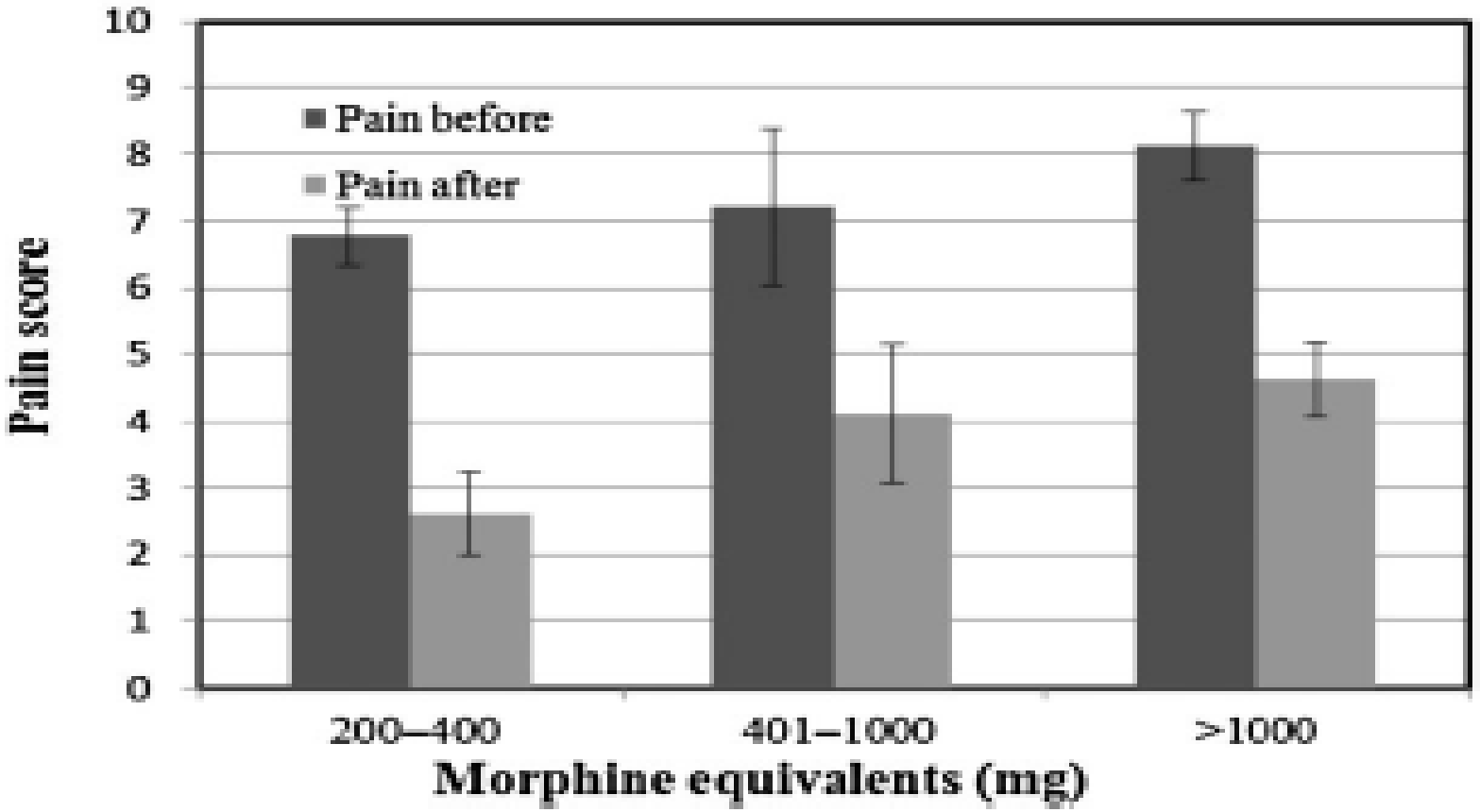
Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients

(Daitch D. Pain Medicine. 2014)

Retrospective chart review of patients on over 200 MEDD converted to Suboxone

- pain scores dropped 51% on average, from 8/10 to 4/10

Pre- and postconversion pain scores by preconversion morphine equivalents dosage



Average 4 point drop!

