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Psychiatry and Addictions Case Conference

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PAIN AND OPIOID USE DISORDER

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SPEAKER DISCLOSURES

✓ No relevant conflicts of interest

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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PAIN AND OPIOID USE DISORDER (OUD)

- Chronic pain and OUD in patients taking long-term opioids
  - –Clinical approach to patients on long-term opioid
  - –Chronic pain treatment
- Managing pain and OUD in hospitalized patients
- Pain in patients taking medication for OUD

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AN “INHERITED” CASE

- 55 yo man with history of failed back surgery on high dose opioids, whose primary care physician recently retired
- Currently taking long-acting oxycodone 90 mg BID and short-acting oxycodone 15 mg 4/day
- Few urine tests done, but each was appropriate
- PDMP shows no additional prescriptions
- PHQ-9 is 16 “because I hurt so much”
- Inactive because “moving makes it worse”

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PAIN AND ADDICTION: COMMON THREADS

- Similar risk factors: SDH, adverse childhood experiences
- Similar neurobiology
- Chronic, recurrent problems
- Treatment involves medication, self-management, and social support
- High dose opioid prescribing is more common in patients with mental health and addiction issues
- High doses are a key risk for patients

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CO-OCCURRENCE PAIN & ADDICTION

- Rates of chronic pain are high in those on MOUD
  - –Methadone: any chronic pain >60%, severe chronic pain 37%
  - –Buprenorphine: chronic pain 36-50%
- In patient with chronic pain, OUD rates vary
  - –Those on long-term opioid therapy, 26% with OUD
  - –Other samples vary, 8-24% with OUD
- NSDUH 7% of those taking opioid pain medication in last year had OUD (includes acute and chronic pain)

PAIN HISTORY PEARLS

- Pain story from the beginning – use reflection!
- Current level of function (activity, sleep)
- Pain related goals
- Co-morbid conditions (apnea, hypogonadism, depression, inactivity)
- Upbringing (ACEs, addiction history going way back)
- “Side effects” including constipation, low energy, poor concentration, thinking about opioids, concerns about addiction/loss of control, others are worried

CDC-Kaiser ACE Study

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RAISING THE ISSUE

- “What have you heard about the risks of opioids?”
- “We didn’t know of these problems when you started”
- “Guidelines suggest avoiding opioids for chronic pain”
- “I am worried about your safety and health over time”
  - Overdose, loss of control, apnea, falls, mood, less sexual satisfaction, increased pain sensitivity
- “Lower doses are safer and some patients have more energy after a taper”
- “We have time to try different things, and go slowly”
- Provide naloxone and rationale for use, including engaging others

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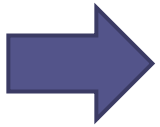
DON'T RUSH THE TAPER!

- While higher doses are less safe than lower doses, tapering is also risky
- Multiple studies demonstrate the risks
- Among 19,377 patients with stable doses >50 mg MED whose dose was tapered >15%, the post-taper period was associated with:
  - Higher incidence of acute care for overdose or withdrawal (incidence RR 1.57)
  - Higher incidence of mental health crisis (incidence RR 1.52)
- Faster tapers are associated with worse outcomes, including mortality
- Care must be taken if tapering from a stable opioid dose is considered

Fenton JJ, et al. *JAMA Netw Open.* 2022;5(6):e2216726
Metz VE, et al. *JGIM*. 2023;39, 1002-9 (2024)

OPIOID USE DISORDER – DSM-5

OPIOID USE DISORDER
Larger amounts than intended
Persistent desire to cut down or quit
Significant time spent taking, obtaining
Craving or urge to use
Failure to fulfill obligations
Continued use despite negative interpersonal consequences
Reduced social, recreational activities
Use in physically hazardous situations
Use despite knowledge of harms
Tolerance (excludes rx medication)
Withdrawal (excludes rx medication)
* Recurrent legal problems deleted



SEVERITY
No SUD: 0-1
Mild: 2-3
Moderate: 4-5
Severe: >5

Moderate-severe OUD ≈ opioid dependence (DSM-IV)

Key principles:
- Negative consequences
- Cravings
- Tolerance
- Withdrawal

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DIAGNOSING OPIOID USE DISORDER

- “Are you concerned about addiction or loss of control of you medication?” “Have others been concerned?”
- “Do you sometimes have worse pain and take more medication, then go without later to make it up?”
- “Have you wanted to cut down or quit?” “Why?”
- “Do you find yourself thinking a lot about your pain medication?”
- Is reduced function a result of pain or opioids?
- Are side effects included in the “continued use in spite of consequences” criteria?

