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Introduction

This guide accompanies the primer for opioid use disorder assessment, treatment, overdose prevention, and care transitions. It can be used in conjunction with the primer or as a standalone tool to learn best practices in caring for hospitalized patients with opioid use disorder.

Case

Victor (he/him) is a 29-year-old man previously unconnected to care admitted to your hospital medicine service for cellulitis.

Nearing the end of hospital day 1, you learn he is tachycardic to 101, diaphoretic, restless, and crying in discomfort. You arrive to his room worried he is septic. He shares that he is in pain, and the oxycodone 5mg you ordered is not working. You examine his leg and see the redness receding from the outlined area of cellulitis. On further examination, you notice he is yawning and has rhinorrhea, gooseflesh skin, and dilated pupils. You want to broach a discussion about what else could be going on, including opioid withdrawal.

1. **All of the following are best practices for discussing opioid use except:**

   a. Tell Victor that you think he is an ‘addict’ and is withdrawing

   b. Use a non-judgmental and non-stigmatizing approach and share you are concerned that you are missing something and ask for permission to inquire about other causes to best care for him

   c. Use the tools of motivational interviewing including open-ended questions, affirmations, reflective statements, and summaries (OARS) to engage in a conversation about the role of opioids in his life, allowing you to go through the Diagnostic Statistical Manual of Mental
Disorders-5 (DSM-5) criteria for opioid use disorder (OUD)

d. Tell Victor that his cellulitis is improving and there is no reason to give him opioids

**Answer:**
The correct answers are B and C. Best practices for conversations about substance use include a non-judgmental and non-stigmatizing approach that focuses on your desire to provide the best care for the patient using a patient-centered, partnership approach. Motivational interviewing is an evidence-based practice that uses various principles and skills to engage people in conversations about behavior change.1-4

*See examples of how to approach this conversation with on the righthand side.*

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**Table 1: Stigmatizing and Non-Stigmatizing, Person-First Language Examples**

<table>
<thead>
<tr>
<th>Stigmatizing Terms – Don’t Use</th>
<th>Non-Stigmatizing Terms – Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Addict, alcoholic, junkie, IV drug user</td>
<td>■ Person with a substance (or opioid, alcohol, stimulant) use disorder, person who uses/injects drugs</td>
</tr>
<tr>
<td>■ Clean</td>
<td>■ In recovery, not-using</td>
</tr>
<tr>
<td>■ Dirty</td>
<td>■ Urine reactive/showed</td>
</tr>
<tr>
<td>■ Relapse</td>
<td>■ Return to use</td>
</tr>
</tbody>
</table>

*See more detailed example in primer.*
Case Continued

You ask for permission to discuss other causes of his symptoms using motivational interviewing and a non-judgmental, non-stigmatizing approach. Using open-ended questions, Victor shares that he is in opioid withdrawal and needs something now.

2. In the hospital setting, what can you offer to treat his opioid withdrawal?
   a. Clonidine, diphenhydramine, loperamide, ondansetron
   b. Methadone
   c. Buprenorphine
   d. Extended-release naltrexone
   e. Oxycodone
   f. Hydromorphone

Answer:

All the above except D can be used to treat opioid withdrawal in the hospital setting. In the community/outpatient setting A and C can be used to treat opioid withdrawal. B can be dispensed through methadone clinics in the outpatient setting for opioid withdrawal. The hospital setting allows full opioid agonists, answers E and F, for opioid withdrawal management even if patients do not want methadone or buprenorphine. However, hospitalists cannot discharge patients on short-acting opioid agonists (e.g., oxycodone and hydromorphone) to manage opioid use disorder/withdrawal in the outpatient setting. Of note, there are no federal restrictions on the use of methadone, buprenorphine, or other opioid agonists for hospitalized patients with OUD.

