Disclosure, Conflict of Interest

- Presenters have nothing to disclose.
- Presenters have no conflicts of interest.
Objectives (Technicians)

1. Recognize the benefits of identifying hospitalized patients with opioid use disorder (OUD), as well as the benefit of initiating treatment while hospitalized
2. Compare and contrast the available medications used to treat OUD
3. List the supportive care medications used in combination with medication-assisted treatment (MAT) to manage symptoms of opioid withdrawal
Objectives (Pharmacists)

1. Explain the benefits of identifying hospitalized patients with opioid use disorder (OUD), and the benefit of initiating treatment while hospitalized
2. Compare and contrast the available medications used to treat OUD
3. Describe the supportive care medications used in combination with medication-assisted treatment (MAT) to manage symptoms of opioid withdrawal
4. Demonstrate how to appropriately manage and treat pain in patients with a history of opioid use disorder
1. Which of the following are FDA approved for treatment of OUD?
   a. Methadone
   b. Disulfiram
   c. Naltrexone
   d. Buprenorphine
   e. Acamprosate

2. How long should patients receive medication for OUD?
   a. Gradual taper after 6 months of therapy
   b. Gradual taper after 1 year of therapy
   c. Indefinitely
   d. Patient-specific lengths of therapy

3. Which of the following would be the most effective option for a patient with OUD and chronic pain?
   a. Buprenorphine
   b. Methadone
   c. Naltrexone
   d. MAT is not indicated for individuals with OUD and chronic pain
Opioid Crisis

- More than 130 people in the US die each day after overdosing on opioids.
- CDC estimates a total “economic burden” of $78.5 million each year due to healthcare costs, productivity losses, addiction treatment and criminal justice.

- 8-12% of patients prescribed opioids will develop an OUD.
- 80% of people who use heroin first misused opioids.
- Opioid misuse has also brought about increases in neonatal abstinence syndrome, HIV and Hep C.
Opioid Overdose Features

- **Classic Triad**
  - Coma
  - Respiratory depression
  - Pinpoint pupils (miosis)

- Untreated patients die of respiratory failure/apnea
- Respiratory support should be enough to prevent death
  - Rapidly efficacious antidote largely eliminating the need for aggressive ventilatory support
    - Naloxone
Naloxone Indications

- For reversal of opioid toxicity characterized by respiratory depression and/or coma
  - Can be used to avoid intubation and an ICU stay

- Diagnostically in undifferentiated CNS depression when overdose is possible or suspected
Naloxone

- MoA: Pure opioid antagonist
- Routes: IV, IM, intranasal
- Rapid onset < 1 minute
- DoA: 20-60 minutes
- Reverses respiratory depression, coma, miosis, and analgesia
- “Safe”
  - Precipitated withdrawal
    - Many providers minimize this risk as uncomfortable but not dangerous
Naloxone

- Manufacturer dosing:
  - 0.4-2 mg IV/IM, repeat every 2-3 minutes if no response
    - If no response after 10 mg - reconsider diagnosis
  - 4 mg (contents of one nasal spray) in one nostril, or 2 mg in each nostril
    - May repeat every 2-3 minutes alternating nostrils
      - Onset slightly delayed versus IV/IM

- American Heart Association dosing:
  - 0.04-0.4 mg
    - Most patients will respond to 0.04-0.05 mg IV

- Goal: reinstatement of adequate spontaneous ventilation (not necessarily CNS arousal)
Naloxone

- Adverse effects
  - Opioid naive: NONE
  - Opioid dependent: precipitated withdrawal
    - Often inconvenient for providers and potentially dangerous to the patient
      - Agitation, HTN, tachycardia, vomiting, diarrhea
      - Extreme discomfort/distress
    - Vomiting while still CNS depressed is very dangerous
      - Coingestion of ethanol or other sedating drugs, head trauma
Changing the Conversation

- Opioid replacement still somewhat controversial
  - Addiction of a new drug dependence
    - i.e. “replacing one addiction with another”
- Detoxification alone has high rates of relapse
  - Assisting a patient through withdrawal and then releasing
- Opioid use disorder is a chronic, relapsing disease
- Instead of declining treatment, the patient isn’t ready “yet”
- Care is easier when treating
- Treatment saves lives!
OUD Diagnosis

