EDUCATION MODULE

PRESCRIBING OPIOIDS IN PATIENTS WITH SUBSTANCE USE DISORDER*

*This module provides information about substance use disorder as a risk factor for opioid overdose and specific risk-reduction guidance. It **supplements** but does not replace the general best practices for opioid prescribing presented in the "**Considerations for Safe and Responsible Opioid Prescribing**" module.*

Background

1. Addiction is a primary, chronic disease characterized by impaired behavioral control of substance use, craving, and diminished recognition of significant problems with one's behaviors and interpersonal relationships. Like other chronic diseases, addiction often involves cycles of relapse and remission.[1-3]

    a. The DSM-V identifies 11 criteria to consider when diagnosing opioid use disorder (OUD). (DSM-V, also see 'Additional Resources' #1)
        i. The presence of 2-3 criteria within a 12-month period indicates mild OUD, 4-5 indicate moderate OUD, and 6 or more indicate severe OUD. (DSM-V)

    b. For individuals taking prescription opioids under medical supervision, two criteria (tolerance and withdrawal) do not count toward an OUD diagnosis. Tolerance is defined by the "need for increased amounts of opioids or diminished effect with continued use at the same amount," and withdrawal is defined by "characteristic opioid withdrawal syndrome or taking opioids to relieve or avoid withdrawal symptoms." (DSM-V)

Updated addiction-related terminology (selected terms)[§]

Current (2018)	Former
Substance use disorder (SUD) (DSM-5)	Substance abuse + substance dependence (DSM-IV)
Opioid use disorder (OUD) (DSM-5)	Opioid abuse + opioid dependence (DSM-IV)
Misuse	Abuse, nonmedical use
OUD pharmacotherapy, OUD medication	Medication assisted treatment
Medically supervised withdrawal	Detoxification
Recovery (includes remission)	
Return to opioid use	Relapse

[§]For definitions of these and additional terms see SAMHSA 2018 (p1-16), DHHS USSG 2016 (ch2), or DSM-V. (see 'Additional Resources' for a summary of various definitions of selected terminology)

2. Opioids are misused by 21% to 29% of adults treated with long-term (> 3 months) opioids for chronic non-cancer pain, and 8% to 12% develop opioid addiction.[4]

3. Pharmacotherapy with buprenorphine, methadone, or naltrexone should be considered for all persons with OUD *in conjunction with* psychosocial treatment (e.g., psychotherapeutic counseling, contingency management, community reinforcement, and family therapy).[2,5,6]
    a. OUD pharmacotherapy as part of a comprehensive treatment plan for OUD reduces illicit

opioid use, increases retention in treatment, and reduces risk of opioid overdose death when compared to treatment without medication.
   b. Buprenorphine and methadone are indicated to manage withdrawal and treat OUD.
   c. Naltrexone is an opioid antagonist used in persons in recovery from OUD to diminish opioid effects and prevent relapse.

4. Buprenorphine, a partial mu opioid receptor (MOR) agonist, is a pharmacologically safer opioid (Schedule III) than pure MORs such as morphine or methadone (Schedule II).[1,2,7]
   a. Partial agonists bind and activate MORs to a lesser degree than full agonists.
   b. Thus, buprenorphine reaches a maximum (ceiling) effect at a certain dose for both analgesic and respiratory depressant effects.
   c. Buprenorphine has a higher binding affinity for the MOR than most full opioid agonists and it can displace or block full agonists from MORs.
   d. If buprenorphine is administered to a patient who is physically dependent on full mu agonist opioids, the patient may experience precipitated withdrawal if insufficient time has elapsed since their last dose of the full agonist opioid.

5. Methadone (see **"Methadone"** module)

Substance use disorder (SUD) and opioid overdose

1. A personal history of an SUD is the strongest and most consistent risk factor for developing opioid misuse or OUD when prescribed opioids. Family history of SUD also increases risk, suggesting that individuals are predisposed to SUD due to genetic and external factors.[3,8,9]

2. Individuals with a history of SUD frequently have co-occurring mental health disorders, poor adherence to psychotherapeutic treatment, and increased risk-taking behavior that increase their risk for OUD and overdose compared with persons without such conditions.[3,10-12]

3. Opioid use disorder is often accompanied by use of other substances. Concurrent use or misuse of other central nervous system (CNS) depressant medications or substances such as alcohol or benzodiazepines may lead to life-threatening respiratory depression or over-sedation (overdose) which is most commonly unintentional.[5,10-13]

4. Recent periods of opioid abstinence, particularly in a controlled environment such as during incarceration or hospitalization, are major risk factors for fatal opioid overdose in individuals with OUD.
   a. The person may lose tolerance to their prior opioid dose in as little as one week, and the risk for a serious overdose is high if they suddenly resume their prior opioid dose.[14,15]

Risk-mitigation interventions to consider when prescribing opioid analgesics in patients with SUD
[Refer to the full prescribing information (**FDA Label**) for important product-specific details]

A. ***Assessment***[1,16]

1. Review the patient's medical records and obtain their self-report of all recent use (past 30 days and particularly the past 1 to 2 days) of prescribed controlled medications and substances, including types (tobacco included), amounts, frequency, and duration.

