OPIOID USE DISORDER (OUD)

CASE-BASED APPROACH TO THE INPATIENT MANAGEMENT OF OPIOID USE DISORDER

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Updates in Hospital Medicine
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DISCLOSURES

None

OBJECTIVES

- Review FDA-approved medications for opioid use disorder.
- Review the DSM-5 diagnostic criteria for opioid use disorder
- Discuss methadone induction and management of co-occurring pain.
- Distinguish between addiction and dependence.
- Define what is meant by shared decision making.
- Discuss buprenorphine induction, management of co-occurring pain, and precipitated withdrawal.
- Highlight ways to stop using stigmatizing language and improve the accuracy of our terminology as it pertains to opioid use disorder.

MEDICATION FOR OPIOID USE DISORDER (MOUD)

"Detoxification may be good for a lot of things, staying off drugs is not one of them." - Walter Ling, MD

Goal

- Prevent euphoria and prevent withdrawal
- Remove compulsive behavior and harmful consequences
- Prevent death

Duration

- Indefinite

MEDICATION FOR OPIOID USE DISORDER (MOUD)

Methadone - 1972

Naltrexone - 1984

Buprenorphine - 2002

METHADONE

Synthetic opioid

Mechanism	Mu-receptor full agonist
Metabolism	Hepatic CYP450 3A4 (2D6, 1A2)
Half-life	24 - 36 hrs
Adverse reactions	QT interval prolongation, respiratory depression, hypotension, sedation
How supplied	PO and IV
Dosing	Varying doses given once daily

METHADONE

Clinical considerations

- Many drug-drug interactions
  - Meds that prolong QT interval
  - Meds that interact with CYP450
  - Serotonergic agents
- High interpatient pharmacokinetic and pharmacodynamic variability
- Conversion ratios to other opioids not accurate
- Analgesia 6 - 8 hrs

NALTREXONE

Full antagonist

Mechanism	Mu-receptor antagonist. Blocks stimulation of dopamine reward system.
Metabolism	Hepatic
Half-life	4 hours
Adverse reactions	Nausea, vomiting, abdominal pain, headache, dizziness, hepatotoxicity
How supplied	PO and IM
Dosing	50 mg po daily or 380 mg IM once monthly

NALTREXONE

Clinical considerations

- High affinity, low dissociation
- Eliminates tolerance --> overdose death
- Risk of severe precipitated withdrawal
- Acute pain: unresponsive to opioids.
- IM formulation: Vivitrol

BUPRENORPHINE

Semi-synthetic opioid

Mechanism	Mu-receptor partial agonist
Metabolism	Hepatic CYP450 3A4 (extensive first-pass metabolism)
Half-life	38 hrs
Adverse reactions	Anticholinergic, hepatotoxicity, CNS depression
How supplied	SL, buccal, IV, IM, transdermal
Dosing	Varying doses

NALTREXONE

Clinical considerations

- Desirable properties in OUD
  - Mixed agonist and antagonist
  - High affinity, low dissociation
  - Long half-life
  - Ceiling effect on respiratory depression
- Risk of precipitated withdrawal
- X-waiver required for prescribing
- Analgesia 4 - 6 hrs

CASE - HG

23M IVDU and daily heroin abuser admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He wants to get clean but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

STIGMATIZING LANGUAGE!

AVOID	PREFERRED
intravenous drug user (IVDU)	person who injects drugs
abuser	person who uses or misuses
clean	person in recovery or abstinent

CASE - HG

23M with opioid use disorder who injects drugs and uses heroin daily admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He is motivated to be in recovery but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

What is the best approach for starting methadone while patient is hospitalized?

A: Federal regulations prohibit the prescribing of methadone in the inpatient setting for treatment of opioid use disorder.
B: Initiate short-acting opioids and titrate as needed to manage withdrawal symptoms for 48 hours then convert to daily methadone equivalent.
C: Start methadone 10 mg q4h prn once COWS $\geq$ 8 (start with 5 mg if medically ill, elderly, or benzos)
D: Start methadone 30 mg po daily

CASE - HG

23M with opioid use disorder who injects drugs and uses heroin daily admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He is motivated to be in recovery but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

What is the best approach for starting methadone while patient is hospitalized?

Correct answer(s):

C: Start methadone 10 mg q4h prn once COWS > 8 (start with 5 mg if medically ill, elderly, or benzos)
D: Start methadone 30 mg po daily

METHADONE INDUCTION

Obtain EKG with first 24 hours to check QT interval.

Methadone initiation: Do not exceed total dose of 40 mg/day.

- OPTION 1: Start methadone 10 mg q4h prn opioid withdrawal (start with 5 mg if medically ill, elderly, or benzos)
- OPTION 2: Start methadone 30 mg po x 1 dose, then additional 10 mg in $\geq$ 4 hrs prn opioid withdrawal

If already established on methadone maintenance, confirm with clinic.

