Received: 15 December 2023 | Accepted: 13 February 2024

DOI: 10.1002/emp2.13134

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
Open Access

WILEY

SPECIAL CONTRIBUTION

Pediatrics

# Acute opioid overdose in pediatric patients

**Stephen Sandelich MD**[1] | **Gwen Hooley MD**[2] | **George Hsu MD**[3] | **Emily Rose MD**[4] | **Tim Ruttan MD**[5] | **Evan S. Schwarz MD**[6] | **Erin Simon DO**[7] | **Carmen Sulton MD**[8] | **Jessica Wall MD, MPH**[9] | **Ann M Dietrich MD**[10]

[1]Department of Emergency Medicine, Penn State College of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA

[2]Department of Emergency Medicine, Children's Hospital of Los Angeles, Los Angeles, California, USA

[3]Department of Emergency Medicine, Augusta University-Medical College of Georgia, Augusta, Georgia, USA

[4]Department of Emergency Medicine, Keck School of Medicine of the University of Southern California, Los Angeles General Medical Center, Los Angeles, California, USA

[5]Department of Pediatrics, Dell Medical School, The University of Texas at Austin, US Acute Care Solutions, Canton, Ohio, USA

[6]Division of Medical Toxicology, Department of Emergency Medicine, University of California Los Angeles, Los Angeles, California, USA

[7]Department of Emergency Medicine, Cleveland Clinic, Akron, Ohio, USA

[8]Departments of Pediatrics and Emergency Medicine, Emory University School of Medicine, Children's Healthcare of Atlanta, Egleston, Atlanta, Georgia, USA

[9]Departments of Pediatrics and Emergency Medicine, Seattle Children's Hospital, Harborview Medical Center, Seattle, Washington, USA

[10]Department of Emergency Medicine, Prisma Health, Greenville, South Carolina, USA

**Correspondence**
Stephen Sandelich, MD, Department of Emergency Medicine, Penn State College of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, PA, USA.
Email: sandelich.md@gmail.com

## Abstract

Recent increases in pediatric and adolescent opioid fatalities mandate an urgent need for early consideration of possible opioid exposure and specific diagnostic and management strategies and interventions tailored to these unique populations. In contrast to adults, pediatric methods of exposure include accidental ingestions, prescription misuse, and household exposure. Early recognition, appropriate diagnostic evaluation, along with specialized treatment for opioid toxicity in this demographic are discussed. A key focus is on Naloxone, an essential medication for opioid intoxication, addressing its unique challenges in pediatric use. Unique pediatric considerations include recognition of accidental ingestions in our youngest population, critical social aspects including home safety and intentional exposure, and harm reduction strategies, mainly through Naloxone distribution and education on safe medication practices. It calls for a multifaceted approach, including creating pediatric-specific guidelines, to combat the opioid crisis among children and to work to lower morbidity and mortality from opioid overdoses.

Supervising Editor: Sing-Yi Feng, MD

KEYWORDS
naloxone, opiate overdose, opioid epidemic, opioid-related disorders, substance-related disorders

## 1 | INTRODUCTION

The opioid crisis in the United States transcends and affects individuals of all demographics. Historically, opioid overdose has been associated with adults, but trends show an increasing incidence among pediatric patients.[1–3] Opioids are the most common cause of fatal poisonings in young children and represent a significant public health challenge.[4–11]

Prompt recognition, resuscitation, and interventions are crucial in managing opioid toxicity in pediatric patients. Emergency clinicians caring for children and adolescents must be prepared to manage opioid toxicity and protect young children from further exposures to decrease future morbidity and mortality.[12,13] While there are policies on the opioid crisis in adults, there is a need for guidelines tailored for pediatric patients.[14–17] This paper discusses the unique opioid overdose characteristics and management in the pediatric population.

## 2 | EPIDEMIOLOGY

The pediatric and adolescent populations are increasingly impacted by the opioid crisis, historically an adult issue. From 2019 to 2021, drug overdose deaths in children aged 10–19 rose by 109%, with opioids being a common factor.[3,9,18–25] Alarmingly, opioid overdoses in children under 5 years of age, particularly infants and adolescents aged 15–19 years, have surged.[26] In 1- to 4-year-olds, accidental overdoses are common, with opioids causing over half of these fatalities recently. Fatal overdoses involving opioids jumped from 24.1% in 2005 to 52.2% in 2018; one-third of these cases were in children under 1 year, many with histories of maltreatment.[9] Adolescents aged 15–19 years are also particularly prone to such overdoses due to risky behaviors and substance experimentation.

Echoing adult trends, pediatric opioid overdoses have shifted from non-synthetic to semi-synthetic and fully synthetic opioids.[23] Between 1999 and 2021, fentanyl was involved in 37.5% of pediatric opioid poisoning deaths, predominantly in adolescents aged 15–19 years.[8] Pediatric emergency department presentations for opioid overdose or use disorder are rising. The complexity of pediatric overdoses, ranging from prescription to synthetic opioids, underscores the urgency for pediatric-specific interventions and policies.[27,28] Factors such as illicit drug availability, social media influence, and insufficient pediatric-focused opioid health policies contribute to this rise.[29–34] Children in environments with adult opioid use or socioeconomic disadvantages face increased risks.[24,35–38]

Parental opioid use significantly elevates a child's risk of opioid misuse.[39,40] Children in homes with adults suffering from opioid use disorders experience both immediate and long-term welfare impacts.[22] In addition, socioeconomic vulnerabilities correlate with higher pediatric opioid misuse rates, disproportionately affecting at-risk groups. In older children, prescription opioid misuse often leads to illicit opioid use or progression to more potent substances like heroin.[41]

