Methadone or Buprenorphine for the Treatment of Pain in Patients with Opioid Use Disorder

Ontario Methadone Prescribers’ Conference
College of Physicians and Surgeons of Ontario
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Faculty/Presenter Disclosure

- Faculty: Andrew J Smith, MDCM
- Relationship with commercial interests
  - None
**Learning Objectives**

By the end of the session, participants will be able to:

1. Outline an approach to managing pain in patients with opioid use disorder

2. Describe an approach to using methadone as part of the treatment of pain in a patient with concurrent opioid use disorder

3. List at least 3 situations in which the use of buprenorphine would be indicated for the treatment of dependence and pain over methadone
Discussion of Off-Label/Investigational Use of Commercial Products

- This activity contains information about clinical and experimental uses of drugs that are not currently approved by Health Canada and/or other national regulatory agencies in Canada.

- Participant are encouraged to consult the Health Canada approved product labelling for any drug mentioned in this program before use.
Question

What percentage of North Americans are currently experiencing pain which has gone on for more than 6 months?

1. 2%
2. 5%
3. 10%
4. 25%
The Burden of Chronic Pain

- Prevalence of chronic pain in the adult population may be 30% (Moulin et al 2001)
- 18% of Canadian adults suffer from moderate to severe chronic pain daily or most days of the week (Nanos Survey 2007-2008)
- Chronic pain is associated with an increase in the use of health services (Tarride, Gordon et al 2005)
- Massive economic burden: $635 billion per annum in US (US Institute of Medicine, 2011)
  - 6x that of depression
  - Mostly due to decreased productivity, not absenteeism
Chronic Pain Defined

- IASP (1986): an unpleasant sensory and emotional experience associated with actual or potential tissue damage

- Acute pain is a vital, protective mechanism that permits us to live in an environment fraught with potential danger

- In contrast, chronic pain serves no such physiologic role and is itself not a symptom, but a disease state

Chronic = pain which lasts beyond the ordinary duration of time that an insult or injury to the body needs to heal

- Beyond 3-6 months in duration

*camh*
Question

What percentage of Ontario middle and high school students (Gr 7-12) used opiates for non-medical purposes in the past year?

1. 5%
2. 7%
3. 10%
4. 12%
## OSDUHS 2013
### Past Year Use – Top 10

<table>
<thead>
<tr>
<th>Substance</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>49.5%</td>
</tr>
<tr>
<td>Cannabis</td>
<td>23.0%</td>
</tr>
<tr>
<td>Binge Drinking</td>
<td>19.8%</td>
</tr>
<tr>
<td><strong>Opioid Pain Relievers (NM)</strong></td>
<td><strong>12.4%(17.8)</strong></td>
</tr>
<tr>
<td>OTC Cough/Cold Medication</td>
<td>9.7% (6.9)</td>
</tr>
<tr>
<td>Waterpipe (“Hookah”)</td>
<td>9.7%</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>8.5%</td>
</tr>
<tr>
<td>Hallucinogens (Ecstasy, mushrooms, mescaline)</td>
<td>7.0%</td>
</tr>
<tr>
<td>Inhalants (Glue or Solvents)</td>
<td>3.4%</td>
</tr>
<tr>
<td>Salvia divinorum</td>
<td>2.6%</td>
</tr>
<tr>
<td><strong>ADHD medications (NM)</strong></td>
<td><strong>1.4%</strong></td>
</tr>
</tbody>
</table>

(www.camh.net)
Opioid therapy can increase pain and reduce function.

1. TRUE
2. FALSE
The Dilemma

What to do when the drug is both a solution and a problem?