- Must confirm methadone clinic involvement, current dosing, and last dose.
- If unable to confirm, do not exceed 40 mg/day

CASE - HG

23M with opioid use disorder who injects drugs and uses heroin daily admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He is motivated to be in recovery but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

What is the best approach for starting methadone while patient is hospitalized?

What is wrong with...

A: Federal regulations prohibit the prescribing of methadone in the inpatient setting for treatment of opioid use disorder.

METHADONE FEDERAL REGULATIONS

Conditions For Distribution And Use Of Methadone Products For The Treatment Of Opioid Addiction

Code of Federal Regulations, Title 42, Sec 8

Methadone products when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR § 12). See below for important regulatory exceptions to the general requirement for certification to provide opioid agonist treatment.

Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of the drug supply, revocation of the program approval, and injunction precluding operation of the program.

Regulatory Exceptions To The General Requirement For Certification To Provide Opioid Agonist Treatment:

1. During inpatient care, when the patient was admitted for any condition other than concurrent opioid addiction (pursuant to 21CFR 1306.07(c)), to facilitate the treatment of the primary admitting diagnosis).
2. During an emergency period of no longer than 3 days while definitive care for the addiction is being sought in an appropriately licensed facility (pursuant to 21CFR 1306.07(b)).

"shall only be dispensed by opioid treatment programs"

EXCEPTIONS:

1. During inpatient care, when admitted for any condition other than concurrent opioid addiction.

2. Emergency period of no longer than 3 days while definitive care...being sought.

CASE - HG

23M with opioid use disorder who injects drugs and uses heroin daily admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He is motivated to be in recovery but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

What is the best approach for starting methadone while patient is hospitalized?

What is wrong with...

B: Initiate short-acting opioids and titrate as needed to manage withdrawal symptoms for 24 hours then convert to daily methadone equivalent.

METHADONE BLACK BOX WARNING

Deaths, cardiac and respiratory, have been reported during initiation and conversion of pain patients to methadone treatment from treatment with other opioid agonists. It is critical to understand the pharmacokinetics of methadone when converting patients from other opioids (see DOSAGE AND ADMINISTRATION). Particular vigilance is necessary during treatment initiation, during conversion from one opioid to another, and during dose titration.

Respiratory depression is the chief hazard associated with methadone hydrochloride administration. Methadone's peak respiratory depressant effects typically occur later, and persist longer than its peak analgesic effects, particularly in the early dosing period. These characteristics can contribute to cases of iatrogenic overdose, particularly during treatment initiation and dose titration.

In addition, cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed during treatment with methadone. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.

Methadone treatment for analgesic therapy in patients with acute or chronic pain should only be initiated if the potential analgesic or palliative care benefit of treatment with methadone is considered and outweighs the risks.

KEY POINTS:

1. Death occurs during initiation and conversion from other opioids.

2. Peak respiratory depressant effects occur later than analgesic effects.

3. QT interval prolongation more common with multiple daily dosing for pain.

CASE - HG

23M with opioid use disorder who injects drugs and uses heroin daily admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He is motivated to be in recovery but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

You start him on methadone 30 mg po daily.

- 6 hours later, he reports uncontrolled withdrawal symptoms.
- You see the patient and his COWS > 10.
- **You give an additional 10 mg dose.**
- **The following day, start methadone 40 mg po qday.**

CASE - HG

23M with opioid use disorder who injects drugs and uses heroin daily admitted for fever and bacteremia diagnosed with endocarditis now requiring IV antibiotics. He is motivated to be in recovery but quickly shuts down any discussion about starting buprenorphine after experiencing precipitated withdrawal a couple months ago. He is requesting to start methadone.

Initiated on methadone 40 mg po qday.

Discharge planning:

- Patient cannot be discharged with a script for methadone.
- Interested in ongoing treatment --> refer to a federally regulated methadone clinic.
- Not transitioning to methadone clinic --> taper based on LOS (5 - 10 mg daily).
- Average opioid maintenance dose: 80 - 120 mg/day.

CASE - MR

56M opioid addict with previous abuse of heroin on MAT with methadone, essential hypertension, and diabetes mellitus admitted for left diabetic foot now status post midfoot amputation and acute post-op pain. Orthopedic surgery is consulting medicine for management of acute pain and concern for pain medication seeking behavior while on methadone.

STIGMATIZING LANGUAGE!

AVOID	PREFERRED
opioid addict	person with opioid use disorder
abuse	use or misuse
medication-assisted treatment	medication for opioid use disorder

CASE - MR

56M PMH opioid use disorder in recovery on MOUD with methadone, essential hypertension, and diabetes mellitus admitted for left diabetic foot now status post midfoot amputation and acute post-op pain. Orthopedic surgery is consulting medicine for management of acute pain while on methadone.