D is incorrect because although extended-release naltrexone is a Food and Drug Administration approved medication for OUD, it does not treat acute opioid withdrawal. Administering extended-release naltrexone to someone with opioids in their system will make their opioid withdrawal worse as it is an opioid antagonist. This could be life threatening if they have other chronic conditions that will make it difficult to tolerate the adrenergic surge of precipitated opioid withdrawal. Extended-release naltrexone can be administered to individuals with OUD who want an opioid antagonist/blocker as treatment and are opioid free for a minimum of seven days.

Answer A is also correct, though this does not address the underlying root cause of opioid withdrawal, and is inferior to buprenorphine and methadone. These medications are adjuncts that only treat opioid withdrawal symptoms. Patients in opioid withdrawal will need methadone, buprenorphine, and/or other opioid agonists for opioid withdrawal. See sidebar for details on adjunct medications.

Treating opioid withdrawal adequately can help patients complete their hospitalization and reduce post-discharge mortality. Opioid agonists (e.g., methadone, oxycodone, hydromorphone), answers B, E, and F, and partial agonists (buprenorphine), answer C, help maintain tolerance and reduce post discharge overdose risk in the setting of return to use. Longer acting medications, such as methadone and buprenorphine can relieve opioid withdrawal for periods of 24 hours. Shorter acting medications, including oxycodone and hydromorphone, require dosing with greater frequencies due to their shorter half-lives. Some patients may require both long- and short-acting opioids to manage opioid withdrawal (e.g., when methadone is being uptitrated in someone with a high opioid tolerance).
Sidebar:
- Clonidine 0.1-0.3 mg PO q6-8h PRN (not to exceed (NTE) 1.2 mg/day) sweating, restlessness, hot flashes, watery eyes, anxiety
- Loperamide 4 mg PO x 1, then 2 mg PRN (NTE 16 mg/24h) loose stools
- Ondansetron 4 mg PO q6h PRN nausea
- Trazodone 25-50mg nightly PRN or Melatonin 3mg nightly PRN insomnia
- Diphenhydramine 25-50 mg, PO q 8h PRN insomnia or anxiety
- Tylenol 650 mg PO q6h or Ibuprofen 400-600 TID PRN pain

3. Does Victor meet OUD criteria?
   a. Yes
   b. No
   c. Unsure

Answer:
The answer is A as Victor meets 9 of the 11 criteria for OUD. The 11 DSM-5 criteria for OUD are:
- Use despite health Consequences
- Inability to Cut down
- Cravings
- Loss of Control
- Compulsion to use
- Risk of bodily harm
- Role failure
- Relationship trouble
- Giving up activities to use
- Tolerance
- Withdrawal

*Remember the 5C’s (consequences, cut down, cravings, control, compulsion) and 3R’s (risk of harm, role failure, relationship trouble) as a shortcut to the DSM-5 criteria or pull out an online calculator.

Victor meets the nine Diagnostic Statistical Manual of Mental Disorders 5 (DSM-5) criteria bolded above for OUD. Those with 2-3 criteria in the last year have a mild OUD, 4-5 moderate OUD, and 6 or more severe OUD. Note that tolerance and withdrawal develop with all opioids. These alone do not meet OUD diagnostic criteria; individuals must meet additional criteria for a diagnosis. In general, if someone is using non-prescribed opioids and experiencing signs and symptoms of opioid withdrawal, including being hospitalized for opioid-related causes, they likely have an OUD. The DSM-5 can be used to make any substance use disorder diagnosis, including alcohol, benzodiazepine, cocaine, methamphetamine, and others.
Case Continued

Now that you diagnosed Victor with OUD, you inquire about what medications for OUD he has tried in the past. He reports he used buprenorphine once, but it made him sick and he is concerned that will happen again. He has never tried methadone. He is interested in cutting back because he would like to reconcile with his siblings with whom he has not connected with for 8 years. He would also like to find stable employment. You discuss buprenorphine, methadone, and extended-release naltrexone (must have at least a 7-day opioid free period) as treatment options. He decides to try methadone, though he is unsure if he would like to continue it after discharge.