The PRACTICE OF EITHER - OR
Case JB: Abdominal Pain Referral to Wasser Pain Management Centre

• 34 yo male, investment banker from NYC with ulcerative colitis dx at 30 yo

• Chronic abdominal pain associated with meals – poorly controlled

• Several flare-ups of rectal pain; diarrhea; bleeding

• Escalating doses hydromorphone

• Adjuvants don’t work

• Running out of meds early
Case JB
A Tale of Two Cities - NYC

- Worsening crampy, abdominal pain since 30yo... Used naproxen
- Worsening urgency, diarrhea, episode of bloody stools
- FH of IBD → Family physician diagnosed likely UC/IBD
- Referred to GI
- Meanwhile prescribed Percocet...
- GI: Colonoscopy..etc...Moderate disease – extensive – proximal to splenic flexure
- RECC: Oral 5-ASA (Mesalamine) to induce remission
- Consider infliximab
- Abdominal, rectal pain/ bloody stools resolved
Case JB
A Tale of Two Cities – Toronto

- Moved to Toronto at 32 yo…New job
- RECURRENCE…crampy abdominal pain
- Percocets…ineffective, dose escalation…
- ER visits – meperidine
- ADRBs – missing GI appointments, always “busy”, calling for early refills, didn’t leave a UDT
- Another flare: FP prescribed hydromorphone…ir
- Pain constant, daily, severely exacerbated by meals…
- SPREADING: lower back – dull ache with sharp radiation upper buttocks; clothes/belt became uncomfortable
- Stopped going to gym/swimming → pool very uncomfortable
Case JB: Med Review

- Hydromorphone IR, then hydromorphone CR added
- Short trials of gabapentin (up to 400mg BID) and pregabalin ineffective
- Bupropion for depression
Case JB: Wasser Clinic Assessment

- Patient taking hydromorphone CR 32mg TID + hydromorphone 4mg 1-2 q 2-4hr, 12/day

- Pain: lower back, abdomen (dull), sharp radiation to legs; cramps worse with meals
  - Worse in morning (9/10), + diaphoresis
  - Poor sleep
  - Often using hydromorphone overnight

- No longer able to work

- Can walk only about 1 block
WELCOME TO OZ!
ADDOP: The Five Pillars of Pain Management

- **Assess:** Symptoms and Risk
- **Define the problem:** where and what is it?
- **Diagnose the kind of pain and treat it**
- **Other issues:** mood, anxiety, sleep, addiction, sex
- **Personal management, self management**

Pearls of Chronic Pain Management

1. Many causes – thorough workup essential

1. Total relief of pain seldom possible

1. Improved function, quality of life, should be main goals

1. Function includes work, ADLs at home, recreation, sleep, sex…

1. The presence of or risk of substance use disorder in a patient does not preclude aggressive treatment of chronic pain
Pillar 1: Risk Assessment

- “Universal Precautions” history (Gourlay et al, 2005)
  - Current and previous pain treatment
  - Aberrant drug-related behaviours
  - Previous drug and alcohol use
  - Family history of drug or alcohol use
  - History of other addictions
  - History of physical, sexual or emotional trauma
  - Depression, anxiety, and other mental health issues
  - Urinary drug screen and identification

- Identify the individuals with the greatest risk of aberrant behaviour NOT to stigmatize, but to improve care
Terminology

Distinguish

- Abuse/Misuse
- Aberrant Drug-Related Behaviours
- Addiction
- Substance dependence
- Substance Use Disorder
- Physical dependence
- Tolerance
Tolerance*
Withdrawal*
More use than intended
Craving for the substance
Unsuccessful efforts to cut down
Spends excessive time in acquisition
Activities given up because of use

Uses despite negative effects
Failure to fulfill major role obligations
Recurrent use in hazardous situations
Continued use despite consistent social or interpersonal problems

*not counted if prescribed by a physician
Case JB: Further History

- Medical History
  - Frequent episodes of bronchitis
  - Asthma – no admissions
  - Multiple fractures – right ankle; left wrist assoc with skiing
  - h/o concussion – playing rugby @ 16yo

- Developmental history
  - Milestones normal
  - School performance problems in Grade 5-6… (family issues)...Bullied
  - Diagnosed with ADD…treated with methylphenidate from Gr 6-8 with some improvement
  - High-school → did well in alternative, private school
Case JB: Further History