- Patient reports methadone dose of 90 mg po qday at XYZ Methadone Clinic for 3 years.
- In recovery since 2015. No illicit drug use in 3 years.
- PMH: type 2 diabetes mellitus and HTN
- SH: Domiciled. Married with 2 grown children. Works as an accountant. No alcohol or tobacco use.
- FH: father died of heroin overdose > 20 years ago; mother has alcohol use disorder in recovery and DM

USING ACCURATE TERMINOLOGY

Patient MR...

A. is addicted to opioids
B. is opioid dependent
C. has an opioid use disorder
D. B + C
E. all of the above

ANSWER: D - opioid dependent and opioid use disorder

USING ACCURATE TERMINOLOGY

A newborn baby exposed to opioids in utero who has signs or symptoms of opioid withdrawal...

A. is addicted to opioids
B. is opioid dependent
C. has an opioid use disorder
D. B + C
E. all of the above

ANSWER: B - opioid dependent

USING ACCURATE TERMINOLOGY

A patient with chronic cancer pain who was been stabilized on fentanyl transdermal patch and MSIR (morphine sulfate immediate release) and takes her medication as prescribed...

A. is addicted to opioids
B. is opioid dependent
C. has an opioid use disorder
D. B + C
E. all of the above

ANSWER: B - opioid dependent

ADDICTION VS DEPENDENCE

Addiction

- A treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. - ASAM 2019

Dependence

- Relying on a substance to function normally. Abruptly stopping leads to unpleasant, dangerous, or life-threatening physical symptoms.

IMPORTANT DISTINCTION:

Opioid agonist therapy is not trading one addiction for another!

CASE - MR

56M PMH opioid use disorder in recovery on MOUD with methadone, essential hypertension, and diabetes mellitus admitted for left diabetic foot now status post midfoot amputation and acute post-op pain. Orthopedic surgery is consulting medicine for management of acute pain while on methadone.

Step one: contact methadone clinic

- Scenario 1: You contact the RN at the clinic and he confirms the dose to be 90 mg daily. Last dose yesterday.
- Scenario 2: No one answers. You only get an answering machine and no one calls you back.

CASE - MR

56M PMH opioid use disorder in recovery on MOUD with methadone, essential hypertension, and diabetes mellitus admitted for left diabetic foot now status post midfoot amputation and acute post-op pain. Orthopedic surgery is consulting medicine for management of acute pain while on methadone.

Scenario 1: You contact the RN at the clinic and he confirms the dose to be 90 mg daily. Last dose yesterday. What is the next best step?

A: Order methadone 90 mg po daily.
B: Divide home methadone dose into divided doses. Order methadone 30 mg po q8h.
C: Calculate the equianalgesic conversion ratio and convert methadone home dose to hydromorphone IV while managing post-op pain.
D: Increase the methadone dose in an attempt to avoid fast-acting opioids given history of OUD. Order methadone 30 mg po q6h.

CASE - MR

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Correct answer(s):

A: Order methadone 90 mg po daily.
B: Divide home methadone dose into divided doses. Order methadone 30 mg po q8h.

ACUTE PAIN AND METHADONE MAINTENANCE

Maintenance opioid needs: continue already established methadone dose

- Consider dividing the dose and administering every 6 - 8 hr to take advantage of analgesic properties
- Do not consider methadone to be adding any considerable pain relief

Acute pain needs: multimodal approach

- Non-pharmacological options: cold and heat therapy
- Non-opioid adjuvant pain medications: APAP, NSAIDS, gabapentin, pregabalin, muscle relaxers
- Opioids: short-acting full agonists

Relapse concern

- No evidence treating acute pain causes relapse
- Untreated pain much more likely to result in relapse

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What is wrong with...

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Scenario 2: No one answers. You only get an answering machine and no one calls you back. What is the next best step?

- A: Hold methadone until confirmation. Try clinic again when they open in the morning.
- B: You see a endocrinology clinic note from last month stating the same dose of methadone. Start methadone 30 mg po q8h.
- C: Confirm the dose on the prescription drug monitoring program (PDMP).
- D: Start methadone 30 mg po daily. Try clinic again when they open in the morning.

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Scenario 2: No one answers. You only get an answering machine and no one calls you back. What is the next best step?

Correct answer:

- **D: Start methadone 30 mg po daily. Try clinic again when they open in the morning.**

WHY ARE THESE INCORRECT?

A. Hold methadone until confirmation. Try clinic again when they open in the morning.

- Risk of opioid withdrawal
- Risk of destabilization

B: You see an endocrinology clinic note from last month stating the same dose of methadone. Start methadone 30 mg po q8h.

- Possible dose change
- Possible discharge from clinic

C: Confirm the dose on the prescription drug monitoring program (PDMP).

- Protected by 42 CFR Part 2

CASE - MR

56M PMH opioid use disorder in recovery on MOUD with methadone, essential hypertension, and diabetes mellitus admitted for left diabetic foot now status post midfoot amputation and acute post-op pain. Orthopedic surgery is consulting medicine for management of acute pain while on methadone. XZY clinic confirmed methadone dose of 90 mg po daily.