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RATIONALE FOR SWITCHING TO MOUD

- Medication treatment for OUD with buprenorphine or methadone is safer than high dose opioids
- Data is limited, but many patients do well with a transition to buprenorphine
- Side effects from opioids, in particular sedation and withdrawal, are often reduced, increasing function
- Stabilizing the patient's opioid systems allows for other forms of pain treatment

“BUT I’M NOT AN ADDICT!”
“I DON’T HAVE A SAFETY PROBLEM!”

- Acknowledge that it is about what happened to them, not who they are
- “Many patients develop OUD as a result of pain treatment”
- Review DSM-5 criteria
- Acknowledge stigma of OUD and high dose opioids for pain
- Buprenorphine for pain is increasingly accepted
- “Do you imagine you will be on high doses of opioids for the rest of your life?”

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WHO SHOULD SWITCH TO BUPRENORPHINE?

- Anyone with an opioid use disorder that is leading to unsafe medication use – yes!
- Patients with opioid use disorder and chronic pain whose function has not improved with high dose chronic opioid therapy – yes
- Any patient with opioid use disorder on high dose opioids – probably worth a trial
- Any patient on high dose opioids – maybe for safety*
- Patients getting functional improvement with low dose opioids – no (maybe taper, maybe not)

* Many buprenorphine products not FDA approved for pain treatment

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TAPER OR SWITCH?

- Offering buprenorphine or taper is a reasonable approach for many patients on higher dose opioids
- Do not taper without buy-in from the patient
- 10% initial reduction should avert most acute withdrawal, but go slowly, adjust, or pause if needed
- OUD diagnostic criteria can emerge as doses are tapered, so continue to offer buprenorphine
- Safety problems may require a more directive approach
- New methadone regulation allow split dosing and quicker take-home doses, so may be an option

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LEARN TO TREAT CHRONIC PAIN

- Opioids for pain or OUD are not the whole plan!
- Educate patients that chronic pain is a disorder not well explained by tissue damage
- Diagnose and treat depression, anxiety, and PTSD
  - Improves pain outcomes
- Use non-opioid pain medications
  - Tricyclic antidepressants for sleep, pain
  - Anticonvulsants, SNRIs for neuropathic pain
- Emphasize active non-medication treatments

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RANDOMIZED TRIAL OF OPIOIDS VERSUS NON-OPIOIDS

- 240 Veterans with moderate-severe chronic back pain or hip/knee OA randomized to opioids versus non-opioids and assessed over 12 months
- Monthly pharmacist visits, compared two prescribing strategies
- Primary outcome was pain-related function (BPI), and pain intensity (BPI) and adverse affects were secondary outcomes
- Results showed no difference in pain-related function, but pain intensity was lower in the non-opioid group
- There were more adverse effects in the opioid group

Krebs EE *JAMA*. 2018;319(9):872-882.

OPIOIDS VERSUS NON-OPIOIDS FOR CHRONIC PAIN

- Opioid prescribing strategy
  - Step 1: IR morphine, oxycodone IR, or hydrocodone/acetaminophen
  - Step 2: morphine SR, oxycodone SR
  - Step 3: fentanyl patch
  - Single opioid preferred not required, max dose 100 mg MED, could rotate opioid if no response
- Non-opioid prescribing strategy
  - Step 1: acetaminophen and NSAIDS
  - Step 2: adjuvants (oral nortriptyline, amitriptyline, gabapentin and topical lidocaine, capsaicin)
  - Step 3: pregabalin, duloxetine, tramadol

A CHRONIC PAIN TREATMENT PLAN

- **Opioids:** May include monitoring (urine, PMP)
- **Non-opioid medications:** For depression, anxiety, PTSD, sleep, pain
- **Non-medication treatments:**
  - Passive
  - Active
- Goal is spending more time on active strategies that the patient implements

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ASSESSING PAIN TREATMENTS

- Passive
  - Medication
  - Surgery/injections
  - Acupuncture
  - Massage
  - Chiropractic
  - TENS
  - Myofascial release
- Active
  - Exercise/activity
  - Physical therapy
  - Coping skills
  - Sleep hygiene
  - Mindfulness skills
  - Biofeedback
- It’s about behavior change!

