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An overview of Medication Assisted Treatment (MAT) and acute pain management on MAT

Victoria Martineau, PharmD
Patricia Pade, MD, FASAM

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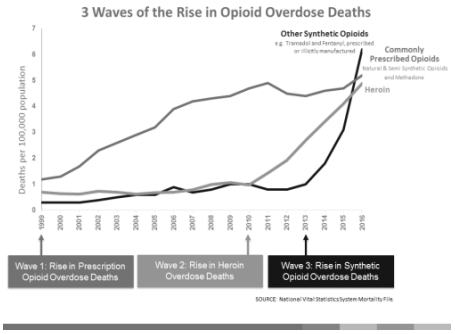
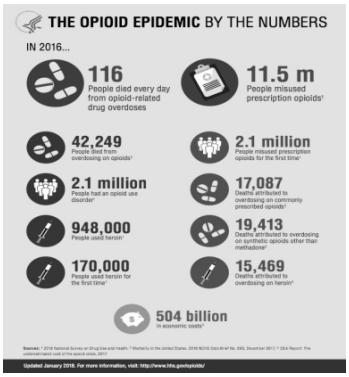
Goals of Discussion

- Recognize opioid use disorder (OUD)
- Discuss the pharmacology of medication assisted treatments (MAT) for OUD
- Describe principles acute pain control while on MAT

Both authors have no disclosures





Response to opioid crisis

- Expanded access to Medication Assisted Therapy (MAT)
  - PAs and NP can now prescribe/Increased limits on Office Based Opioid therapy
  - Expansion of telemedicine
  - ED initiation of treatment
  - Enhanced integration of behavioral health in primary care
- Promotion of harm reduction measures
  - Overdose education and naloxone for rescue
- Innovative use of community/peer support efforts
- Research in new formulations and medications
  - New formulations of buprenorphine
- Lessen opioid/controlled substance prescribing

Opioid Use Disorder (OUD)

DSM-5 Criteria - OUD

- Opioids taken in larger amounts, longer than intended
- Unsuccessful efforts to cut down or control use
- A great deal of time spent obtaining, using or recovering from use
- Craving
- Recurrent use results in failure to fulfill work, home, school obligations
- Continued use resulting in interpersonal/social problems
- Recurrent use in hazardous situations
- Important social, occupational or recreational activities are reduced due to use
- Continues use despite knowledge of physical, psychological problems related to use
- **Tolerance and withdrawal: NOT criteria if opioids are used solely under appropriate medical supervision**

SEVERITY:
Mild (2-3)
Moderate (4-5)
Severe (≥6)

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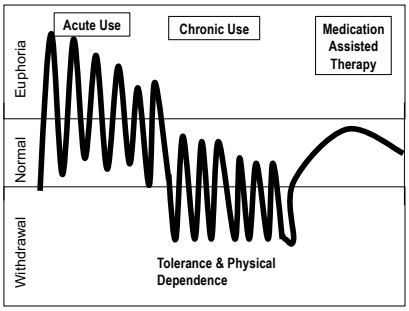
Medication Assisted Therapy



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Pharmacology of MAT

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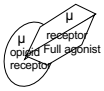
Full opioid agonist: Methadone



- Full agonist binding activates the μ opioid receptor
- Additive effect when combined with other full agonists
- Is highly reinforcing and has higher potential for abuse
- Abrupt discontinuation will result in withdrawal

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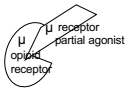
Partial opioid agonist: Buprenorphine



- Partial agonist binding activates the μ opioid receptor and kappa antagonist
- Competitive agonist with high binding affinity/slow disassociation
- Is less reinforcing than full agonists (lower risk for abuse)
- Abrupt discontinuation will result in withdrawal
- Available as sublingual, buccal, transdermal, and injection

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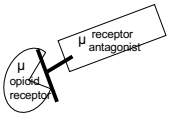
Opioid antagonists: Naloxone and Naltrexone



- Antagonist binding to the μ opioid receptor occupies without activating
- Is not reinforcing
- Blocks abused opioid agonist binding