What is the next best step(s) to address and manage the acute pain?

A: Implement shared decision making
B: Order non-pharmacological pain management strategies
C: Order non-opioid pharmacotherapy including scheduled acetaminophen
D: Order short-acting opioid analgesics
E: All of the above

CASE - MR

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What is the next best step(s) to address and manage the acute pain?

Correct answer(s):

E: All of the above

WHAT IS SHARED DECISION-MAKING?

SAMHSA: Substance Abuse and Mental Health Services Administration defines as...

- An **emerging best practice** in behavioral and physical health
- Aims to help people in treatment and recovery have **informed, meaningful, and collaborative discussions** with providers
- Providing **objective** information
- Allows people in treatment and recovery to then weigh that information against **their personal preferences and values**
- **Empowers** people who are seeking treatment or in recovery to work together with their service providers
- Allows people to **be active in their own treatment**

CASE - MR

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So you talk to Mark...

- He is scared to take additional pain medications. --> You are able to provide counseling.
- He broke his arm a couple years ago. ---> He is able to explain what has worked in the past.
- He thinks it would be helpful to involve his wife in the discussion. --> Incorporate family support.

CASE - MR

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Recommendations:

1. Divide home methadone dose and give 30 mg po q8h.
2. Start acetaminophen 975 mg po tid.
3. Start gabapentin 100 mg po tid.
4. Add oxycodone 10 - 15 mg po q4h prn pain. Continue to reassess for appropriateness of dose titration to maintain adequate pain control.

CASE - MR II

56M PMH opioid use disorder in recovery on MOUD with Suboxone, essential hypertension, and diabetes mellitus admitted for left diabetic foot infection. Orthopedic surgery consulted and recommends midfoot amputation in 2 days. Orthopedic surgery defers pain management to the primary team.

- Patient has been stable on buprenorphine/naloxone 8 mg SL bid for 3 years.
- In recovery since 2015. No illicit drug use in 3 years.
- PMH: type 2 diabetes mellitus and HTN
- SH: Domiciled. Married with 2 grown children. Works as an accountant. No alcohol or tobacco use.
- FH: father died of heroin overdose > 20 years ago; mother has alcohol use disorder in recovery and DM

CASE - MR II

56M PMH opioid use disorder in recovery on MOUD with Suboxone, essential hypertension, and diabetes mellitus admitted for left diabetic foot infection. Orthopedic surgery consulted and recommends midfoot amputation in 2 days. Orthopedic surgery defers pain management to the primary team.

How should you manage his maintenance Suboxone 8 mg SL bid perioperatively?

- A: stop Suboxone since it is a partial agonist and will impede acute pain control
- B. increase Suboxone to 8 mg SL q8h to take advantage of 6 - 8 hr analgesia window
- C: continue Suboxone 8 mg SL bid
- D: transition to dose equivalent of methadone

CASE - MR II

56M PMH opioid use disorder in recovery on MOUD with Suboxone, essential hypertension, and diabetes mellitus admitted for left diabetic foot infection. Orthopedic surgery consulted and recommends midfoot amputation in 2 days. Orthopedic surgery defers pain management to the primary team.

How should you manage his maintenance Suboxone 8 mg SL bid perioperatively?

Correct answer(s):

C: continue Suboxone 8 mg SL bid

WHY ARE THESE CONSIDERED LESS OPTIMAL?

A: stop Suboxone since it is a partial agonist and will impede acute pain control

- Transition back may be difficult as would likely require an induction
- Risk of destabilization

B. increase Suboxone to 8 mg SL q8h to take advantage of 6 - 8 hr analgesia window

- Likely easier to control pain with addition of a full agonist

D: transition to dose equivalent of methadone

- No clear dose conversion
- Risk of destabilization

PERIOPERATIVE MANAGEMENT OF BUPRENORPHINE

Step 1: Determine total 24-hour home dose of buprenorphine

- ≤ 8 mg
  - Continue home dose throughout perioperative period (do not discontinue prior to surgery)
- > 8 mg
  - Proceed to Step 2

MGB Recommendations for the Perioperative Management of Home Buprenorphine-Naloxone. Assessed 7/29/2021.

PERIOPERATIVE MANAGEMENT OF BUPRENORPHINE

Step 2: Determine anticipated opioid requirements/pain after surgery

Moderate to high opioid requirements

- > 16 mg:
  - before surgery: consider dose reduction to 16 mg/24 hr
  - day of surgery: consider further dose reduction to 8 mg/24 hr + full agonist opioids prn
  - discharge planning: full agonist opioid taper plan + resume home dose of buprenorphine
- ≤ 16 mg: consider continuing home dose

Low opioid requirements

- continue home regimen throughout perioperative period

PERIOPERATIVE MANAGEMENT OF BUPRENORPHINE

TAKE HOME MESSAGE:

AVOID stopping buprenorphine

CASE - MR II

56M PMH opioid use disorder in recovery on MOUD with Suboxone, essential hypertension, and diabetes mellitus admitted for left diabetic foot infection. Orthopedic surgery consulted and recommends midfoot amputation in 2 days. Orthopedic surgery defers pain management to the primary team.