**Psych history**
- h/o depression mid-late 20s; treated
- Serial “monogamy”; sexual compulsivity
- Sexually abused by older cousin – age 9-10
- Physically, emotionally abused by father and witnessed same of mother

**Family History**
- Alcohol and cocaine use d/o in father
- “Dad used to have weird rituals”
- Paternal aunt hospitalized for “nervous breakdown”
Case JB: Substance Use

- First drink @16 yo; first drunk @ 16
- High responder
- Maximum alcohol consumption: 6 units/24 hours
- Last use – 4 years ago
- CAGE ¼
- Cocaine – first use at 16 yo: “the lights went on…I knew I would have too much fun with that…”
- 2-3 cigarettes periodically, usually with alcohol
- THC: didn’t like effect; recently smoked with friend → MARKED effect on alleviating abdominal pain
Case BB: Physical Exam & UDT

- Physical Exam
  - 34 yo man, well groomed, speech fluent, anxious, flushed, mildly diaphoretic
  - Diffuse abdominal swelling and tenderness
  - No stigmata, some piloerection
  - +++ tenderness R>L SI joint
  - P6→3 RRLA, tremor felt
  - Sensory testing: allodynia / hyperalgesia over lower abdomen and upper buttocks
  - Throat-clearing and rare blinking tics

- UDT (Immuno) U Cr 2.8  pH 6.8
  POS: Opiates, amphetamines
Pillar 3: Diagnose Pain and Treat Rationally

Nociceptive vs Neuropathic

Cancer vs Non-Cancer

Acute vs Chronic

Mild, Moderate and Severe
Pillar 3: Diagnosis: Nociceptive vs. Neuropathic

- **Nociceptive**: Normal stimulation of nociceptors
- **Neuropathic**: Abnormal nervous system activation

- **Somatic**
- **Visceral**
- **Central**
- **Peripheral**

Appropriate pharmacotherapy for pain

- NSAIDs
- Opioids
- Adjuvant
- Cannabinoids
- Topicals
Pharmacologic Steps in Neuropathic Pain

TCA ← Gabapentin or Pregabalin

SNRI ← Topical Lidocaine*

Tramadol or CR Opioid Analgesic

Fourth Line Agents **

Add additional agents sequentially if partial but inadequate pain relief***

* 5% gel or cream - useful for focal neuropathy such as postherpetic neuralgia..
** eg Cannabinoids, methadone, lamotrigine, topiramate, valproic acid
*** Do not add SNRI to TCA

Moulin et al. 2007
Non-pharmacologic therapy – 3 Ps

- Self-Management
- Cognitive and Behavioural Therapy (CBT)
- Meditation
- Mindfulness techniques
- Exercise
- Physical therapy
- Interventional approaches: nerve stimulation or block
- Acupuncture
- Botox
- ETC...
Case JB: Wasser Clinic Diagnoses

- IBD – untreated

- Chronic abdominal pain
  - Visceral nociceptive pain
  - Chronic neuropathic component
  - Poorly managed on high-dose opioids – unstable opioid regimen Meq (720 mg/day)
  - Complicated by high tolerance and likely opioid-induced hyperalgesia

- ? SI joint/ankylosing spondylitis

- Risk: high – FH+, h/o mood comorbidity, h/o trauma, LD, ? UDT result
Case JB: Wasser Recommendations

- GI – consideration of DMARD Rx, etc
- Imaging of spine, SI joints, HLA B27
- UDT: GCMS today
- d/c all hydromorphone
- Outpatient morphine taper: Kadian (morphine) 400mg qDay + Statex 10mg up to 4/day; weekly dispensing
- Taper by 10% (40mg) every 2 weeks until at 200mg/day, then reassess
- Opiate contract
- UDTs on regular basis
- Consider psych eval
A Canadian Approach to Opioids

