Epidemiology (*Lancet* 2019;393(10182):1760-72; *N Engl J Med* 2012;367(2):146-55; *Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health*, 2021)

- Opioid use disorder (OUD): problematic pattern of opioid use leading to clinically significant impairment or distress and continued use despite significant related problems
- 9.5 million people in the U.S. age 12 or older used heroin and/or prescription opioids for a nonmedical reason in 2020; 2.7 million people had OUD
- Risk factors for developing OUD: ↑ risk is associated with adverse childhood experiences (ACEs), younger age (35-44 yr), being male, under- or unemployed, psychiatric disease, complex musculoskeletal pain, or other substance use disorder

Assessment and Evaluation (*ASAM Principles of Addiction Medicine*, 6th ed, 2019)

- Three-step process for identification and diagnosis:
  1. *SCREEN* for at-risk opioid use. NIDA single-item screening question: "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (If patient asks what is meant by nonmedical reasons, can clarify by saying "for the feeling or experience it causes")
  2. *ASSESS* pattern of opioid use and determine if the patient meets OUD criteria based on *DSM-5* (see dx criteria below)
  3. *EVALUATE* the patient's opioid use history, current use, treatment hx, and risk of return to use. A mnemonic is RIPTEAR:
     Risk of Current Use—History of overdose? Symptoms of withdrawal?
     Initiation—When did opioid use begin?
     Pattern of use—Route of administration
     Treatment—History of treatment episodes and outcomes
     Effects—Explore positive and negative experiences
     Abstinence—What were circumstances around prior abstinence?
     Return to use prevention plan—Discuss patient-centered plans to prevent return to heavy use or reduce risk of use
- ***DSM-5* Criteria**: OUD diagnosed based on 11 criteria: mild (2-3 criteria), moderate (4-5 criteria), or severe (6+ criteria) OUD. Meeting criteria for tolerance and withdrawal alone when taking opioids as prescribed does not meet criteria for OUD.
- OUD in remission when criteria with exception of craving no longer met for 3 mo (early remission) or 12 mo (sustained remission)

Criteria include: using more opioids than intended; problems controlling opioid use; spending more time finding, using, or recovering from opioids; craving; continued use of opioids causing a failure to meet life obligations; continued opioid use in risky situations; continued opioid use despite associated mental or physical health problems; tolerance; and withdrawal

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Opioid-Related Overdose

Epidemiology (*MMWR Morb Mortal Wkly Rep* 2018;67(5152):1419-27)

- Opioid overdose deaths continue to rise

- The overdose crisis can be thought of as occurring in 3 waves:
  1st wave associated with an ↑ in prescribed opioids in the 1990s
  2nd wave associated with a rapid ↑ in heroin use in 2010
  3rd wave associated with an ↑ in synthetic opioids (illicitly manufactured fentanyl) started in 2013, with ongoing contamination of drug supply

Signs and Symptoms (see also Chapter 5) *(ASAM Principles of Addiction Medicine, 2019)*

- Small, constricted pupils
- Increased somnolence or loss of consciousness
- Reduced resp rate/breathing
- Limp, flaccid extremities or body
- Pale, blue, or cold skin
- Most worrisome sign is respiratory depression with a patient becoming apneic and hypoxic. Note, toxicology testing is not necessary to initiate treatment for opioid overdose.

Management of Opioid Overdose (https://www.cdc.gov/drugoverdose/pdf/patients/Preventing-an-Opioid-Overdose-Tip-Card-a.pdf; *Ann Intern Med* 2018;169(3):137-45)

- Acute management of suspected overdose includes calling for help (911 or code if in hospital/clinic), administering naloxone, delivering rescue breathing, if no or minimal response administering additional naloxone
- Nonfatal opioid overdose is opportunity to initiate medication for OUD (MOUD)
- Health systems should adopt "no wrong door" approach for patients after OD
- Any healthcare setting, including primary care, the ED, inpatient hospital, etc, is opportunity to initiate treatment and connect patients with ongoing care
- Programs aimed at curbing overdose death should:
  - Integrate overdose education and naloxone provision and training
  - Offer immediate access to MOUD
  - Offer harm reduction services or partner with harm reduction organizations (see Chapter 17 for more)

Managing Withdrawal *(ASAM Principles of Addiction Medicine, 6th ed, 2019)*

- Abrupt reduction or cessation of opioids may result in opioid withdrawal
- The management of opioid withdrawal should be considered part of a continuum of treatment initiation for OUD; withdrawal management alone assoc. w/ high rates of recurrent opioid use
- Can assess withdrawal severity with the Clinical Opiate Withdrawal Scale (see below)
- **1st-line tx—**methadone or buprenorphine
- Methadone for withdrawal management 5-10 mg prn up to 40 mg in first 24 hr (allowable to administer in hospital settings or opioid treatment programs)
- Buprenorphine or buprenorphine/naloxone can be started at 2-8 mg sublingual and given 2-8 mg prn for withdrawal symptoms up to 24 mg in first 24 hr

- Ideally MOUD continued for maintenance unless patient prefers taper after informed discussion about risks (recurrence, overdose, death)
- **2nd-line tx**—adjunctive medications: clonidine 0.1-0.2 mg q4-6hr prn restlessness/anxiety, dicyclomine 20 mg q6hr prn stomach cramping, trazodone 50 mg qHS prn insomnia, ibuprofen 400-800 mg q8hr prn myalgias/arthralgias, hydroxyzine 25-50 mg po q4-6hr prn anxiety

Pregnancy *(ASAM Principles of Addiction Medicine, 6th ed, 2019)*

- Medically managed withdrawal not recommended (ie, tapering off methadone/buprenorphine); MOUD should be started and continued

Treatment

Initial Evaluation *(ASAM Principles of Addiction Medicine, 6th ed, 2019)*

- Evaluate use and treatment history (see RIPTEAR mnemonic above)
- Consider infectious disease screening for HIV, viral hepatitis, particularly if using via injection
- Determine patient's goals. Engage in shared decision-making for deciding on tx strategy.