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V)

- Use in larger amounts and/or for a longer time than intended
- Persistent desire or unsuccessful effort to cut down or control use
- Excessive time and/or energy obtaining opioids or recovering from opioid effects
- Craving, strong desire, or urge for opioids
- Failure to fulfill obligations at school, work, or home related to opioid use
- Continued use despite social or interpersonal problems related to opioid use
- Use despite medical or psychological problems related to opioid use
- Important activities given up or reduced due to opioid use
- Use in situations where it is physically hazardous

2-3 = mild, 4-5 = moderate, 6+ = severe
Medication-Assisted Therapy (MAT)

- MAT: the use of medications in combination with counseling and behavioral therapies to treat substance use disorders and prevent opioid overdose
  - Provide a “whole patient” approach
What percentage of patients with OUD are receiving treatment with MAT?
Medication-Assisted Therapy (MAT)

- Most individuals with OUD are not currently receiving treatment
  - Only ~20% have received specialty care within the previous year
- Only \( \frac{1}{3} \) of patients receiving specialty treatment are prescribed MAT
  - <7% of patients with OUD
- Only \( \frac{1}{2} \) of patients receiving specialty treatment remain in continuous care after 6 months
Medication Assisted Therapy (MAT)

- Available Pharmacologic Treatments
  - Buprenorphine (Subutex)
  - Buprenorphine + naloxone (Suboxone)
  - Methadone
  - Naltrexone

- Patients who receive treatment with methadone or buprenorphine experience lower mortality, primarily due to a reduction in drug-related overdose
  - Improved mortality outweighs risks associated with treatment
Medication-Assisted Therapy (MAT)

**Buprenorphine**
- MoA: partial opioid receptor agonist to ameliorate craving and withdrawal
- Very high affinity for mu receptors, blocks the effects of other opioids

Naloxone: added as an abuse deterrent
- Injection of crush tablets or liquefied films will result in precipitated withdrawal
- If the dosage is taken appropriately (SL), naloxone is not absorbed

**Methadone**
- MoA: binds to opioid receptors in ascending pathways, ameliorating craving through substitution (cross tolerance)

**Naltrexone**
- MoA: Pure opioid antagonist, acts as a competitive antagonists at opioid receptor sites
- Highest affinity for mu receptors
- Prevents relapse by preventing opioids from agonizing the mu receptor
Comparison of Effectiveness

**Buprenorphine**
- Often viewed as advantageous over methadone
- Faster at home treatment
- Self-administered
- More expensive
- Less DDI
- Ceiling effect: blocks effects of other opioids
- Possibly milder withdrawal due to *partial* mu agonist activity

**Methadone**
- Efficacy in reducing/eliminating heroin use has long been established
  - Available in pain clinics /specialized dosing centers (may be distant from patients)
  - Methadone clinic patients may experience stigmatization
  - More public concern for overdose and diversion
- Patients typically must show compliance for at least 2 years to be allowed to take home a 1 month supply of medication
Comparison of Adverse Effects

**Buprenorphine**
- Less risk of sexual dysfunction (but still present)
- Less respiratory depression (more difficult to reverse if present)
- Death during induction phase is rare
- **Makes acute pain management with opioids problematic (blocks effects of full agonists)**
- Less dysphoria
- Lower overdose risk
- Lower risk of dependence

**Methadone**
- Greater risk of sexual dysfunction (hypogonadism in men)
- Greater risk of respiratory depression (more readily reversible if present)
- Higher risk of death during induction phase
- **More effective in pain management**
- Higher risk of dysphoria
- Well absorbed orally, higher overdose risk
- More DDIs
  - Carbamazepine, CYP3A4 inhibitors, tamoxifen, QTc prolonging drugs
- **QTc prolongation, >500 msec:**
  - Consider discontinuation/dose reduction
  - Address other factors promoting QT prolongation
  - Consider alternative therapy
True or False?

Buprenorphine is a partial opioid agonist, making it more effective for pain management compared to methadone.
False!

