Session 2
Determining Treatment Plan for Patients with Opioid Use Disorder
Session Learning Objectives


2. Summarize the clinical pharmacology, efficacy, and safety of methadone, buprenorphine, and naltrexone in treating opioid use disorders.

3. Examine the need for and use of medications to manage patients with opioid use disorder.

4. Assess and diagnose patients with opioid use disorder while considering severity, chronicity, individual characteristics, and psychiatric and medical comorbidities.

5. Develop an individualized, patient-centered treatment plan by evaluating appropriate medication and psychosocial intervention options.

Legislative Topics

- **2000**: Drug Addiction Treatment Act (DATA 2000)
- **2016**: Comprehensive Addiction and Recovery Act (CARA)
- **2016**: Final Rule on 275 Patient Limit
- **2019**: SUPPORT for Patients and Communities Act (HR6)

- Allows physicians to prescribe an FDA approved opioid for the treatment of opioid use disorder.
- Physicians must meet certain qualifications:
  - At least 8 hours of education
  - Patient limits: 30, 100
  - Application must be submitted online at the SAMHSA website
  - Receive "X-number" after application approval

Final Rule on 275 Patient Limit

- Announced in August 2016
- Allows qualified providers to increase patient limit to 275
  - Requires “qualified practice setting”
  - Requires new waiver application
  - Must reaffirm eligibility every 3 years (90 days before end of waiver year)
CARA & SUPPORT Acts

- CARA expanded prescribing to NPs and PAs
- SUPPORT Act expanded prescribing to CRNAs, CNMs, and CNSs
- Requires 24 hours of education

Patient Limits

**Beginning 1st Year**
- 30 patients per practitioner during first year of the waiver.
- May start at 100 patients when meeting certain requirements.

**After 1st Year**
- Can increase to 100 patients – a new waiver must be obtained.

**After 2nd Year**
- Can increase to 275 patients – a new waiver must be obtained.

*Census*: Patient remains on your census until the last prescription has run out.

*Hospitalized Patients*: w/ primary admitting diagnosis other than OUD, buprenorphine can be ordered by non-waivered physician.
Medication Requirements

- **FDA Approval**
  - Drug must be approved by FDA for use in treating opioid use disorders (OUD).

- **DEA Schedules**
  - Medication must be DEA schedule III, IV, or V (methadone is schedule II).

- **Buprenorphine Schedule**
  - Schedule III
  - Certain (not all) formulations are approved for the treatment of OUD.

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DEA Controlled Substance Classification

- **Schedule II**
  - High potential for misuse
  - High potential for misuse includes: morphine, codeine, hydrocodone, methadone, hydromorphone, oxycodone, fentanyl, oxymorphone, tapentadol

- **Schedule III**
  - Moderate to low potential for misuse
  - Moderate to low potential for misuse includes: acetaminophen with codeine, testosterone, buprenorphine

- **Schedule IV**
  - Low risk of misuse
  - Low risk of misuse includes: benzodiazepines, tramadol

- **Schedule V**
  - Low potential for misuse
  - Low potential for misuse includes: cough preparations with codeine, pregabalin
Requirements for Opioid Treatment Programs (OTP)

By Prescription:

The practitioner can prescribe approved medication in the same manner as in an office-based practice with the same patient limits (30, 100, 275).

By Order to Dispense:

The practitioner can order approved medication to be dispensed in OTP setting in a manner similar to methadone with no specific limits on number of patients.

DEA Compliance

DEA continues routine practitioner inspections to assess:

- Compliance with the 30/100/275 patient limit.
- Record keeping.
- Security measures related to on-site drug storage if buprenorphine is dispensed or administered from the office.
Audience Response

Is someone who has their DEA waiver more likely to have DEA agents come to their practice?

A. Yes, and it's a good reason not to get your waiver.
B. Yes, and there are simple things you can do to make it less likely.
C. Yes, because they are trying to get doctors to prescribe under a waiver.
D. No.

Opioid Pharmacology
Opiates and Opioids

**Opiates:**
*Natural compounds present in opium:* e.g., morphine, codeine, thebaine

**Opioids:**
Manufactured as:
- **Semi-synthetic opioids:** derived from an opiate, e.g., heroin, oxycodone, hydromorphone, buprenorphine
- **Synthetic opioids:** completely synthesized to function similarly to natural opiates, e.g., methadone, fentanyl

Endogenous Opioids and Their Receptors
Most of the clinically-significant effects of prescribed and illicit opioids are attributed to activity at the mu-opioid receptor.