Daitch D et al. Pain Medicine. 2014

Naltrexone – opioid antagonist

- Post detox use naltrexone 50mg/d po for those with OUD
  - can block 0.5+ gm of heroin IV or equivalent
- Start 1-2 wks after last short acting opioid (3-4 wks post methadone)
  - ¼ pill day 1; ½ pill day 2; 1 pill day 3 onwards
  - Witnessed ingestion is best – or injectable once here
- Contraindicated cirrhosis, OD risk high once d/c
- Use for first 6-12 months of sobriety from OUD
- Analgesia with non-opioids or get consult

Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial

Evgeny Krupitsky, Edward V Nunes, Walter Ling, Ari Illeperuma, David R Gastfriend, Bernard L Silverman

Lancet 2011; 377: 1506–13

Published Online
April 28, 2011
DOI:10.1016/S0140-6736(11)60358-9

See Comment page 1468

Bekhterev Research Psychoneurological Institute, St Petersburg State Pavlov Medical University, St Petersburg, Russia (Prof E Krupitsky MD); New York State Psychiatric Institute and Department of Psychiatry, Columbia University, New York, NY, USA (Prof E V Nunes MD); Department of Psychiatry and

Summary

Background Opioid dependence is associated with low rates of treatment-seeking, poor adherence to treatment, frequent relapse, and major societal consequences. We aimed to assess the efficacy, safety, and patient-reported outcomes of an injectable, once monthly extended-release formulation of the opioid antagonist naltrexone (XR-NTX) for treatment of patients with opioid dependence after detoxification.

Methods We did a double-blind, placebo-controlled, randomised, 24-week trial of patients with opioid dependence disorder. Patients aged 18 years or over who had 30 days or less of inpatient detoxification and 7 days or more off all opioids were enrolled at 13 clinical sites in Russia. We randomly assigned patients (1:1) to either 380 mg XR-NTX or placebo by an interactive voice response system, stratified by site and gender in a centralised, permuted-block method. Participants also received 12 biweekly counselling sessions. Participants, investigators, staff, and the sponsor were masked to treatment allocation. The primary endpoint was the response profile for confirmed abstinence during weeks 5–24, assessed by urine drug tests and self report of non-use. Secondary endpoints were self-reported opioid-free days, opioid craving scores, number of days of retention, and relapse to physiological opioid dependence. Analyses were by intention to treat. This trial is registered at ClinicalTrials.gov, NCT00678418.

Findings

Between July 3, 2008, and Oct 5, 2009, 250 patients were randomly assigned to XR-NTX (n=126) or placebo (n=124). The median proportion of weeks of confirmed abstinence was 90·0% (95% CI 69·9–92·4) in the XR-NTX group compared with 35·0% (11·4–63·8) in the placebo group (p=0·0002). Patients in the XR-NTX group self-reported a median of 99·2% (range 89·1–99·4) opioid-free days compared with 60·4% (46·2–94·0) for the placebo group (p=0·0004). The mean change in craving was −10·1 (95% CI −12·3 to −7·8) in the XR-NTX group compared with 0·7 (−3·1 to 4·4) in the placebo group (p<0·0001). Median retention was over 168 days in the XR-NTX group compared with 96 days (95% CI 63–165) in the placebo group (p=0·0042). Naloxone challenge confirmed relapse to physiological opioid dependence in 17 patients in the placebo group compared with one in the XR-NTX group (p<0·0001). XR-NTX was well tolerated. Two patients in each group discontinued owing to adverse events. No XR-NTX-treated patients died, overdosed, or discontinued owing to severe adverse events.

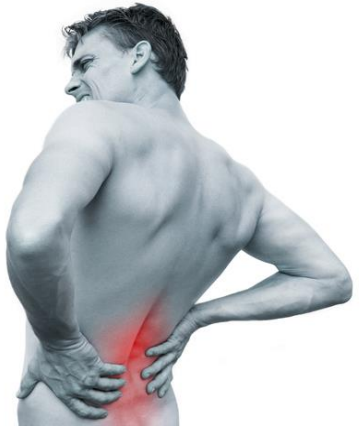
Naloxone Take Home Kits

- Nasal or injectable naloxone kits given to people prescribed opioids for pain or addiction
- Train Pt and others living with them
- Can save lives in OD situations
- Sometimes Pt uses it on a friend
- Find out what is available/allowable in your area

Take Home Naloxone

- T

Case - Mr. D.



