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SPECIAL CONTRIBUTION

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Emergency department management of opioid use disorder in pediatric patients

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Abstract

Opioid use disorder (OUD) has emerged as a significant public health crisis affecting individuals across all age groups. However, there remains a critical gap in understanding the specific nuances and challenges associated with OUD in pediatric populations. This article provides a comprehensive review of the epidemiology, definition of OUD, screening recommendations for OUD, and evidence-based management strategies for OUD in pediatric patients.

KEYWORDS

buprenorphine, methadone, opioid use disorder, opioid-related disorders, OUD, pediatric, substance-related disorders

1 | INTRODUCTION

As emergency departments (EDs) are grappling with the effects of the opioid crisis, the pediatric population is notably affected. National surveys estimate that 17% of high school seniors in the United States have used prescription opioids in their lifetime for medical purposes, and 13% have used them for nonmedical purposes.[1] In 2016, over 150,000 adolescents met the criteria for an opioid use disorder (OUD).[2] According to the Treatment Episode Data Set of opioid-related admissions from 2008 to 2017, 60% were male, 74% white, and 10% African

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TABLE 1 DSM-5 criteria for diagnosis of opioid use disorder.[5]

- Opioids are often taken in larger amounts or over a longer period 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 need for markedly increased amounts of opioids to achieve intoxication or desired effect
  - markedly diminished effect with continued use of the same amount of an opioid
- Withdrawal, as manifested by either of the following:
  - the characteristic opioid withdrawal syndrome
  - the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

American.[3] However, few, if any, guidelines exist to support management of OUD in this population, which poses a challenge to EDs. Additionally, there are very few educational resources addressing OUD in adolescents.[4] Given the pervasiveness of opioid use among adolescents and the associated risks, emergency physicians must be knowledgeable in caring for adolescents with OUD, which includes harm reduction.

2 | DEFINITION/CRITERIA

When discussing opioid use, there are several terms to understand. Opioid misuse is defined as using an opioid in any way other than as directed by a physician. This includes using one's prescription in greater amounts or for longer periods than prescribed.[2] The DSM-5 defines OUD as "a problematic pattern of abuse leading to clinically significant impairment or distress" with at least two of the characteristics found in Table 1 over 12 months. Importantly, tolerance and withdrawal do not count if the patient takes prescribed medications as directed.[5]

The criteria for OUD revolves around the behaviors associated with addiction. Notably, the term "abuse" is no longer included in the DSM criteria and should not be used. An essential aspect of managing OUD in the ED is recognizing and treating opioid withdrawal. Opioids bind to the mu-opioid receptor, which is involved in several neurotransmitter pathways, including dopaminergic pathways, which lead to euphoria and reward pathways.[1] Over time, opioid use alters the release of neurotransmitters and the regulation of neuroreceptors, leading to a physical dependence on opioids. The same stimulus causes either less release of neurotransmitters or less stimulation at the receptor causing someone to need higher amounts of drugs to obtain the same feeling.

Opioid withdrawal occurs when an individual who is physically dependent on opioids suddenly stops using them, precipitating extremely uncomfortable symptoms. Withdrawal signs and symptoms include arthralgias, myalgias, diaphoresis, piloerection, lacrimation, chills, rhinorrhea, mydriasis, tachycardia, abdominal pain, nausea, vomiting, diarrhea, and yawning as well as anxiety and irritability.[6] While not life threatening in comparison with sedative/hypnotic withdrawal, suboptimal treatment leads to continued use of dangerous illicit opioids, which is associated with significant morbidity and mortality. By initiating treatment in adolescents with OUD who present in acute withdrawal or want help, emergency physicians can better alleviate their symptoms, engage them in treatment, and connect them to treatment and other recovery resources.[7]

3 | SCREENING

Screening for OUD in the ED is an essential part of the management and initiation of treatment of patients with OUD. However, screening approaches need to be different for adolescents with targeted screening being recommended [8,9] for high-risk populations who present with overdoses to the ED; however, the Substance Abuse and Mental Health Services Administration and the American Academy of Pediatrics recommend universal screening in the primary care setting.[10,11] Given the escalating opioid crisis and its increasing impact on adolescents, ideally, we recommend implementing universal adolescent specific screening in the ED in patients who are medically stable. However, we recognize the already abundant amount of screening performed in the ED and that time and resources are finite. One approach is to complete a standard social assessment as part of the patient history, for example, the HEEADSSS assessment (home environment, education and employment, eating, peer-related activities, drugs, sexuality, suicide/depression, and safety from injury and violence) in the initial assessment in the ED. This assessment can be completed verbally or electronically, and a positive "screen" can trigger a more targeted and detailed assessment.[11] Additional substance use screening tools validated for adolescents include the Screening to Brief Intervention; Brief Screener for Tobacco, Alcohol, and Other Drugs; and the Car, Relax, Alone, Friends/Family, Forget, Trouble.[9,11] All of these can be completed electronically on a tablet by the patient while they are waiting. This may improve privacy for the patient and offloads the screening process from staff. Some EDs have already implemented this approach for screening in their adolescent population. Further research is needed to identify the ideal screening tool and method in

