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OPIOIDS (J DONROE AND D FIELLIN, SECTION EDITORS)

# Treatment of Opioid Use Disorder in Pediatric Medical Settings

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## Abstract

**Purpose of Review** The purpose of this review is to examine the impact of the opioid epidemic in adolescents and young adults and recent findings regarding the treatment of opioid use disorder (OUD) in pediatric medical settings.

**Recent Findings** Existing guidelines for the treatment of chronic pain in adults are not intended to be applied to adolescents, who arguably may need different interventions that balance the need to mitigate the long-term impact of chronic pain with the need to limit opioid misuse. Screening, brief intervention, and referral to treatment is an important upstream strategy to prevent opioid misuse in youth. Medications such as buprenorphine, naltrexone, and methadone are important treatment options for youth with OUD but remain underutilized in this population.

**Summary** More research is needed to better understand how to best prevent opioid misuse and treat OUD in adolescents and young adults.

**Keywords** Opioids · Opioid use disorder · Adolescents · Young adults · Prevention · Treatment

## Introduction

Opioid misuse and opioid use disorder (OUD) are urgent public health issues affecting all segments of society, including the pediatric population of adolescents and young adults through age 21 [1, 2, 3•]. Adolescents and young adults (henceforth, "youth") are two of the age groups at highest risk for prescription opioid misuse. In 2017, 3.3 million youth in the USA misused prescription opioids in the past year (3.1% of adolescents and 7.3% of young adults), and nearly 2200 adolescents and young adults misused prescription pain relievers for the first time every single day [1].

Opioid misuse during adolescence is associated with acute and serious medical consequences, including emergency department (ED) visits and overdose [4, 5] which may occur even among naïve users. Between 1999 and 2015, hospitalizations for opioid poisonings nearly doubled for adolescents and young adults aged 15–19 [6]. Drug overdose is now the leading cause of accidental death in the USA [7]. Fatal opioid overdose rates increased by 253% among adolescents aged 15 to 19 years between 1999 and 2016 [8•]. These findings reinforce the importance of implementing efforts to prevent opioid misuse and treat OUD in general pediatric medical settings that serve patients in adolescence and early young adulthood, when opioid misuse reaches peak levels and the neurodevelopmentally driven risk of emergent OUD is striking.

A paramount problem related to opioid misuse among adolescents and young adults is their inherent neurodevelopmental vulnerability to developing addiction [9]. This vulnerability leads to heightened risk of future heroin use, intravenous (IV) drug use, OUD, and its related medical and psychological consequences [10]. In fact, one in three patients in treatment for OUD initiated opioid use before their 18th birthday and two in three before age 25 [11]. Trajectory analysis suggests that a portion of people who misuse oral prescription opioids initiate heroin use due to its ready availability, lower cost, and strong potency [10]. A 2018 study of young adults who use heroin

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found a mean age of first prescription opioid misuse of 16.8 years, with a transition to heroin use within 4 years [12]. In 2017, 14,000 adolescents used heroin in the past year [1].

This report reviews recent scientific literature and expert guidance on the prevention of opioid misuse and the treatment of opioid use disorders for youth. Where the literature base is limited, results and recommendations are based on extrapolation from studies with older adults.

## Pain Management in Pediatric Settings

In response to the opioid epidemic, great attention has been placed on the importance of appropriately treating chronic pain. The 2016 Centers for Disease Control guideline for prescribing opioids for chronic pain offers recommendations for adults ages 18 and above with chronic pain not related to active cancer, or palliative and end of life care [13]. However, these guidelines are not intended to be applied to adolescents, who arguably may need different interventions that balance the need to mitigate the long-term impact of chronic pain with the need to limit the impact of chronic opioid exposure on the developing brain and the risk of opioid misuse in this age group [14•]. A large nationally representative longitudinal cohort study found that chronic pain during adolescence is an independent risk factor for opioid misuse in adulthood [15]. Overall, there is a striking dearth of studies examining the appropriate and most efficacious use of opioids for chronic pain in adolescents. In fact, the 2017 Cochrane Review "Opioids for Chronic Non-Cancer Pain in Children and Adolescents" concluded that there was no evidence from randomized controlled trials to support or refute the use of opioids to treat chronic non-cancer pain in this population [16]. Compounding the problem, studies of non-opioid pain management strategies in this group are also extremely limited.

