Acute Pain Management for People with Opioid Use Disorder

An evidence-based approach to analgesia in those on medication-assisted treatment.

ABSTRACT: Medication-assisted treatment for opioid use disorder (OUD), which incorporates methadone, buprenorphine, or naltrexone, has been shown to reduce all-cause mortality rates in patients with this disease—and the numbers of patients receiving such treatment is substantial. In 2016, among U.S. patients with OUD, nearly 350,000 were treated with methadone, more than 60,000 were treated with buprenorphine, and more than 10,000 were treated with naltrexone. Managing acute pain in patients receiving this treatment can be a significant nursing challenge. The authors discuss the attributes of the three medications used to treat OUD and, through a composite patient case, review how to manage acute pain effectively in patients receiving this type of treatment.

This article is one in a series on palliative care developed in collaboration with the Hospice and Palliative Nurses Association (https://advancingexpertcare.org), which offers education, certification, advocacy, leadership, and research on palliative care.

Keywords: medication-assisted treatment, opioid use disorder, pain management, palliative care, substance use disorder

Brenda Jackson is a 55-year-old woman admitted for a stem cell transplant to treat Hodgkin's lymphoma. (This case is a composite based on our experience.) She has a history of heroin addiction and is taking combination buprenorphine–naloxone 16 mg/4 mg sublingual film daily to prevent relapse. She has mediastinal pain that is managed with nonopioid medications. She understands that mucositis is a potential adverse effect of her treatment.

During her admission assessment, she asks how her pain will be managed and whether her buprenorphine–naloxone treatment will continue. She says she has experienced unrelieved pain during previous admissions and worries that if she doesn't continue taking buprenorphine–naloxone she might relapse into heroin use after discharge. To address Ms. Jackson's concerns and educate the other nurses who will be caring for her, the advanced practice nurse reviews the nursing literature on the management

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of pain in the acute care setting for patients receiving medication-assisted treatment for opioid use disorder (OUD). Such medication-assisted treatment incorporates methadone, buprenorphine, or naltrexone and has been shown to reduce all-cause mortality rates in patients with OUD.[1,2] (See Table 1.[3-17])

In 2016, nearly 350,000 U.S. patients with OUD were treated with methadone, more than 60,000 were treated with buprenorphine, and more than 10,000 were treated with naltrexone.[18] Many nurses may be unfamiliar with how to adequately manage acute pain in such patients, especially in the setting of serious illness or injury. While multimodal analgesia—incorporating antiinflammatories, antidepressants, and anticonvulsants, if indicated, as well as nonpharmacologic strategies—should play an important role in the care of all patients experiencing acute pain, this article discusses additional measures nurses may take in caring for patients like Ms. Jackson, who have been receiving medication-assisted treatment for OUD and are experiencing acute pain in the hospital setting. Understanding the treatment such patients receive is critical to providing excellent nursing care.

THE U.S. OPIOID EPIDEMIC

The U.S. opioid epidemic was declared a national emergency in 2017. In 2016, upward of 63,000 people in the United States (nearly 20 per 100,000) died from drug overdoses, with more than 42,000 of these deaths attributed to opioids.[19,20] The number of people with cancer who also have OUD is not known, but studies in which cancer patients were screened for risk of opioid misuse found that anywhere from 20% to 43% of these patients were at risk.[21-23]

Changing terminology. In the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*), published in 2013, the American Psychiatric Association changed the terminology related to substance use, combining the categories of substance abuse and substance dependence from the fourth edition into a single category—substance-related disorders—which may involve any of the following 10 substance categories[24]:

- alcohol
- caffeine
- cannabis
- hallucinogens
- inhalants
- opioids
- sedatives, hypnotics, and anxiolytics
- stimulants
- tobacco
- other or unknown substances

According to *DSM-5*, disorders involving these substances (except for caffeine) can be classified as substance use disorders (SUDs).