Buprenorphine is a partial opioid agonist

Acute pain management is more difficult - blocks the effects of full opioid agonists
Naltrexone

- Must have washout period from opioids before starting naltrexone
  - Will precipitate withdrawal
  - Patients should have essentially no opioid agonist in the system prior to starting
    - Start 7-10 days after last dose of most opioids
    - Longer for methadone

- Dose
  - 25 mg PO on day 1, if no withdrawal, can increase to 50 mg on day two
    - Maintenance: 50 mg/day
  - IM depot (Vivitrol): 380 mg IM every 4 weeks

- Does NOT specifically provide treatment for cravings
  - Adherence may be an issue for PO formulation
  - Patients may simply stop taking and begin to use opioids again very quickly
    - IM formulation improves adherence
Duration of Treatment

- Opioid replacement therapy may go on indefinitely
- There is typically NOT a clear endpoint upon initiation of therapy
- Decision to taper should be a result of a complex assessment of patient-specific factors regarding risk for relapse
Guidelines and Guidance

- **American Society of Addiction Medicine (ASAM)**
  - Treatment choice should be a *shared decision*
    - Success depends largely on patient-specific factors (AEs, transportation, time, social support)
    - Patients who fail buprenorphine may do well on methadone and vice versa
    - Patients may have several treatment failures before finally achieving long-term abstinence
  - Methadone and buprenorphine generally recommended

- **Naltrexone** has certain places in therapy
  - Prison, inpatient rehab, difficult access, homelessness

- **World Health Organization (WHO)**, British Columbia Centre on Substance Use and B.C. Ministry of Health, and American Society of Addiction Medicine (ASAM), recommend MAT as first line therapy within their guidelines and agree upon its superiority compared to abrupt discontinuation with withdrawal
### Changing the Approach

<table>
<thead>
<tr>
<th>Old Approach</th>
<th>Better Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Specialty care referral for OUD treatment  ○ Creates stigmas</td>
<td>● Provide care where patients are more likely to be</td>
</tr>
<tr>
<td>● Limited OUD education  ○ Reduced screening</td>
<td>● OUD training and screenings</td>
</tr>
<tr>
<td>● Limited provider time and provider shortages  ○ Reduced access</td>
<td>● Potentially integrating pharmacists as additional providers</td>
</tr>
</tbody>
</table>
Interprofessional Practice

- Multiple professionals in a shared work site working as a team
  - Share and integrate information
  - Coordination in generating treatment plans and providing services
- Improves access to services and care and improves health outcomes
- Increases patient safety and level of care
- Decreases patient complications
- Decreases hospital length of stay (LOS) and readmissions
- Decreases percentage of patients who leave the hospital against medical advice
- Decreases errors, staff turnover and mortality
Role of the Pharmacist

- Medication management
- Opioid/Benzo tapers
- Induction and stabilization
- Risk mitigation
- Referrals
MAT at Providence
Alaska Medical Center
In 2016, PAMC saw 141,218 patients with substance use disorders, 31,344 (22%) of whom were identified as using opioids.

Those who used opioids experienced elevated mortality rates by a factor of nearly 3, when compared to patients without SUDs (2.3% vs .8%, respectively).

OUD can lead to dangerous medical complications and can be challenging to manage during an acute hospital stay.

Patients and caregivers focused on "detox," thinking the addiction problem will not return.

These patients generally relapse in the weeks/months following, and face elevated risk of a fatal overdose.

This approach creates fatigue and distrust between hospital caregivers and patients who need medical attention.
Patient Population

- Individuals with OUD have greater medical service utilization with higher hospitalization and re-hospitalization rates
- Patients are less likely to complete medical treatment and more likely to leave AMA
- Patients often have a number of comorbidities
  - Chronic pain syndromes
  - HIV
  - Hepatitis C
  - Psychiatric disorders
  - Heart disease
  - Respiratory disease
  - Sleep disorder
  - Cancer
  - Diabetes
Guiding Principles

- Chronic medical condition to be managed by compassionate respectful interventions
- Evidence-based strategies for withdrawal prevention and management, and pain management
- Caregiver education and communication tools
- Building positive relationships between caregivers and patients
- Caregivers recognize moral judgements do not produce positive outcomes
- Caregivers partner with patients and visitors to discuss safety
- Trauma informed care guides practice
- Patients that suffer from addiction deserve medical care
- MAT is the standard of care, along with evidence-based standards such as multimodal pain control
Opioid Dependence and OUD Screening