Nonetheless, prescription opioids remain an important treatment option for post-operative pain in adolescents. Current recommendations discourage long-term use of opioids past the immediate post-operative period [17]. However, data indicate that a sizable number of adolescents receive persistent opioids after surgery. In a national cohort study of 13–21 year old patients, 4.8% of past-year opioid-naïve patients filled opioid prescriptions > 90 days after surgery [18•]. Certain procedures, such as cholecystectomy and colectomy, were associated with higher rates of persistent opioid use 6 months post-procedure (15.2% and 7.3% respectively). Similarly, a retrospective cohort study of 12–18-year-old patients treated for trauma found that more than 20% filled two or more outpatient opioid prescriptions within 12 months of hospital discharge and 13% were taking prescription opioids 4 or more years after their injury [19]. Furthermore, 10% of these patients subsequently experienced an opioid overdose [19]. Thus, multimodal therapies including non-opioid anti-inflammatory medications, local pain management techniques, and extensive counseling on pain expectations are recommended to minimize opioid prescribing [17]. A small study found that only 42% of opioid doses prescribed to pediatric patients after post-operative discharge were consumed, and only 4% of families disposed of extra medications, highlighting the importance of counseling on tapering, storage, and disposal when prescribing opioids for pediatric pain [17, 20]. Current research is underway to develop an opioid risk screening tool for patients with traumatic injury with an ultimate goal of reducing the likelihood of opioid misuse and addiction in this population [21].

## Upstream Interventions to Prevent Opioid Misuse in Pediatric Populations: Screening, Brief Intervention, and Referral to Treatment for Marijuana, Alcohol, and Tobacco

Adolescent opioid misuse is most often preceded by use of other substances and adolescents that use alcohol, marijuana, or tobacco or tobacco (including e-cigarettes) that also misuse opioids are more likely to develop OUD [22]. According to the Office of National Drug Control Policy, "Early detection and treatment of a substance use problems by a doctor, nurse, or other health care professional is much more effective and less costly than dealing with the consequences of addiction or criminal justice involvement later on." [23] Early intervention that successfully reduces substance use during adolescence could play a significant role in reducing initiation of opioid misuse and ultimately reversing the current crisis of opioid addiction. Evidence suggests that embedding efforts to address substance use in primary care, including integrated treatment for opioid use disorder, is both acceptable and feasible [24].

Screening, brief intervention, referral to treatment or SBIRT is a clinical framework that has been developed to guide healthcare providers in identifying and addressing substance use. SBIRT begins with risk level identification through screening followed by delivery of a "just right" intervention that matches intensity to risk level. The latest review by the US Preventive Services Task Force issued an "I" statement for adolescent SBIRT [25] due to insufficient evidence that interventions delivered in primary care can effectively reduce substance use or related problems. Nonetheless, based on promising work [26–31], the American Academy of Pediatrics recommends SBIRT as part of routine medical care for all patients over the age of 12 [32•], and SBIRT is increasingly accepted by providers as an integral part of routine care. [33, 34] While an in-depth review of adolescent SBIRT is out of scope for this chapter, the following section presents a brief overview.

## SBIRT Core Principles

The objective of adolescent SBIRT is to screen for level of substance use experience (varying from no use of any substance to severe substance use disorder [SUD] with more than one substance) and then deliver an intervention targeted to risk and tailored to individual characteristics. For example, an intervention for an adolescent who reports no past-year substance use and is scheduled for upcoming wisdom tooth extraction might be to provide brief advice regarding pain control after the procedure, including only using prescription medications as prescribed and contacting the dentist if pain persists [34]. Because the risk of substance use initiation and escalation increases with age throughout adolescence, the American Academy of Pediatrics recommends that all adolescents receive a brief intervention intended to prevent, delay, or reduce use and that healthcare providers deliver a clear message that "non-use" is the healthiest choice for this age group [32].