- NOUGG – with representation from all MRAs in Canada
- Treatment of pain
- Evidence-based
- Collaborative
- Autonomy
- Clinician and Patient Input
- Practice Improvement
- Implementation
- Practice Resources
Overview of NOUGG Guidelines

1. Deciding to initiate opioid therapy

1. Conducting an opioid trial

1. Monitoring long-term opioid therapy

1. Opioids in specific populations

1. Managing opioid misuse and addiction in CNCP patients
NOUGG Guidelines

CLUSTER 1: Deciding to Initiate

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Keyword</th>
</tr>
</thead>
<tbody>
<tr>
<td>R01</td>
<td>Before initiating opioid therapy, ensure comprehensive documentation of the patient’s pain condition, general medical condition and psychosocial history (Grade C), psychiatric status, and substance use history. (Grade B).</td>
<td>Comprehensive assessment</td>
</tr>
<tr>
<td>R02</td>
<td>Before initiating opioid therapy, consider using a screening tool to determine the patient’s risk for opioid addiction. (Grade B).</td>
<td>Addiction-risk screening</td>
</tr>
<tr>
<td>R03</td>
<td>When using urine drug screening (UDS) to establish a baseline measure of risk or to monitor compliance, be aware of benefits and limitations, appropriate test ordering and interpretation, and have a plan to use results. (Grade C).</td>
<td>Urine drug screening</td>
</tr>
<tr>
<td>R04</td>
<td>Before initiating opioid therapy, consider the evidence related to effectiveness in patients with chronic non-cancer pain. (Grade A).</td>
<td>Opioid efficacy</td>
</tr>
<tr>
<td>R05</td>
<td>Before initiating opioid therapy, ensure informed consent by explaining potential benefits, adverse effects, complications and risks (Grade B). A treatment agreement may be helpful, particularly for patients not well known to the physician or at higher risk for opioid misuse. (Grade C).</td>
<td>Risks, adverse effects, complications</td>
</tr>
<tr>
<td>R06</td>
<td>For patients taking benzodiazepines, particularly for elderly patients, consider a trial of tapering (Grade B). If a trial of tapering is not indicated or is unsuccessful, opioids should be titrated more slowly and at lower doses. (Grade C).</td>
<td>Benzodiazepine tapering</td>
</tr>
</tbody>
</table>
Before initiating opioid therapy, consider the evidence related to effectiveness in patients with chronic non-cancer pain.

<table>
<thead>
<tr>
<th>Examples of CNCP conditions for which opioids were shown to be effective in placebo-controlled trials*</th>
<th>Examples of CNCP conditions that have NOT been studied in placebo-controlled trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tramadol only</strong></td>
<td><strong>Weak or strong opioid</strong></td>
</tr>
</tbody>
</table>
| **Fibromyalgia** | • Diabetic neuropathy  
• Peripheral neuropathy  
• Postherpetic neuralgia  
• Phantom limb pain  
• Spinal cord injury with pain below the level of injury  
• Lumbar radiculopathy  
• Osteoarthritis  
• Rheumatoid arthritis  
• Low-back pain  
• Neck pain | • Irritable bowel syndrome  
• Pelvic pain  
• Temporomandibular joint dysfunction  
• Atypical facial pain  
• Non-cardiac chest pain  
• Lyme disease  
• Whiplash  
• Repetitive strain Injury  |

*A limitation of these trials was that the duration of opioid therapy was a maximum of three months.
Opioid Efficacy – NOUGG Review

- The updated systematic review of opioids for CNCP included 62 randomized trials.
- Opioids were compared to placebos in 47 randomized trials.
- The effect size for improvement in pain was medium (0.58 95% CI: 0.48 to 0.67, extracted from 47 RCTs).
- For functional outcomes, the effect size was small (0.34 95% CI: 0.25 to 0.43, extracted from 31 RCTs).
GCMS

POS fentanyl, norfentanyl
Hydromorphone
Alprazolam
D-methamphetamine, amphetamine
Pay no attention to that man behind the curtain....
Urgent Follow-Up