<table>
<thead>
<tr>
<th>ENDOGENOUS LIGAND</th>
<th>OPIOID RECEPTOR TYPES</th>
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<tbody>
<tr>
<td>Beta Endorphins</td>
<td>Mu</td>
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<tr>
<td>Enkephalins</td>
<td>Delta</td>
</tr>
<tr>
<td>Dynorphins</td>
<td>Kappa</td>
</tr>
<tr>
<td>Nociceptin/OrphaninF/Q</td>
<td>ORL-1</td>
</tr>
</tbody>
</table>
Mu-Opioid Receptor

- G-protein coupled receptor
- Subtypes and > 100 polymorphisms to the mu-opioid receptor gene
- High affinity for beta-endorphin and enkephalins
- High affinity for morphine
- Low affinity for dynorphins
- Acute changes in neuronal excitability via "disinhibition" of presynaptic release of GABA

Opioid Characteristics that Increase Euphoria

- **Route of Administration**
  - Faster route has a greater misuse potential
  - Smoking → Injecting IV → Injecting SQ → Oral/Intranasal

- **Drug Half-Life**
  - Shorter half-life has a greater misuse potential
  - Fentanyl → Heroin → Methadone

- **Lipophilicity**
  - Faster across blood-brain barrier
  - Higher lipophilicity has a greater misuse potential
  - Fentanyl → Heroin → Morphine → Methadone
Opioid Agonists and Antagonists

- **Opioid Agonists and Antagonists**

- **Mu Receptor**
  - **Antagonist Binding**
  - **Full Agonist Binding**
  - **Partial Agonist Binding**

- **% Mu Receptor Intrinsic Activity**
  - **Full Agonist** (e.g. heroin, methadone, oxycodone)
  - **Partial Agonist** (e.g. buprenorphine)
  - **Antagonist** (e.g. naloxone, naltrexone)

- **Drug Dose**
  - no drug
  - low dose
  - high dose
**Opioid Antagonist**

**An antagonist**
- occupies without activating.
- is not reinforcing/rewarding.
- blocks or displaces opioid agonists.
- includes naloxone and naltrexone.

**Full Opioid Agonist**

**A full agonist**
- activates the Mu receptor.
- is reinforcing/rewarding.
- is the riskiest opioid type (i.e., sedation and respiratory depression).
- includes fentanyl, heroin, methadone, & others.
Partial Opioid Agonist

A partial agonist
- activates the Mu receptor with ceiling effect.
- is relatively less reinforcing/rewarding.
- is a less risky opioid type (i.e., sedation and respiratory depression).
- includes buprenorphine.

Receptor Affinity

Buprenorphine’s Affinity
- Affinity is the strength with which a drug physically binds to a receptor.
- Buprenorphine’s affinity is very high; it will displace full agonists.
- Receptor binding strength, high or low, is NOT the same as receptor activation (agonist or antagonist).
Receptor Dissociation

Dissociation

- Dissociation is the speed (slow or fast) of disengagement of the drug from the receptor.
- Buprenorphine's dissociation is slow.
- Buprenorphine stays on the receptor for a long time and blocks full agonist from binding.

Therefore, Full Agonists cannot bind.

Acute Opioid Withdrawal

Symptoms / Signs

<table>
<thead>
<tr>
<th>Mild</th>
<th>Anxiety, drug craving</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yawning, sweating, runny nose, tearing eyes, restlessness, insomnia</td>
</tr>
<tr>
<td></td>
<td>Dilated pupils, gooseflesh, muscle twitching, muscle &amp; joint aches</td>
</tr>
<tr>
<td></td>
<td>Nausea, extreme restlessness, elevated BP, heart rate &gt; 100, fever</td>
</tr>
<tr>
<td>Severe</td>
<td>Vomiting, diarrhea, abdominal cramps, curled-up body position</td>
</tr>
</tbody>
</table>

Clinical Opiate Withdrawal Scale (COWS):
- pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh
  - 5-12 mild
  - 13-24 moderate
  - 25-36 moderately severe
  - >36 severe
Determinants of Withdrawal Risk

- Exposure to steady state level of medication:
  - Neuro-adaptation to opioids
- Higher intensity withdrawal from:
  - Higher steady state levels
  - Longer term exposure
  - Faster rate of medication clearance
  - Short vs. long half-life agents

Spontaneous Acute Opioid Withdrawal

- Develops spontaneously in a person with physical dependence.
  - Someone who suddenly stops, or markedly decreases the opioid.
- Half-life opioids:
  - Severity is usually less with longer half-life opioids.
  - Duration depends on half-life of opioids person uses.