In general, adolescents are entitled to confidential health care around issues related to substance use. State laws govern confidentiality provisions, and it is recommended that healthcare providers become familiar with local laws and use clinical judgment when balancing an adolescent's right to confidential healthcare around drug and alcohol use with the need to protect the patient's health and safety. The American Academy of Pediatrics [32], the American Academy of Family Physicians [35], and the Society for Adolescent Health and Medicine [36] have position statements and guidelines addressing confidentiality and informed consent for adolescents less than age 18. Further, the Center for Adolescent Health and the Law (CAHL.org) provides detailed information about each state's regulations surrounding confidential healthcare for adolescents.

## Screening

Validated screening tools that can quickly and accurately identify youth that are likely to have a SUD are critical for SBIRT. Several screening tools for identifying SUD in adolescents and adults have been developed. Problem-based screens categorize adolescents into "low" vs "high" risk for SUD based on the number of problems endorsed, while frequency-based screens use past-year frequency of use for triaging. Problem-based tools are clinically inefficient because they cannot distinguish risk level for individual substances, and thus require physician assessment which typically relies on identifying advanced signs or symptoms of SUD resulting in very poor sensitivity [37, 38]. Newer tools, such as the NIDAMED screening tool [39], the National Institute on Alcoholism and Alcohol Abuse Youth Alcohol Screening Tool [40], the "Screening to Brief Intervention" (S2BI) [41] and "Brief Screen for Tobacco, Alcohol and other Drugs" (BSTAD) [42] use past-year frequency of use questions to assess SUD risk, generating separate risk levels for alcohol, tobacco, and marijuana.

Using a self-report format may support more disclosure than interview administered screens and is a preference for adolescents [43, 44]. However, even when tools are self-administered, reviewing responses with each patient remains a key component of SBIRT as asking about substance use appears to play an important role in triggering counseling [45], which is recommended for all adolescents—even those who do not report substance use [32].

## Brief Intervention

Brief intervention, the "BI" in SBIRT, is an umbrella term that refers to the conversation that follows a substance use screen result. All youth should receive a brief intervention after screening, which may range from a few words of anticipatory guidance to a discussion and encouragement to accept a referral to a substance use treatment program or provider. Youth SBIRT guidelines recommend brief advice that emphasizes non-use as a means for preserving physical and mental health and maximizing potential for individuals that report no use or sporadic use in the past year. An emphasis on abstinence is particularly important for individuals who report opioid misuse because even sporadic opioid misuse is an important risk factor for OUD [10].

For adolescents for whom substance use has become more regular, brief interventions combine motivational interviewing techniques and psychoeducation to explicitly encourage behavior change (i.e., reduced use and/or risky behaviors). Several structured brief interventions, including the Brief Negotiated Interview [46], the 5 As [47], and CHAT [48] all have positive impacts.

## Referral to Treatment for Adolescents with Opioid Use Disorder

Referral to treatment, the "RT" in SBIRT, describes a conversation that encourages and supports adolescents in need of treatment to access appropriate services. RT is comprised of two distinct activities: discussing recommendations in a way that helps the adolescent to recognize the benefits of treatment and increases willingness to access help and connecting the teen to appropriate services [49]. Level of care considerations that take into account preferences of the adolescent and family are much more likely to resonate than those that are informed strictly by clinical presentation. Figure 1 is an algorithm to assist in determining level of care recommendations largely based on patient preferences [49].