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COGNITIVE BEHAVIORAL THERAPY FOR CHRONIC PAIN

- Evidence-based skill building intervention
- Changes the focus to what patients can do for themselves
- Includes education: chronic pain ≠ tissue damage
- Can use Managing Chronic Pain: A Cognitive Behavioral Therapy Approach by John Otis
- YouTube video: “Understanding pain: what to do about it in less than five minutes” at https://www.youtube.com/watch?v=C_3phB93rvI

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COGNITIVE BEHAVIORAL THERAPY TOPICS

Pain Modifier	CBT Topic
• Poor sleep?	• Sleep hygiene
• Too much or too little activity?	• Time-based pacing
• Muscle tension?	• Progressive relaxation
• Restricted breathing?	• Diaphragmatic breathing
• Negative thoughts?	• Cognitive restructuring
• Increased stress?	• Stress management
• Anger?	• Anger management
• Not having any fun?	• Pleasant activity scheduling

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EXAMPLE: TIME-BASED PACING

- “Both too much exercise and too little exercise makes pain worse. How about for you?”
- “Everyone with chronic pain needs an activity they can do pretty much every day.”
- Assess current activity level and find one that they can commit to trying **nearly every day**.
- Can become a functional metric to follow over time

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DO NOT ABANDON YOUR PATIENTS!

- They are very vulnerable
- They are at risk to die
- They need your support
- Learn to use buprenorphine so you don't have to refer
- Make it clear that whatever the opioid plan may be, you want to remain their provider
- Take a broad approach to treating chronic pain

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HOSPITAL TREATMENT OF PAIN AND OUD

- Initial evaluation in the hospital
- Inpatient pain and withdrawal management
- Choice of ongoing MOUD
- Low-dose buprenorphine initiation

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INITIAL EVALUATION

- Most patients will not be seeking OUD treatment prior to admission
- Many/most will have acute pain
- Withdrawal and pain management is urgent to allow access to medical/surgical treatment and to avoid patient directed discharge
- Acute illness will take priority until later in the hospital stay, when outpatient MOUD can be decided
- “Do you want to talk now or get your withdrawal treated first?”
- Fentanyl adds urgency to need for acute withdrawal treatment
  - High dose fentanyl may need rapid treatment

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MEDICATION FOR PAIN AND WITHDRAWAL

- For most inpatients, methadone is preferred
  - Works quickly, familiar to patients
  - Reduces need for high dose full agonists for pain
  - Start with 30-40 mg and **reassess in 2-3 hours**
  - Can add 10 mg prn doses the first day
  - Give total 1st day's dose the next morning
  - Treat subjective opioid withdrawal symptoms
- If no acute pain condition and in withdrawal (not common), buprenorphine can be initiated at full dose

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INITIAL PAIN AND WITHDRAWAL RX

- Quickly provide both if needed!
- Use short-acting full agonists at adequate doses for acute pain
- Consider PCA or scheduled oral opioids when patient is using high-dose fentanyl
- Treat promptly in collaboration with nursing
- Re-evaluate the patient within 2 hours to provide reassurance and additional treatment if needed
- Active management helps!

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CHOOSING A SHORT ACTING OPIOID

Opioid Receptor Affinity

Drug	K_i (nM)	Drug	K_i (nM)	Drug	K_i (nM)
Tramadol	12,486	Hydrocodone	41.58	Butorphanol	0.7622
Codeine	734.2	Oxycodone	25.87	Levorphanol	0.4194
Meperidine	450.1	Diphenoxylate	12.37	Oxymorphone	0.4055
Propoxyphene	120.2	Alfentanil	7.391	Hydromorphone	0.3654
Pentazocine	117.8	Methadone	3.378	Buprenorphine	0.2157
		Nalbuphine	2.118	Sufentanil	0.1380
		Fentanyl	1.346		
		Morphine	1.168		

Affinity measures how tightly an opioid binds the receptor

Higher Affinity = Increased percentage of a time period in which the ligand interacts with mu-opioid receptors

