

Opioid Use Disorder, Adolescents, and the Importance of Treatment in the Emergency Department

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Abstract: Deaths from opiate overdoses are climbing every year, especially from fentanyl. Adolescents are particularly vulnerable to the acute and chronic harms associated with drug use, addiction, and overdose. Providers in the acute care setting have a unique opportunity to address a population of adolescents with opioid use disorder who are at the highest risk of harm and who may be more receptive to help. It is critical that providers are familiar with the tools that are available to assist and have some facility with their application.

Key Words: opioid use disorder, opiate withdrawal, naloxone, buprenorphine
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TARGET AUDIENCE

This CME activity is intended for physicians and advanced practitioners who care for adolescents in the acute care setting, including emergency departments, urgent care, and primary care clinics.

LEARNING OBJECTIVES

After completion of this article, the reader should be better able to:

1. Explain how adolescents are at particular risk of opioid use disorder and at risk of overdose.
2. Identify the signs and symptoms of opiate use disorder and opiate withdrawal and discuss appropriate treatment.
3. Describe harm reduction approaches, naloxone, and outpatient treatment with buprenorphine.

Opiate overdose deaths have risen across the country, with rates rising as much as 169% from 2019 to 2021.¹ Among adolescents, there has been a 182% increase in deaths, largely driven by the use of fentanyl in the same period.²

Fentanyl is 100 times as powerful as morphine and 50 times more potent than heroin. It comes in pill and powdered form and can be ingested orally, smoked, inhaled, or injected.³ Rapid onset

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Dr. Buresh has disclosed that the FDA has only approved the use of buprenorphine for treatment of OUD down to age 16. Please consult the product's labeling for approved information.

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and resolution are characteristics of fentanyl use and are two of the things that make it so addictive. Because it is so potent, it only takes a minuscule amount to have a desired effect. Fentanyl can be found in any number of illicit substances. It is often added to counterfeit drugs being sold as "Xanax" or "Adderall," mixed with methamphetamine or cocaine, and in many places, it is found in high concentrations in "Percocet" or pills that are made to look like prescription tablets of the oral analgesic.⁴ In addition, some markets are now seeing the fentanyl supply adulterated with additional agents to potentiate and prolong its effect. Most recently xylazine has been used for this purpose. Xylazine is a central alpha 2 agonist, similar to clonidine, that was developed for use in veterinary medicine. When mixed with other respiratory depressants like fentanyl, it can cause sedation and respiratory depression that does not respond completely to traditional measures.⁵

Adolescents are particularly vulnerable to harm from opioid misuse for social, developmental,⁶ and logistical reasons.⁷

DIAGNOSIS OF OPIOID USE DISORDER

Opioid use occurs along a spectrum. On one side of the spectrum is abstinence, followed by occasional recreational use, then increasingly dangerous use associated with potential harms, ongoing use despite harms, and finally habitual and compulsive use that is difficult to decrease and is associated with deleterious financial, social, or health consequences. This end of the spectrum is often characterized by people spending a significant amount of their time, money, and effort devoted to the use of the drug. People often are experiencing negative social and professional consequences of the ongoing use and are unable to decrease that use without suffering withdrawal symptoms. Various points along this range constitute mild, moderate or severe opioid use disorder (OUD), depending on how many symptoms the patient has and how severe they are (Table 1).⁸ Many people who use drugs move back and forth along this spectrum over time and, like most chronic diseases, people with addiction experience remissions and relapses. Many people with severe OUD will eventually recover. With heroin, it was thought that only about 15% of people developed severe OUD.⁹ It is not known how often this happens with fentanyl, nor how often this happens among the adolescent population, but there are reasons to suspect that it may happen more often with this drug in this population.

WITHDRAWAL

Withdrawal is a hallmark of moderate to severe OUD. It is characterized by a constellation of subjective and objective findings after the cessation of use of an opioid. The time that it takes to go into withdrawal depends on the usual dose of the drug, the route of administration, and the pharmacokinetics. Some frequent users will report the onset of withdrawal symptoms within 2 hours of their last use, while others can take up to 12 hours to experience symptoms. The symptoms usually last for a week, with the first 1 to 3 days being the worst. Cravings for the drug can last much longer, though.¹⁰

Withdrawal symptoms can consist of subjective symptoms such as restlessness, anxiety, mood instability, feeling burning or cold in the skin, joints, and bones, nausea, and stomach cramping,