There is surprisingly little research on the topic of the referral to treatment portion of SBIRT [50–53], though programs that integrate substance use counselors into primary care settings have shown promise both regarding feasibility and acceptability and in

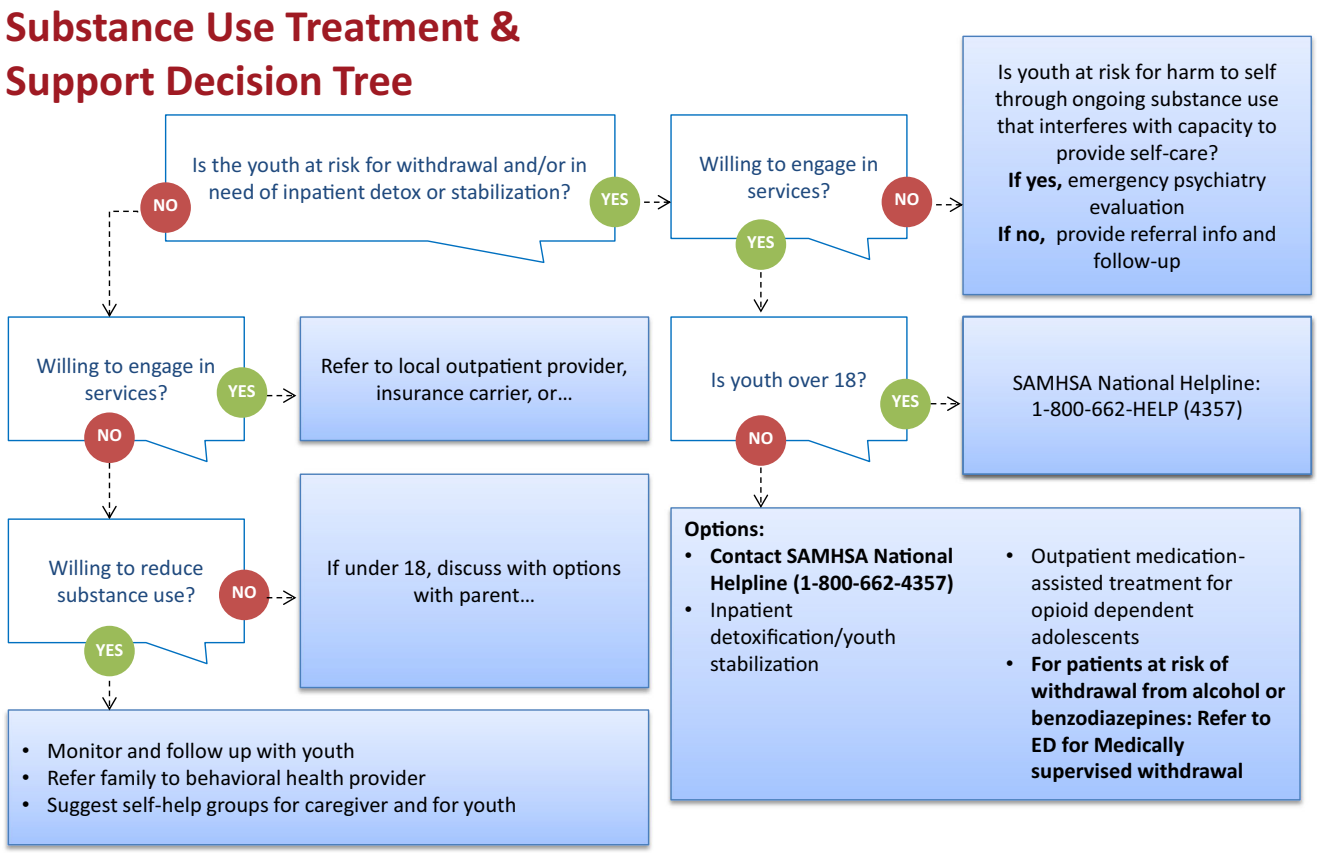


**Fig. 1** Youth substance use disorder treatment level of care decision support. [49]

reducing mental health care visits (and thus presumably costs) in the long term [24, 55, 56]. A perception that adolescents are often unwilling to accept a referral is one of the most commonly cited barriers to referral [50], underscoring the need for innovative service delivery models and enhanced provider training.