Higher Affinity = lower K_i

Volpe 2011

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FOR PATIENTS ALREADY ON MOUD

- Don’t mess with the methadone or buprenorphine!
  - Consider splitting the dose (check with the patient first)
- Verify methadone dose with opioid treatment program
- Treat acute pain with short-acting full agonists
  - Will likely need higher doses due to tolerance
- Do not hold MOUD in the intensive care setting

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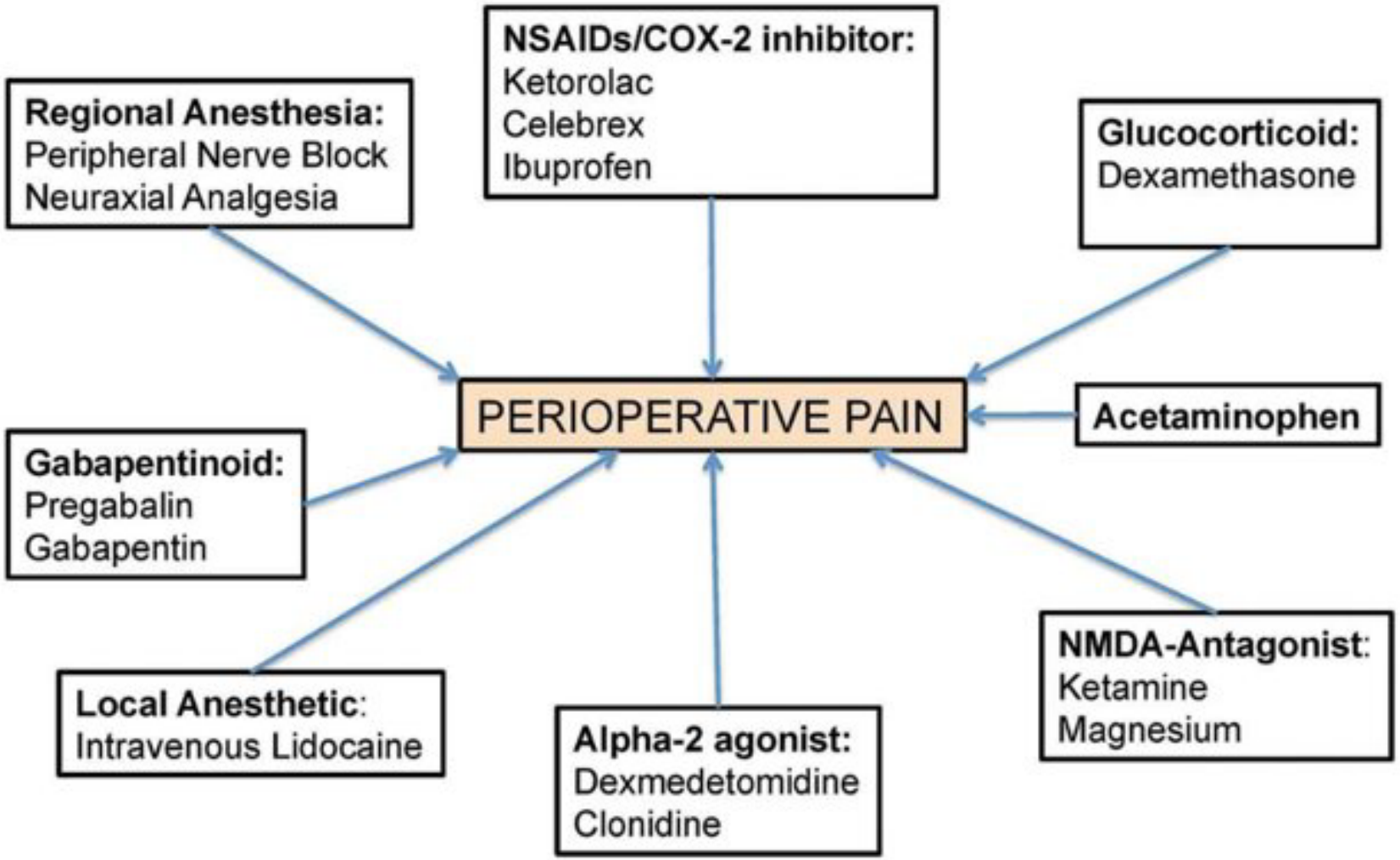
Multimodal Opioid-Sparing Analgesia