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>4-6 hours</td>
<td>~ 3 days</td>
<td>4-7 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>1-2 days</td>
<td>~ 7 days</td>
<td>12-14 days</td>
</tr>
</tbody>
</table>
Precipitated in a physically dependent person, by administration of an:
- opioid antagonist drug (e.g. naloxone, naltrexone), or
- opioid partial agonist drug (e.g. buprenorphine)

- Qualitatively similar to a spontaneous withdrawal but it has a faster onset.
- Duration depends upon half-life of drug.

<table>
<thead>
<tr>
<th>Opioid antagonist drug/ Opioid Partial Agonist Drug</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naloxone</td>
<td>Minutes</td>
<td>Minutes</td>
<td>~ 20 minutes</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Minutes</td>
<td>Minutes</td>
<td>1-2 days</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Minutes</td>
<td>Minutes</td>
<td>1-2 days</td>
</tr>
</tbody>
</table>

**Precipitated Acute Opioid Withdrawal**

*Full Agonist* (e.g. heroin, methadone, oxycodone)

A Net Decrease in Receptor Activity if a Partial Agonist Displaces Full Agonist

**Partial Agonist** (e.g. buprenorphine)

Buprenorphine will precipitate withdrawal when it displaces full agonist off the Mu receptors.
Audience Response

Which of the following is a characteristic of a partial agonist?

A. It activates the Mu receptor with a ceiling effect.
B. It is relatively more reinforcing/rewarding.
C. It is a riskier opioid type (i.e., sedation and respiratory depression).
D. Methadone is an example of a partial agonist.

ROBERT’S CASE
Robert’s Case

Robert is a 35-year-old middle school math teacher using illicit hydrocodone and intranasal heroin. He has been using on and off since age 24. Robert has been through more than 15 episodes of medically supervised withdrawal (“detox”).

His last treatment included a 28-day residential program during his summer break while attending daily NA meetings. He remained in recovery for three months but relapsed one month ago and is having difficulty maintaining employment because he “calls in sick too much.”

Robert’s Case

His wife is in recovery and insisted that he return to treatment after she discovered he was taking hydrocodone pills from several doctors for a back injury following an automobile crash. She is unaware that he is also using heroin daily.

There is family history of alcohol use disorder. He denies alcohol or tobacco use. His only current medical problem is mild hypertension. His back pain has resolved. He is hepatitis C and HIV negative.
Robert's Case

I know I'm addicted. My wife stopped using when she was pregnant with our daughter, and she just got her 12-year chip. She moved on with her life, but I'm stuck. My back injury threw me into a tailspin. At first, I really needed the painkillers, but now I'm just using them to ‘feel normal’ and to prevent withdrawal. I really need your help. If my wife finds out I’m back on heroin, she’ll leave me this time.

Activity 4: Case Discussion – Robert

- **Task:** With your group, discuss Robert's case.

- **Discuss:** Review the case with your group in break-out session. Does he meet DSM-5 criteria for an opioid use disorder? If so, is it mild, moderate or severe?

- **Time Allocated:** 5 minutes
Treatment Medications For Opioid Use Disorder: Methadone

Methadone Hydrochloride

- Full Opioid Agonist
- Oral
  - 80-90% bioavailability liquid, tablet, and disket formulations
- Proper dosing for OUD
  - 20-40 mg for acute withdrawal
  - > 80 mg for craving, "opioid blockade"
- Duration of action
  - 24-36 hours to treat OUD
  - 6-8 hours to treat pain
- Can be administered parenterally (IV, SQ or IM)
  - at 80% of the total daily oral dose administered in a divided dose every 12 hours (e.g., 40 mg by mouth every day = 16 mg IV every 12 hours)

Mercadante S. (2013) Handbook of Methadone Prescribing and Buprenorphine Therapy
Methadone Safety

**Half-Life**
- Long, variable, unpredictable half-life
- Serum t½ 20-120 hours
- 4-7 days to reach steady state: “Start low, go slow”