the ED setting to identify adolescents at higher risk for OUD while minimizing the impact of ED workflow. However, EDs should not hesitate to implement screening programs in the absence of perfect evidence, given the scale of the problem and the potential benefit of treatment programs.[12] While adolescents are minors, they do generally have the right to confidentiality from their parents regarding presentations due to substance use disorders (SUDs). Situations where confidentiality may need to be broken include a concern for the patient's life or there is a strong likelihood of harm and all other alternatives have been exhausted. Physicians need to be aware of local regulations that impact adolescent confidentiality.[13]

4 | IDENTIFICATION

Opioid use in adolescents has a range of presentations from worsening school performance to a fatal overdose. Opioid use may be discovered following an arrest, by their parents, because of being fired from work, expulsion from school, or when the patient presents for an unrelated complaint. Unfortunately, dependence, which may indicate an OUD, may only be recognized when the adolescent withdraws when they cannot access opioids, such as on vacations, during a hospitalization, due to lack of funds to buy opioids, or during a jail sentence. OUD may mimic other medical and SUDs such as gastroenteritis, sedative/hypnotic withdrawal, or cannabinoid hyperemesis syndrome. Signs might be subtle such as social isolation; changing peer groups; mood changes (irritability, depression, and anger); and increasing negative behaviors such as lying, stealing, and school absences.[14]

Patients will require a comprehensive psychosocial assessment, including a family history of substance use and psychiatric disorders, social living situations, and access to opioids. However, this is not necessary to either initiate buprenorphine in the ED or refer them to treatment. Additionally, while urine drugs screens (UDS) may be useful in addiction clinics, they are not necessary to initiate medications for opioid use disorder (MOUD) in the ED. If one is obtained, a negative test does not eliminate the use of opioids or other drugs as many synthetic drugs, such as fentanyl and fentanyl analogs, are not detected on standard UDS.[15]

5 | MANAGEMENT

Treating OUD in pediatric patients involves a comprehensive approach that includes MOUD, behavioral therapies, and supportive services. Behavioral health specialists are critical in counseling and supporting patients and families. They help patients develop coping strategies and provide resources for ongoing support. Peer support teams play a valuable role in treating OUD. These teams are made up of individuals with personal addiction and recovery experience. Importantly, MOUD should not be contingent on having these resources, particularly in the ED. Options for MOUD include buprenorphine, naltrexone, and methadone (Table 2). Naltrexone requires prolonged abstinence prior to induction so is generally not an option in the ED. Given its pharmacologic properties and regulatory restrictions, methadone is not typically initiated in EDs. Thus, buprenorphine is the preferred therapy. Unfortunately, there is paucity of published information about MOUD in adolescents in the ED.

A way to assess the severity of withdrawal and whether to initiate MOUD is with the Clinical Opioid Withdrawal Scale (COWS).[16] The COWS score is a validated 11-item tool that classifies the severity of the withdrawal symptoms as mild, moderate, or severe.[17] While patients in acute withdrawal can be treated symptomatically, the scoring scale assists clinicians in determining when buprenorphine may be initiated.[18] While individual practice may vary, most protocols recommend initiating buprenorphine for a COWS score of 8 or greater.[19]

No specific laboratory evaluation is required prior to initiating MOUD. As this population is at high risk for sexually transmitted diseases, screening or testing should be considered in the ED or at follow up. Ideally if agreeable by the patient, parents should be involved in the discussion of MOUD with the patient in order to provide support to the patient and so that they understand the rationale and importance of MOUD to treat OUD. A direct and open discussion is best given stigma and misconceptions that the patient or their parents may have.

5.1 | Buprenorphine

Buprenorphine is a partial mu-opioid receptor agonist that increases treatment retention, decreases drug use, and improves abstinence from opioids.[20] Three crucial properties of buprenorphine underpin its use in the treatment of OUD. It is a partial mu-agonist, with a very high affinity for the mu receptor, and a slow dissociation from the receptor.[21,22] These factors make buprenorphine an ideal treatment for OUD as it will reliably outcompete other opioids at the mu receptors, while the ceiling effect makes respiratory depression significantly unlikely. Its high affinity blocks full agonists, such as fentanyl and heroin, at the mu receptor. Standard commercial buprenorphine products are combined with naloxone to deter inappropriate use.[23,24] When administered in the sublingual form, the naloxone is not significantly bioavailable; however, when injected or insufflated, it is better absorbed causing withdrawal. Importantly, anyone with a DEA license allowing them to prescribe schedule 3 substances may prescribe buprenorphine. A special waiver, known as an "x-waiver," is no longer required to prescribe buprenorphine.[25]