Medication for OUD *(ASAM Principles of Addiction Medicine, 6th ed, 2019)*

- Methadone or buprenorphine 1st line with strong evidence for effectiveness, reducing recurrent opioid use, overdose, and mortality
- Extended-release naltrexone 2nd line option for patients who have been counseled on risks vs benefits and prefer it to agonist medication (see table below)
- Low-dose buprenorphine-naloxone induction (ie, "micro-dosing" induction) is an option for patients with ongoing need for full agonist opioids for pain or where standard induction is challenging, eg, patients using nonprescribed fentanyl with a history of precipitated withdrawal or patients transitioning from methadone

Sample Buprenorphine Low-Dose Induction Protocols

	Day 1	2	3	4	5	6	7+
1. Buprenorphine SL Approach	0.5 mg once	0.5 mg BID	1 mg BID	2 mg BID	4 mg BID	4 mg TID	Titrate prn
2. Buprenorphine Transdermal + SL Approach	-	1 mg qHS	1 mg BID	2 mg BID	4 mg BID	4 mg TID	Titrate prn
	Transdermal patch 20 μg/hr Continue until first SL dose or throughout induction						

For either option 1 or 2, full opioid agonist is continued or slowly tapered until ~day 5, then stopped

Ongoing Management

- Ongoing follow-up important. Check-in visits, frequently at first, space out as stabilize. Like any chronic care management follow-up visits involve evaluating ongoing symptoms (cravings, withdrawal, use), benefits or challenges with medication, need for additional support or treatment modifications, focus on patient-identified goals.

- If person not doing well, modify treatment. Continued substance use by patient not a sufficient reason to discontinue MOUD but may reflect the need for a change in treatment plan. Consider: increasing medication dose, increasing supports and adjunctive therapies (psychosocial services, peer support, housing supports, level of care). If persistent challenges, explore changing meds (ie, buprenorphine to methadone).
- Incorporate harm reduction into ongoing management

Managing Patients Already Treated With MOUD *(J Hosp Med 2019;10;633-35; Ann Intern Med 2006;144(2):127-34; J Gen Intern Med 2020;35(12):3635-43)*

- If hospitalized, pts should be continued on MOUD. Buprenorphine and methadone can be administered during hospitalization for acute medical/surgical issue without special licensure. If on methadone, pt's dose should be confirmed with OTP.
- If patients have acute pain or in perioperative period:
  - For methadone: cont home dose and use short-acting opioids
  - For buprenorphine: cont home dose (consider splitting dose to TID or QID) and use short-acting opioids

Medication	Methadone	Buprenorphine-Naloxone	Extended-Release Naltrexone	Extended-Release Buprenorphine
Action on opioid receptor	Full opioid agonist	Partial opioid agonist	Opioid antagonist	Partial opioid agonist
Usual dose	60-120 mg PO daily	8-24 mg SL daily	380 mg IM monthly	100-300 mg SC monthly
Ideal for the following treatment	Moderate to severe OUD; long history of opioid use; high opioid tolerance; preference for methadone	Mild to severe OUD; preference for buprenorphine	Long-term stability in OUD treatment; institutionalized without access to OAT; after being counseled on risks and benefits prefers antagonist treatment	Moderate to severe OUD patients who have initiated treatment with transmucosal buprenorphine-naloxone for at least 7 d
Benefits	Improved treatment retention Reduce overdose mortality Improved OUD remission Effective in pregnancy Easy to initiate treatment No maximum dosage	Can be prescribed in outpatient setting by MD/NP/PA w/ X-waiver More flexible dosing schedule Lower risk of respiratory depression or sedation Minimal risk of overdose in opioid-tolerant patient Few side effects Short time to therapeutic dose	Does not cause sedation or respiratory depression; no need for prescriber waiver	Similar benefits to buprenorphine-naloxone with the added benefit of monthly dosing; does require X-waiver

Disadvantages	Requires visits to federally regulated opioid treatment program Potential risk for overdose in induction period Regulations require daily observed doses on initiation; take-home doses only after months of stability Notable side-effect profile somnolence, ↑Qtc Risk of drug interaction given its cytochrome P450 effects	Possible to precipitate withdrawal on initiation Lower retention of patients when inadequately dosed Requires waivered prescriber under current regulations (although no longer requires training if treating 30 or fewer patients at a time)	Does not reduce craving Can precipitate withdrawal if inadequate period of abstinence Risk of fatal overdose if individual uses opioids after dosing interval given loss of tolerance Inferior effectiveness compared to opioid agonist Limited safety data in pregnant patients Insomnia and depressed mood	Similar disadvantages to buprenorphine-naloxone including risk of precipitating withdrawal
Special populations	Appropriate in pregnancy & breastfeeding May require dose adjustment in renal/hatic failure	Appropriate in pregnancy and breastfeeding May need dose adjustment in severe hepatic impairment	May be useful in patients with history of OUD and current alcohol use disorder	Monthly XR-buprenorphine not recommended in pregnancy due to excipient NMP; weekly formulation considered safe in pregnancy (*Contemp Clin Trials* 2020;93:106014)