1. NIDA ASSIST or TAPS
   - Nurse-administered. Goal to screen all patients

2. COWS or CIWA
   - Assess for withdrawal

3. Provider is Contacted
   - For all positive screened patients

   - Non Pharmacotherapy
Buprenorphine Initiation

- Discontinue all opioid medications
- Monitor with COWS q4h; d/c 24h after last buprenorphine increase
- Suboxone = Buprenorphine/Naloxone tablet 8 mg/2 mg
- Day 1: Half tablet of Suboxone 8/2 for dose of 4mg/1 mg SL prn COWS ≥8
  - NTE 24 mg TDD buprenorphine
- Day 2+: calculate daily dose by totaling previous day's administration
  - Suboxone 4 mg/1mg COWS ≥ 8 (NTE 24mg TDD buprenorphine)
# Methadone

<table>
<thead>
<tr>
<th>Continuation</th>
<th>Initiation</th>
</tr>
</thead>
</table>
| Confirm dose at clinic  
*If last dose:*  
• <48h: continue home dose  
• 48-72h: reduce by 25%  
• >72h: follow initiation pathway |  
• Monitor with COWS q4h  
• Hold for RR <12  
• Starting dose: Methadone 10 mg po tid  
• Titration: increase q3days in 15 mg increments ÷ tid  
  • With clinical judgment, can increase q2days  
  • 10 mg tid → 15 tid → 20 tid  
  • Goal 80 – 120 mg, targeting w/d sx & cravings  
  • Liaise w/psych CL for TDD >80 mg  
• Oxycodone 5 – 20 mg po q3h prn COWS ≥ 8  
• Transition to daily dosing prior to discharge |
Pain Management

- In patients who are receiving treatment for opioid use disorder, there is a concern of relapse while treating pain
- Acute pain does occur in these patients and does require management
- Common misconceptions:
  - Maintenance opioid therapy provides analgesia
  - Addiction relapse will occur if opioids are used for analgesia
  - Reporting pain is “drug seeking” behavior
Pain Management

- Analgesic action of methadone and buprenorphine is only ~4-8 hours
  - Dosing interval for opioid use disorder is much longer
- Patients will have developed tolerance to analgesic effects
- Opioids may cause hyperalgesia over time
- Use of opioids for acute pain has NOT been proven to induce relapse
  - Inadequate pain management IS associated with relapse
- Some patients may exhibit drug seeking behavior
  - Differentiating between legitimate need and abuse is key
Updated 6.6.19

Acute Pain Management & Medication Assisted Treatment

- Pts w/OUD usually have higher opioid tolerance & may require higher doses than opioid-naïve pts. They may have lower threshold for pain, experiencing hyperalgesia and allodynia.
- For all patients:
  1. *Multimodal Pain Management Postop* order set (some Rx auto d/c after 3 days)
  2. Consider IV Lidocaine or IV Ketamine (per PAMC policy)
  3. Neuraxial/Regional anesthesia if appropriate
Multimodal Pain Management Order Set

- Acetaminophen
- NSAIDs
  - Celecoxib
  - Ibuprofen
  - Naproxen
  - Ketorolac
- Gabapentin or pregabalin
- Oral opioids
  - Oxycodone
  - Morphine
  - Hydromorphone
- IV opioids
  - Morphine
  - Hydromorphone
Pain Management

Buprenorphine (Suboxone, Subutex, Zubsolv, Sublocade, Bunavail)

Due to buprenorphine’s high affinity for mu receptor, low dose/affinity opioids are ineffective for pain

1. Continue home dose buprenorphine & divide to q8h dosing
   • Add buprenorphine 2-6 mg q6h prn for TDD 32 mg; determine requirement & schedule
   • Return to home dosing regimen when acute pain resolved