Table 1. Medication-Assisted Treatments for OUD[3-17]

Medication	Action	Dose	Where Obtained?	Comments
Methadone (Methadose, Dolophine)	Full mu opioid agonist; can reduce cravings for 24 hours	60–120 mg by mouth daily	Administered in federally licensed OTPs for observed dosing, with one take-home weekend dose per week Patients showing progress may be eligible to take home additional doses, based on their time in treatment.	• Provides analgesia for 4–8 hours • More than once daily dosing is necessary for pain management. • Many drug–drug interactions • Can cause QTc prolongation
Buprenorphine Buprenorphine–naloxone (Suboxone, Bunavail) Buprenorphine implant (Probuphine) Buprenorphine injection (Sublocade)	Partial mu opioid agonist; occupies mu receptors, reduces craving	8–24 mg in sublingual or transmucosal form daily after induction Sublingual (Suboxone): 16 mg/4 mg daily Transmucosal (Bunavail): 8.4 mg/1.4 mg daily 80 mg every 6 months Two initial 300-mg monthly doses, followed by 100-mg monthly maintenance doses. Increasing the maintenance dose to 300 mg monthly may be considered in patients for whom the benefits outweigh the risks.	Prescribed by physicians, NPs, and PAs who have additional training and a DEA waiver	• May provide analgesia if divided into three or four doses administered every 6 or 8 hours. Higher doses are required if mu opioids are also administered. • Fewer drug–drug interactions than methadone • Although implants are intended to be in place for six months, they can be removed earlier.
Naltrexone injection (Vivitrol) Naltrexone	Full mu opioid receptor antagonist	380 mg IM monthly 50 mg daily by mouth or three times weekly in two 100-mg doses, followed by one 150-mg dose	Injection can be administered by any clinicians with prescribing authority in their state.	• Also used to treat alcohol use disorder • Blocks the euphoric effects of opioids

DEA = Drug Enforcement Administration; OTP = opioid treatment program; OUD = opioid use disorder; PA = physician assistant.

Although the effects of the substances may vary, a SUD is characterized by pathological behaviors that fall into four general categories: impaired control, social impairment, risky use, or tolerance and withdrawal.[25] (See *Clarifying Substance Use Terminology*.[25]) OUD is categorized as one of several SUDs.

METHADONE

Methadone, a mu opioid agonist, has been used to treat addiction since 1965.[26] When administered daily for OUD, methadone blocks the euphoric effects of opioids and reduces craving.[10] Patients in maintenance treatment should be titrated to a dose that prevents opioid withdrawal symptoms for 24 hours.[10]

When used to treat OUD, methadone is available through federally licensed opioid treatment programs (OTPs). For the most part, patients are seen daily for directly observed therapy within the first 90 days of treatment, though OTPs may dispense one take-home dose per week to accommodate patients through weekend closures, and patients who demonstrate progress may earn an additional take-home dose per week. Within subsequent 90-day treatment periods, patients demonstrating progress may become eligible to take home additional doses, based on their time in treatment.[13] Given the counseling services and close follow-up federal OTPs require for methadone treatment, methadone may be the most beneficial medication-assisted treatment for patients with OUD who are at risk for misuse or diversion.[8]

Methadone's duration of action is substantially shorter when the drug is used for pain relief than to suppress opioid withdrawal symptoms (four to eight hours versus 24 to 48).[3] For analgesic purposes, methadone can be prescribed by any clinician who is authorized to prescribe Schedule II medications and familiar with the drug's unique properties.

People with liver or renal disease can be treated with methadone if the drug is started at a low dose, titrated slowly, and the patient is carefully monitored for signs of respiratory or central nervous system depression.[10] Methadone interacts significantly with several other drugs.[11,26] To minimize the potential for adverse interactions, clinicians may need to adjust dosages of either the methadone or any competing medications the patient is taking. Since methadone can prolong QTc intervals, concurrent use of other medications that also prolong QTc intervals, such as ondansetron and haloperidol, may put patients at risk for torsade de pointes, a potentially fatal cardiac arrhythmia.[6,11,26] Patients taking methadone in conjunction with other medications that prolong QTc intervals require close monitoring. Clinicians should consider ordering electrocardiographic studies for such patients, as well as for those with a history of prolonged QTc interval and those whose methadone dose is greater than 120 mg per day.[27]

Naltrexone is best suited for patients who want to completely abstain from using any type of opioid therapy or do not tolerate opioid agonist therapies, such as methadone or buprenorphine.