- 47 year old married at home father, degree is psychology, no family history of SUD
- Age 19: L4-5 discectomy for prolapse
- Post-op give Tylenol #3
  - He mixed these with ETOH to get high
- 10 years later – recurrent disc – surgery
- Initially successful then increasing low back pain over the next year

Mr. D, cont'd

- GP managed
  - Tried different medications, low dose at 1st
  - Hydromorphone short acting up to 80 mg/d
    - Would run out early, would crush and smoke
  - Fluoxetine 60 mg/d
  - Lorazepam 4 mg/d
  - Pain still unmanageable on above regime
  - Referred on

Mr. D., cont'd

- Multidisciplinary hospital based pain clinic
  - Medications altered, various medications combined
  - Opioids were increased over time to the level below:
  - Fentanyl Patch 150 mcg/h q2 d (prescribed q3d)
  - +/- fentanyl solution 100 mcg/2ml vile 3-5/d
  - Fentanyl film 600 mcg bid = 1200 mcg/d
  - Tramadol (24h) 50 mg ii bid = 6 tabs/d = 300 mg/d
  - Methadone tablets 60 mg bid = 120 mg/d
  - Hydromorphone - short acting 80 mg/d (snorting)
  - Morphine equivalent dose = 1,830+ mg/d

Mr. D., cont'd

- Other medications
  - Fluoxetine 80 mg/d (adverse rxn - duloxetine)
  - Diazepam 2.5 mg bid (+still using lorazepam)
  - Decongestant with pseudoefedrine 2 tabs/d
  - Caffeine pills and energy drinks
- He still felt pain, otherwise felt "Great!"
- Function: ran triathlons, others see sedation
- Total cost to wife's insurance = $3,000/wk

Mr. D., cont'd

- Voluntary admission to a medically supervised residential treatment facility: education, 12 step, group, 1:1, CBT, etc.
- Methadone and fluoxetine same dose at 1st
- Stopped tramadol on admission
- Stopped all fentanyl after 2 d taper
- Added quetiapine 25 mg q6h
- No withdrawal seen

Mr. D., cont'd

- Tapered the methadone over 3 weeks to 5 mg tid
- Dose held until in withdrawal
- Switched to buprenorphine patch 10 mcg initially – not quite enough
- Then over to sublingual bup/nx titrated to 6 mg/d where he has been maintained successfully

Mr. D. f/u

Follow-up at 12 months – doing great!

- Meds
  - Bup/nx 6 mg/d
  - Fluoxetine 60 mg/d and tapering
  - Quetiapine 125 mg/d and tapering
- Has attended 12 step daily, has a sponsor
- No relapses or slips, despite divorcing
- No more pain issues
- GAF 95/100

Mr. D., Reflections

- Primary pain disorder or substance use disorder?
- Opioid induced hyperalgesia?
- How can the opioids besides methadone be stopped abruptly without withdrawal?
- How can bup/nx and 12 step combined control both the pain and addiction issues?

Pain & SUD

1. Similar treatment goals – restore function, improve mood and sleep, reduce suffering, minimize medication burden and side effects
2. If the patient is in recovery and has acute or chronic pain – discuss all options and risks before making a plan (informed consent)
3. If the patient has a past history of a SUD or is at high risk for one then explore non-opioid options first when feasible, close monitoring

Pain & SUD

4. Active alcohol or benzodiazepine use disorder? Pt not eligible for conventional opioid therapy due to the elevated risk of unintentional overdose
5. Active opioid use disorder? Buprenorphine/naloxone, methadone maintenance therapy is recommended. Other once daily opioids may be an option. Explore abstinence based treatment: Detox with naltrexone after

Pain & SUD

6. Once on bup/nx or methadone for pain and addiction, non-opioid medications and non-pharmacologic strategies should be used for flares and mild to moderate new pain conditions
7. If another opioid is added for severe pain then make it time limited
8. If the pain condition is ongoing, consideration can be given to increasing the methadone or bup/nx. Caution should be applied and consultation obtained if possible before adding another opioid long term (no evidence)

Pain & SUD

9. If the patient has an active cocaine or other stimulant use disorder then it is unwise to give take home doses of any opioid due to the risk of diversion and fueling the stimulant use
10. Prescribing cannabinoids to people with cannabis use disorders or other active substance use disorders is contraindicated

Opioids - Highlights

- Risks and benefits of opioid therapy need to be weighed and documented for each patient:
- Absence of quality evidence of pain relief VS…
- Risks: OD, testosterone suppression, depression, sleep apnea, cardiac events, addiction, diversion, and additional pain

Opioids - Highlights

- Patients with physiologic dependence on opioids and/or benzodiazepines who need to come down or off can be assisted by a variety of approaches:
  - Replacement and tapering
  - Symptom management
  - Agonist therapy
  - Antagonist therapy (naltrexone)
  - Education and non-pharmacologic options

Thank you!