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Methadone Pharmacokinetics

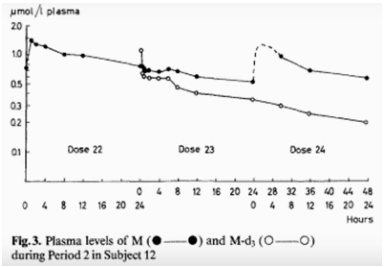


Fig. 3. Plasma levels of M (●——●) and M-d_3 (○——○) during Period 2 in Subject 12

Buprenorphine Pharmacokinetics

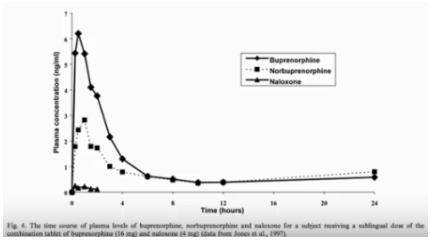
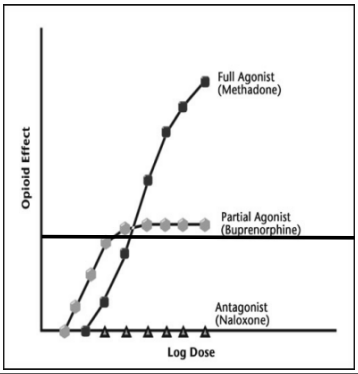
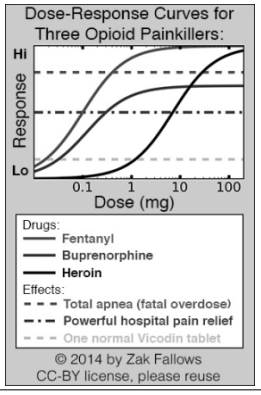


Fig. 4. The time course of plasma levels of buprenorphine, norbuprenorphine and naloxone for a subject receiving a sublingual dose of the combination tablet of buprenorphine (16 mg) and naloxone (4 mg) (data from Jones et al., 1997).





Methadone and Buprenorphine as analgesics

- Both are approved for use in chronic pain
- Daily dosing used for MAT does not provide analgesia
  - Dosing frequency must be increased due to alpha/beta phases
  - Tolerance
  - Hyperalgesia

Naltrexone

- Opioid antagonist
  - Binds competitively, but blocks opioid effect
- As oral tablet usual dose is 50 mg daily
  - t ½ = 14 hours, 50% blockade gone after 72 hours
- Comes in depo form – 380 mg IM every 4 weeks
  - Peak plasma concentration in 2-3 days, declines in 1 days
- Blocks opioid analgesia – blockade can be overcome with 6-20x the usual dose of opioids without significant respiratory depression

Acute Pain Control for Patients on MAT

Obstacles to Good Care

Providers:
- Bias and perception of OUD as moral failing, not a disease
- Physicians fear deception
- Lack of education about medications
- Providing MAT outside the mainstream of medicine
- Lack of good standards

Patients:
- Fear of mistreatment
- Fear of being judged or labeled
- Fear of withdrawal
- Studies show:
  - Active opioid use disorder - less pain tolerance than matched controls
  - On MAT – less pain tolerance
  - H/O of OUD have less pain tolerance than siblings without addiction.

General Principles

- Multi-modal pain control
- Opioid debt: Patients physically dependent on opioids (including methadone and buprenorphine) will need daily equivalence before an analgesic effect with opioids
  - Opioid analgesic requirements are often higher due to tolerance and increased pain sensitivity
  - Treating opioid withdrawal (which is painful) can improve pain management
- Giving opioids for pain will not create an addict in opioid dependent patients.

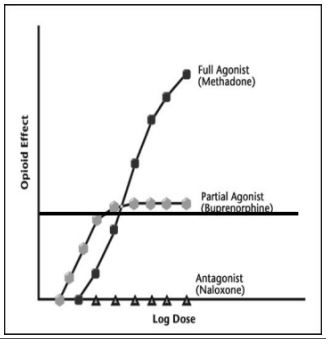
 Alford DP, Compton P, Samet JH. Ann Intern Med 2006

Multi-Modal pain control

Consider scheduled dosing for the following:
- Acetaminophen
  - Avoid combination opiate/APAP products
- NSAIDs – oral and topical
- Gabapentin
- Lidocaine patches