**QTc Prolongation, Risk of Torsades de Pointes**
- Dose-related: >100mg daily
- Multifactorial: ↓K, ↓Mg, other drugs ↑QTc
- CYP450: 3A4, 2D6 interactions
- QTc > 500 msec → Torsades de Pointes

Methadone Maintenance in OTP

- **Highly Structured**
  - Daily nursing assessment
  - Weekly individual and/or group counseling
  - Random supervised drug testing
  - Psychiatric services
  - Medical services

- **Methadone Dosing**
  - Observed daily - “Take homes” based on stability and time in treatment
  - Max: 27 “take homes”
  - Varies by state, county, and individual clinics

Methadone Summary: Benefits

- **Increases**
  - overall survival
  - treatment retention
  - employment

- **Improves**
  - birth outcomes

- **Decreases**
  - illicit opioid use
  - hepatitis and HIV seroconversion
  - criminal activity

Methadone Summary: Limitations

- **Highly regulated: Narcotic Addict Treatment Act 1974**
  - Created methadone clinics (Opioid Treatment Programs)
  - Separate system not involving primary care or pharmacies

- **Limited access**

- **Inconvenient**

- **Stigma**
  - “Methadone is substituting one drug for another... I don't believe in methadone.”
Some of the benefits of methadone include:

A. Decreased employment.
B. Increased hepatitis and HIV seroconversion.
C. Increased survival.
D. Decreased rates of unplanned pregnancy.

Treatment Medications For Opioid Use Disorder: *Naltrexone*
Naltrexone

- Mu-opioid receptor antagonist
- Not a controlled substance
  - no special prescribing restrictions
- Patients physically dependent
  - must be opioid free for a minimum of 7-10 days before treatment
- Also FDA approved for the treatment of alcohol use disorders
- Oral naltrexone (generic and brand Revia™)
  - Well tolerated
  - Duration of action 24-48 hours
  - FDA approved 1984
- IM injection extended-release naltrexone (Vivitrol)
  - IM injection (w/ customized needle) once/month
  - FDA approved 2010

Naltrexone Safety

- Generally well tolerated
  - initial headache, nausea, dizziness
- Depressed mood and suicidality rarely
  - no cause-and-effect established
- Reduce opioid tolerance
  - patients who return to pretreatment use have greater risk of fatal opioid overdose
- IM injection site reactions
  - bruise, induration, nodules, pain, pruritus, swelling, tenderness

The Medical Letter. 2017, 59(1522), 89-90.
Naltrexone and the Liver

- Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses.
- Naltrexone does not appear to be hepatotoxic at the recommended doses.
- Naltrexone is contraindicated in acute hepatitis or liver failure.

Oral Naltrexone Efficacy

Meta-analysis of 13 RCTs 1,158 participants:

- Naltrexone maintenance treatment versus placebo or other treatments.
- Only 28% of people were retained in treatment in the included studies.
- No statistically significant differences were noted for all the primary outcomes considered.
- More effective than placebo in sustaining abstinence in studies where patients were legally mandated to take the drug.
Injectable Extended-Release Naltrexone (XR-NTX) Efficacy

- **Multicenter** (13 sites in Russia) funded by Alkermes
- **DB RPCT**, 24 weeks, n=250 w/ opioid use disorder
- **XR-NTX vs placebo**, all offered biweekly individual drug counseling
- **Increased**
  - weeks of confirmed abstinence (90% vs 35%)
  - patients with confirmed abstinence (36% vs 23%)
- **Decreased** craving (-10 vs +0.7)

Krupitsky E et al. Lancet. 2011

XR-NTX Efficacy: Retention

- **Mean # doses (Max = 6)**
  - Heroin: 2.3
  - Non-heroin opioid: 2.5
- **Drop-out risk factors**
  - Homelessness
  - Opioid injection use (regardless of opioid-type)
  - Mental illness

Cousins SJ et al. J Sub Abuse Treat 2016
Naltrexone Summary

Benefits:
- Good for patients who do not want opioid agonist therapy.
- No risk of diversion (not a controlled substance).
- **No risk of overdose by drug itself.**
- Can be administered in any setting (office-based or OTP).
- Long-acting formulation.
- Treats both opioid use disorder and alcohol use disorder.

Limitations:
- Difficulty starting—must be fully withdrawn from opioid; > short-acting (6 days); long-acting opioids (7-10 days).
- Not suitable for patients with severe liver disease.
- Loss of tolerance to opioids increases the risk of overdose if return to pretreatment use occurs.
- Not recommended for pregnant women. Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine.