TABLE 1. Diagnosis of OUD, From the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition***To confirm a diagnosis of OUD, at least 2 of the following should have been observed in the last 12 mo**

- 1 Opioids are taken in larger amounts or over a longer period than was intended
- 2 There is a persistent desire or unsuccessful efforts to cut down or control opioid use
- 3 A great deal of time is spent in activities needed to obtain, use, or recover from an opioid
- 4 Craving, or a strong desire to use opioids
- 5 Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home
- 6 Continued opioid use despite having persistent or recurrent social or interpersonal problems exacerbated by opioid use
- 7 Important social, occupational, or recreational activities are given up or reduced because of opioid use
- 8 Recurrent opioid use in situations in which it is physically hazardous
- 9 Continued opioid use despite knowledge of having a recurrent physical or psychological problem that is likely to be caused or exacerbated by use
- 10 Exhibits tolerance as evidenced by:
 - 10 a. the need for a markedly increased dose to achieve the same effect
 - 10 b. markedly diminished effect with the same dose of opioid
- 11 Exhibits withdrawal as seen by:
 - 11a. Characteristic opioid withdrawal syndrome
 - 11b. The use of the same or closely related substance to avoid or relieve withdrawal symptoms

among others. Signs that practitioners can observe include dilated pupils, goose flesh, vomiting, diarrhea, diaphoresis, tachycardia, and agitation. The Clinical Opioid Withdrawal Scale (COWS) score is a standard tool that uses 11 subjective and objective measures to determine the severity of withdrawal.¹¹ This scale is very useful in starting medications for opioid use disorder (MOUD) and clinicians should become familiar with it (Fig. 1).

ADOLESCENT VULNERABILITY

Adolescents are particularly vulnerable when it comes to OUD for both social and physiologic reasons. The majority of adolescents initiate drug use for either sensation seeking or as a coping mechanism.⁸ Drug use seems to occur more often in people with mental health problems.¹² In one study, up to 41% of adolescents and young people who died of an overdose had a co-occurring mental health problem.³ It is perhaps not a coincidence that the rates of adolescents dying of an overdose have increased in conjunction with a rise in anxiety and depression among the same age group. It is likely that these mental health problems and the rise in overdoses have both been exacerbated by the COVID-19 pandemic.

Adolescents who die from an overdose are often using alone. They are more likely to overdose in their own house than other age groups are. Even though there is often someone at home with them, they are the least likely of all age groups to receive naloxone in an overdose, making them less likely to survive.¹³ Part of this may be due to the increasing isolation that adolescents experienced and grew up with during the COVID-19 pandemic, and part of this is likely due to the fear of the stigma that surrounds drug use.

The stigma associated with the use of drugs may, in fact, be one of the most lethal aspects of the problem for teenagers. Stigma and the fear of stigma are often the things that prevent adolescents who use drugs from getting help. One way to help address that stigma is to adopt a harm reduction approach (Table 2).

HARM REDUCTION

Harm reduction is a set of nonjudgmental pragmatic strategies aimed at keeping people from getting sick or hurt and supporting them in making healthy choices (Table 1). It does not mandate abstinence as a precondition of care. It is based on the idea that all persons have value and are worthy of care, whether

or not they use drugs.¹⁴ Like all approaches and techniques, using harm reduction well takes practice, patience, and humility, but it can be life-saving. Research has shown that patients who feel more connected to their providers and more invested in the treatment plan are more likely to follow their treatment. The longer people who use drugs stay in treatment, the less likely they are to die from an overdose or experience other harms.¹⁵

Perhaps the most important harm reduction technique is to be open to listening without judgment. People who use drugs often do so for a reason. It is important to respect those reasons, even when you do not agree with them. Another important idea is to minimize risks and harms while drug use is ongoing. Encouraging people to use the safest route of administration is an easy start. Swallowing pills is generally safer than snorting or smoking, which are both safer than intravenous injection. Intravenous use is still preferable to intramuscular use. If injection is going to happen, then ensuring that people are using clean “works,” cookers, needles, cottons, syringes, and diluent is critically important to stopping the spread of hepatitis C and HIV, as well as skin and soft tissue infections, and endocarditis. Referring people to places where they can get this equipment is often very helpful. Advising people to use a tester dose, a much smaller dose than usual, is another good strategy. This is especially important when using a new batch of drugs that the person has not yet used before, even if they got it from the same source. Because there is no body that oversees the illicit drug manufacturing and distributing process, drugs are often of widely varying potency and frequently adulterated with other substances. Finally, advising people to never use alone is critically important. Often if people take turns using, one person can monitor the others to ensure that they continue to breathe. If this is not possible, there are phone numbers that people can call when using (<https://neverusealone.com/> 877-696-1996). Someone will stay on the line with them and then alert EMS if they stop responding for a certain period. That is not nearly as helpful as having another person present, though, especially if that person has naloxone.

