PRESBYTERIAN

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

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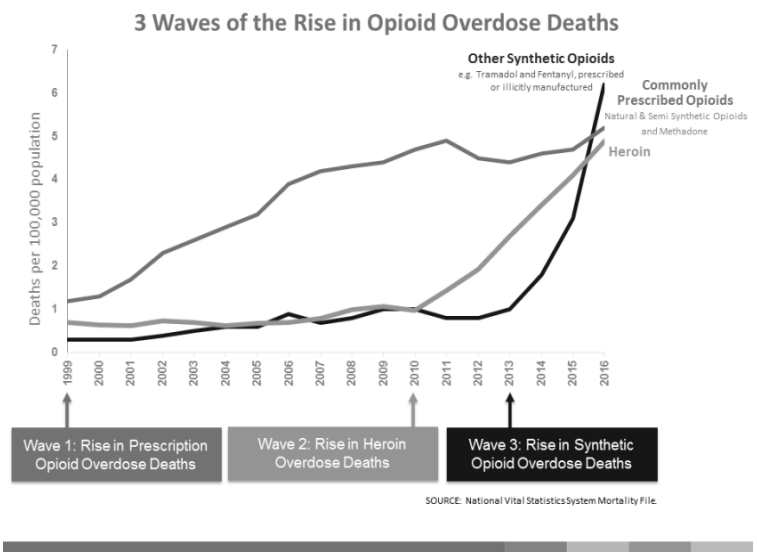
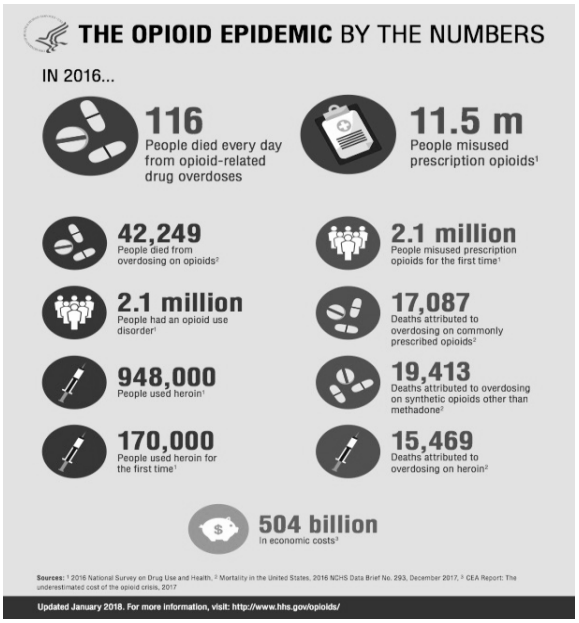
Goals of Discussion

- 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


3 Waves of the Rise in Opioid Overdose Deaths
Other Synthetic Opioids
e.g. Tramadol and Fentanyl, prescribed or illicitly manufactured
Commonly Prescribed Opioids
Natural & Semi Synthetic Opioids and Methadone
Heroin
Deaths per 100,000 population
0
1
2
3
4
5
6
7
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Wave 1: Rise in Prescription Opioid Overdose Deaths
Wave 2: Rise in Heroin Overdose Deaths
Wave 3: Rise in Synthetic Opioid Overdose Deaths
SOURCE: National Vital Statistics System Mortality File.


THE OPIOID EPIDEMIC BY THE NUMBERS
IN 2016...
116
People died every day from opioid-related drug overdoses
11.5 m
People misused prescription opioids¹
42,249
People died from overdosing on opioids²
2.1 million
People misused prescription opioids for the first time¹
2.1 million
People had an opioid use disorder¹
17,087
Deaths attributed to overdosing on commonly prescribed opioids²
948,000
People used heroin¹
19,413
Deaths attributed to overdosing on synthetic opioids other than methadone²
170,000
People used heroin for the first time¹
15,469
Deaths attributed to overdosing on heroin²
504 billion
In economic costs³
Sources: ¹ 2016 National Survey on Drug Use and Health, ² Mortality in the United States, 2016 NCHS Data Brief No. 293, December 2017, ³ CEA Report: The underestimated cost of the opioid crisis, 2017
Updated January 2018. For more information, visit: http://www.hhs.gov/opioids/