Audience Response

A good candidate for naltrexone may show the following:

A. Abstinence from opioids for 4-6 days depending on the half-life of the opioid.
B. Able to come to clinic for a nursing visit every 12-16 days for injection of the medication.
C. It is a good choice for someone with severe liver damage.
D. Have comorbid opioid and alcohol use disorders.
Treatment Medications For Opioid Use Disorder: *Buprenorphine*

**Buprenorphine**

- is a semi-synthetic analogue of thebaine.
- was approved by the FDA in 2002 as Schedule III — up to 5 refills.
- has a high receptor affinity.
- has a slow dissociation.
- has a ceiling effect for respiratory depression.
- is a partial Mu-opioid agonist, kappa antagonist.
Buprenorphine: Active Effect

- Buprenorphine has poor oral bioavailability when swallowed. All therapeutic formulations use other routes.
- Sublingual administration bypasses first-pass metabolism and allows bioavailability around 30%.
- Most buprenorphine is excreted into the biliary tract; small fractions enter the urine and are detectable in urine tests.


Buprenorphine

Partial Agonist at the Mu-Opioid Receptor

- Analgesia (Analgesic effect is 6-8 hours)
- Ceiling effect on respiratory and CNS depression
- OUD treatment effect is 24-36 hours at therapeutic dose
Combination: Buprenorphine/Naloxone

If dissolved sublingually:

- Buprenorphine is active
- Naloxone is not active

If swallowed:

- Buprenorphine not active (minimal oral bioavailability)
- Naloxone not active

If injected or used intranasally:

- Buprenorphine is active
- Naloxone active x 20 minutes so attenuates the parenteral "rush"

Not time-released:

- Tablets/film strip can be split

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Opioid Blockade

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Mu Opioid Receptor Binding Potential

Binding Potential (Bmax/Kd)
Buprenorphine Efficacy: Retention

- **Completion 52-week trial:**
  - Taper: 0%
  - Maintenance: 75%

- **Mean % urine neg:**
  - Maintenance: 75%

- **Mortality**
  - Taper: 20%
  - Maintenance: 0%

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Buprenorphine Efficacy: Summary

Studies (RCT) show buprenorphine (16-24 mg) more effective than placebo and equally effective to moderate doses (80 mg) of methadone on primary outcomes of:

- Retention in treatment
- Abstinence from illicit opioid use
- Decreased opioid craving
- Decreased mortality
- Improved occupational stability
- Improved psychosocial outcomes

Characteristics of buprenorphine that make it a good treatment for a person with an opioid use disorder include:

A. Low receptor affinity.
B. Fast dissociation.
C. Full Mu-opioid agonist and partial kappa antagonist.
D. Ceiling effect for respiratory depression.

Treatment Medications For Opioid Use Disorder: 
Buprenorphine Safety
Buprenorphine Safety

- Highly safe medication for both acute and chronic dosing.
- No evidence of significant disruption in cognitive or psychomotor performance with buprenorphine maintenance.
- No evidence of organ damage with chronic dosing of buprenorphine “mono” or “combo.”

Adverse Effects

- Constipation (PAMORA), excessive sweating
- 2° Hypogonadism:
  - ↓ HPG axis → ↓ Testosterone
- QTc prolongation but less than with methadone
- Hemodialysis safe
- Decreased bone health – Opioid Class Effect, ↓ Saliva, Osteoclast activity
Adverse Effects of Medications

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Constipation, hyperhidrosis, respiratory depression (particularly combined with benzodiazepines or other CNS depressants), sedation, QT prolongation, interactions with other medications that alter cytochrome P450 metabolism, sexual dysfunction, severe hypotension including orthostatic hypotension and syncope, misuse potential, NOWS</td>
</tr>
<tr>
<td>Buprenorphine (with or without naloxone)</td>
<td>Constipation, nausea, precipitated withdrawal, excessive sweating, insomnia, peripheral edema, respiratory depression when with benzodiazepines or other CNS depressants, misuse potential, NOWS Implant: Nerve damage during insertion/removal, accidental overdose or misuse if extruded, local migration or protrusion Subcutaneous: Injection site itching or pain, death from intravenous injection</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Nausea, anxiety, insomnia, precipitated withdrawal, hepatotoxicity, vulnerability to opioid overdose, depression, suicidality, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders Intramuscular: Pain, swelling, induration (including some cases requiring surgical intervention)</td>
</tr>
</tbody>
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**Overdose Risk Minimal**

- **Respiratory Depression and Overdose Risk**
  - No reports of significant respiratory depression in clinical trials.
  - Overdose and misuse (e.g., injecting) of buprenorphine combined with other CNS depressants result in respiratory depression and risk overdose.