## 3 | PEDIATRIC INGESTION TYPE

In contrast to adult overdoses, pediatric overdoses often occur when young children accidentally encounter substances at home or during normal exploratory behavior. For instance, opioid analgesic patches, such as those containing fentanyl, pose a unique risk. These patches can be accidentally transferred to children through ingestion, skin contact, or found and inappropriately applied by a child, leading to severe toxicity due to their high potency.[42–44] In addition, accidental ingestions can result from dosing errors with prescribed medication.[45,46] Notably, secondhand exposure is an emerging concern, where children come into contact with opioids through drug paraphernalia or environmental contamination in households with frequent opioid use.[47–49]

Among adolescents, recreational misuse of opioids presents a different profile. Teenagers are more likely to experiment with prescription opioids, and alarmingly, there has been a rise in the use of synthetic opioids like fentanyl, often clandestinely mixed into other recreational drugs.[27,50] Innovative delivery systems, such as opioid-laced edibles and vaping products, have also gained popularity in this age group.[51,52]

## 4 | DIAGNOSTIC EVALUATION

The initial steps in diagnosing acute opioid intoxication are obtaining a thorough history and performing a complete physical examination while maintaining a high degree of suspicion in situations where the child's mental status is altered or there is evidence of respiratory depression. While the foundational principles of diagnosis and treatment remain consistent across age groups, pediatric patients require a more tailored approach. The medical history should include questions about current medication use, substance use, and possible exposure to adulterated drugs. When taking a medical history, adult patients typically can provide self-reported information or confirm their substance use. In contrast, pediatric patients, particularly younger children, cannot provide their history, necessitating reliance on information from caregivers. This can lead to incomplete or potentially inaccurate histories, with added complexity in cases of suspected neglect or abuse. It is essential to identify the source of the substances to ascertain the child's safety. It is also crucial to obtain information about the patient's vital signs, respiratory status, level of consciousness, and any other symptoms or signs that may suggest opioid overdose. Children under

**TABLE 1** Diagnostic criteria for acute opioid overdose in pediatric patients.

| Symptom/sign | Description | Relevance to opioid overdose |
|---|---|---|
| Altered mental status | Changes in consciousness from drowsiness to stupor or coma. | Opioids depress the central nervous system. |
| Respiratory depression | Reduced respiratory rate, depth, and effort. | Opioids depress respiratory centers in the brainstem. |
| Miosis (pupillary constriction) | Constricted pupils, poor light response. | Opioids stimulate parasympathetic activity, causing constriction. |
| Bradycardia | Slower than normal heart rate. | Opioids can slow heart rate by increasing vagal tone. |
| Hypotonia | Decreased muscle tone and strength. | Central nervous system depression leads to muscle weakness. |
| Decreased bowel sounds | Reduced or absent sounds upon abdominal auscultation. | Opioids increase gastrointestinal tract smooth muscle tone. |
| Cyanosis (in severe cases) | Bluish skin/mucous membranes due to low oxygen. | Severe respiratory depression may lead to hypoxia. |
| Hypothermia | Abnormally low body temperature. | Decreased metabolic rate and impaired thermoregulation. |

2 years of age are more vulnerable to intentional poisonings secondary to their reliance on caregivers and higher susceptibility because of their smaller size.[53,54]

The physical examination for adults and children focuses on mental status, respiratory function, and neurological assessment. However, in pediatrics, there is an increased emphasis on evaluating developmental and age-appropriate responses, such as varying normal heart rates in children of different ages, especially when assessing conditions like bradycardia.[55,56] Clinical diagnostic signs of opioid toxicity are outlined in Table 1.

Laboratory evaluation is similar to adult patients and should assess electrolytes, blood glucose, and liver and renal function. A standard urine drug screen is not usually necessary to diagnose or treat an acute opioid overdose; however, it may be required to identify polyingestions, determine placement in a treatment program and identify an unknown exposure, especially in younger children or assist with legal proceedings in pediatric cases of child neglect.[56–58] Although physicians often obtain standard urine drug screens in the workup of suspected opioid ingestion, they have a significant false negative rate. A negative urine drug screen does not exclude the possibility of opioid toxicity.[59–62] Notably, there are various extended drug screens available that will assess for the presence of a greater number of substances. These tests are generally not rapid and take a few days to result, limiting their usefulness for the acute overdose situation. Even when results are available during the emergency department evaluation, results rarely change management.[63] However, they should be considered in a young child, with physical findings concerning for possible exposure, as this may significantly alter the child's management and disposition.

Pediatric patients are particularly vulnerable to unintentional exposure to adulterated products, especially in environments where adult opioid use is present.[64–73] These products can cause severe respiratory depression and hypotension. Opioids may be combined with other drugs of abuse; therefore, even if a patient denies any opioid use, it may still be on the differential. Clinicians should be aware of the current trends in opioid use in their community, the potential for adulterations, and management changes that may result. Poly-substance/polypharmacy is another essential consideration in diagnosing acute opioid overdose in pediatric patients.[74]

## 5 | MANAGEMENT OF ACUTE OVERDOSE

The management priority in patients with acute opioid overdose is similar to that in adults and includes airway support, oxygenation, and early administration of an opioid antagonist (naloxone). Table 2 lists the management considerations for acute opioid overdose in children.

Pediatric patients with unwitnessed opioid ingestion may present with an altered level of consciousness; therefore, we considered naloxone administration in the undifferentiated altered mental status patient.[73,75,82,86] Severe opioid toxicity will initially present with respiratory depression leading to respiratory arrest followed by cardiac arrest.[76] The focus of treatment should be prompt recognition and activation of the emergency response system and administration of high-quality cardiopulmonary resuscitation (CPR). It is reasonable to administer naloxone to a child in respiratory arrest with a pulse in addition to standard basic life support/pediatric advanced life support (BLS/PALS) care.[76–81] No studies demonstrate improved outcomes for administering naloxone during cardiac arrest and providing high-quality CPR should be the initial focus of a child found to be in arrest. Naloxone may be administered to a patient in arrest, provided it does not interfere with high-quality CPR.