While ED initiation of treatment for OUD is an accepted practice in adults,[26–34] there is a less robust body of research evaluating adolescent and pediatric induction, and many of the recommendations are either based on expert opinion or are not based on evidence obtained in the ED setting.[10,35–39] Buprenorphine is approved for patients 16 years and older but is used off label in younger patients.[40] Given these limitations, many programs rely on adult literature for developing programs to initiate MOUD.[41] There are currently three randomized control studies evaluating the effectiveness of buprenorphine in the adolescent population.[19,42,43] These studies included patients 16–24, 13–18, and 15–21 years of age, respectively, and took place in out-

TABLE 2 Medications for opioid use disorder.

Medication	Mechanism of action	Important considerations
Buprenorphine	Partial agonist	Induction strategy needed to avoid precipitated withdrawal
Methadone	Full agonist	Can be very challenging to continue in the outpatient setting in pediatric patients
Naltrexone	Antagonist	Need to be off all opioids for at least 7 days prior to induction

patient treatment centers or research clinics. They demonstrate that buprenorphine is more effective than monotherapy with clonidine, and that longer treatment courses of buprenorphine are beneficial in pediatric populations with OUD. Buprenorphine was demonstrated to be very safe, with no adverse reactions noted in any of the three randomized control studies.

There are multiple described traditional buprenorphine strategies.[44] A traditional induction program requires a period of abstinence prior to the induction of buprenorphine to avoid precipitated withdrawal (PW), defined as abrupt and severe withdrawal symptoms following the administration of buprenorphine. PW is the most feared complication of buprenorphine induction, and patients should be warned that this infrequently occurs and can be treated with more buprenorphine in addition to other supportive medications. Once adequate withdrawal is established, using clinical scoring such as the COWS and the patient's historical reporting of their last dose of opioids, buprenorphine induction should be initiated. Importantly, there are alternative microdosing approaches where buprenorphine induction can proceed even with very low COWS.

In the adult population, there is a movement toward low-dose induction (micro-dosing) to alleviate some of the shortcomings of traditional induction, such as PW or a need for a long abstinence period prior to induction.[45–47] Additionally, some are concerned that traditional approaches may no longer work due to the preponderance of fentanyl and analogs in the heroin supply,[48] although this is controversial and not universally accepted. Most adult literature centers on case studies and series.[49–66] There are multiple approaches to microdosing, which can start as low as 0.5 mg per day. There is presently one case series of two adolescent patients with sickle cell disease who were successfully induced with a low-dose induction [67] and another case report of an adolescent patient who was initiated with rapid low-dose induction and subsequently transitioned to extended-release buprenorphine.[68] Additionally, some experts advocate for a high dose or macrodose approach such as an induction dose of 12–16 mg or more, compared with a more standard dose of 8 mg.[69] This is then generally followed by maintenance dosing of 8 mg two or three times a day.

At follow-up, ongoing monitoring and adjustments to the treatment plan are necessary to ensure the best possible outcomes for the patient. Whether a standard, microdose, or macrodose approach are used, buprenorphine should be offered to adolescents with OUD in the ED. If for whatever reason the patient is not a candidate or declines buprenorphine, symptomatic medications such as clonidine, antiemetics, and hydroxyzine can be prescribed to treat withdrawal symptoms and the patient should still be referred for addiction treatment.

5.2 | Methadone

Methadone was developed by German scientists [70,71] before being introduced in the United States in 1946 and approved as an analgesic and antitussive by the United States Food and Drug Administration in 1947.[72] In 1971, regulations allowed the use of methadone for the treatment of OUD, although in a very restrictive manner. Regulations enacted in the next few years better allowed for maintenance therapy with methadone; however, there were still significant restrictions. Methadone could only be dispensed for OUD in methadone maintenance programs or opioid treatment programs (OTPs).[73] Regulations also required daily, onsite dosing for at least the first 90 days; mandatory counseling; suggested dosing; and drug testing.[74,75] Patients under 16 years of age were restricted from treatment, and special procedures were required for adolescents aged 16–18 years.[38,74,76]

Methadone is a full opioid agonist with a long half-life and inactive metabolites, making it ideal for treating OUD. While it prolongs the QT interval, cardiovascular screening is not mandated prior to initiation, though caution should be used in patients taking other QT prolonging medications. Due to its long half-life, it is slowly titrated to avoid respiratory depression. To treat OUD, it must be dispensed from an OTP, although it can be administered in a hospital but not prescribed. Methadone dispensation from OTPs will not appear in state prescription drug monitoring programs. While it is an efficacious option for treating OUD, it is generally not recommended in the ED in adolescents at this time. Additionally, transitioning a patient from methadone to buprenorphine should only be done by someone with expertise in addiction medicine.