## Overview of Treatment Options for OUD in Adolescents

### Mild Opioid Use Disorders

Opioid use disorder is defined by 11 criteria specified in the Diagnostic and Statistical Manual of Psychiatry (DSM-5) [54]. Individuals who endorse 2 or 3 are diagnosed with mild OUD; moderate and severe OUDs are diagnosed when individuals endorse 4 or 5, or 6 or more, respectively. Youth with mild OUD may have begun to experience adverse consequences as a result of use. Very little research has been done with this group and treatment guidance is lacking, though the American Academy of Pediatrics has provided guidance on managing a full spectrum of substance use in adolescents [32]. Counseling that encourages abstinence combined with close monitoring may help to prevent progression to more severe OUD. While medications that are used to suppress withdrawal symptoms and cravings are generally not indicated for this group, referral to an experienced counselor and close follow up in primary care may have a significant impact on long-term outcomes.

### Moderate and Severe OUD

The American Academy of Pediatrics recommends that all youth with OUD that have symptoms of opioid withdrawal and cravings should be offered medications as part of comprehensive treatment that also includes supportive counseling and evaluation and treatment for commonly co-occurring medical and mental health disorders [57••]. Brief medically supervised opioid withdrawal (sometimes referred to as "detoxification") is associated with very high rates of relapse and thus not recommended as a standalone treatment [58].

Opioid agonist medications are a well-established component of effective treatment for adults with OUD [59, 60, 61, 62••]. Two forms of opioid agonist medications are available: methadone and buprenorphine. Methadone is a full opioid agonist that has been used for treatment of OUD since the 1970s, though federal law prohibits methadone prescribing for the treatment of OUD from primary care settings [63]. With few exceptions, methadone programs cannot accept patients under the age of 18; as a result, use of methadone with adolescents is extremely limited. Nonetheless, referral to an

opioid treatment program may be a reasonable option for older adolescent primary care patients who could benefit from the highly structured treatment approach offered in this setting.

Buprenorphine is a partial opioid agonist medication with efficacy for treating OUD similar to methadone [64]. In 2000, the US congress passed the Drug Abuse Treatment Act (DATA) allowing physicians who receive 8 h of specialized training (now extended to 24 h for advance practice providers such as Physician Assistants or Nurse Practitioners) to apply to the Drug Enforcement Agency (DEA) for a waiver to prescribe buprenorphine, thus allowing patients to be prescribed agonist treatment for OUD from general medical settings for the first time in US history, and subsequently, buprenorphine was approved by the Federal Drug Administration (FDA) for patients as young as 16 in 2002 [59, 65]. Buprenorphine has been studied extensively in adults, and three randomized controlled trials with youth have established efficacy in younger OUD patients [66–68•], finding that buprenorphine reduced opioid use and related consequences in youth, though improvements were not sustained once the medication was terminated.

Naltrexone is an opioid antagonist that has been established as an effective treatment for opioid use disorder in adults, though less research has been conducted with youth. A recent comparative efficacy study in adults found that while naltrexone is more difficult to initiate due to the potential for evoked withdrawal, participants who started naltrexone had results similar to those who were treated with buprenorphine [69]. Naltrexone may be a safer treatment option in adolescents with co-occurring alcohol or benzodiazepine disorders, and those for whom possessing a medication with diversion potential may be a liability.

The state of Massachusetts has produced detailed guidance for prescribing medication for OUD specifically for primary care providers that care for youth [70].

## OUD Treatment Access Among Adolescents

Despite evidence demonstrating that use of medications for the treatment of OUD saves lives [59], data suggests that youth experience barriers to accessing this treatment. An analysis of data on episodes of specialty treatment for heroin or prescription opioid use reported that only 2.4% of adolescents in treatment for heroin received medications (vs. 26.3% of adults) and only 4% of adolescents in treatment for prescription OUD received medications [72]. Similarly, a retrospective cohort study of Medicaid-enrolled youth with OUD across 11 states found that only 4.7% of adolescents and 26.9% of young adults received either buprenorphine, naltrexone, or methadone within 3 months of diagnosis of OUD [73••]. A majority of the sample (52%) received behavioral health services only; however, receipt of buprenorphine, naltrexone, and methadone was each independently associated with longer retention in care compared to receipt of behavioral health services alone.