When hospitalized patients receive methadone for OUD, treatment should be continued unless contraindicated (for example, if the patient shows signs of increased sedation or a prolonged QTc interval). To verify the methadone dosage, clinicians must contact the OTP that was providing the patient's treatment prior to admission, because methadone dispensed at an OTP is not reported by state prescription drug monitoring programs.[28] If an OTP patient is admitted when the OTP is closed, clinicians should refer to their state's clinical guidelines and the policies of their

Clarifying Substance Use Terminology[25]

Impaired control
Use of larger amounts of substances or for longer periods than intended; unsuccessful attempts to reduce use; excessive time spent acquiring, using, or recovering from use; cravings so intense that interferes with other thought processes.

Social impairment
Continued substance use despite interference with work, school, family, or social obligations; loss of interest or involvement in formerly meaningful social or recreational activities.

Risky use
Continued substance use despite physical or psychological harm; repeated use in dangerous situations.

Tolerance
The need to increase intake of a substance to achieve the desired effect.

Withdrawal
The body's response to abrupt cessation of a substance once it has developed a tolerance to the substance.

Figure 1. The Clinical Opiate Withdrawal Scale

Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptoms. 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 increased 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

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
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practice site for dosing information. Opioid withdrawal symptoms may occur if the hospital dosage is significantly lower than the dosage the patient was receiving prior to admission. Nurses should assess patients for opioid withdrawal using a standardized scale, such as the Clinical Opiate Withdrawal Scale (COWS).[29, 30] (See Figure 1.)

treatment for OUD can also be prescribed by NPs and physician assistants who have completed the required 24 hours of training and obtained the special waiver to prescribe from the Drug Enforcement Administration, containing a prescribing identification number.[15] These clinicians do not have to be specially trained in addiction medicine.

Opioid withdrawal symptoms may occur if the hospital dosage is significantly lower than the dosage the patient was receiving prior to admission.

Acute pain management may be inadequate with the once-daily dose of methadone typically used in OUD treatment. In our clinical experience, we've found it helpful to divide the daily methadone dose into smaller doses that can be administered every six or eight hours, but this can be done only with the OTP's permission. Another option for acute pain management would involve adding additional methadone doses in six- or eight-hour intervals to the existing methadone dosage.[12]

If additional methadone is to be used in the hospital setting, it should be prescribed by a clinician who is aware of the risks associated with methadone use. Additional monitoring may be necessary to avoid oversedation or QTc interval prolongation.

Some patients may benefit from the addition of another mu opioid agonist, such as morphine or hydromorphone. If pain is severe and cannot be well controlled with oral analgesics, a patient-controlled analgesic bolus is an acceptable option. The plan of care should always include plans for management after discharge. (For more information, see the *National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use*, produced by the American Society of Addiction Medicine, available at www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf.)

For special considerations in caring for patients receiving methadone for OUD, see *Methadone Key Points*.

BUPRENORPHINE

A partial mu opioid agonist, buprenorphine has been used for medication-assisted treatment since Congress passed the Drug Addiction Treatment Act in 2000.[31, 32] Although some OTPs prescribe buprenorphine treatment for OUD, patients need not attend a federal OTP to receive buprenorphine; they can be treated in general ambulatory care settings.[8] Buprenorphine

Buprenorphine binds tightly to the mu opioid receptor. At higher doses, it reaches a maximum level of analgesic effect—that is, increasing doses do not produce a greater effect—and can act as an antagonist, blocking other mu opioid agonists from fully binding to the mu opioid receptors. Because it's a partial agonist, when used alone, it carries less risk of overdose.[33] Since its effects can last for up to 72 hours, preventing other opioids from binding to these receptors, any additional opioids administered during this period may have an inadequate analgesic effect.[5]

Buprenorphine for medication-assisted treatment is available in various formulations, including buccal/sublingual, six-month implants, and monthly subcutaneous injection.[34] To minimize the risk of tampering and injection of the product, some formulations combine oral buprenorphine with naloxone, a mu