Rarely, a patient with respiratory failure may have decreased tidal volumes with deceptively normal respiratory rates.[82,83] End-tidal $CO_2$ monitoring may be helpful in these situations. Airway protection may be necessary for central nervous system depression or vomiting. Naloxone is not beneficial if a patient has been intubated and is mechanically ventilated, as it may cause increased agitation and necessitate increased sedation. In patients who present with recent ingestion (in the last hour) and are alert with a reassuring mental status, gastrointestinal decontamination with activated charcoal may be considered, with a dose of 1 g/kg administered orally.[84] Activated charcoal

**TABLE 2** Treatment modalities for acute opioid overdose in pediatric patients.

| Treatment | Dosage/method | Notes/special considerations |
|---|---|---|
| Naloxone administration | 0.1 mg/kg IV initially; alternative routes available. | Monitor for symptom recurrence; consider continuous infusion if needed. |
| Respiratory support | Oxygen, bag-valve-mask, or intubation based on patient status. | Airway management is critical in severe respiratory depression. |
| Fluid resuscitation | IV fluids; dosage based on patient weight and clinical need. | Use isotonic fluids; monitor for fluid overload. |
| Gastrointestinal decontamination | Activated charcoal, 1 g/kg orally for recent ingestions. | Avoid in patients with altered mental status to prevent aspiration. |
| ICU admission for severe cases or frequent naloxone redosing | ICU admission for severe cases or frequent naloxone redosing. | ICU admission for severe cases or frequent naloxone redosing. |

administration should be avoided in patients with an altered mental status, as it may be aspirated if the patient vomits. Activated charcoal or whole bowel irrigation with airway protection in place may be required if there has been significant ingestion or, in the case of body packers or stuffers.[85,86] Large-volume packaging or stuffing may require surgical decontamination.[87–89] Intravenous or inhaled opioid overdoses do not warrant the use of gastric decontamination.

## 6 | NALOXONE ADMINISTRATION

Naloxone has a rapid onset of action and typically works within 1 min if given intravenously.[90–92] One dose of naloxone typically lasts 45–70 min. The recommended dosing of naloxone is 0.1 mg/kg IV with an initial maximum of 2 mg per dose. A lower dose may be used to avoid precipitated opioid withdrawal in older children or adolescents who may not be opiate naive. They should receive an initial dose of 0.04 mg IV, which can be titrated up to effect.[93,94]

Larger doses of naloxone may be required to reverse drugs with high receptor affinity (e.g., fentanyl and fentanyl analogs, buprenorphine, codeine, and diphenoxylate-atropine).[95,96] Escalating naloxone doses may be given, although >10 mg within 30 min may have diminishing returns.[97] If multiple doses of naloxone are required, a continuous infusion may be necessary.[98] Infusion rates are titrated to maintain respiratory effort while avoiding withdrawal symptoms.

Naloxone is most rapidly absorbed if administered intravenously but may be given in many alternative routes if IV access has not been obtained. Intranasal, intraosseous, intramuscular, subcutaneous, endotracheal, and even intralingual administration (with injection into the sublingual vein) may be used.[96] Intranasal naloxone is equally efficacious as intravenous or intramuscular and has been integrated into many prehospital protocols.[99–106] While most of the data on prehospital naloxone administration are focused on adults, some data on children show that intranasal naloxone administration is as efficacious as intravenous administration.[107,108] Naloxone is safe. However, there have been rare adverse events in adults, including pulmonary edema, at an incidence of 0.2%–3.6%. It has been infrequently reported in adolescents, and a single case report in a 3-year-old is in the literature.[109]

## 7 | DISCHARGE/DISPOSITION

Patients who respond to naloxone may develop recurrent central nervous system or respiratory depression as the effects of the naloxone wear off before the opioids they are treating.[78,110–113] The time a patient requires monitoring depends on the medication, route, time of ingestion, and required intervention. The onset of action of intravenous opioid use is immediate; subcutaneous takes effect within 15 min, nasal within 30 min, and oral ingestions may take 4–6 h for peak effects.[114,115] Most opioid effects last a total of 3–6 h. Fentanyl is the shortest acting with about 1 h of activity, and methadone is the longest acting opioid, lasting 24–48 h. Naloxone is shorter acting than most opioids, with a duration of action of 30–70 min.

Some patient populations may require admission to the hospital. These include infants and young children, suspected abuse, unsafe social situations, ingestion of long-acting agents, any concerns of suicidality or self-harm, and patients with signs of recurrence of respiratory depression or noncardiogenic pulmonary edema. Adolescent patients who are monitored for a time based on the type of ingestion after administration of naloxone can be safely discharged to home if clinically improved.[116–118] Discharge criteria can be seen in Table 3.