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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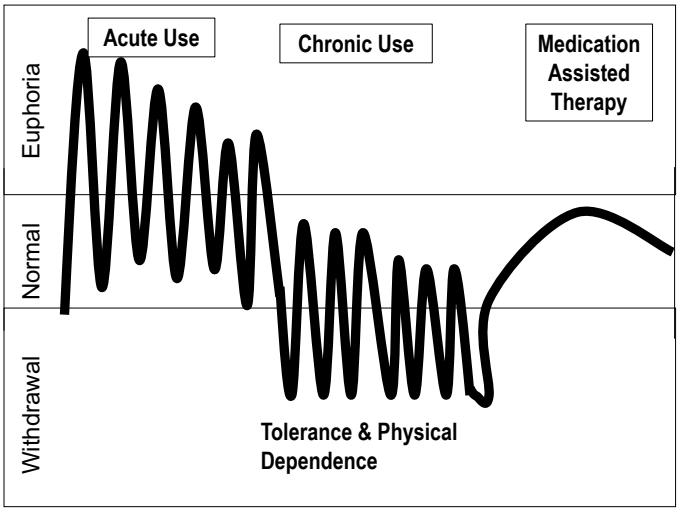
Medication Assisted Therapy



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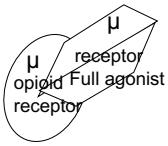
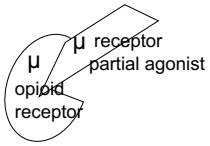
Pharmacology of MAT

Full opioid agonist: Methadone



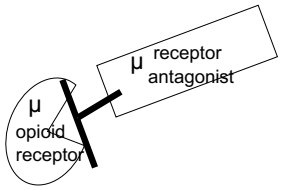
- Full agonist binding activates the μ opioid receptor
- Additive effect when combined with other full agonists
- Is highly reinforcing and has higher potential for abuse
- Abrupt discontinuation will result in withdrawal

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

Opioid antagonists: Naloxone and Naltrexone



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

Methadone Pharmacokinetics

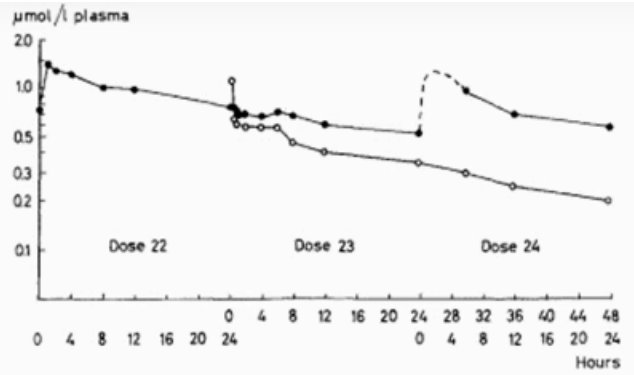


Fig. 3. Plasma levels of M (●——●) and M-d_3 (○——○) during Period 2 in Subject 12

Buprenorphine Pharmacokinetics

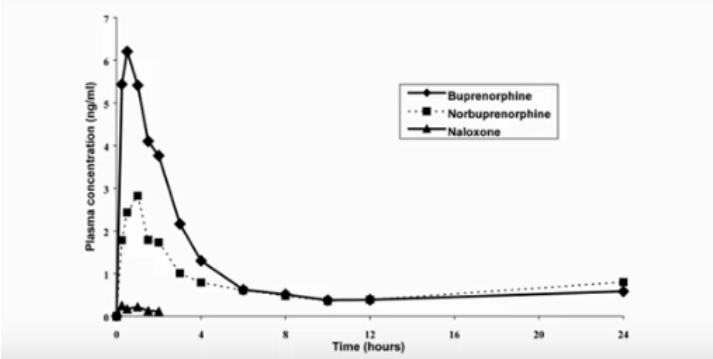
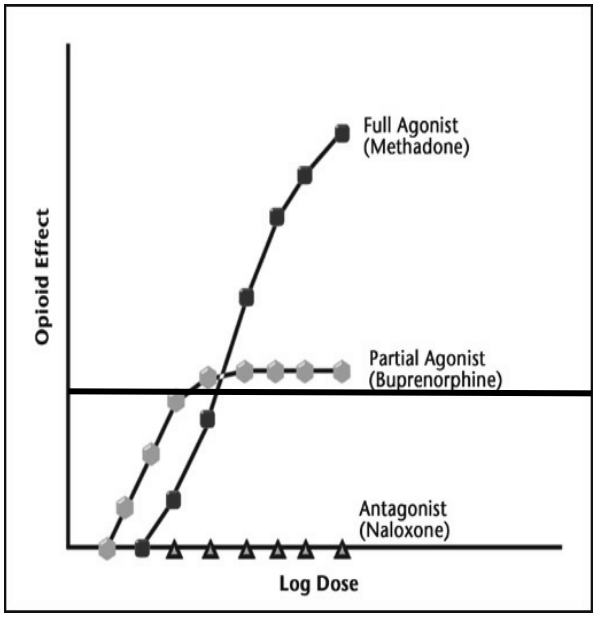


Fig. 4. The time course of plasma levels of buprenorphine, norbuprenorphine and naloxone for a subject receiving a sublingual dose of the combination tablet of buprenorphine (16 mg) and naloxone (4 mg) (data from Jones et al., 1997).