Other agents:
- Ketamine
- Regional anesthesia
- Short-acting opioids

Opioid debt



MAT agents

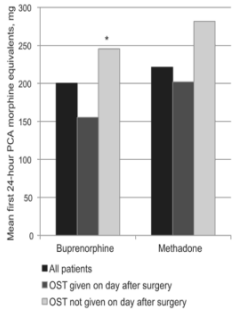
Short-acting opioids

Opioid affinities for mu receptor

Opioids	Range of Ki Value
Levorphanol	0.19 to .23[32]
Buprenorphine	0.21 to 1.5
Naltrexone	0.4 to 0.6 (antagonist effects)[20]
Fentanyl	0.7 to 1.9
Methadone	0.72 to 5.6
Naloxone	1 to 3 (antagonist effects)[20]
Morphine	1.02 to 4
Pentazocine	3.9 to 6.9
Codeine	65 to 135

Table 5. Mu Receptor Affinities of Various Opioids

Macintyre PE et al, Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy; Anaesth Intensive Care 2013; 41:222-230



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Methadone

- Contact methadone clinic – dosing will not appear in PMP
  - Verify current dose AND date of last administration
- Consider continuing outpatient dosing
  - Split total daily dose TID to address pain
  - Add short-acting opiates – side effects will be additive and patients will be tolerant
- When to reduce methadone dose (10-20% reduction in TDD):
  - Respiratory failure
  - Somnolence
  - QTc >500
  - Concurrent benzodiazepine – **Avoid if possible**

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Buprenorphine

- Consider continuing outpatient dosing
  - Split total daily dose TID to address pain
  - Add short-acting opiates if necessary – higher doses are required to overcome binding affinity
  - Avoid risk of overdose on other opiates during buprenorphine discontinuation
  - Avoid risk of relapse
  - Avoid the need to re-induce

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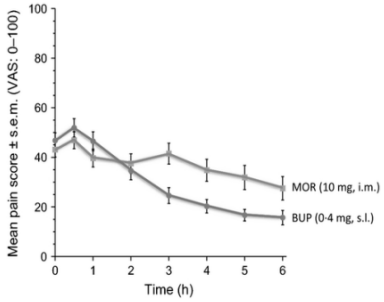
Analgesic efficacy of buprenorphine



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The clinical analgesic efficacy of buprenorphine, Volume: 39, Issue: 6, Pages: 577-583, First published: 29 July 2014, DOI: (10.1111/jcpt.12196)

Naltrexone

- Recommend:
  Oral: wait 72 hours before surgery
  IM: schedule surgery at end of cycle
- Must overcome blockade, but also loss of tolerance
- Restart naltrexone once abstinent from opioids (depending on length of time)
- Use multi-modal approach for pain control and opioid sparing.
- If acute pain service available, would consult.

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Case 1

45 year old woman admitted with a broken femur. She has a history of diabetes and Hepatitis C. She says that she takes methadone 120 mg daily and has been attending a methadone clinic for 1 year. This is her second hospital day.

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Inpatient Addiction Medicine Service

General Principles

- PMP check
- Urine drug screening
- Pregnancy test for women of child-bearing age
- Use of non-opioid treatments
- Confirm dosing at the methadone clinic

Methadone Clinic Contact Record

- Methadone clinic name
- How long attending clinic
- What is the daily dose and when did they last dose
- Do they have take homes
- What is the patient's compliance
- We include the following statement on our record:

If no dose taken in past 2-5 days, give ½ dose first day, dosing advance cautiously as clinically appropriate and/or in collaboration with addiction medicine or the methadone clinic

If no dose taken for >5 days, requires further medical evaluation - consult addiction medicine or the methadone clinic.

Case 2

35 year old man who is admitted for RLQ pain. Diagnosed with appendicitis and has surgery. He has been on Buprenorphine/naloxone 8 mg a day for 9 months and reports no heroin use since starting the medication. He took his dose the the day of admission. You are asked to see him the following day.

Case 3

62 year old male patient who has been treated for his OUD successfully with naltrexone 50 mg qd for 6 years. He needs to be admitted for a knee replacement.

Recovery Support

- Stress, pain, insomnia, illness, isolation are major triggers for relapse.
- Important to understand what recovery supports patient has in place, and what recovery supports may be needed.
- Help patient utilize the tools acquired in treatment.
  - Coping skills
  - Relaxation techniques
  - Mindfulness
- 12 step – sponsor support, Big Book
- Relapse prevention strategies

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