NALOXONE

Naloxone is an opioid antagonist. It binds tightly to the mu- and kappa-opioid receptors, displacing any opiate that might already be there. In this way, it reverses the respiratory depression

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 <i>Measured after patient is sitting or lying for one minute</i> 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	GI Upset: <i>over last 1/2 hour</i> 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting	
Sweating: <i>over past 1/2 hour not accounted for by room temperature or patient activity.</i> 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: <i>observation of outstretched hands</i> 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching	
Restlessness: <i>Observation during assessment</i> 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: <i>Observation during assessment</i> 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 <i>If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored</i> 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 <i>Not accounted for by cold symptoms or allergies</i> 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.

FIGURE 1. The COWS.

that is associated with an opioid overdose. It can be administered intravenously, intramuscularly, or intranasally. It is commercially available to the general public as an intranasal inhaler and also as an intramuscular autoinjector.¹⁶

Naloxone is very effective at reversing opioid overdoses, but it will not reverse the effects of other sedatives. It also has no effect on someone who is not intoxicated with opioids. There is no maximum dose, and it does not have to be dose adjusted for age, body weight, surface area, or organ dysfunction. Distributing naloxone widely in communities where there is a high incidence of opioid use has been shown to reduce overdoses. Depending on how targeted the population is that is receiving the naloxone, the number needed to prescribe to prevent one overdose death is 63.¹⁷ If given to someone who is intoxicated with opioids, it will reverse

all of the effects of the opioid, not just the respiratory depression. Unfortunately, this can cause acute withdrawal symptoms.

Withdrawal Treatment

Withdrawal can be very difficult to treat. Of course, giving a short-acting full opioid agonist can ameliorate symptoms, but it only delays them. Other medications, such as ondansetron for vomiting, loperamide for diarrhea, acetaminophen for joint pains, and clonidine for agitation, are also helpful. These work well as adjuncts but do not treat the primary problem. The 2 medications that work and are Food and Drug Administration approved for management of withdrawal symptoms are buprenorphine and methadone. Methadone is a very long-acting full agonist that can only be given in specially licensed dispensaries where patients

TABLE 2. Harm Reduction Techniques

Behaviors	Things
1 Trauma-informed approach	1 Availability when patient is ready
2 Nonjudgmental conversations	1a
3 Avoiding stigmatizing language	2 Provision of naloxone
4 Allowing the patient to choose treatments and services	3 Safer use supplies
5 Provision of community resources	4 Condoms
6 Discussion of safer use strategies	5 Testing for HIV, hepatitis C, syphilis, pregnancy
6a	6 Provision of Fentanyl and/or Xylazine test strips
6b	7 Referrals to treatment, counseling, peer counseling
6c	8 Referrals for sexually transmitted infection treatment and pre-exposure prophylaxis for HIV services

have to present in-person each day to get their dose. It is not often used in adolescents, and so will not be discussed further here.¹⁸

BUPRENORPHINE

Buprenorphine is a partial agonist that is useful for treating withdrawal and preventing cravings. Whereas fentanyl causes maximal activation of the receptor, buprenorphine only causes partial stimulation. It is a long-acting medication with a half-life of approximately 38 hours. It does not often cause the same euphoria and does not cause the respiratory depression seen with other opioid agonists, especially when given to people who have experience using opioids.¹⁹ Buprenorphine binds the opioid receptor with a high affinity. In fact, people who have taken a therapeutic dose of buprenorphine will not be able to get intoxicated with other opioids taken later.²⁰ In this way, buprenorphine is an important tool in overdose prevention.

The detrimental part of this high receptor affinity is that if people take buprenorphine while they are intoxicated with opioids, it will replace the full agonist on the receptor and they may go into acute precipitated withdrawal.²¹ For this reason, it is important to wait until people are already in moderate withdrawal to start the medication. Most protocols advocate for performing a COWS score to assess the severity of the withdrawal. The COWS scale gives a result from 0 to 48. Most protocols advocate for waiting until people have a COWS score of at least 8 before starting treatment to avoid precipitating withdrawal (Fig. 1).