4. What methadone dose would you start?
   a. None, there is no methadone clinic in the area
   b. 5mg
   c. 20mg
   d. 80mg

Answer:
The best answer is C, 20mg. Outpatient methadone titrations used in opioid treatment programs (OTPs, also known as methadone clinics) are adapted for hospital use. Generally, on day 1, patients receive 20-40mg of methadone. In individuals with a high tolerance (e.g., using fentanyl daily), a 30 mg starting dose is reasonable. If someone appears comfortable and their tolerance is unclear, start with 10 or 20 mg. You can give an additional 10mg every 3-4 hours for a maximum of 40 on day 1. On day 2, start with the total methadone dose they received on day 1 and give up to 10mg every 3-4 hours after the morning methadone dose for a maximum of 50mg on day 2. On day 3, start with the total methadone dose they received on day 2 and up to 10mg every 3-4 hours after the morning methadone dose for a maximum of 60mg on day 3. Thereafter, you can increase the methadone by up to 10mg every 3-5 days. Methadone's pharmacology accounts for this titration. Methadone peaks 2-4 hours after administration, has a half-life of 24-36 hours, and reaches steady state in 5 days. In the setting of synthetic opioids (e.g., fentanyl), methadone titrations are rapidly evolving.
A is not the best answer because even if there is no local methadone clinic, methadone can be used to manage opioid withdrawal in the inpatient setting. Discussing local methadone availability may allow Victor to consider buprenorphine instead.

B is incorrect because Victor endorses a high tolerance with daily fentanyl use.

D is incorrect because this is a new methadone start. The starting dose of methadone is between 10mg to 40mg on day 1.

Case Continued

You share with Victor that there is no nearby methadone clinic. He considers this and is now interested in buprenorphine, and potentially continuing it after discharge if he can start the medicine without becoming sick. He is excited that buprenorphine can be prescribed by a primary care doctor and that he can access it without going to an opioid treatment program (methadone clinic). As you share this with Victor, you recall buprenorphine’s properties. In addition to being a mu opioid receptor partial agonist, it is a kappa receptor antagonist and delta agonist, mediating its antidepressant and analgesic properties. See Table 2 to learn more about methadone and buprenorphine.

5. What dose of buprenorphine would you start?
   a. Gradual, low-dose, or “microdose” (hereinafter referred to as gradual)
   b. 2mg
   c. 8mg
   d. 16mg
   e. Need more information

<table>
<thead>
<tr>
<th>Table 2.</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Retention</td>
<td>Higher than buprenorphine due to structured treatment</td>
<td>Daily-monthly; can also provide as directly observed therapy in some OTPs</td>
</tr>
<tr>
<td>Office Visits</td>
<td>Daily visits to Opioid Treatment Program (OTP – methadone clinic). Take home doses allowed eventually</td>
<td>Any clinician during hospitalization</td>
</tr>
<tr>
<td>Prescribe in Hospital</td>
<td>Any clinician during hospitalization</td>
<td>Any clinician during hospitalization</td>
</tr>
<tr>
<td>Prescribe at Discharge</td>
<td>Methadone can currently only be dispensed at OTPs</td>
<td>Any clinician due to the MAT Act</td>
</tr>
<tr>
<td>Sedation</td>
<td>Yes at high doses, non-tolerant patients, or slow metabolizers</td>
<td>Ceiling effect for respiratory depression</td>
</tr>
<tr>
<td>Withdrawal When Starting</td>
<td>Start anytime. Days-weeks to reach comfortable dose</td>
<td>Must be in withdrawal or initiate via gradual titration to reduce risk of withdrawal</td>
</tr>
</tbody>
</table>

Methadone and Buprenorphine Comparison
Answer:
The correct answer is E, we need more information to make a person-centered decision. Traditionally, clinicians started buprenorphine when patients were in mild-moderate opioid withdrawal based on scoring at least 8-10 on the Clinical Opiate Withdrawal Scale (COWS). Individuals are in mild-moderate withdrawal when they have at least 1 objective sign of withdrawal (e.g., mydriasis, sweating, rhinorrhea, tachycardia, diarrhea, tremor) and 1 subjective sign (e.g., nausea, myalgias, chills).