Methadone Key Points

- Patients with opioid use disorder may undergo significant withdrawal if opioids are abruptly discontinued. Contacting the opioid treatment program (OTP) at patient admission is vital.
- Before starting any new medications concurrently with methadone, check for potential drug–drug interactions and alert the prescriber to minimize the potential for adverse events.
- Electrocardiograms should be considered when the patient is taking methadone, especially when other medications that prolong the QTc interval are concurrently prescribed.
- If the patient requires long-term administration of an opioid in addition to methadone, coordinate with the OTP to ensure there is a clinician willing to prescribe and manage the opioid prescriptions after discharge.

Buprenorphine Key Points

- If buprenorphine is discontinued during hospitalization, the patient may require higher doses of other opioids for 24 to 72 hours thereafter to achieve pain relief.[5]
- Nurses must monitor for respiratory depression if buprenorphine is discontinued and higher doses of opioids are utilized during the time that buprenorphine is still binding to the mu receptors (24 to 72 hours).[5]
- Before buprenorphine is restarted following discontinuation, patients should be in a state of mild withdrawal from any opioids used in the interim in order to prevent acute withdrawal.[5]
- Nurses should coordinate with buprenorphine prescribers, especially when patients require supplemental opioids for pain management after discharge.[37]
- Nurses should inform patients that there may be an increased risk of relapse into substance use and potential overdose if medication-assisted treatment isn't continued after hospital discharge.[8] A vital component of postdischarge care is effective coordination between clinicians managing pain and those treating opioid use disorder.

receptor antagonist used to reverse opioid-induced respiratory depression.[34] In pregnancy, naloxone is not recommended except in cases of life-threatening overdose.[8] Buprenorphine formulations developed to treat OUD should not be confused with those used for pain management, which contain much lower buprenorphine doses. Like methadone, buprenorphine may provide pain relief for about eight hours, but it can prevent opioid withdrawal symptoms for more than 24 hours.[35] Patients who have OUD but no chronic pain may be prescribed buprenorphine on a once-a-day schedule, while patients who have both OUD and chronic pain are often scheduled to take buprenorphine every eight hours to allow the drug to provide 24 hours of coverage for both pain and addiction.[35]

To address acute pain in patients taking buprenorphine therapy for OUD, it's necessary to work collaboratively with the prescriber. Clinicians can consult acute pain management protocols when caring for these patients (see the Medical Professionals Opiate Toolkit 2017 at https://starkmhar.org/wp-content/uploads/2016/12/12-22-16_Physician-toolkit-final_WEB.pdf or the 2018 Arizona Opioid Prescribing Guidelines at www.azdhs.gov/documents/audiences/clinicians/clinical-guidelines-recommendations/prescribing-guidelines/az-opioid-prescribing-guidelines.pdf).

In Ms. Jackson's case, one approach would be to wean her from the buprenorphine–naloxone, reducing the dose by 1 to 2 mg every two weeks (or longer, if possible) and discontinuing it 72 hours before her stem cell transplant.[36] Although it's possible to wean a patient from buprenorphine over three days, such rapid reduction may cause opioid withdrawal symptoms, which may be mitigated by administering another opioid, such as methadone.[5] Alternatively, clinicians may divide the daily buprenorphine dose into three or four doses administered every six or eight hours while Ms. Jackson is hospitalized.[5] If a patient has a buprenorphine six-month implant, removal and discontinuation may not be possible. In such cases, higher than usual opioid doses can be used to override the buprenorphine effect.

For special considerations in caring for patients receiving buprenorphine for OUD, see *Buprenorphine Key Points*.[5, 8, 37]

NALTREXONE

In 2010, naltrexone, which had been used to treat alcohol dependence since 2006, was approved for use in preventing relapse into opioid dependency.[9] Naltrexone therapy can be administered in ambulatory care settings by any clinician who is licensed to prescribe medications.[14] It can be taken daily in 50-mg oral doses, or three times weekly in two 100-mg oral doses followed by a third 150-mg dose.[8] Alternatively, an extended-release formulation can be injected intramuscularly every four weeks.[8, 38]