2. Conduct urine (or saliva) drug testing to check for the presence of prescribed controlled medications (adherence) and to detect undisclosed use of non-prescribed controlled medications or illicit drugs (misuse/addiction).

3. Check the state prescription drug monitoring program (PDMP) data from the patient's home and surrounding states to confirm the history of controlled medications and to investigate use of multiple prescribers or pharmacies, which raise concern for substance use disorder or diversion.

4. Assess for a DSM-5 diagnosis of currently active SUD if the patient has a history of SUD, recent controlled substance misuse, or recent illicit substance use.

B. ***Treatment: Pain management in patients with SUD***[1,2,16]

1. Optimize treatment of co-occurring mental health disorders (anxiety, depression).

2. Optimize non-pharmacologic interventions to manage pain.

3. Optimize treatment with non-opioid analgesics such as acetaminophen, NSAIDs/cyclooxygenase 2 (COX-2) inhibitors, topical analgesics, and adjuvant analgesics (selected antidepressants, such as tricyclics and serotonin-norepinephrine reuptake inhibitors; and selected anticonvulsants, such as gabapentin and pregabalin).

4. Strongly consider consulting a pain medicine or addiction medicine specialist regarding pain management for persons with active or recent SUD. Communicate with the patient's SUD treatment providers if opioid analgesics are prescribed.[5]

5. Prescribe take-home naloxone for opioid-treated persons with a history of SUD, including those who have recently initiated OUD pharmacotherapy, to reverse life-threatening respiratory depression if an overdose occurs. Educate the patient, family/household members, and caregivers about signs and symptoms of opioid overdose and train them to properly use naloxone if an opioid-related overdose is suspected.[5,17,18] (See 'Follow Up' section, #5 in the **"Considerations for Safe and Responsible Opioid Prescribing"** module)

6. Patients with pain and active, untreated OUD:
    a. Defer treatment of pain beyond non-opioid interventions until OUD pharmacotherapy is initiated and the patient consents to care in collaboration with the patient's OUD treatment provider (if a different clinician).[2,6,19]

b. Initiate or refer for OUD pharmacotherapy—which can also help manage pain—in conjunction with psychosocial treatment.
    i. Methadone to treat OUD may be dispensed only by a certified opioid treatment program.
    ii. Buprenorphine therapy may be prescribed for patients with OUD by trained and certified health care professionals with a DATA waiver/DEA "X" license in most office-based settings in accordance with the Drug Addiction and Treatment Act (DATA 2000).[2]

7. Patients with OUD who are in medication-assisted recovery with buprenorphine pharmacotherapy:
    a. Defer treatment of pain beyond non-opioid interventions until the patient consents to care in collaboration with the patient's OUD treatment provider.[2,6,19]

    b. Buprenorphine to treat OUD may also provide modest analgesia for a co-occurring pain condition and should be continued without interruption.

    c. For mild-to-moderate acute pain, consider temporarily dividing the total buprenorphine dose to three times per day to improve pain relief, as buprenorphine's analgesic effect only lasts 6 to 8 hours.

    d. If pain relief is inadequate or if the acute pain is moderate to severe, first confirm that the patient is taking buprenorphine by urine drug testing using a method that is designed to detect synthetic opioids like buprenorphine. If confirmed, the daily dose of buprenorphine (sublingual) may be increased to a maximum of 24mg per day.

    e. If pain relief is inadequate, consult a specialist in pain medicine or addiction medicine regarding pain management.[5]

8. Patients with OUD who are in medication-assisted recovery with methadone pharmacotherapy:
    a. Defer treatment of pain beyond non-opioid interventions until the patient consents to care in collaboration with the patient's OUD treatment provider.[2,6,19]

    b. Contact the patient's opioid treatment program (OTP) directly to confirm the patient's methadone dose and the last day of dose administration. Confirm recent use of the methadone with a urine drug screen that is able to detect synthetic opioids. Maintenance methadone for OUD should be continued without interruption as it also may provide analgesia for a co-occurring pain condition.

    c. Suggest that the OUD treatment provider consider dividing the methadone dose to every 6-12 hours to improve pain relief. The analgesic effect of methadone lasts only 4 to 8 hours in comparison with its typical daily dosing schedule for the treatment of OUD and half-life of approximately 24 to 36 hours (range, 8 to 59 hours).

    d. For pain severe enough to require opioid analgesics in patients who are administered daily methadone maintenance to treat OUD, additional doses and higher opioid analgesic dosage will likely be necessary for pain control due to opioid tolerance. If

considering prescribing opioid analgesics in the outpatient setting for a patient enrolled in an OTP, coordinate treatment with the OTP provider and prescribe short-acting opioids as time-scheduled treatment rather than as-needed.