UDT results reviewed
Additional history obtained

- Accessing opioids from street – fentanyl → smoking

- Started using methamphetamine to counteract sedation associated with opioid use

- Benzos to counteract amphetamines
Reformulation of Dx and Plan

Substance use disorder – opioid, amphetamines, benzos
IBD – untreated
Chronic abdominal pain
? SI joint/ankylosing spondylitis

Refer to Medical Withdrawal Service at CAMH

Discontinue all opioids – rotate onto Suboxone for pain/opioid use disorder

Follow-up at CAMH
For patients with chronic non-cancer pain who are addicted to opioids, three treatment options should be considered:

1. Methadone or buprenorphine treatment (Grade A)
2. Structured opioid therapy (Grade B), or
3. Abstinence-based treatment (Grade C)

Consultation or shared care, where available, can assist in selecting and implementing the best treatment option (Grade C)
Methadone – Treatment for Addiction and Pain

- Full opioid agonist
- NMDA antagonist \(\rightarrow\) neuropathic pain and tolerance
- Long-acting: Elimination half-life = ~ 22 hours (5-130 hr interindividual variability)
- Reduces illicit opioid and other drug use
  - Cocaine
  - Amphetamines
  - Sedatives
  - Cannabis
- NB: Counseling, adequate dosing, contingency management, harm reduction program orientation
- Few studies on effectiveness of MMT for prescription opioid dependence
- Better treatment retention compared to Suboxone
Methadone Toxicity

- 7-fold increase in methadone Rxs 1997 – 2004
- 17-fold increase in mortality

Methadone Toxicity

• Methadone overdose deaths and sales rates in the US peaked in 2007.

• In 2010, methadone accounted for 3% of opioid Rxs nationally

• 39.8% of single-drug opioid-related deaths

• Involved in 31.4% of OPR deaths

• Overdose death rate for methadone far outranked that for other OPR multi-drug and single-drug deaths

CDC 2013
Clinician Knowledge and Therapeutic Alliance Reduces Risk & Improves Outcomes

One of the biggest barriers to appropriate treatment of chronic non-cancer pain and addiction is insufficient pain management education for physicians

Why Bup/Nal vs Methadone?
Ontario Drug Benefit – LU Code 437

For the treatment of opioid dependence in patients who have failed, have significant intolerance, have a contraindication to, or who are at high risk for toxicity with methadone

- use of benzodiazepines
- alcohol abuse or dependence
- elderly
- patients who are dependent on codeine or abuse opioids on a less than daily basis
- on medications that interfere with methadone metabolism
- at high risk for prolonged QT interval.

NOTE: Physicians should complete an accredited course on opioid addiction and buprenorphine treatment before prescribing Suboxone.

http://www.camh.ca/en/education/about/AZCourses/Pages/BUP.aspx
Buprenorphine

- Partial opioid agonist
- Ceiling effect
Buprenorphine - Pharmacology

- Lipophilic → ideal for TD preparations (vs 40% S/L bioavailability)
- Slow-onset and long-offset
- Transmucosal route – even longer… t1/2 19-27 hr
- High affinity to u-opioid receptor…competing with other opioids that bind there
- Has slow rate of dissociation from u receptor → prolonged duration of action compared with other opioids
- Agonist at delta -OR and ORL receptors
Buprenorphine - Pharmacology

- ORL-1
  - In brain - anti-analgesic effect in animals; dampens dopaminergic reward system
  - At spinal level – anti-nociception
  - Slows onset of opioid tolerance
  - Agonism…may be effective for treatment of neuropathic pain

- KAPPA-OR ANTAGONIST…blocks dysphoric and psychotomimetic effects of K agonism

- Inhibition of voltage-gated Na channels
Buprenorphine - Pharmacology

- Metabolized though hepatic CYP3A4 (primary), CYP2C8, CYP2C9
  - 3 metabolites: norbup, norbup-3-glucuronide, bup-3-glucuronide
  - Glucuronide-conjugated byproducts eliminated in feces by biliary excretion 4-6d after admin
  - Minimal urinary excretion