5.3 | Long acting injectables

There are now two buprenorphine extended-release products (BUP-XR), Sublocade® and Brixadi®, available for clinical use. The package insert for Sublocade® reads that it should only be initiated after a patient is on a steady dose for 7 days. It is then administered monthly as a subcutaneous injection. The dose is 300 mg for the first 2 months, followed by 100 mg in subsequent months but can be increased to 300 mg if required for symptom control. It is equivalent to approximately 16–24 mg/day of the sublingual formulation, and patients should wait at least 26 days between injections. Due to its long-acting nature, withdrawal symptoms may be delayed following discontinuation. In a case report, Sublocade® was administered to a 16-year-old after only 3 days of sublingual buprenorphine.[68] New research indicates that Sublocade® could be initiated in the ED after a single dose of sublin-

gual buprenorphine.[77] Brixadi® was approved in May 2023. It comes in weekly and monthly injections. A new trial demonstrates that it can be injected in the ED without a sublingual dose in adult patients.[78]

5.4 | Precipitated withdrawal

PW is the most feared complication of buprenorphine induction and also occurs after naloxone administration. When PW occurs after administering the combination buprenorphine/naloxone product, it is the buprenorphine, not the naloxone causing PW. PW signs and symptoms include arthralgias, discomfort, anxiety, nausea, vomiting, diarrhea, tremor, muscle spasms, rhinorrhea, headaches, fever, chills, tachycardia, hypertension, and piloerection. It occurs quickly after induction, generally within 20 min.

PW can last from several hours to a couple of days. Significant hypertension and tachycardia precipitated by a short-acting antagonist, such as naloxone, are expected to resolve after a brief observation. Buprenorphine can be administered to patients with PW from either buprenorphine, naltrexone, or naloxone.[79,80] While potentially counterintuitive, additional doses of buprenorphine will improve most patients' symptoms, and they can then be started on maintenance therapy upon discharge from the ED.

5.5 | Supportive and adjunctive medications

In addition to partial mu-agonist medications, multiple adjunctive treatments support adolescents symptomatically through the withdrawal process, during induction, and in the case of PW. In patients with normal or elevated blood pressure, an alpha-2 agonist may be administered. Clonidine binds to a central alpha-2 adrenergic receptor that shares potassium channels with opioids and blunts withdrawal symptoms.[81] Lofexidine® is presumed to exert the same mechanism of action as clonidine but is more expensive. Heart rate and blood pressure monitoring should be continued when administering these medications, and they should not be used if the patient is hypotensive.

Benzodiazepines are a good supplement to clonidine due to their excellent safety profile and emergency physicians are familiar with their use. In animal models, other gamma-aminobutyric-ergic drugs reduce catecholamine release during severe withdrawal, and benzodiazepines are demonstrated to improve withdrawal.[82,83] In addition to clonidine, either diazepam, lorazepam, or midazolam may be utilized. They are best utilized as a single dose in the ED and should not be prescribed to the patient.

Other symptoms of PW can be addressed individually. For nausea, vomiting, restlessness, and insomnia: promethazine, diphenhydramine, or hydroxyzine are utilized, respectively. Loperamide, octreotide, or bismuth subsalicylate treat diarrhea or abdominal cramping. For pain and myalgia, acetaminophen or nonsteroidal anti-inflammatories are recommended. For muscle cramping, baclofen can be utilized.

QT prolongation can occur when multiple medications are used to treat opioid withdrawal symptoms, although it is rare. In addition, those with electrolyte abnormalities from vomiting or diarrhea can also have an increased risk. Therefore, a baseline electrocardiogram and cardiac monitoring can be considered in at-risk patients.

6 | DISCHARGE/DISPOSITION AND HARM REDUCTION

Adolescents presenting with OUD after an overdose do not necessarily need to be admitted to the hospital for buprenorphine induction and further treatment if symptoms are controlled in the ED. However, there is a wide range of practice variation regarding admission or discharge from the ED. This may be due to unique psychosocial differences in adolescents compared with adults causing providers to feel more comfortable admitting them. At discharge, patients should be referred to a treatment program that offers MOUD. While continuation of MOUD is extremely important, the patient (and possibly their family) will likely need other behavioral and psychological interventions. We believe these are likely to be very important in and adolescent with a SUD. Academic centers may have internal programs while community settings may need to make external referrals. In many areas, there are programs willing to collaborate with EDs to improve the handoff of care.