An opioid antagonist, naltrexone blocks the euphoric effects of opioids.[9] It should not be confused with naloxone. Naltrexone is best suited for patients who want to completely abstain from using any type of opioid therapy or do not tolerate opioid agonist therapies, such as methadone or buprenorphine. People who work in jobs in which urine drug testing is routinely conducted and who choose not to disclose a diagnosis of OUD may be good candidates for naltrexone therapy.[39] Naltrexone must be discontinued in patients who have acute pain or are anticipated to have chronic pain that will require opioid treatment. Oral naltrexone should be discontinued 72 hours prior to surgery and intramuscular naltrexone injection should be discontinued one month prior to surgery.[8] In the event of an unplanned hospitalization for trauma or acute illness, patients receiving naltrexone may require 10 to 20 times the usual opioid dose to overcome the naltrexone blockade of the mu opioid receptors.[5] Even with high doses of opioids, there may be insufficient pain relief and a greater risk of adverse effects. For safety reasons, initial pain management should be monitored closely.[40] For patients with naltrexone in their systems, multimodal pain management supplemented with

nonopioid analgesics may be required to ensure appropriate pain relief.[40]

Naltrexone has a documented risk of hepatotoxicity, so clinicians should monitor liver function.[9] If the patient has pain that requires opioid therapy beyond hospitalization, collaboration with the outpatient clinician who is managing the naltrexone will be necessary to determine an optimal OUD treatment strategy.

For special considerations in caring for patients receiving naltrexone for OUD, see *Naltrexone Key Points*.

Naltrexone Key Points

- Naltrexone must be discontinued if patients require pain management with opioid therapy.
- If patients require opioids for pain relief and have naltrexone in their system, they may require 10 to 20 times the usual opioid dose.
- Nurses should coordinate with the outpatient prescriber and ensure plans are in place for postdischarge care, especially if the patient needs continued pain management with opioids.

MS. JACKSON'S TREATMENT

The advanced practice nurse discussed with Ms. Jackson the recommended treatment for acute pain in patients receiving medication-assisted treatment for OUD and reassured her that her clinicians would work together to manage her pain. Ms. Jackson continued receiving her home dose of buprenorphine–naloxone after admission, and throughout her transplant procedure and hospital stay. She was able to attend 12-step meetings held weekly in the hospital and was visited by community volunteers from a local OUD treatment program. When she developed mucositis and could no longer take buprenorphine by mouth, the buprenorphine–naloxone was discontinued, and she started receiving hydromorphone by patient-controlled analgesia (PCA) with doses adjusted to treat her pain. She had significant pain the first day after buprenorphine discontinuation because the drug was still in her system (where it prevented other opioids from binding to the mu opioid receptors). By the third day, however, her pain was well controlled with hydromorphone by PCA.

When the mucositis resolved, she discontinued the PCA hydromorphone; 16 hours later, after she experienced mild opioid withdrawal, her buprenorphine–naloxone was restarted.

Ms. Jackson's treatment plan included ongoing assessment using the COWS to assess the symptoms that occurred during the transition from hydromorphone to buprenorphine–naloxone. Buprenorphine–naloxone was restarted at a dose recommended by her prescribing clinician. The care team managed her withdrawal symptoms as follows: nausea with prochlorperazine, diarrhea with loperamide and intravenous fluids, and anxiety with lorazepam.[41] She was discharged to home on her usual dose of buprenorphine–naloxone 16 mg/4 mg daily, which she decided to take in divided doses to more adequately address her transplant-related pain.

THE NURSE'S ROLE: ADVOCATE

As nurses, we encounter people with OUD in the hospital setting. Patients with serious illnesses and comorbid OUD face additional stressors: concerns about receiving adequate pain management and the fear of relapse into drug use. Nurses can best care for this patient population by learning about OUD and its treatment. We can help patients cope during hospitalization by accessing such resources as local 12-step programs and support groups or reaching out to community volunteers, who may be willing to visit during hospitalization. Nurses can educate other clinicians on the care of people with OUD. We play a key role in advocating appropriate pain management in this patient population while providing compassionate, nonjudgmental care. ▼

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