Gabriel et al, Expert Opin Pharmacother. 2019 Jun;20(8):949-961

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CHOICE OF ONGOING MOUD

- Take time, sit down, and listen
- Don’t assume everyone will want MOUD long-term
- Provide harm reduction resources (Narcan, etc.)
- Assess prior experiences with buprenorphine
  - Precipitated withdrawal or worsening fentanyl withdrawal?
- Present methadone and buprenorphine as similarly effective, but delivered in different settings

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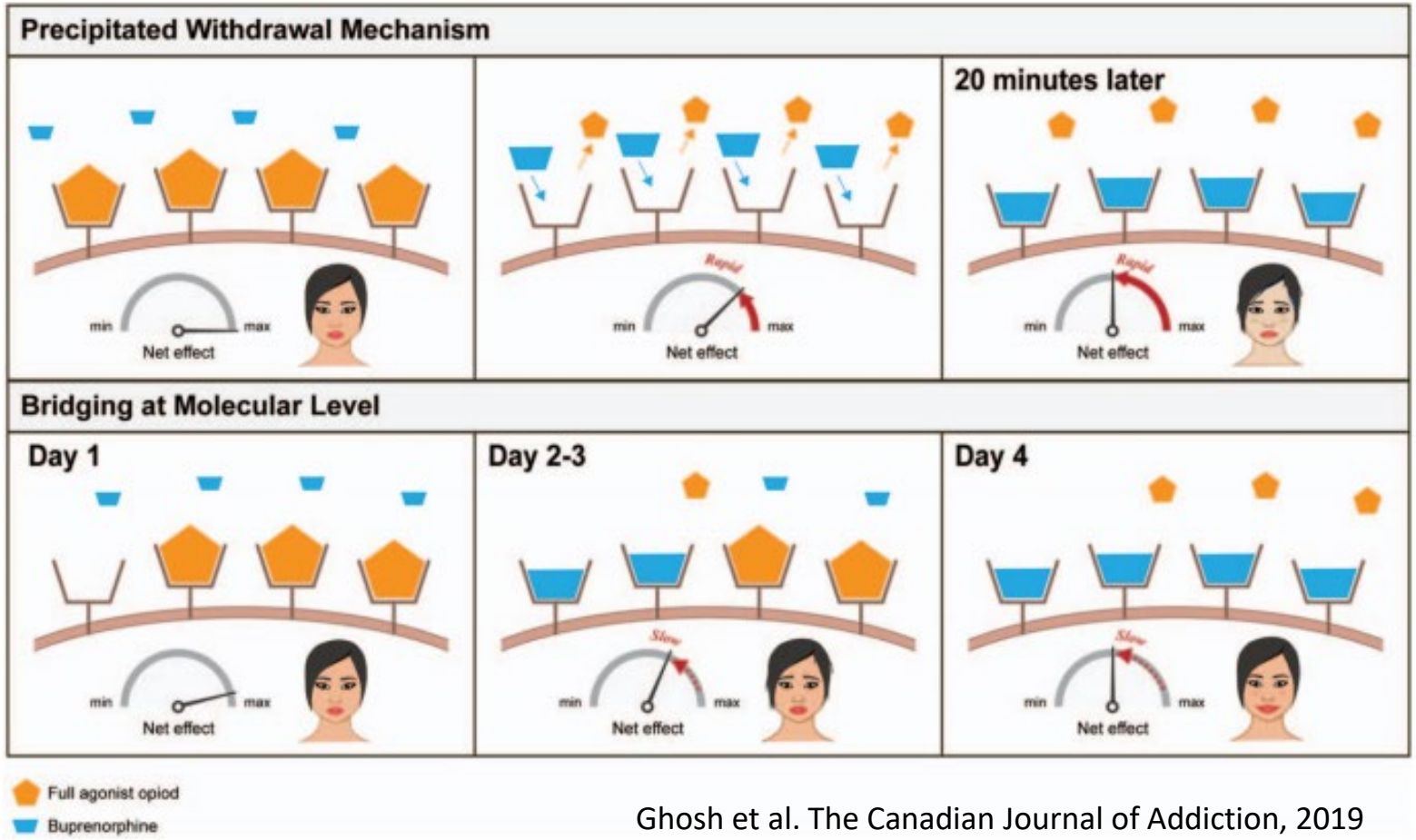
BUPRENORPHINE INITIATION