- **France experience:**
  - IV buprenorphine + high potency benzodiazepines → deaths
Misuse Potential of Buprenorphine

- **Euphoria:**
  - in non-opioid dependent individuals

- **Misuse:**
  - Potential less than full opioid agonists
  - Among opioid-dependent individuals is relatively low
  - Most illicit use is to prevent or treat withdrawal and cravings
  - Combination product theoretically less likely to be misused by IV route.

**Level of Evidence: Moderate**

- **Prior to induction:** obtain LFTs, INR, hepatitis serologies.
  - Avoid delay in starting treatment, can obtain LFTs at same time as induction.

- **Monitor LFTs.**
  - No empirical evidence to guide the frequency. Semi-annual is adequate if no other risk factors.
  - If patient does have clinical/laboratory evidence of hepatotoxicity, evaluate possible causes of liver injury.
    - Consideration should be given to lowering dose or discontinuing.
  - Subsequent studies have NOT shown significant increases in LFTs during SL buprenorphine treatment for patients with and without chronic hepatitis C.

**LFT Recommendations**

- Prior to induction: obtain LFTs, INR, hepatitis serologies.
  - Avoid delay in starting treatment, can obtain LFTs at same time as induction.

- Monitor LFTs.
  - No empirical evidence to guide the frequency. Semi-annual is adequate if no other risk factors.
  - If patient does have clinical/laboratory evidence of hepatotoxicity, evaluate possible causes of liver injury.
    - Consideration should be given to lowering dose or discontinuing.
  - Subsequent studies have NOT shown significant increases in LFTs during SL buprenorphine treatment for patients with and without chronic hepatitis C.
Which of the following are key drivers for buprenorphine misuse?

A. A person can easily create a euphoric effect by injecting buprenorphine, even if they are opioid tolerant.
B. Most illicit use is to prevent or treat withdrawal and cravings.
C. Many prescribers feel equipped to utilize this medication.
D. Starting to treat patients with an opioid use disorder is a low threshold opportunity.

Treatment Medications For Opioid Use Disorder: *Comparative Effectiveness*
Comparative Effectiveness: All Cause Mortality Rates

All cause mortality rates in and out of opioid substitution treatment with methadone or buprenorphine and overall pooled all cause mortality rates, 1974-2016.

Comparative Effectiveness: Overdose Mortality Rates in and out of Opioid Substitution Treatment

Overdose mortality rates in and out of opioid substitution treatment with methadone or buprenorphine and overall pooled overdose mortality rates, 1974-2016.
Comparative Effectiveness: Summary

- Methadone is associated with better retention in treatment than buprenorphine in OTP.
- Higher doses of both medications are associated with better retention in OTP.
- For patients with OUD, methadone and buprenorphine had similar therapeutic efficacy. Evidence quality was low to moderate.

XR-NTX versus BUP-NX

1. It is more difficult to initiate patients to extended-release naltrexone than buprenorphine/naloxone.
2. Once initiated, both medications were equally safe and effective.
Mortality Risk During and After Opiate Agonist Therapy (OAT)

- On methadone, 25 fewer deaths/1000 person years vs patients who discontinue it; Mortality risk in OAT is <1/3 of that expected in the absence of OAT.
- The mortality risk in the induction phase of methadone (1st 4 weeks) is high, but subsequently decreases with stabilization at 6 deaths/1000 person years in the remaining time in treatment. This did not occur with buprenorphine.
- The mortality risk in the 4 weeks immediately after cessation of OAT is high and could exceed 30 deaths/1000 person years.
- Buprenorphine probably also effective in reducing mortality, but quantification of averted deaths requires further studies.

Treatment Medications For Opioid Use Disorder: Treatment Access
The study examined the association between expansion of methadone and buprenorphine treatment and the prevalence of heroin overdose deaths.