## 8 | HARM REDUCTION

When young children present following an acute opioid overdose, providers should consider the safety of the home environment. Since most ingestions in young children are exploratory or accidental, determining how the child accessed opioids is vital. While many adults may have legitimately prescribed medications, caregivers are responsible for ensuring these medications are properly stored.[119] Lack of appropriate supervision is a form of child neglect reportable to child protective services; however, the American Academy of Pediatrics notes that even careful caregivers can have a brief supervision lapse and recommends assessing the child's overall ongoing risk in the home.[120] Furthermore, identifying parents and caregivers who suffer from an untreated opioid use disorder is crucial as they place children under their care at risk, and intervention to protect these children is critical.[121] Physicians are mandated reporters of child abuse

**TABLE 3** Disposition criteria for pediatric patients post-opioid overdose.

| Criteria | Observation period | Disposition decision |
|---|---|---|
| Response to naloxone | Minimum of 2–4 h post last naloxone dose. | Discharge with close follow-up if stable; admission if recurrent symptoms. |
| Age of patient and ingestion details | Longer observation for younger children (<5 years) or unknown ingestion time. | Admission recommended for infants and very young children, especially with intentional ingestion or unknown substance. |
| Ingestion of long-acting opioids | At least 24 h due to prolonged drug effects. | Admission for observation due to risk of delayed symptoms. |
| Suspected child abuse or neglect | As required by law and institutional policy. | Mandatory reporting to child protective services; admission or safe discharge plan based on social situation. |
| Recurrence of respiratory depression | Extended observation post-recurrence. | Admission, potentially to intensive care, depending on severity and frequency of recurrence. |
| Noncardiogenic pulmonary edema | Based on clinical stability and improvement. | Admission to intensive care for respiratory support and monitoring. |
| Co-ingestions or poly-substance abuse | Dependent on the substances involved and their effects. | Admission for monitoring of potential interactions and cumulative effects. |

and neglect and have a duty to report a reasonable suspicion of neglect, so it is essential to involve social work colleagues when available in determining the overall safety of the home environment and whether reporting to child protective services is warranted.[122] Given the mortality associated with opioid overdose, most opioid ingestions in children should be reported to child protective services.[120,121] Given the risk of bias based on race or other socioeconomic factors for mandated reporting, many institutions have instituted protocols to report all pediatric ingestions to child protective services to avoid selective reporting.

One of the most efficacious forms of harm reduction is the distribution of intranasal naloxone. Increased access to naloxone decreases the risk of fatal opioid overdoses. All patients or families with members at high risk for an overdose should be prescribed or provided with take-home naloxone.[123] The lay public can be trained to administer naloxone successfully,[124,125] and there has been a case study of a pediatric patient who received a home naloxone nasal spray with improved symptoms.[126] A study focusing on pediatric opioid fatal overdoses also recommends disseminating naloxone to households where individuals are in recovery or have a history of substance misuse.[49] Families should be counseled that minors can purchase naloxone in most states. While many states have standing orders that allow the purchase of naloxone without a prescription, the U.S. Food and Drug Administration also approved naloxone for over-the-counter sale in March 2023.[127]

Families should be educated on the safe administration, storage, and disposal of pain medications. Physicians should communicate the importance of adequately disposing of unused and expired medicines in the home to reduce the risk of children and adolescents having access to prescription drugs, including opioids.[128] In pediatric patients with accidental exploratory ingestions at home, ensuring a safe home environment with adequate disposition planning is imperative. This may require consultation with hospital social workers, when available, and local child protective services to ensure safety.

**TABLE 4** Recommendations.

| **Early recognition of a potential opioid overdose, including in young children, is essential.** |
|---|
| All acutely intoxicated pediatric patients require a thorough evaluation, including considerations of an intentional opioid dose or unsafe environment in the youngest children. |
| Improved access to naloxone will help save lives and mitigate the devastating consequences of opioid overdose in all ages. |
| Providing comprehensive training on naloxone administration will help to mitigate the consequences of opioid overdose in all ages. |

Patients who desire substance use treatment should be provided with referrals to inpatient or outpatient facilities that can assist in initiating medication-assisted treatment for opiate use disorder.[129]

## 9 | CONCLUSION

The issue of acute opioid overdose in pediatric patients demands that all emergency physicians have an acute awareness and consider the unique features of an opioid overdose in a child. In addition to recognition of subtle presentations, early treatment may reverse the devastating consequences of an opioid overdose, and timely involvement of social work may help protect the at-risk child. The devastating consequences of opioid overdose on children's lives necessitate immediate action to prevent, identify, and address this problem (Table 4).

### ACKNOWLEDGMENTS

The authors gratefully acknowledge the American College of Emergency Physicians Pediatric Emergency Medicine Committee and the Pain Management and Addiction Medicine Section.

### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## ORCID

*Stephen Sandelich MD* https://orcid.org/0009-0000-2940-4699


## REFERENCES


1. Garofoli M. Adolescent substance abuse. *Prim Care*. 2020;47(2):383-394.
2. Groenewald CB. Opioid-prescribing patterns for pediatric patients in the United States. *Clin J Pain*. 2019;35(6):515-520.
3. Levy S. Youth and the opioid epidemic. *Pediatrics*. 2019;143(2):e20182752.
4. Centers for Disease Control and Prevention National Center for Injury Prevention and Control. *Opioid Overdose: Understanding the Opioid Overdose Epidemic*. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. 2022. Accessed 19 May, 2023. https://www.cdc.gov/opioids/basics/epidemic.html#:~:text=The%20number%20of%20drug%20overdose,in%202020%20involved%20an%20opioid
5. Abudu B, Burton BN, Said ET, Wilkins YML, Brzenski A, Gabriel RA. A population-based study of sociodemographic and clinical factors among children and adolescents with opioid overdose. *J Clin Anesth*. 2020;59:61-66.
6. Administration SAaMHS. *Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55)*. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2020.
7. Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826.
8. Gaither JR. National trends in pediatric deaths from fentanyl, 1999–2021. *JAMA Pediatr*. 2023;177(7):733-735.
9. Gaw CE, Curry AE, Osterhoudt KC, Wood JN, Corwin DJ. Characteristics of fatal poisonings among infants and young children in the United States. *Pediatrics*. 2023;151(4):e2022059016.
10. Jones CM, Einstein EB, Compton WM. Changes in synthetic opioid involvement in drug overdose deaths in the United States, 2010–2016. *JAMA*. 2018;319(17):1819-1821.
11. Rudd RA, Paulozzi LJ, Bauer MJ, et al. Increases in heroin overdose deaths – 28 States, 2010 to 2012. *MMWR Morb Mortal Wkly Rep*. 2014;63(39):849-854.
12. Biancuzzi H, Dal Mas F, Brescia V, et al. Opioid misuse: a review of the main issues, challenges, and strategies. *Int J Environ Res Public Health*. 2022;19(18):11754.
13. Forti RJ. Opiate overdose. *Pediatr Rev*. 2007;28(1):35-36.
14. National Institute on Drug Abuse. *Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide*. National Institute on Drug Abuse; 2014.
15. National Academies of Sciences, Engineering, and Medicine. *Medications for Opioid Use Disorder in Adolescents and Young Adults: Clinical Effectiveness, Cost-Effectiveness, and Guidelines*. National Academies of Sciences, Engineering, and Medicine; 2019.
16. Committee on Substance Use and Prevention. Medication-assisted treatment of adolescents with opioid use disorders. *Pediatrics*. 2016;138(3):e20161893.
17. World Health Organization. *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence*. World Health Organization; 2009.
18. Allen JD, Casavant MJ, Spiller HA, Chounthirath T, Hodges NL, Smith GA. Prescription opioid exposures among children and adolescents in the United States: 2000–2015. *Pediatrics*. 2017;139(4):e20163382.
19. Champagne-Langabeer T, Cardenas-Turanzas M, Ugalde IT, et al. The impact of pediatric opioid-related visits on U.S. emergency departments. *Children (Basel)*. 2022;9(4):524.
20. Hudgins JD, Porter JJ, Monuteaux MC, Bourgeois FT. Prescription opioid use and misuse among adolescents and young adults in the United States: a national survey study. *PLoS Med*. 2019;16(11):e1002922.
21. Krane EJ, Weisman SJ, Walco GA. The national opioid epidemic and the risk of outpatient opioids in children. *Pediatrics*. 2018;142(2):e20181623.
22. Stulac S, Bair-Merritt M, Wachman EM, et al. Children and families of the opioid epidemic: under the radar. *Curr Probl Pediatr Adolesc Health Care*. 2019;49(8):100637.
23. Tanz LJ, Dinwiddie AT, Mattson CL, O'Donnell J, Davis NL. Drug overdose deaths among persons aged 10–19 years—United States, July 2019-December 2021. *MMWR Morb Mortal Wkly Rep*. 2022;71(50):1576-1582.
24. Winstanley EL, Stover AN. The impact of the opioid epidemic on children and adolescents. *Clin Ther*. 2019;41(9):1655-1662.
25. Yaster M, McNaull PP, Davis PJ. The opioid epidemic in pediatrics: a 2020 update. *Curr Opin Anaesthesiol*. 2020;33(3):327-334.
26. Kaur M, Lee J. Treatment of pediatric opioid overdose in the United States. *Pediatrics*. 2019;144(2_MeetingAbstract). https://doi.org/10.1542/peds.144.2MA1.00j
27. Kuehn BM. Fentanyl drives startling increases in adolescent overdose deaths. *Jama*. 2023;329(4):280-281.
28. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(5152):1419-1427.
29. Columbia University: The National Center on Addiction and Substance Abuse. *National Survey of American Attitudes on Substance Abuse XVI: Teens and Parents*. Columbia University: The National Center on Addiction and Substance Abuse; 2011.
30. Drug Enforcement Administration. Social media—Drug trafficking threat. 2022. https://www.dea.gov/sites/default/files/2022-03/20220208-DEA_Social%20Media%20Drug%20Trafficking%20Threat%20Overview.pdf
31. Costello CR, Ramo DE. Social media and substance use: what should we be recommending to teens and their parents? *J Adolesc Health*. 2017;60(6):629-630.
32. Moreno MA, Briner LR, Williams A, Walker L, Christakis DA. Real use or "real cool": adolescents speak out about displayed alcohol references on social networking websites. *J Adolesc Health*. 2009;45(4):420-422.
33. Moreno MA, Parks MR, Zimmerman FJ, Brito TE, Christakis DA. Display of health risk behaviors on MySpace by adolescents: prevalence and associations. *Arch Pediatr Adolesc Med*. 2009;163(1):27-34.
34. Strasburger VC. Policy statement–children, adolescents, substance abuse, and the media. *Pediatrics*. 2010;126(4):791-799.
35. Agbese E, Stein BD, Druss BG, Dick AW, Pacula RL, Leslie DL. Mental health conditions and substance use disorders among youth subsequently diagnosed with opioid use disorder or opioid poisoning. *J Addict Med*. 2022;16(3):357-359.
36. Altekruse SF, Cosgrove CM, Altekruse WC, Jenkins RA, Blanco C. Socioeconomic risk factors for fatal opioid overdoses in the United States: findings from the Mortality Disparities in American Communities Study (MDAC). *PLoS One*. 2020;15(1):e0227966.
37. Marshall T, Olson K, Youngson E, et al. Preexisting mental health disorders and risk of opioid use disorder in young people: a case-control study. *Early Interv Psychiatry*. 2023;17:963-973.
38. van Draanen J, Tsang C, Mitra S, Karamouzian M, Richardson L. Socioeconomic marginalization and opioid-related overdose: a systematic review. *Drug Alcohol Depend*. 2020;214:108127.
39. Griesler PC, Hu MC, Wall MM, Kandel DB. Nonmedical prescription opioid use by parents and adolescents in the US. *Pediatrics*. 2019;143(3):e20182354.