In addition to continuing his home dose of Suboxone 8 mg SL bid...

- Contact anesthesiology to discuss possibility of a regional block
- Implement non-pharmacological pain management strategies
- Utilize non-opioid pharmacotherapy
- **Use high-affinity IV full agonist opioids (i.e. hydromorphone IV)**

CASE - CW

47M PMH chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability. Reports being on chronic opioids for 14 years. Had a pain contract but lost her prescriber 2 years ago due to a dirty urine. Has since been purchasing/obtaining illicit opioids and states they have always been in the form of pharmaceutical grade oxycodone.

STIGMATIZING LANGUAGE!

AVOID	PREFERRED
dirty	positive
clean	negative

CASE - CW

47M PMH chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability. Reports being on chronic opioids for 14 years. Had a pain contract but lost her prescriber 2 years ago due to urine toxicology screen positive for fentanyl. Has since been purchasing/obtaining illicit opioids and states they have always been in the form of pharmaceutical grade oxycodone.

- Admits to oral and insufflation. Denies ever injecting drugs.
- Her husband who obtained illicit oxycodone died 2 months ago from accidental opioid overdose.
- Ran out of "Percocet" 24 hours ago.

CASE - CW

What is the most likely explanation for her urine toxicology screen negative for oxycodone and positive for fentanyl?

A: Laboratory error.

B: Percocet tablets were actually non-pharmaceutical grade pressed fentanyl tablets

C: All oxycodone has metabolized. Fentanyl false-positive.

D: She is not being forthcoming

urine opiates	negative
urine oxycodone	negative
urine fentanyl	positive

CASE - CW

What is the most likely explanation for her urine toxicology screen negative for oxycodone and positive for fentanyl?

B: Percocet tablets were actually non-pharmaceutical grade pressed fentanyl tablets

urine opiates	negative
urine oxycodone	negative
urine fentanyl	positive

USING ACCURATE TERMINOLOGY

Opioids refer to all natural, semisynthetic, and synthetic opioids.

- Opiates (natural) - heroin, morphine, codeine
- Semisynthetic - oxycodone, hydrocodone, hydromorphone, and oxymorphone
- Synthetic - methadone, fentanyl

Image: https://premierbiotech.com/innovation/opi-vs-oxy/. Accessed 8/12/2021

CASE - CW

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Does she have an opioid use disorder?

Refer to Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

DSM-5 CRITERIA

SEVERITY

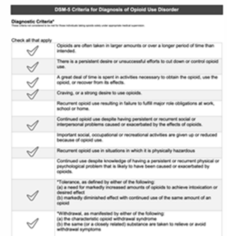
Mild: 2 - 3 symptoms

Moderate: 4 - 5 symptoms

Severe: ≥ 6 symptoms

Our patient:

8 symptoms = Severe



DSM-5 Criteria for Diagnosis of Opioid Use Disorder

Diagnostic Criteria*

Check all that apply

✓	Opioids are often taken in larger amounts or over a longer period of time than intended.
✓	There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
✓	A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
✓	Craving, or a strong desire to use opioids.
	Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home.
✓	Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
	Important social, occupational or recreational activities are given up or reduced because of opioid use.
✓	Recurrent opioid use in situations in which it is physically hazardous
	Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
✓	*Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of an opioid
✓	*Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

CASE - CW

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Does she have an opioid use disorder?

Refer to Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

Diagnosis: severe opioid use disorder.

CASE - CW

47M PMH chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability. Reports being on chronic opioids for 14 years. Had a pain contract but lost her prescriber 2 years ago due to urine toxicology screen positive for fentanyl. Has since been purchasing/obtaining illicit opioids and states they have always been in the form of pharmaceutical grade oxycodone.

Is she experiencing opioid withdrawal syndrome?

Refer to Clinical Opiate Withdrawal Scale (COWS)

CLINICAL OPIATE WITHDRAWAL SCALE (COWS)

APPENDIX 1
Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:________ Date and Time ___/___/___:____

Reason for this assessment ________

Resting Pulse Rate ______beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset** *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating *over past 1/2 hour not accounted for by room temperature or patient activity* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute

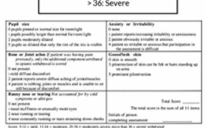
SEVERITY

5 - 12: Mild

13 - 24: Moderate

25 - 36: Moderately severe

> 36: Severe



Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score ______ The total score is the sum of all 11 items Initials of person completing assessment ______

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal
This version may be copied and used clinically.

CASE - CW

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Is she experiencing opioid withdrawal syndrome?

Refer to Clinical Opiate Withdrawal Scale (COWS)

COWS = 18
Diagnosis: moderate opioid withdrawal syndrome

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder.