Discharge from the ED is a critical opportunity for education. Families should be educated on the safe administration, storage, and disposal of pain medications. Research demonstrates that although friends or relatives are the most common sources of prescription opioids that youths misuse, 20% percent of adolescents and 25% of young adults who misuse prescription opioids obtain them directly from a physician.[15,84] Physicians should communicate the importance of properly disposing of unused and expired medications in the home to reduce the risk of children and adolescents having access to prescription drugs, including opioids. Opioid medications should be locked and stored when not in use.[85]

Naloxone is a life-saving medication that can reverse opioid overdoses.[85] It has minimal side effects and does not possess the potential for misuse. Increased access to naloxone, especially at ED discharge, decreases the risk of fatal opioid overdoses. Take-home naloxone should be considered for all patients at risk for overdose.[84,86] Families should be counseled that minors can purchase naloxone in most states, and minors should be educated on how to use naloxone. While it is now available over the counter, the best practice is to dispense it directly to the patient if possible, otherwise, they should receive a prescription. In addition to naloxone, patients should be offered other harm-reduction services before discharge.

7 | CONCLUSION

The response to the opioid crisis must focus on preventing new cases of opioid misuse while improving the treatment of those with OUD. All pediatric patients suspected of having an OUD should ideally be screened and offered treatment in the ED. In addition to starting buprenorphine in the ED and linking patients to treatment, patients

with an OUD or following an opioid overdose should receive take-home naloxone and other forms of harm reduction.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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REFERENCES

1. McCabe SE, West BT, Teter CJ, Boyd CJ. Medical and nonmedical use of prescription opioids among high school seniors in the United States. *Arch Pediatr Adolesc Med*. 2012;166(9):797-802.
2. Key substance use and mental health indicators in the United States: results from the 2016 National Survey on Drug Use and Health (HHS Publication No. SMA 17–5044, NSDUH Series H-52). *Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration*. Substance Abuse and Mental Health Services Administration.;2017.
3. Welsh JW, Dennis ML, Funk R, Mataczynski MJ, Godley MD. Trends and age-related disparities in opioid use disorder treatment admissions for adolescents and young adults. *J Subst Abuse Treat*. 2022;132:108584.
4. Garcia-Vassallo G, Edens EL, Heward B, Auerbach MA, Wong AH, Camenga D. Management of adolescents with OUD: a simulation case for subspecialty trainees in addiction medicine and addiction psychiatry. *MedEdPORTAL*. 2021;17:11147.
5. Diagnostic and statistical manual of mental disorders: DSM-5™, 5th ed, Diagnostic and statistical manual of mental disorders: DSM-5™, 5th ed.(2013).
6. Pergolizzi JV Jr, Raffa RB, Rosenblatt MH. Opioid withdrawal symptoms, a consequence of chronic opioid use and opioid use disorder: current understanding and approaches to management. *J Clin Pharm Ther*. 2020;45(5):892-903.
7. Canamo LJ, Tronco NB. Clinical opioid withdrawal scale (COWS): implementation and outcomes. *Crit Care Nurs Q*. 2019;42(3):222-226.
8. Love JS, Hughes A, Hendrickson RG. Pediatric opioid-related emergency visits offer critical opportunities for opioid safety screening and planning. *Am J Emerg Med*. 2022;55:199-200.
9. Smith JR, Hazen EP, Kaminski TA, Wilens TE. Literature review: substance use screening and co-morbidity in medically hospitalized youth. *Gen Hosp Psychiatry*. 2020;67:115-126.
10. Screening and Treatment of Substance Use Disorders among Adolescents. Advisory. Publication No. PEP20-06-04-008. Substance Abuse and Mental Health Services Administration.;2021.
11. Levy SJ, Williams JF. Substance use screening, brief intervention, and referral to treatment. *Pediatrics*. 2016;138(1).
12. Ozechowski TJ, Becker SJ, Hogue A. SBIRT-A: adapting SBIRT to maximize developmental fit for adolescents in primary care. *J Subst Abuse Treat*. 2016;62:28-37.
13. Pathak PR, Chou A. Confidential care for adolescents in the U.S. health care system. *J Patient Cent Res Rev*. 2019;6(1):46-50.
14. Whelan KT, Heckmann MK, Lincoln PA, Hamilton SM. Pediatric withdrawal identification and management. *J Pediatr Intensive Care*. 2015;4(2):73-78.
15. Sharma B, Bruner A, Barnett G, Fishman M. Opioid use disorders. *Child Adolesc Psychiatr Clin N Am*. 2016;25(3):473-487.
16. Tompkins DA, Bigelow GE, Harrison JA, Johnson RE, Fudala PJ, Strain EC. Concurrent validation of the Clinical Opiate Withdrawal Scale (COWS) and single-item indices against the Clinical Institute Narcotic Assessment (CINA) opioid withdrawal instrument. *Drug Alcohol Depend*. 2009;105(1-2):154-159.
17. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*. 2003;35(2):253-259.
18. Guo CZ, D'Onofrio G, Fiellin DA, et al. Emergency department-initiated buprenorphine protocols: a national evaluation. *J Am Coll Emerg Physicians Open*. 2021;2(6):e12606.
19. Marsch LA, Moore SK, Borodovsky JT, et al. A randomized controlled trial of buprenorphine taper duration among opioid-dependent adolescents and young adults. *Addiction*. 2016;111(8):1406-1415.
20. Wakeman SE, Larochelle MR, Ameli O, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. *JAMA Netw Open*. 2020;3(2):e1920622.
21. Chiang CN, Hawks RL. Pharmacokinetics of the combination tablet of buprenorphine and naloxone. *Drug Alcohol Depend*. 2003;70(2):S39-S47. Suppl.
22. Walsh SL, Preston KL, Stitzer ML, Cone EJ, Bigelow GE. Clinical pharmacology of buprenorphine: ceiling effects at high doses. *Clin Pharmacol Ther*. 1994;55(5):569-580.
23. Soyka M. Buprenorphine and buprenorphine/naloxone soluble-film for treatment of opioid dependence. *Expert Opin Drug Deliv*. 2012;9(11):1409-1417.
24. Soyka M. Buprenorphine-naloxone buccal soluble film for the treatment of opioid dependence: current update. *Expert Opin Drug Deliv*. 2015;12(2):339-347.
25. *X-Waiver No Longer Required to Treat Opioid Use Disorder*. In. Vol 2024: American College of Emergency Physicians; 2023.
26. Bahji A, Cheng B, Gray S, Stuart H. Reduction in mortality risk with opioid agonist therapy: a systematic review and meta-analysis. *Acta Psychiatr Scand*. 2019;140(4):313-339.
27. Herring AA, Perrone J, Nelson LS. Managing opioid withdrawal in the emergency department with buprenorphine. *Ann Emerg Med*. 2019;73(5):481-487.
28. Hickman M, Steer C, Tilling K, et al. The impact of buprenorphine and methadone on mortality: a primary care cohort study in the United Kingdom. *Addiction*. 2018;113(8):1461-1476.
29. Kimber J, Larney S, Hickman M, Randall D, Degenhardt L. Mortality risk of opioid substitution therapy with methadone versus buprenorphine: a retrospective cohort study. *Lancet Psychiatry*. 2015;2(10):901-908.
30. Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. *Lancet*. 2011;377(9776):1506-1513.
31. Lee JD, Nunes EV Jr, Novo P, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:bOT): a multicentre, open-label, randomised controlled trial. *Lancet*. 2018;391(10118):309-318.
32. Manhapra A, Rosenheck R, Fiellin DA. Opioid substitution treatment is linked to reduced risk of death in opioid use disorder. *Bmj*. 2017;357:j1947.
33. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *Bmj*. 2017;357:j1550.
34. Tanum L, Solli KK, Latif ZE, et al. Effectiveness of injectable extended-release naltrexone vs daily buprenorphine-naloxone for opioid dependence: a randomized clinical noninferiority trial. *JAMA Psychiatry*. 2017;74(12):1197-1205.
35. Medication-assisted treatment of adolescents with opioid use disorders. *Pediatrics*. 2016;138(3).