- All analgesic EXCEPT norbup-3-gluc

- Norbup and norbup-3-gluc → RESP DEPRESSION, SEDATION…
  - NOT so with bup and bup-3-glucuronide

- NB other meds that compete for metabolic pathways..eg benzos
Hyperalgesia: “Opioid-induced Pain”

Tolerance

resistance to opioid

desensitization  down-regulation

↑ Dose

Hyperalgesia

hyperesthesia +/- allodynia

- anatomically distinct
- qualitatively different
- long- and short-term therapy

NMDA

Dynorphin

μ-opioidRc

↑ cAMP

↓ Dose
Possible Antihyperalgesic Action of Buprenorphine

Pergolizzi J et al. Pain Practice. 2010
Partial Agonist?

Partial agonist = inability to produce the same level of effect as some reference full-agonist drug in a given situation

- What do we mean?
  - Intrinsic activity → biological stimulus imparted by drug to a receptor
  - Efficacy → level of drug-induced effect for a given outcome (manifested at a particular endpoint) eg…ANALGESIA, RESP DEPRESSION

- BUP has low in vitro intrinsic activity as measured in several receptor binding assays → PARTIAL AGONIST MONIKER

- Does BUP produce less effect compared to a reference drug?

Partial Agonist?

- Morphine also produces <100% effect
- Bup acts at multiple receptors → total analgesic effect results from activity at several receptors
- Bup displays > 98% noci efficacy in animal models
- PET scans of human brains show that full analgesia achieved with bup doses that occupy < 100% of opioid receptors

Buprenorphine – Full Agonist – Clinical Evidence

- Inclusion: human, within-study comparison of same pain type and with drugs commonly considered to be full agonists, quantification of pain severity or pain relief; comparison using the same pain scales

- EXCLUSION: non-human; use as part of a combination; use in opioid addiction (e.g., Suboxone)

- 24 clinical trials identified + 1 case report and 1 dose-response curve

- Based on complete or comparable pain relief, buprenorphine had full clinical analgesic efficacy in 25/26 of these studies

- Tiggerstedt et al (1980) im bup vs im morphine
  - Post-op pain,
  - Randomized, double-blind, multiple-dose, non-crossover trial
  - 60 pts p abdominal surgery

Buprenorphine – ? Ceiling

- Analgesic efficacy of iv buprenorphine
- Post-op over 24 hours
- 50 pts recovering from elective C-section
- Received bup in 0.2mg aliquots over 3-15 mins until pain relieved
- All px achieved complete analgesia with 0.4 – 7mg buprenorphine

Budd K et al. Anaesthesia. 1981
Potential Advantages of Buprenorphine in Chronic Pain

- Efficacy demonstrated in various pain conditions, comparable to “full agonists”

- Ceiling effect for respiratory depression

- Less development of tolerance via KAPPA antagonism, ORL agonism

- Antihyperalgesic effect

- Less effect on hypogonadism (ORT experience)

- Less immunosuppression compared with morphine and fentanyl (limited evidence – preclinical and clinical)

- Ease of use un elderly and in renal impairment

- ? Efficacy in neuropathic pain
Bup-Nal s/l for chronic pain

- AIM: systematic review of s/l bup for chronic pain

- ELIGIBILITY: cancer and non-cancer pain using s/l bup and bup/nal

- EXCLUSION: acute pain, peri-operative, opidep, opidep with pain, NAS, medically supervised w/d, non-s/l routes all excluded

- 10 studies met inclusion criteria
  - 1979 – 2012
  - 1,190 px from US and Europe
  - N: 5-453
  - Duration: few days – 8.8 months (2 didn’t report duration)