Youth experience similar treatment disparities for OUD as adults. A study of commercially insured youth diagnosed with OUD found that between 2000 and 2014, females were less likely than males to receive medication treatment, as were non-Hispanic black and Hispanic youth compared to White youth [74•]. Surprisingly, a history of overdose also decreases the likelihood of accessing treatment [75]. A study of 13–22-year-old youth presenting to either inpatient, ED, or outpatient services after an overdose found that 31.3% received any type of treatment within 30 days of overdose; however, only 1.8% received a medication [76•].

Both the low prevalence of medication treatment in youth and the disparities in treatment access may be explained by a number of factors, including lack of treatment facilities, drug-related discrimination by the medical community, lack of support for use of medications by parents, and inability to pay out-of-pocket costs for treatment [59, 75]. Workforce shortages also may explain the low rates of medication use among adolescents with OUD. Anecdotally, very few pediatricians or child psychiatrists are waivered to prescribe buprenorphine [64]. Further, only some addiction specialists or general psychiatrists treat adolescents with OUD [63, 77].

## Prevention and Initiation of OUD Treatment in the ED

The ED is an important setting for interventions that focus on preventing opioid misuse, as youth are more likely than younger pediatric populations to receive opioid medications during ED visits [78]. For example, a multi-site study of youth presenting to EDs found that increasing patient age was associated with a significant increase in opioid prescribing [78], and another found that 8.7% of ED patients 14 through 21 years old reported a history of prescription opioid misuse [79]. Patients who experience an overdose are often resuscitated and evaluated in an ED, presenting an opportunity to initiate medication treatment and make linkages to OUD treatment programs. ED-based interventions have been developed for adults [80, 81] though few have specifically addressed the prevention of opioid misuse, or treatment of OUD in youth and more work needs to be done in this area.

## Treatment of Opioid Use in Pediatric Primary Care Settings

Providing treatment for adolescents with OUD within primary care settings that regularly engage this age group could help to close the enormous treatment gap for youth and also help improve retention in care, which to date has presented a major

challenge. While the waiver requirement has limited access to buprenorphine for all patients and especially adolescents, due to low penetrance among healthcare professionals, those who do complete training may garner new insights into caring for patients with addiction beyond opioid physiology, providing a benefit to both clinicians and the patients they treat [63].

Expanding primary care by integrating behavioral health clinicians as part of a team that also prescribes medication for addiction treatment and screening and treatment for commonly co-occurring medical and mental health disorders offers great benefit, given that mental health and substance use disorders are highly associated with the leading causes of morbidity and mortality for youth [83]. As when caring for other complex patients, primary care providers benefit from specialist consultation, and a small pilot study recently found this model feasible and acceptable to patients and providers [24]. The burgeoning field of Addiction Medicine, recently recognized by the American Board of Medical Specialties, may ultimately be of sufficient size to fulfill this role. In order to address the immediate and pressing need to support healthcare providers in the meantime, the Substance Abuse and Mental Health Services Association (SAMHSA) supports the Providers Clinical Support System (PCSS) [84] to provide trainings, educational materials and individual mentors on demand to support clinicians caring for patients with OUD and the Opioid Response Network [85] which provides technical assistance for prevention, treatment, and recovery. Services from these organizations are available free of charge and both support pediatric- and adolescent-focused programs in addition to adult programs.

Even when robust outpatient services are available, some adolescents with OUD will need a higher level of care when disease activity flares. Stabilization early in treatment may be difficult in an environment filled with triggers, particularly when housing is unstable or mental health symptoms create acute safety concerns. Deciding where to refer an adolescent for OUD treatment is dictated by specific needs of the patient, treatment availability, insurance complexities, and patient preference [49]. Despite recommendations, some patients will not agree to enter a higher level of care and in these situations, ongoing primary care follow-up is critical in assuring that teens ultimately stabilize or accept placement. In all cases, patients discharged from treatment programs need long-term medical follow up in order to address the chronic nature of OUD.

## Conclusions

Opioid misuse and OUD continue to pose a substantial threat to the health of youth, and more research is needed to determine how to best address these challenges. However, the urgency of the current opioid crisis requires healthcare professionals to rely on the current evidence base and expert guidance to implement the most promising strategies for these problems.

## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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