Symptomatic management - the "PRNs":

ibuprofen	loperamide
acetaminophen	hydroxyzine
dicyclomine	trazodone
ondansetron	famotidine
clonidine	Maalox

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder.

What is the next best step to manage her opioid withdrawal syndrome and treat her opioid use disorder?

A: Methadone PO
B: Buprenorphine/naloxone sublingual film
C: Naltrexone PO
D: Oxycodone with plans for a fast taper off and arrange follow-up at the bridge clinic. She has never injected and her supply has been cut off. This is her first presentation. She may not require maintenance MOUD.
E: Invest in shared decision making.

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder.

What is the next best step to manage her opioid withdrawal syndrome and treat her opioid use disorder?

Correct answer(s):

E: Invest in shared decision making.

MOUD COMPARISON

Methadone
- Daily commitment
- Strict protocols
- Drug interactions
- No risk of precipitated withdrawal

Buprenorphine
- Maintenance supply
- More private
- Respiratory depression ceiling
- Risk of precipitated withdrawal

Naltrexone
- Eliminates tolerance
- Increased overdose risk
- Not as effective
- Must be opioid-free for 7-12 days

CASE - CW

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What is the next best step to manage her opioid withdrawal syndrome and treat her opioid use disorder?

What's wrong with...

D: Oxycodone with plans for a fast taper off and arrange follow-up at the bridge clinic. She has never injected and her supply has been cut off. This is her first presentation. She may not require maintenance MOUD.

2020: WAKEMAN ET AL: DIFFERENT PATHWAYS FOR OUD

Comparative Effectiveness of Different Treatment Pathways for Opioid Use Disorder
JAMA Network Open. 2020;3(2)

Design	Retrospective comparative effectiveness research study
Population	40, 885 adults with opioid use disorder
Goals/Outcomes	Opioid-related overdose or serious acute care use during 3 and 12 months after initial treatment.
Interventions	6 different treatment pathways: 1) no treatment; 2) inpt detox or residential services; 3) intensive behavioral health; 4) buprenorphine or methadone; 5) naltrexone; 6) non-intensive behavioral health
Results	Only treatment with buprenorphine or methadone was associated with reduced risk of overdose and serious opioid-related acute care compared with no treatment

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder.

What is the next best step to manage her opioid withdrawal syndrome and treat her opioid use disorder?

A: Methadone PO. Consult social work to arrange for methadone clinic intake appointment.
B: Buprenorphine/naloxone SL. Plan for induction this admission.
C: Naltrexone 50 mg po daily. Provide outpatient prescription. Instruct patient to take first dose in 7 days.

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder.

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CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder.

What is the next best step to manage her opioid withdrawal syndrome and treat her opioid use disorder?

- Patient is not interested in methadone.
- Has experienced self-induced precipitated withdrawal in the past. Expresses concern about having to experience it again.

B: Buprenorphine/naloxone SL. Plan for induction this admission.

BUPRENORPHINE/NALOXONE INDUCTION

Traditional Approach

1. Calculate clinical opioid withdrawal score (COWS)
2. Once COWS > 8, give buprenorphine/naloxone 4 mg SL now - OR - 2 mg SL now and may repeat in 30 min
3. Reassess in one hour. If symptoms improved but still present, give additional 4 - 8 mg SL
4. Continue to give 4 - 8 mg every 4 hours until symptoms resolve (up to 16 - 24 mg/day)

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder. She agrees to a buprenorphine/naloxone induction.

Buprenorphine/naloxone induction:

11:00 AM:

- COWS = 18
- Give buprenorphine/naloxone 2 mg SL x 1 dose.
- Reassess in one hour.

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder. She agrees to a buprenorphine/naloxone induction.

Buprenorphine/naloxone induction:

1:00 PM. Total dose received: buprenorphine/naloxone 2 mg SL.

- COWS = 10
- Give another dose of buprenorphine/naloxone 4 mg SL x 1
- Reassess in one hour

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder. She agrees to a buprenorphine/naloxone induction.

Buprenorphine/naloxone induction:

2:00 PM. Total dose received buprenorphine/naloxone 6 mg SL.

- COWS = 8
- Give another dose of buprenorphine/naloxone 8 mg SL x 1
- Reassess in one hour.

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder. She agrees to a buprenorphine/naloxone induction.

Buprenorphine/naloxone induction:

5:00 PM. Total dose received buprenorphine/naloxone 14 mg SL.

- COWS = 3
- Start buprenorphine/naloxone 8 mg SL bid in am

CASE - CW

47M PMH severe OUD and chronic low back pain on chronic opioids presents to the hospital with complaints of whole body aches, diarrhea, abdominal cramps and irritability due to opioid withdrawal syndrome. Patient is requesting treatment for opioid use disorder. She agrees to a buprenorphine/naloxone induction.