36. Medication for adolescents and young adults with opioid use disorder. *J Adolesc Health*. 2021;68(3):632-636.
37. Borodovsky JT, Levy S, Fishman M, Marsch LA. Buprenorphine treatment for adolescents and young adults with opioid use disorders: a narrative review. *J Addict Med*. 2018;12(3):170-183.
38. Feder KA, Krawczyk N, Saloner B. Medication-assisted treatment for adolescents in specialty treatment for opioid use disorder. *J Adolesc Health*. 2017;60(6):747-750.
39. Yule AM, Lyons RM, Wilens TE. Opioid use disorders in adolescents-updates in assessment and management. *Curr Pediatr Rep*. 2018;6(2):99-106.
40. Terranella A, Guy GP, Mikosz C. Buprenorphine dispensing among youth aged ≤19 years in the United States: 2015–2020. *Pediatrics*. 2023;151(2).
41. Trope LA, Stemmle M, Chang A, et al. A novel inpatient buprenorphine induction program for adolescents with opioid use disorder. *Hosp Pediatr*. 2023;13(2):e23-e28.
42. Marsch LA, Bickel WK, Badger GJ, et al. Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial. *Arch Gen Psychiatry*. 2005;62(10):1157-1164.
43. Woody GE, Poole SA, Subramaniam G, et al. Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. *Jama*. 2008;300(17):2003-2011.
44. Spreen LA, Dittmar EN, Quirk KC, Smith MA. Buprenorphine initiation strategies for opioid use disorder and pain management: a systematic review. *Pharmacotherapy*. 2022;42(5):411-427.
45. Ahmed S, Bhivandkar S, Lonergan BB, Suzuki J. Microinduction of buprenorphine/naloxone: a review of the literature. *Am J Addict*. 2021;30(4):305-315.
46. Cohen SM, Weimer MB, Levander XA, Peckham AM, Tetrault JM, Morford KL. Low dose initiation of buprenorphine: a narrative review and practical approach. *J Addict Med*. 2022;16(4):399-406.
47. De Aquino JP, Parida S, Sofuoglu M. The pharmacology of buprenorphine microinduction for opioid use disorder. *Clin Drug Investig*. 2021;41(5):425-436.
48. Facher L. Fentanyl isn't just causing overdoses. It's making it harder to start addiction treatment. *STAT*. November 16, 2022.
49. Azar P, Nikoo M, Miles I. Methadone to buprenorphine/naloxone induction without withdrawal utilizing transdermal fentanyl bridge in an inpatient setting-Azar method. *Am J Addict*. 2018;27(8):601-604.
50. Bhatraju EP, Klein JW, Hall AN, et al. Low dose buprenorphine induction with full agonist overlap in hospitalized patients with opioid use disorder: a retrospective cohort study. *J Addict Med*. 2022;16(4):461-465.
51. Brar R, Fairbairn N, Sutherland C, Nolan S. Use of a novel prescribing approach for the treatment of opioid use disorder: buprenorphine/naloxone micro-dosing—a case series. *Drug Alcohol Rev*. 2020;39(5):588-594.
52. Button D, Hartley J, Robbins J, Levander XA, Smith NJ, Englander H. Low-dose buprenorphine initiation in hospitalized adults with opioid use disorder: a retrospective cohort analysis. *J Addict Med*. 2022;16(2):e105-e111.
53. De Aquino JP, Fairgrieve C, Klaire S, Garcia-Vassallo G. Rapid transition from methadone to buprenorphine utilizing a micro-dosing protocol in the outpatient veteran affairs setting. *J Addict Med*. 2020;14(5):e271-e273.
54. DeWeese JP, Krenz JR, Wakeman SE, Peckham AM. Rapid buprenorphine microdosing for opioid use disorder in a hospitalized patient receiving very high doses of full agonist opioids for acute pain management: titration, implementation barriers, and strategies to overcomes. *Subst Abus*. 2021;42(4):506-511.
55. Hamata B, Griesdale D, Hann J, Rezazadeh-Azar P. Rapid microinduction of buprenorphine/naloxone for opioid use disorder in a critically ill intubated patient: a case report. *J Addict Med*. 2020;14(6):514-517.