9. Patients with a remote history of OUD (e.g., in long-term remission without OUD pharmacotherapy):

    a. If pain control of a chronic pain condition with non-opioid therapy is inadequate, a trial of an opioid analgesic may be considered in consultation with pain medicine and addiction medicine specialists, with very close monitoring of patient medication adherence, and weighing the pain and functional benefits against the increased risks of overdose and active OUD.[5,16]

Additional Resources

**The information presented in this module highlights some fundamental concepts of opioid prescribing for adult outpatients. It excludes certain populations (pediatrics, pregnancy, patients with active cancer or receiving palliative or end-of-life care) and settings (perioperative, emergency, in-patient). The information provided is intended to support safe and effective opioid therapy and minimize serious adverse outcomes, particularly overdose. It is not intended to be exhaustive nor substitute for consulting a medication's full prescribing information for complete details and warnings. Links and references to selected, more comprehensive clinical and prescribing resources are provided to facilitate safe and effective opioid prescribing.*

1. DSM-V Criteria for Substance Use Disorder, DSM-V Criteria for Opioid Use Disorder, DSM-V Opioid Use Disorder Checklist
2. FDA-approved drug label information: FDA Online Label Repository or Daily Med (NIH/National Library of Medicine)
3. Behavioral Health Treatment Services Locator. A confidential and anonymous source of information for persons seeking treatment facilities for SUD and/or mental health problems
    a. Opioid Treatment Program Locator for methadone treatment programs
    b. Buprenorphine Physician and Treatment Program Locator
4. Buprenorphine Resource Center and training for eligible office-based health care professionals to become certified to prescribe buprenorphine for patients with OUD under the Drug Addiction Treatment Act of 2000 (DATA 2000)
5. American Society of Addiction Medicine
    a. American Society of Addiction Medicine SUD treatment resources
    b. The ASAM criteria. The most widely used and comprehensive set of guidelines for placement, continued stay and transfer/discharge of patients with addiction and co-occurring conditions
6. National Institute on Drug Abuse
    a. NIDA Resources for Health Care Professionals
    b. Pain Management, Opioid, and Addiction Science Resources

7. Opioid Abuse in Chronic Pain—Misconceptions and Mitigation Strategies.[20]
8. PCSS-O Training - Prescribers' Clinical System for Opioid Therapies
9. Prescriber Clinical Support System for Medication Assisted Treatment
10. Opioid Overdose Prevention Toolkit (SAMHSA) How to help prevent opioid-related overdoses and deaths for first responders, healthcare professionals, and persons recovering from opioid overdose
11. Prescribe to prevent Overdose education and naloxone prescribing and dispensing information
12. SCOPE of Pain (Boston University) Safe and Competent Opioid Prescribing Education

Summary of various definitions of selected terminology[3] (p1—16)

- **Misuse**: *Taking a medication in a manner or dose other than prescribed; taking more than prescribed because of inadequate pain relief; taking someone else's drug, even if for a legitimate medical purpose (i.e., diversion).*
    - Substance misuse is presently the preferred term for "substance abuse" which is increasingly avoided by professionals because it can be shaming. Although misuse is not a diagnostic term, it generally suggests use in a manner that could cause harm to the user or those around them.
- **Abuse**: *Intentionally taking a medication for a non-medical purpose (e.g., euphoria, sleep, relaxation); physically altering a delivery system or changing the route of intended administration.*
    - Previously defined in DSM-IV as use that is unsafe (e.g., drunk or drugged driving), use that leads a person to fail to fulfill responsibilities or gets them in legal trouble, or use that continues despite causing persistent interpersonal problems (e.g., fights with a spouse).
- The DSM-5 integrates the two DSM-IV disorders, substance abuse and substance dependence, into a single disorder called substance use disorder with mild, moderate, and severe sub-classifications based on the number of diagnostic criteria fulfilled.
- FDA (label) defines abuse as the intentional non-therapeutic use of an over-the-counter or prescription drug, even once, for its rewarding psychological or physiological effects.
- **Addiction:** *Although addiction is not a diagnostic term, it refers to substance use disorders at the severe end of the spectrum that are characterized by compulsive substance use and impaired control over use.*

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