Discharge planning:

- Buprenorphine/naloxone 8 mg SL bid
- You confirm her PCP has an X-waiver and is willing to manage her buprenorphine/naloxone.
- You provide her with a prescription for a 7-day supply to bridge to her next PCP appointment.
- Social worker has arranged for substance use disorder intensive outpatient program.

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis

- 4-day binge of heroin, crystal meth, and crack cocaine above a baseline of daily heroin use.
- "heroin, meth, and crack", injected into left AC and neck "a few hours ago."
- Seen by ortho who recommends CT wrist and admission for IV antibiotics.
- Admit to general medicine.

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis

- Arrives on the floor.
- Patient requesting Suboxone this admission.
- COWS = 10. He has experienced self-inflicted precipitated withdrawal and requests to wait.
- Urine toxicology screen positive for amphetamine, cocaine, and fentanyl.

CASE - LC

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The following day...

- RN pages provider: pt is feeling very sick from opioid withdrawal, wants Suboxone, wants to see you ASAP
- Pt pacing around the room. Diaphoretic, ripping his shirt off, anxious, crying, piloerection
- COWS 18 = moderate opioid withdrawal
- 30+ hrs since last use

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

Criteria for traditional induction:

- COWS > 8
- 6 -12 hrs since last use of short-acting opioid

Give buprenorphine 4 mg SL x 1 now

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

20 minutes later...

- Profuse sweating, walking around the room, stripping down naked, runs to the shower, dru heaves and refuses to come out
- COWS = 25

PRECIPITATED OPIOID WITHDRAWAL!

WHAT IS PRECIPITATED WITHDRAWAL?

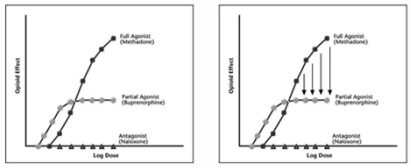

Image: https://www.nuabt.org/education/technical_explanation_buprenorphine.cfm. Accessed 5/21/2021

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

Patient is experiencing PRECIPITATED opioid withdrawal

Why did this happen?

Fentanyl pharmacokinetics

- highly lipophilic
- large volume of distribution
- slow dissociation

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

Patient is experiencing PRECIPITATED opioid withdrawal

What do you do next?

A: Proceed with small, frequent doses of buprenorphine until precipitated withdrawal overcome (DHHS TIP).
B: Proceed with high-dose buprenorphine ("macro-dosing") induction approach.
C: STOP! Treat the symptoms. Retry traditional induction tomorrow.
D: STOP! Give full mu-R agonist. Plan for low-dose buprenorphine ("micro-dosing") induction approach tomorrow.

PRECIPITATED WITHDRAWAL

A: Proceed with small, frequent doses of buprenorphine until precipitated withdrawal overcome (DHHS TIP).

3. Management of precipitated withdrawal

Recommendations:
Level of Evidence: **Low-clinical experience**
If an unexpected precipitated withdrawal occurs during the early phases of the induction period, supportive treatment with or without medication will be necessary.
Types of supportive **treatment:**

1. Repeated 2 mg doses of buprenorphine every 1-2 hours
2. Clonidine 0.1 mg every 8 hours (caution regarding hypotension)
3. Antiemetics for nausea
4. Non-steroidals for arthralgias and myalgias

Some patients may resist supportive treatment and return to full agonist opioid use as a method to self-medicate their precipitated withdrawal.

Image: https://pcssnow.org/wp-content/uploads/2014/02/PCSS-MATGuidanceBuprenorphineInduction.CasaIonte.pdf

PRECIPITATED WITHDRAWAL

B: Proceed with high-dose buprenorphine ("macro-dosing") induction approach.

Approach?
- Add further buprenorphine to increase opioid agonist effect/occupy more receptors

What's the rationale?
- Don't lose the opportunity
- Reduce risk of overdose

Implications?
- Patient's discomfort
- Could lead to the patient's reluctance to undergo induction in the future

PRECIPITATED WITHDRAWAL

C: STOP! Treat the symptoms. Retry traditional induction tomorrow.

Approach?
- Reassurance and symptomatic medication. Consider adding a benzodiazepine prn.

What's the rationale?
- Gain an additional 24 hrs of drug metabolism.

Implications?
- Potential lost opportunity
- Risk of returning to illicit drug use

PRECIPITATED WITHDRAWAL

D: STOP! Give full mu-R agonist. Plan for low-dose buprenorphine ("micro-dosing") induction approach tomorrow.