- Standard initiation is difficult in the hospital due to concurrent short-acting full agonist opioids for pain
- Low-dose initiation without stopping full agonists is a promising/acceptable option
- Uses slowly increasing doses to avoid precipitated withdrawal
- Literature limited to case reports and two substantial retrospective inpatient cohorts
- Low-dose initiation shows less promise in the outpatient setting, likely due to difficulty continuing full agonist opioids

Button D, et al. J Addict Med. 2022 16(2);e105-e111
Bhatraju EP, et al. J Addict Med. 2022 16(4);461-5

MECHANISM OF LOW-DOSE INITIATION



Ghosh et al. The Canadian Journal of Addiction, 2019

Low doses ease buprenorphine onto receptors, slowly displacing full agonists and avoiding precipitated withdrawal

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SAMPLE 1-WEEK DOSING SCHEDULE

Day	Actual Dose/Day	Fraction of Buprenorphine-Naloxone Film	Opioid
Day 1	0.5mg once	1/4 film (2/0.5mg) once	Continue current dose
Day 2	0.5mg BID	1/4 film (2/0.5mg) BID	Continue current dose
Day 3	1mg BID	1/2 film (2/0.5mg) BID	Continue current dose
Day 4	2mg BID	1 film (2/0.5mg) BID	Continue current dose
Day 5	4mg BID	2 films (2/0.5mg) BID	Continue current dose
Day 6	8mg daily	1 film (8/2mg) once	Continue current dose
Day 7	8mg in AM, 4mg in PM	1 film (8/2mg) in AM ½ film (8/2mg) in PM	STOP opioid
Ongoing	8mg BID	1 film (8/2mg) BID	

Adapted from Marwah, et al. *Can Fam Physician*, 2020. Terasaki, et al Pharmacotherapy 2019

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PAIN IN PATIENTS TAKING MOUD

- Confusion among providers about best practices
- Surgeons may be reluctant to perform elective surgeries, fearing difficulty with perioperative pain control
- Assumed buprenorphine would block analgesia
- Prior guidelines suggested stopping buprenorphine before surgery
- New guidance and general consensus: “don’t mess with the bup!”
- For both methadone and buprenorphine, patients may need higher opioid doses for pain control

Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction TIP 40 CSAT 2004
J Addict Med. 2020 Mar/Apr;14(2S Suppl 1):1-91.

ACUTE PAIN AND MOUD

- Options for acute pain and MOUD (e.g. acute dental issues, ankle fracture)
  - Multimodal pain management (e.g. acetaminophen and NSAIDS taken together, gabapentin, diclofenac)
  - Split the buprenorphine dose – analgesic effect 6-8 hours
  - Increase the buprenorphine dose (maybe, if on a low dose to start)
  - Add full agonist opioid – buprenorphine will not block analgesia
- Make patient-centered decisions

Alford DP, Compton P, Samet JH. Ann Intern Med. 2006

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SURGICAL PLANNING AND MOUD

- Elective or semi-elective surgeries (THA, ankle fracture needing surgery)
- Communication with surgery team very helpful
  - Advocate/reassure about safety, current addiction status (in treatment)
  - Offer to manage pain post or peri-op
- Options:
  - “Don’t mess with the bup (or methadone)!”
  - “Don’t let anybody else mess with the bup!”
  - Multimodal pain management – consider involving pain specialists
  - Some recommend lowering the buprenorphine dose to 12-16 mg before surgery if its high – no evidence
  - Use full agonists anticipating the need for higher doses

PAIN AND OPIOID USE DISORDER

- Chronic pain and addiction overlap in complex ways and touch many parts of the medical system
- Patients with OUD and pain are at risk for poor outcomes both in the clinic and when hospitalized
- Best result will include plans for opioid medications, non-opioid medications, and non-medication treatment plan

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QUESTIONS OR COMMENTS?

Thanks to Jonathan Buchholz, Amy Kennedy, Jim Walsh and the Swedish Addiction Medicine fellows for selected slides and ideas