40. Griesler PC, Hu MC, Wall MM, Kandel DB. Assessment of prescription opioid medical use and misuse among parents and their adolescent offspring in the US. *JAMA Netw Open*. 2021;4(1):e2031073.
41. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med*. 2016;374(2):154-163.
42. Hilado MA, Getz A, Rosenthal R, Im DD. Fatal transdermal fentanyl patch overdose in a child. *Cureus*. 2020;12(1):e6755.
43. Stoecker WV, Madsen DE, Cole JG, Woolsey Z. Boys at risk: fatal accidental fentanyl ingestions in children: analysis of cases reported to the FDA 2004–2013. *Mo Med*. 2016;113(6):476-479.
44. Teske J, Weller JP, Larsch K, Tröger HD, Karst M. Fatal outcome in a child after ingestion of a transdermal fentanyl patch. *Int J Legal Med*. 2007;121(2):147-151.
45. Basco WT Jr, Ebeling M, Garner SS, Hulsey TC, Simpson K. Opioid prescribing and potential overdose errors among children 0 to 36 months old. *Clin Pediatr (Phila)*. 2015;54(8):738-744.
46. Mc Donnell C. Opioid medication errors in pediatric practice: four years' experience of voluntary safety reporting. *Pain Res Manag*. 2011;16(2):93-98.
47. Bishop-Freeman SC, Young KA, Aurelius MB, Hudson JS. Pediatric opioid fatalities: what can we learn for prevention? *J Forensic Sci*. 2021;66(4):1410-1419.
48. Ghosh P, Pruitt C, Shah N, Kulkarni A, Slattery A, Nichols M. Unintentional opioid ingestions presenting to a pediatric emergency department. *Pediatr Emerg Care*. 2021;37(10):498-501.
49. Hunter AA, Schwab-Reese L, DiVietro S, McCollum S. An examination of fatal child poisonings in the United States using the National Violent Death Reporting System (NVDRS), 2012–2017. *Clin Toxicol (Phila)*. 2022;60(3):342-347.
50. Cook-Sather SD, Urban E, Romano VA, Romano MA. When fentanyl finds an outlier: talking with teenagers about the danger. *Pediatrics*. 2021;148(4):e2021051368.
51. Blundell M, Dargan P, Wood D. A cloud on the horizon-a survey into the use of electronic vaping devices for recreational drug and new psychoactive substance (NPS) administration. *Qjm*. 2018;111(1):9-14.
52. Morris JD, Pebley K, Little MA. Vaping opioids: should we be worried? *Am J Health Promot*. 2023;37(8):1171-1173.
53. Gauthey M, Capua M, Brent J, Finkelstein Y. Poisoning with malicious or criminal intent: characteristics and outcome of patients presenting for emergency care. *Clin Toxicol (Phila)*. 2019;57(7):628-631.
54. Yin S. Malicious use of pharmaceuticals in children. *J Pediatr*. 2010;157(5):832-836.e831.
55. Baldo BA, Rose MA. Mechanisms of opioid-induced respiratory depression. *Arch Toxicol*. 2022;96(8):2247-2260.
56. Casavant MJ. Urine drug screening in adolescents. *Pediatr Clin North Am*. 2002;49(2):317-327.
57. Ferrer Bosch N, Martínez Sánchez L, Trenchs Sainz de la Maza V, Velasco Rodríguez J, García González E, Luaces Cubells C. [Use of urine drug screening in the emergency department of a paediatric hospital]. *An Pediatr (Engl Ed)*. 2018;88(1):19-23.
58. Rahmandar MH. Urine drug testing in adolescents: common questions and uses. *Pediatr Ann*. 2023;52(5):e166-e169.
59. Kale N. Urine drug tests: ordering and interpreting results. *Am Fam Physician*. 2019;99(1):33-39.
60. Moeller KE, Kissack JC, Atayee RS, Lee KC. Clinical interpretation of urine drug tests: what clinicians need to know about urine drug screens. *Mayo Clin Proc*. 2017;92(5):774-796.
61. Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. *Mayo Clin Proc*. 2008;83(1):66-76.
62. Reisfield GM, Goldberger BA, Bertholf RL. 'False-positive' and 'false-negative' test results in clinical urine drug testing. *Bioanalysis*. 2009;1(5):937-952.
63. Christian MR, Lowry JA, Algren DA, Thornton SL, Deng S, Garg U. Do rapid comprehensive urine drug screens change clinical management in children? *Clin Toxicol (Phila)*. 2017;55(9):977-980.
64. DEA. The growing threat of xylazine and its mixture with illicit drugs. DEA Joint Intelligence Report. 2022.
65. Ayub S, Parnia S, Poddar K, et al. Xylazine in the opioid epidemic: a systematic review of case reports and clinical implications. *Cureus*. 2023;15(3):e36864.
66. Ball NS, Knable BM, Relich TA, et al. Xylazine poisoning: a systematic review. *Clin Toxicol (Phila)*. 2022;60(8):892-901.
67. Deutsch SA, De Jong AR. Xylazine complicating opioid ingestions in young children. *Pediatrics*. 2023;151(1):e2022058684.
68. Joynt PY, Wang GS. Fentanyl contaminated "M30" pill overdoses in pediatric patients. *Am J Emerg Med*. 2021;50:811.e813-811.e814.
69. Kacinko SL, Mohr ALA, Logan BK, Barbieri EJ. Xylazine: pharmacology review and prevalence and drug combinations in forensic toxicology casework. *J Anal Toxicol*. 2022;46(8):911-917.
70. Macmadu A, Carroll JJ, Hadland SE, Green TC, Marshall BD. Prevalence and correlates of fentanyl-contaminated heroin exposure among young adults who use prescription opioids non-medically. *Addict Behav*. 2017;68:35-38.
71. Meyer GM, Meyer MR, Mischo B, Schofer O, Maurer HH. Case report of accidental poisoning with the tranquilizer xylazine and the anesthetic ketamine confirmed by qualitative and quantitative toxicological analysis using GC-MS and LC-MS(n.). *Drug Test Anal*. 2013;5(9-10):785-789.
72. Ruiz-Colón K, Chavez-Arias C, Díaz-Alcalá JE, Martínez MA. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: a comprehensive review of the literature. *Forensic Sci Int*. 2014;240:1-8.
73. Sanello A, Gausche-Hill M, Mulkerin W, et al. Altered mental status: current evidence-based recommendations for prehospital care. *West J Emerg Med*. 2018;19(3):527-541.
74. Lim JK, Earlywine JJ, Bagley SM, Marshall BDL, Hadland SE. Polysubstance involvement in opioid overdose deaths in adolescents and young adults, 1999–2018. *JAMA Pediatr*. 2021;175(2):194-196.
75. Toce MS, Chai PR, Burns MM, Boyer EW. Pharmacologic treatment of opioid use disorder: a review of pharmacotherapy, adjuncts, and toxicity. *J Med Toxicol*. 2018;14(4):306-322.
76. Lavonas EJ, Akpunonu PD, Arens AM, et al. 2023 American Heart Association focused update on the management of patients with cardiac arrest or life-threatening toxicity due to poisoning: an update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2023;148(16):e149-e184.
77. Dezfulian C, Orkin AM, Maron BA, et al. Opioid-associated out-of-hospital cardiac arrest: distinctive clinical features and implications for health care and public responses: a scientific statement from the American Heart Association. *Circulation*. 2021;143(16):e836-e870.
78. Topjian AA, Raymond TT, Atkins D, et al. Part 4: pediatric basic and advanced life support 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Pediatrics*. 2021;147(1):S469-S523.
79. Cheng A, Magid DJ, Auerbach M, et al. Part 6: resuscitation education science: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2020;142(_suppl_162):s551-s579.
80. Saybolt MD, Alter SM, Dos Santos F, et al. Naloxone in cardiac arrest with suspected opioid overdoses. *Resuscitation*. 2010;81(1):42-46.
81. van Lemmen M, Florian J, Li Z, et al. Opioid overdose: limitations in naloxone reversal of respiratory depression and prevention of cardiac arrest. *Anesthesiology*. 2023;139(3):342-353.
82. Bachmutsky I, Wei XP, Kish E, Yackle K. Opioids depress breathing through two small brainstem sites. *eLife*. 2020;9:e52694.