Cote J et al. Pain Medicine 2014
Bup-Nal s/l for chronic pain

- ALL observational except 1 RCT
- 4 studies – general chronic pain; others OA, SCD, nociceptive cancer pain, chronic pain in the elderly; pediatric chronic ca pain; chronic ca pain
- Manufacturer funding, provision of drug, or conflict of interest 5/10 trials
- 4 studies → with prior opioid therapy → MED up to 840mg/day
- 6 studies—used initial low dose (<400ug)

- No trials deemed high quality evidence
- ALL Studies reported s/l bup demonstrated some effectiveness for analgesia in chronic pain
- Due to lack of high-quality trials→ there is insufficient evidence to determine effectiveness of s/l buprenorphine for the treatment of chronic pain
- NEEDS MORE HIGH-QUALITY TRIALS

Cote J et al. Pain Medicine 2014
But....

AIM:
- Evaluate effectiveness of conversion to Bup/Nal SL for patients with significant levels of persistent pain on high doses of full agonist opioid medication (200 – 1370 MEqD)
- Continuous or worsening pain despite opioid analgesia;
- MEq >200mg/day
- Remain on bup s/l after initial conversion for 60 days
- Conversion at home

- Primary outcome: reduction in self-reported pain after conversion to Bup/Nal S/L
- Secondary outcome: change in QOL

RESULTS:
- 51% reduction in pain score: 7.2 – 3.5 (P <0.001) reporting reduced pain
- QOL: 6.1 – 7.1 (P= 0.005)...

Tolerance and poor analgesia with increasing doses of opioids may be exhibiting OIH...

Clinical experience: Many patients can and do begin to reduce dosage of bup/nal after 4-6 months of therapy post rotation

Limitation: chart review with no control group
Back to the beginning…

- How to treat chronic pain in patients with substance use disorder?
- Current guidelines: 1) methadone; 2) buprenorphine; 3) no opioids
- Methadone…properties, risks
- Need evidence-based guidelines to manage more effectively pain in patients with opioid dependence
- Blondell et al (2010): treatment with steady doses of bup/nal for 6 months resulted in superior treatment retention vs detox with abstinence
- → POORLY MANAGED PAIN IN OPIOID DEPENDENT PATIENTS INCREASED RISK OF RELAPSE

Neumann AM et al. J Addict Dis. 2013
Methadone vs Bup/Nal in Chronic Pain and Addiction

- RCT: compare influence of 6 months of methadone and bup/nal on analgesia, illicit drug use, treatment retention and function in a group of px with pain/addiction in a primary care setting

- > 18yo with well-documented CNCP PLUS addiction to prescription opioids

- Excl: homeless, parole, unable to consent, co-occuring psych, prolonged QT or previous cardiopulm issues, taking med contraindicated with methadone or bup, h/o ORT, pregnant

- N= 54 randomly assigned to one of two 6 month treatment protocols
  - Bup/nal  4-16mg divided 1-4 daily (26)
  - Methadone 10-60mg/day (28)

- Requested to participate in chem dependency treatment for 12-16 weeks, encouraged to attend 12-step, no other use

- Monthly f/u, UDT at each visit

Neumann AM et al. J Addict Dis. 2013
Methadone vs Bup/Nal in Chronic Pain and Addiction

RESULTS

- Across both conditions, significantly less pain at 6 months (5.5) than at initial (6.3) P: 0.043… **12.75 % reduction in pain** at medium effect size
- No difference in treatment retention between two treatments
- At 6 months, 5 pts in bup/nal reported use of opioids vs none in methadone group (P: 0.039)
- No significant change in function from baseline

Neumann AM et al. J Addict Dis. 2013
Methadone vs Bup/Nal in Chronic Pain and Addiction

- Both BUP/NAL and methadone can be used to treat chronic pain in patients with opioid dependence
- Small analgesic effect
- No significant difference in function (? NRS not sensitive enough to assess)
- Treatment retention NO DIFFERENCE between methadone and Bup/Nal (per previous)
- More illicit opioid use with Bup/Nal → consistent with previous research
- UDT pos cocaine associated with non-completion of treatment…echoes poorer outcomes/retention opidep populations
- LIMITATIONS: small open label study, not double-blind and double-dummy