56. Hämmig R, Kemter A, Strasser J, et al. Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. *Subst Abuse Rehabil*. 2016;7:99-105.
57. Klaire S, Zivanovic R, Barbic SP, Sandhu R, Mathew N, Azar P. Rapid micro-induction of buprenorphine/naloxone for opioid use disorder in an inpatient setting: a case series. *Am J Addict*. 2019;28(4):262-265.
58. Lee DS, Hann JE, Klaire SS, Nikoo M, Negraeff MD, Rezazadeh-Azar P. Rapid induction of buprenorphine/naloxone for chronic pain using a microdosing regimen: a case report. *A A Pract*. 2020;14(2):44-47.
59. Martell JP, Konakanchi JS, Sethi R. Treating opioid use disorder with rapid micro induction technique of sublingual buprenorphine/naloxone in an outpatient setting-a case report. *J Addict Dis*. 2022;40(3):439-443.
60. Martin L, Lennox R, Regenstreif L, O'Shea T. Case report:"striving to skip the withdrawal" using buprenorphine–naloxone microdosing for hospitalized patients. *Can J Addict*. 2019;10(4):35-40.
61. Menard S, Jhawar A. Microdose induction of buprenorphine-naloxone in a patient using high dose methadone: a case report. *Ment Health Clin*. 2021;11(6):369-372.
62. Payler DK. Substitution of heroin and methadone with buprenorphine using an overlap method without needing to wait for withdrawal. *Drugs Alcohol Today*. 2016;16(4):259-266.
63. Raheemullah A, Benhamou OM, Kuo J, Lembke A. Buprenorphine microdosing cross tapers: a time for change. *Int J Environ Res Public Health*. 2022;19(24).
64. Rozylo J, Mitchell K, Nikoo M, et al. Case report: successful induction of buprenorphine/naloxone using a microdosing schedule and assertive outreach. *Addict Sci Clin Pract*. 2020;15(1):2.
65. Terasaki D, Smith C, Calcaterra SL. Transitioning hospitalized patients with opioid use disorder from methadone to buprenorphine without a period of opioid abstinence using a microdosing protocol. *Pharmacotherapy*. 2019;39(10):1023-1029.
66. Wong JSH, Nikoo M, Westenberg JN, et al. Comparing rapid microinduction and standard induction of buprenorphine/naloxone for treatment of opioid use disorder: protocol for an open-label, parallel-group, superiority, randomized controlled trial. *Addict Sci Clin Pract*. 2021;16(1):11.
67. Buchheit BM, Joslin T, Turner HN, Wong TE. Ambulatory microdose induction of buprenorphine-naloxone in two adolescent patients with sickle cell disease. *Pediatr Blood Cancer*. 2021;68(1):e28766.
68. Azar P, Wong JSH, Jassemi S, et al. A case report: rapid micro-induction of buprenorphine/naloxone to administer buprenorphine extended-release in an adolescent with severe opioid use disorder. *Am J Addict*. 2020;29(6):531-535.
69. Herring AA, Vosooghi AA, Luftig J, et al. High-dose buprenorphine induction in the emergency department for treatment of opioid use disorder. *JAMA Netw Open*. 2021;4(7):e2117128.
70. Fishman SM, Wilsey B, Mahajan G, Molina P. Methadone reincarnated: novel clinical applications with related concerns. *Pain Med*. 2002;3(4):339-348.
71. Pates R. Methadone matters, evolving community methadone treatment of opiate addiction Gillian Tober and John Strang Martin Dunitz. *J Subst Use*. 2004;9:102-103. ISBN: 1-83184-159-5, 2003, 302 pp. with index, £28.95.
72. Treatment IoMUCoFRoM. Federal regulation of methadone treatment. In Rettig RA, ed. Federal regulation of methadone treatment. *5, Federal Regulation of Methadone Treatment*. National Academies Press (US); 1995. A Y.
73. Joudrey PJ, Edelman EJ, Wang EA. Drive times to opioid treatment programs in urban and rural counties in 5 US states. *Jama*. 2019;322(13):1310-1312.
74. *Federal Guidelines for Opioid Treatment Programs*. HHS Publication No. (SMA) XX-XXXX. Substance Abuse and Mental Health Services Administration: Substance Abuse and Mental Health Services Adminis-