**Conclusions:**
- Increased access to opioid agonist treatment was associated with a reduction in heroin overdose deaths
- Evidence-based medication treatment of OUD may decrease heroin overdose deaths

### After Nonfatal Opioid Overdose and Association With Mortality

**N=17,568**
- 12 m after overdose 11% on MMT (median 5 m), 17% on buprenorphine (median 4 m), 6% on naltrexone (median 1 m)

**Compared with no medication for OUD**
- MMT and buprenorphine treatment associated with decreased all-cause mortality and opioid-related mortality
- No associations between naltrexone and all-cause mortality or opioid-related mortality
Overcoming My Fear of Treating OUD

Dr. P was reluctant to obtain a waiver to prescribe buprenorphine for the treatment of OUD until her patient, Ms. L, with longstanding OUD, died from a fatal opioid overdose.

Caring for these patients has become the most meaningful part of my practice. Providing some sense of normalcy for patients whose lives are roiled by overdose and estrangement is the most profound therapeutic intervention I’ve engaged in as a caregiver. I did not know what Ms. L meant all those years ago when she said that she only wished to feel normal again. I wish that I’d listened more closely. I wish that I had not been afraid.
Role of Non-Pharmacological Treatment

- **Psychosocial services are often helpful.** Psychosocial services encourage utilization.

- **Additional Behavioral Therapy:** Three trials showed that additional behavioral therapy does NOT significantly improve outcomes over that achieved by buprenorphine PLUS “medical management” or “medical counseling.”

- **Patients should not be denied medication** should they refuse psychosocial services or if psychosocial services are not available.

Psychosocial Treatment Examples

- Individual counseling
- Group therapy
- Marital/family counseling
- Mutual help groups (e.g. AA, NA)
- SMART Recovery
- Women for Sobriety
- Secular Organizations for Sobriety (SOS)

Audience Response

Psychosocial treatment for persons with opioid use disorder should include:

A. A mandate to be in therapy to access medications.
B. Requirements to be in therapy early in treatment that decrease over time in treatment.
C. Offering of person-centered therapy options.
D. Having on-site counseling available including 24 hour call coverage.
Providers Clinical Support System (PCSS)

Through trainings and clinical coaching programs, PCSS's mission is to increase healthcare providers' knowledge and skills in the prevention, identification, and treatment of substance use disorders with a focus on opioid use disorders.

https://pcssnow.org/
SAMHSA grant to the American Academy of Addiction Psychiatry (AAAP) with a coalition of 22 national healthcare partner organizations. The consortium provides training and TA via local experts across the US, focusing on applying evidence-based practices to meet locally identified needs.

https://opioidresponsenetwork.org/

The ASAM National Practice Guideline (NPG) was updated in 2020.

- It provides information on evidence-based treatment of opioid use disorder (TOUD).
- It is the first text to address all the FDA-approved medications available to treat addiction involving opioid use and opioid overdose in a single document.
The ASAM Criteria

The ASAM Criteria is the most widely used and comprehensive set of guidelines for placement, continued stay, and transfer/discharge of patients with addiction and co-occurring conditions. It matches people to the level of care that safely and efficiently meets their needs and that is not biased towards inpatient or outpatient care. Patients should receive the least intensive but safe level of care.

Patient Resources

1. ASAM’s Opioid Addiction Treatment: A Guide for Patients, Families, and Friends
2. National Institute on Drug Abuse (NIDA) Patient Materials
3. National Alliance on Mental Illness (NAMI)
Activity 5: Revisiting Robert’s Case

- **Task:** Working with your group, develop Robert’s treatment plan.

- **Discuss:** Let’s revisit Robert’s case from a treatment perspective. Based on the content covered in this module, identify the appropriate treatment plan for Robert.

- **Time Allocated:** 10 minutes

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**Key Treatment Considerations:**

1. What medication and/or psychosocial treatment options would you recommend for Robert and why?

2. Assess Robert’s case to determine if he meets DSM-5 criteria for an opioid use disorder. If so, how? Is it mild, moderate, or severe?

3. What are the treatment options for Robert?

4. How would you assess the need for pharmacotherapy (e.g., methadone, buprenorphine, naltrexone) for Robert?

5. Is Robert a candidate for office-based opioid treatment (OBOT)? Why or why not?

6. What should the initial treatment plan include?
Activity 5: Revisiting Robert’s Case

- **Task:** Large Group Report Out
- **Discuss:** Let’s revisit Robert’s case from a treatment perspective. Based on the content covered in this module, identify the appropriate treatment plan for Robert.
- **Time Allocated:** 10 minutes

DETERMINING A TREATMENT PLAN FOR PATIENTS WITH OPIOID USE DISORDER

End of Session 2