Neumann AM et al. J Addict Dis. 2013
Back to JB…

- Substance use disorder – opioid, amphetamines, benzo
- IBD – untreated
- Chronic abdominal pain
  - Visceral nociceptive pain
  - Chronic neuropathic component
  - Poorly managed on high-dose opioids – unstable opioid regimen Meq (720 mg/day)
  - Complicated by high tolerance and likely opioid-induced hyperalgesia
- ? SI joint/ankylosing spondylitis
- Refer to Medical Withdrawal Service at CAMH
- Discontinue all opioids – rotate onto Suboxone for pain/opioid use disorder
- Follow-up at CAMH
JB – 4 months later

- Admitted to Medical Withdrawal Unit
- Suboxone titrated to 8mg total daily dose
- Nabilone 0.5mg BID
- FP taking over Suboxone prescribing, etc (through ECHO telementoring)
- Followed by GI → started DMARD → UC in remission

- Allodynia and hyperalgesia resolved
- Moderate abdominal pain - aching/sometimes cramping 3-4/10 → negligible on current regimen

- Participation in Power Over Pain group
- Participation in 12-step program: Sober since discharge!
- Returned to work 1 month ago
- Back to gym
**Pillar 5: Personal Responsibility and Self-Management**

- Who’s working harder?

- Lack of buy-in and self management is likely a key component of the ‘refractory’ patient

- Proactive management of realistic expectations

- Need to educate patient and family about pain management techniques

- Therapeutic alliance is key

- Clinicians need to practice (not just talk about) interprofessional model
  - Lack of prompt recovery → we tend to repeatedly apply medical model – more consults, tests, drugs
  - Other modalities – psychological and otherwise – are left out
Pain as a Motivational Disorder

- A daily reminder of derailment
- Traumatic
- Robs assertiveness
- A neurological signal to cease and desist
- Multifactorial – multiple concurrent disorders
- Overwhelming
- Isolating
Pillar 5: Pain Recovery

- Reimagining pain from uncontrollable to manageable
- Fostering optimism and combating despair
- Promotion of patient feelings of success, self-control and efficacy
- Patients attribute success to their own role
- Education in specific skills: pacing, relaxation, problem-solving
- Emphasis on active patient participation and responsibility
Treating Acute Pain in MMT Patients

G11.5
For patients with acute pain that warrants short-term opioid therapy, MMT physicians may temporarily split the methadone dose with an additional 10-15 mg evening dose, or prescribe opioids in addition to methadone.

G11.6
If opioids are prescribed for acute pain, the MMT physician should choose an opioid that the patient has not misused in the past, and dispense the opioid in small amounts (controlled dispensing).

The MMT physician should limit the prescription to the number of days that opioids are typically needed for that particular acute pain condition.
Chronic Pain in MMT

G11.8
The MMT physician may prescribe methadone in split doses for patients with severe chronic pain who require opioids. Usually this should only be done after the patient is on a stable once daily dose and is receiving 5-6 take-home doses per week.

G11.9 **CAUTION**
The MMT physician should only attempt long-term opioid therapy for methadone patients with chronic non-cancer pain if:
1) the patient has severe pain from a well-documented diagnosis of a serious nociceptive or neuropathic condition that would usually require opioid analgesics.

1) the patient has had insufficient analgesic benefit from an adequate trial of non-opioid treatments and from a trial of split methadone dosing.
Acute-On-Chronic Pain

G11.10

If opioids are prescribed in addition to methadone, the recommended opioids for most patients are codeine and tramadol, followed by morphine.

The MMT physician should use strategies to minimize diversion and misuse.

The MMT physician should periodically attempt a trial of opioid tapering, particularly in patients on higher opioid doses who continue to report severe pain.
Thank You!