New methods of starting buprenorphine are rapidly developing. These gradual titrations mean that individuals no longer have to be in withdrawal to start buprenorphine. This may also reduce the risk of precipitated withdrawal which can happen when starting buprenorphine due to buprenorphine’s partial agonism and high affinity for mu opioid receptors.

This is important given the prevalence of fentanyl across the United States. Though fentanyl is a short-acting opioid, it behaves like a long-acting opioid with regular use as it accumulates in adipose tissue. Further guidance on starting buprenorphine is below.

Clinicians should inform patients of the options available to start buprenorphine in their hospital. You can offer a urine toxicology screen (including methadone, if available) to confirm the opioids in a patient’s system when starting buprenorphine. Clinicians should also inquire about last opioid use, types of opioids used, and ensure other long-acting opioids (e.g., MS Contin, methadone) were not recently used.

Buprenorphine initiation options include:

1. Traditional initiation generally starts with 2-8mg of buprenorphine. You can start buprenorphine when the patient is in mild-moderate opioid withdrawal with a COWS score of 8-10. However, it is ultimately up to the patient when during their withdrawal they want to start buprenorphine.

2. Gradual buprenorphine regimens vary, and an example is below. Of note, most patients will require full opioid agonists (e.g., hydromorphone, oxycodone) as they start buprenorphine because gradual buprenorphine doses are too low to treat opioid withdrawal. If patients have acute pain, they may need full-agonist opioids in addition to buprenorphine.
   a. Day 1: Buprenorphine 0.5mg q6h = 2mg total (continue full opioid agonist, i.e., oxycodone 15-20mg q4, hydromorphone 6-8mg q4, methadone 40 mg daily)
   b. Day 2: Buprenorphine 1mg q6h = 4mg total (continue full opioid agonist)
   c. Day 3: Buprenorphine 2mg q6h = 8mg total (continue full opioid agonist)
   d. Day 4: Buprenorphine 16-32mg in daily or divided dose. Start to decrease/stop full agonists (except if needed for acute pain)

Therapeutic buprenorphine doses range from 16-24mg daily, but as with methadone, some need less, and some need more. In addition, buprenorphine provides analgesia for 6-8 hours. This means that buprenorphine can be dosed 2-4 times daily to maximize its analgesic properties. Dose buprenorphine daily if it is not needed to treat concurrent pain. Ultimately, this should be guided by the patient.
The formulations of buprenorphine approved for OUD include buprenorphine-naloxone SL films, buprenorphine-naloxone SL tabs (also available as a buprenorphine monopoduct), and extended-release buprenorphine (subcutaneous injection that lasts 30 days). In the hospital setting other buprenorphine formulations may support gradual buprenorphine starts including buccal buprenorphine, buprenorphine patches, and intravenous buprenorphine. These formulations allow low doses of buprenorphine to be administered. Buprenorphine films and tabs of 2mg doses can also be quartered to administer 0.5mg doses, but hospital pharmacy and therapeutics committees vary in allowing this process due to variable dosing and absorption.20

Case Continued
Victor proceeds with a gradual buprenorphine start and does well on buprenorphine-naloxone SL film 8-2mg TID and is ready for discharge on oral antibiotics. You discharge Victor with a two-week supply of buprenorphine-naloxone SL films, intranasal naloxone for overdose reversal, his remaining antibiotic doses, and a follow-up appointment.

Victor follows up with his primary care clinician in one week and feels well on his buprenorphine-naloxone dosing. His opioid cravings are controlled, and he has not returned to fentanyl use.
References