83. Bouillon T, Bruhn J, Roepcke H, Hoeft A. Opioid-induced respiratory depression is associated with increased tidal volume variability. *Eur J Anaesthesiol*. 2003;20(2):127-133.
84. Boehnert MT, Lewander WJ, Gaudreault P. Advances in clinical toxicology. *Pediatr Clin North Am*. 1985;32(1):193-211.
85. Hassanian-Moghaddam H, Amraei F, Zamani N. Management recommendations for body stuffers at emergency units. *Arh Hig Rada Toksikol*. 2019;70(2):90-96.
86. Heymann-Maier L, Trueb L, Schmidt S, et al. Emergency department management of body packers and body stuffers. *Swiss Med Wkly*. 2017;147:w14499.
87. Covarelli P, Burini G, Castellani E, et al. Therapeutic options for body packers: surgical or conservative treatment? A single center experience and review of literature. *Ann Ital Chir*. 2015;86(4):371-377.
88. Schaper A, Hofmann R, Bargain P, Desel H, Ebbecke M, Langer C. Surgical treatment in cocaine body packers and body pushers. *Int J Colorectal Dis*. 2007;22(12):1531-1535.
89. Yegane RA, Bashashati M, Hajinasrollah E, Heidari K, Salehi NA, Ahmadi M. Surgical approach to body packing. *Dis Colon Rectum*. 2009;52(1):97-103.
90. Algera MH, Kamp J, van der Schrier R, et al. Opioid-induced respiratory depression in humans: a review of pharmacokinetic-pharmacodynamic modelling of reversal. *Br J Anaesth*. 2019;122(6):e168-e179.
91. Handal KA, Schauben JL, Naloxone SalamoneFR. Naloxone. *Ann Emerg Med*. 1983;12(7):438-445.
92. Wahler BM, Lerche P, Ricco Pereira CH, et al. Pharmacokinetics and pharmacodynamics of intranasal and intravenous naloxone hydrochloride administration in healthy dogs. *Am J Vet Res*. 2019;80(7):696-701.
93. Moss RB, Carlo DJ. Higher doses of naloxone are needed in the synthetic opiod era. *Subst Abuse Treat Prev Policy*. 2019;14(1):6.
94. Rzasa Lynn R, Galinkin JL. Naloxone dosage for opioid reversal: current evidence and clinical implications. *Ther Adv Drug Saf*. 2018;9(1):63-88.
95. Armenian P, Vo KT, Barr-Walker J, Lynch KL. Fentanyl, fentanyl analogs and novel synthetic opioids: a comprehensive review. *Neuropharmacology*. 2018;134(Pt A):121-132.
96. Chamberlain JM, Klein BL. A comprehensive review of naloxone for the emergency physician. *Am J Emerg Med*. 1994;12(6):650-660.
97. Jordan MR, Morrisonponce D. *Naloxone*. StatPearls Publishing; 2023.
98. Goldfrank L, Weisman RS, Errick JK, Lo MW. A dosing nomogram for continuous infusion intravenous naloxone. *Ann Emerg Med*. 1986;15(5):566-570.
99. Barton ED, Colwell CB, Wolfe T, et al. Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the prehospital setting. *J Emerg Med*. 2005;29(3):265-271.
100. Dietze P, Jauncey M, Salmon A, et al. Effect of intranasal vs intramuscular naloxone on opioid overdose: a randomized clinical trial. *JAMA Netw Open*. 2019;2(11):e1914977.
101. Kerr D, Kelly AM, Dietze P, Jolley D, Barger B. Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. *Addiction*. 2009;104(12):2067-2074.
102. Merlin MA, Saybolt M, Kapitanyan R, et al. Intranasal naloxone delivery is an alternative to intravenous naloxone for opioid overdoses. *Am J Emerg Med*. 2010;28(3):296-303.
103. Robertson TM, Hendey GW, Stroh G, Shalit M. Intranasal naloxone is a viable alternative to intravenous naloxone for prehospital narcotic overdose. *Prehosp Emerg Care*. 2009;13(4):512-515.
104. Skulberg AK, Tylleskär I, Valberg M, et al. Comparison of intranasal and intramuscular naloxone in opioid overdoses managed by ambulance staff: a double-dummy, randomised, controlled trial. *Addiction*. 2022;117(6):1658-1667.
105. Vanky E, Hellmundt L, Bondesson U, Eksborg S, Lundeberg S. Pharmacokinetics after a single dose of naloxone administered as a nasal spray in healthy volunteers. *Acta Anaesthesiol Scand*. 2017;61(6):636-640.
106. Williams K, Lang ES, Panchal AR, et al. Evidence-based guidelines for EMS administration of naloxone. *Prehosp Emerg Care*. 2019;23(6):749-763.