Buprenorphine comes in either pills or films that dissolve under the tongue. Suboxone is a brand name combination product that contains both buprenorphine and naloxone. The naloxone is not absorbed sublingually or in the gastrointestinal tract, so it is not pharmacologically active. However, if the Suboxone is injected, smoked, or inhaled, the naloxone does become active and can precipitate withdrawal. Including the naloxone is intended to make sure that Suboxone is taken only by mouth.

Most traditional buprenorphine induction protocols start with 4 mg of buprenorphine (or 4/1 mg of buprenorphine/naloxone if using Suboxone) once the COWS score is 8 or more.²² An additional 4-mg dose is given after an hour if the patient tolerated the first one without experiencing precipitated withdrawal, for a total dose of 8 mg (or 8/2 mg of the combination product). Many patients will need a third, and some will need a fourth 4-mg dose between one and several hours later for recurring withdrawal symptoms. The more heavily people have used opioids, the higher the dose of buprenorphine they will need. Rarely, up to

32 mg/d may be required. Most people do well with 8 to 16 mg/d (16 mg/d is the Food and Drug Administration-recommended limit), and adolescents are usually more comfortable with 8 to 12 mg/d. Once they have found the dose that makes them feel comfortable on the first day, they continue that total daily dose the following day (Appendix 1). People should follow up with a treatment provider after a week to have their dose adjusted. There is no limit to the duration of buprenorphine treatment. Some people are on it chronically, while others taper off of it after several months to a year. It seems to work better to help people reduce or stop their use if they are on it for longer periods.^{23,24} People can stay in the emergency department while they are getting started on the buprenorphine, or if they are motivated and will follow directions, they can get a prescription and start the buprenorphine at home (Appendix 2).²⁵ They should be reminded that they need to wait until they are in moderate withdrawal before starting the medication to avoid precipitating withdrawal.

Buprenorphine and methadone are two of the most effective medications for the treatment of OUD. They decrease all-cause mortality in people with OUD by 40% to 60%.²⁶ That means that the number needed to treat is 2; for every 2 people who get started on one of these medicines, one life is saved.

CHANGES IN REGULATIONS

On January 12, 2023, the Drug Enforcement Administration (DEA) removed the requirement for special training and certification to dispense buprenorphine under Section 1262 of the Consolidated Appropriations Act, 2023 (the DEA X Waiver).²⁷ Now anyone with a standard DEA license allowing them to prescribe schedule III substances can prescribe buprenorphine with no limit on the number of patients they can treat. However, beginning in June 2023, all providers who are renewing their DEA license must have completed 8 hours of training on opioid or other substance use disorders to renew their DEA license according to the DEA's new Medication Access and Training Expansion Act.²⁸

DISPOSITION

Most people with OUD can be treated as outpatients, even after an overdose requiring reversal with naloxone. Some may require hospital admission for medical comorbidities, and MOUD can be initiated in the inpatient setting, but treatment of withdrawal alone is rarely an indication for admission unless the patient is unable to tolerate oral intake. Importantly, if people are

being admitted for an acutely painful condition or a surgical procedure, buprenorphine may complicate the management of acute pain. Expert consultation is recommended in this case.

The majority of patients with OUD may be discharged after initiating buprenorphine in the ED or with instructions and a prescription for home induction once they are in mild to moderate withdrawal. It is also imperative to ensure that patients have access to naloxone. It is critical to help discharged patients link to ongoing care for MOUD. With the elimination of the DEA X Waiver, any primary care physician that can prescribe opioids can also prescribe buprenorphine. However, few may be comfortable with this treatment, especially in adolescents. It is important to understand what resources are available in your community for continuing MOUD. The Substance Abuse and Mental Health Services Administration has a MOUD locator on their website that lists providers by state who will prescribe MOUD.²⁹ It is important to discharge people with enough medication for them to have time to arrange follow-up. Usually 7 to 10 days is sufficient. State or county health departments often have additional resources.

SUMMARY

While the deadly opioid epidemic has continued to worsen, we have more tools available than ever before to address it. Naloxone is incredibly effective if delivered in time and is now over-the-counter. Naloxone is easy to distribute, carry, and deliver. All medical professionals should be conversant in how and when to use it and should participate in efforts to get more naloxone out into communities, where it can be used by bystanders. Today there is more access to buprenorphine, which has the potential to avert half of all overdose deaths. It is safe, easy to use, and can be life-changing. We have a moral imperative to become facile with treating OUD in this vulnerable population.

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