tration; 2015. https://store.samhsa.gov/sites/default/files/guidelines-opioid-treatment-pep15-fedguideotp.pdf
75. Kreek MJ, Vocci FJ. History and current status of opioid maintenance treatments: blending conference session. *J Subst Abuse Treat*. 2002;23(2):93-105.
76. SAMHSA. (2015, January 26). CIB: Coverage of Behavioral Health Services for Youth with Substance Use Disorders [press release]. Joint CMCS and SAMHSA Informational Bulletin. 2015. Accessed on August 9, 2024. https://www.medicaid.gov/federal-policyguidance/downloads/cib-01-26-2015.pdf
77. Hassman H, Strafford S, Shinde SN, Heath A, Boyett B, Dobbins RL. Open-label, rapid initiation pilot study for extended-release buprenorphine subcutaneous injection. *Am J Drug Alcohol Abuse*. 2023;49(1):43-52.
78. D'Onofrio G, Hawk KF, Perrone J, et al. Incidence of precipitated withdrawal during a multisite emergency department-initiated buprenorphine clinical trial in the era of fentanyl. *JAMA Netw Open*. 2023;6(3):e236108.
79. Herring AA, Schultz CW, Yang E, Greenwald MK. Rapid induction onto sublingual buprenorphine after opioid overdose and successful linkage to treatment for opioid use disorder. *Am J Emerg Med*. 2019;37(12):2259-2262.
80. Oakley B, Wilson H, Hayes V, Lintzeris N. Managing opioid withdrawal precipitated by buprenorphine with buprenorphine. *Drug Alcohol Rev*. 2021;40(4):567-571.
81. Aghajanian GK, Wang YY. Common alpha 2- and opiate effector mechanisms in the locus coeruleus: intracellular studies in brain slices. *Neuropharmacology*. 1987;26(7b):793-799.
82. Elman I, D'Ambra MN, Krause S, et al. Ultrarapid opioid detoxification: effects on cardiopulmonary physiology, stress hormones and clinical outcomes. *Drug Alcohol Depend*. 2001;61(2):163-172.
83. Suzuki T, Tsuda M, Narita M, Funada M, Mizoguchi H, Misawa M. Diazepam pretreatment suppresses morphine withdrawal signs in the mouse. *Life Sci*. 1996;58(4):349-357.
84. Yaster M, McNaull PP, Davis PJ. The opioid epidemic in pediatrics: a 2020 update. *Curr Opin Anaesthesiol*. 2020;33(3):327-334.
85. Matson KL, Johnson PN, Tran V, Horton ER, Sterner-Allison J. Opioid use in children. *J Pediatr Pharmacol Ther*. 2019;24(1):72-75.
86. Jimenez DE, Singer MR, Adesman A. Availability of naloxone in pharmacies and knowledge of pharmacy staff regarding dispensing naloxone to younger adolescents. *J Adolesc Health*. 2019;65(5):698-701.

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