107. Heard C, Creighton P, Lerman J. Intranasal flumazenil and naloxone to reverse over-sedation in a child undergoing dental restorations. *Paediatr Anaesth*. 2009;19(8):795-797. discussion 798–799.
108. Malmros Olsson E, Lönnqvist PA, Stiller CO, Eksborg S, Lundeberg S. Rapid systemic uptake of naloxone after intranasal administration in children. *Paediatr Anaesth*. 2021;31(6):631-636.
109. Grout S, Dave M, Lefort R. Naloxone-associated pulmonary edema in a 3-year-old with opioid overdose. *J Am Coll Emerg Physicians Open*. 2022;3(3):e12740.
110. Clarke SF, Dargan PI, Jones AL. Naloxone in opioid poisoning: walking the tightrope. *Emerg Med J*. 2005;22(9):612-616.
111. Etherington J, Christenson J, Innes G, et al. Is early discharge safe after naloxone reversal of presumed opioid overdose? *Cjem*. 2000;2(3):156-162.
112. Heaton JD, Bhandari B, Faryar KA, Huecker MR. Retrospective review of need for delayed naloxone or oxygen in emergency department patients receiving naloxone for heroin reversal. *J Emerg Med*. 2019;56(6):642-651.
113. Zuckerman M, Weisberg SN, Boyer EW. Pitfalls of intranasal naloxone. *Prehosp Emerg Care*. 2014;18(4):550-554.
114. Willens JS, Myslinski NR. Pharmacodynamics, pharmacokinetics, and clinical uses of fentanyl, sufentanil, and alfentanil. *Heart Lung*. 1993;22(3):239-251.
115. Ziesenitz VC, Vaughns JD, Koch G, Mikus G, van den Anker JN. Pharmacokinetics of fentanyl and its derivatives in children: a comprehensive review. *Clin Pharmacokinet*. 2018;57(2):125-149.
116. Santos C, Adam A, Calello D, Nelson L. Safety of a brief emergency department observation protocol for patients with presumed fentanyl overdose. *Ann Emerg Med*. 2019;73(1):99-100.
117. Scheuermeyer FX, DeWitt C, Christenson J, et al. Safety of a brief emergency department observation protocol for patients with presumed fentanyl overdose. *Ann Emerg Med*. 2018;72(1):1-8.e1.
118. Willman MW, Liss DB, Schwarz ES, Mullins ME. Do heroin overdose patients require observation after receiving naloxone? *Clin Toxicol (Phila)*. 2017;55(2):81-87.
119. Lumba-Brown A. Drug overdose. In: McInerny TK, Adam HM, Campbell DE, eds. *American Academy of Pediatrics Textbook of Pediatric Care*. American Academy of Pediatrics; 2016.
120. Hymel KP. When is lack of supervision neglect? *Pediatrics*. 2006;118(3):1296-1298.
121. Wood JN, Pecker LH, Russo ME, Henretig F, Christian CW. Evaluation and referral for child maltreatment in pediatric poisoning victims. *Child Abuse Negl*. 2012;36(4):362-369.
122. Christian, Committee on Child Abuse and Neglect. The evaluation of suspected child physical abuse. *Pediatrics*. 2015;135(5):e1337-e1354. Pediatrics. 2015;136(3):583.
123. 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.
124. Eggleston W, Calleo V, Kim M, Wojcik S. Naloxone administration by untrained community members. *Pharmacotherapy*. 2020;40(1):84-88.
125. Goldberg SA, Dworkis DA, Liao VT, et al. Feasibility of bystander administration of public-access naloxone for opioid overdose. *Prehosp Emerg Care*. 2018;22(6):788-794.

126. Lebin JA, Chen BC, Valento MJ. Reversal of pediatric opioid toxicity with take-home naloxone: a case report. *J Med Toxicol*. 2019;15(2):134-135.
127. U.S. Food and Drug Administration. *FDA Approves First Over-the-Counter Naloxone Nasal Spray [press release]*. U.S. Food and Drug Administration; 2023.
128. Sharma B, Bruner A, Barnett G, Fishman M. Opioid use disorders. *Child Adolesc Psychiatr Clin N Am*. 2016;25(3):473-487.
129. Weiner SG, Baker O, Bernson D, Schuur JD. One year mortality of patients treated with naloxone for opioid overdose by emergency medical services. *Subst Abus*. 2022;43(1):99-103.

**How to cite this article:** Sandelich S, Hooley G, Hsu G, et al. Acute opioid overdose in pediatric patients. *JACEP Open*. 2024;5:e13134. https://doi.org/10.1002/emp2.13134