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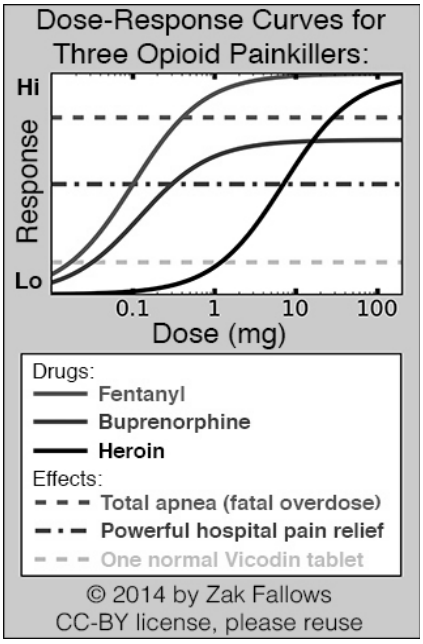

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Methadone and Buprenorphine as analgesics

- 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

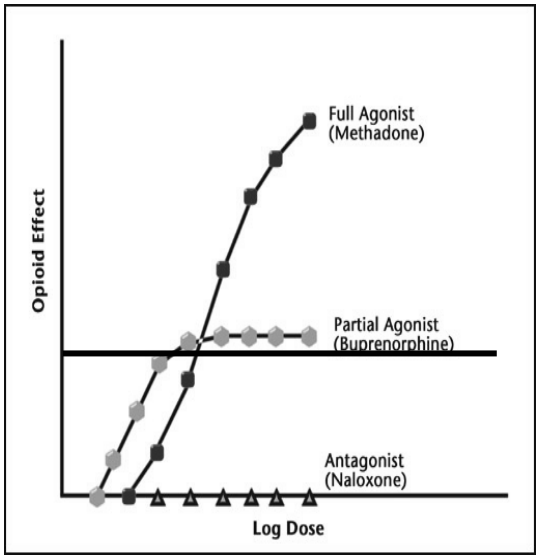
Consider scheduled dosing for the following:

- 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

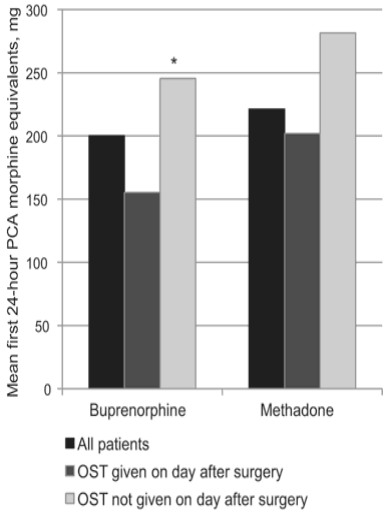
Short-acting opioids

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[19]

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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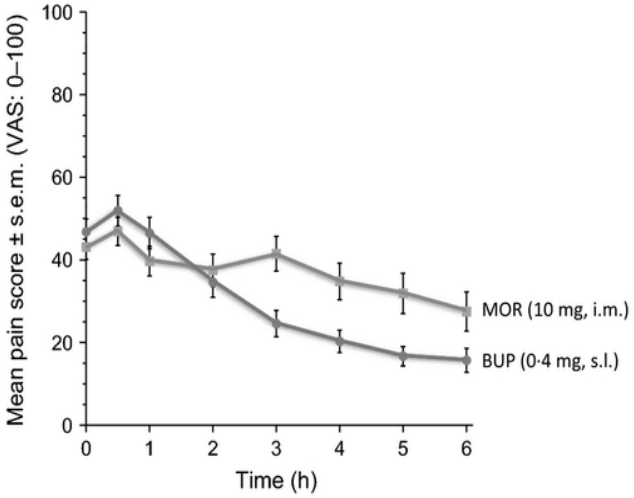
Buprenorphine

- 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

Analgesic efficacy of buprenorphine



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.

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.

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

References

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