Approach?
- Revert to treatment with full opioid agonists, such as methadone
- Plan for low-dose buprenorphine induction once patient is comfortable

Rationale?
- More humane experience for the patient

Implications?
- Much longer process
- +/- Risk of returning to illicit drug use

2021: BUTTON ET AL. LOW-DOSE BUPRENORPHINE INITIATION

Low-dose buprenorphine initiation in hospitalized adults with opioid use disorder: a retrospective cohort analysis

Design	Retrospective cohort analysis at urban academic tertiary care center
Population	Patients with OUD seen by a hospital-based addiction medicine consult service who underwent low-dose buprenorphine initiation
Goals/outcomes	Completion low-dose initiation (defined by reaching 16 mg/day -OR- a lower stable buprenorphine dose through shared-decision making)
Interventions	Low-dose buprenorphine approach using 1 of 3 protocols (standard, acute pain, methadone)
Results	68 patients underwent 72 low-dose buprenorphine initiations. 50 (69%) completed in the hospital; 9 (13%) transitioned to outpatient; 13 (18%) were terminated early

2021: BUTTON ET AL. LOW-DOSE BUPRENORPHINE INITIATION

Practice Considerations for in-hospital initiation:

1. Acute, severe illness
2. Co-occurring pain
3. History of precipitated withdrawal
4. Opioid withdrawal intolerance
5. Transition from high dose methadone
6. Rapid hospital discharge

Dosing:
- Day 1: 20 mcg buprenorphine transdermal patch (Butrans)
- Days 2 - 7+: patch + very slow titration of buprenorphine/naloxone SL, increasing the dose every 24 hours

WHAT IS BUTRANS?

Buprenorphine transdermal patch (Butrans)
- FDA-approved treatment of chronic pain
- Continuous administration of buprenorphine
- Steady state is achieved by the third day of buprenorphine patch use
- Designed to stay in place for 7 days

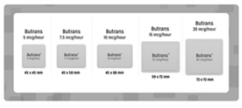

Image: https://butrans.com/patient/what-is-butrans.html. Accessed 8/20/2021.

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis. Traditional buprenorphine induction performed. Pt is now in severe precipitated withdrawal.

COWS = 25 after 4 mg SL. Proceed with high-dose buprenorphine ("macro-dosing") induction approach.

- You give a dose and reassess every 1-2 hours with goal of COWS < 8
- Patient receives 4 mg - 8 mg - 8 mg over course of 5 hours
- COWS peaks at 32 but eventually decreases to 5
- Start buprenorphine/naloxone 8 mg SL tid
- Next morning COWS = 2

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

REWIND...

- Arrives on the floor.
- Patient requesting Suboxone this admission.
- COWS = 10. He has experienced self-inflicted precipitated withdrawal and requests to wait.
- Urine toxicology screen positive for amphetamine, cocaine, and fentanyl.

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

REWIND...

Traditional vs low-dose buprenorphine, hmm?

What are the risk factors for precipitated withdrawal?

PRECIPITATED WITHDRAWAL

Patient characteristics associated with complicated inductions:

- Recent use of fentanyl
- Recent use of methadone
- Recent benzodiazepine use
- No prior history of buprenorphine use
- Low initial dose of buprenorphine/naloxone

J Subst Abuse Treat. 2010 Jul; 39(1): 51–57.

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

REWIND...

Traditional vs low-dose buprenorphine, hmm?

- Prolonged and recent heavy fentanyl use

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

REWIND...

Low-dose buprenorphine induction!

Tonight...

- Give methadone 10 mg po x 1 dose for COWS 12, repeat q4h prn COWS > 8 (NTE 40 mg/24 hrs)
- Plan for low-dose buprenorphine induction with transdermal patch tomorrow morning

CASE - LC - REDO

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

Button et al: Standard Protocol

- Day 1: place 20 mcg buprenorphine transdermal patch
- Day 2: patch + 1 mg SL bup/nx bid
- Day 3: patch + 2 mg SL bup/nx bid
- Day 4: patch + 4 mg SL bup/nx bid
- Day 5: patch + 6 mg SL bup/nx bid
- Day 6: patch + 8 mg SL bup/nx bid
- Day 7: increase bup/nx as needed NTE 24 mg/24 hours and remove patch

CASE - LC

26M PMH with multiple substance use disorders: opioids (on methadone and buprenorphine in the past), alcohol, stimulants (cocaine and methamphetamine), and tobacco, depression and PTSD from childhood sexual trauma and homelessness. Presents to ED with complaints of redness and swelling of left wrist x 3 days c/w cellulitis.

FAST FORWARD...

Day 7: Successfully completes the protocol.

Discharge planning...

- Provide a prescription for a 7-day supply of buprenorphine/naloxone 24 mg SL daily
- You confirm he has an initial appointment with an addiction psychiatrist in 5 days
- Cellulitis resolved. Completed course of antibiotics prior to discharge.

SUMMARY

- Medication for opioid use disorder is medication treating a chronic medical condition.
- Methadone can be described as an inpatient in the management of opioid withdrawal syndrome and opioid use disorder.
- Inpatient providers should take a proactive approach in initiating treatment for opioid use disorder prior to discharge.
- Low dose buprenorphine induction should be considered in patients with co-occurring pain or active medical issues, history or fear of precipitated withdrawal, recent fentanyl use, or transitioning from methadone.