2. If increased buprenorphine & multimodals are ineffective OR expected moderate/severe pain

   Oral (preferred)
   • Hydromorphone 4 – 8 mg po q3h prn

   Intravenous
   • Hydromorphone 1 – 2 mg IV q2h prn

   if oral ineffective or unavailable
# Pain Management

## Methadone

Home dose methadone alone cannot be relied upon for acute pain management

1. Divide methadone to q8h dosing
   - Return to home dosing regimen when acute pain resolved

2. Utilize prn medications for 24 hours to determine baseline requirements, then convert to standing + prn

<table>
<thead>
<tr>
<th>Oral (preferred)</th>
<th>Intravenous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone 5 – 20 mg po q3h prn</td>
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</tr>
<tr>
<td>Hydromorphone 4 – 8 mg po q3h prn</td>
<td>if oral ineffective or unavailable</td>
</tr>
<tr>
<td>Morphine 15 – 45 mg q3h prn</td>
<td>Morphine 5 – 10 mg IV q2h prn</td>
</tr>
</tbody>
</table>
Patient established on methadone 90 mg once daily requires treatment for acute pain

1. What is the most appropriate way to manage this patient’s methadone while being treated for acute pain?
   a. Continue methadone 90 mg once daily
   b. Increase methadone every 3 days in 15 mg increments
   c. Divide methadone 90 mg into q8h dosing
   d. Hold methadone while utilizing other PRN opioids
a. Continue methadone 90 mg once daily
b. Increase methadone every 3 days in 15 mg increments
c. **Divide methadone 90 mg into q8h dosing**
d. Hold methadone while utilizing other PRN opioids
## Opioid Withdrawal Symptom Management

*Use in combination with Medication Assisted Treatment*

<table>
<thead>
<tr>
<th>Scheduled</th>
<th>As needed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clonidine</strong> 0.1 mg po q6h</td>
<td><strong>Pain</strong>  Acetaminophen 650 mg po q6h prn</td>
</tr>
<tr>
<td>• Hold if SBP &lt; 90, HR &lt; 50</td>
<td>ibuprofen 600 mg po q8h prn</td>
</tr>
<tr>
<td><strong>Hydroxyzine</strong> 50 mg po q4h</td>
<td>Toradol 15 – 30 mg IM/IV q6h prn</td>
</tr>
<tr>
<td>• If ≥60 yo, ↓ to 25 mg</td>
<td>Tizanidine 2 mg po q4h prn muscle cramps</td>
</tr>
<tr>
<td><strong>Gabapentin</strong> 300 mg po q8h</td>
<td></td>
</tr>
<tr>
<td><em>For sleep, pick one:</em> Hydroxyzine 50 – 100 mg po qhs</td>
<td><strong>Nausea/Vomiting</strong>  Zofran 4 mg po/IV q4h prn</td>
</tr>
<tr>
<td></td>
<td>Dicyclomine 10 mg po q4h prn stomach cramps</td>
</tr>
<tr>
<td>Mirtazapine 15 mg po qhs</td>
<td></td>
</tr>
<tr>
<td>Melatonin 0.5 mg po q1700</td>
<td><strong>Diarrhea</strong>  Loperimide 4 mg once followed by 2 mg prn</td>
</tr>
<tr>
<td></td>
<td>loose stool; not to exceed 16 mg daily</td>
</tr>
</tbody>
</table>
Social Work and Case Management

- Psychosocial care
- Discharge planning
  - Bridge to buprenorphine prescriber or methadone clinic
- Education
- Naloxone kit with instructions
- Communicate follow-up appointments with outpatient clinic
Summary

- OUD is a chronic, relapsing disease
- The combination of therapy + medications (MAT) has been shown to be more effective than detox, medication alone or behavioral therapies
- Methadone and buprenorphine are generally preferred, but naltrexone does have its place in therapy
- Therapy should be patient-specific instead of a “one size fits all” approach
- An interprofessional approach is safest, more accessible and provides the best patient outcomes
- Treatment should be accessible where patients are most likely to need it
- Patients with OUD have many additional comorbidities, and inpatient OUD treatment allows them better opportunities to receive treatment
1. Which of the following are FDA approved for treatment of OUD?
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   b. Disulfiram
   c. Naltrexone
   d. Buprenorphine
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Post-Test

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Thank you
Questions?
References

Opioid Use Disorder and Medication Assisted Therapy at Providence Alaska Medical Center

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