# Management of Opioid Misuse and Opioid Use Disorders Among Youth

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## Abstract

In response to the growing impact of the current opioid public health crisis in the United States on adolescents and young adults, pediatricians have an expanding role in identifying opioid use early, preventing escalation of risky use, reducing opioid-related harms, and delivering effective therapies. Research and expert consensus suggest the use of brief interventions focused on reducing risks associated with ongoing opioid use and using motivational interviewing strategies to engage youth in treatment. Because fatal opioid overdose remains a major cause of opioid-related mortality among youth, delivering overdose education as part of any visit in which a youth endorses opioid use is one evidence-based strategy to decrease the burden of opioid-related mortality. For youth that are injecting opioids, safe injection practices and linkage to needle or syringe exchanges should be considered to reduce complications from injection drug use. It is crucial that youth be offered treatment at the time of diagnosis of an opioid use disorder (OUD), including medications, behavioral interventions, and/or referral to mutual support groups. The 2 medications commonly used for office-based OUD treatment in adolescents are extended-release naltrexone (opioid antagonist) and buprenorphine (partial opioid agonist), although there is a significant treatment gap in prescribing these medications to youth, especially adolescents <18 years of age. Addiction is a pediatric disease that pediatricians and adolescent medicine physicians are uniquely poised to manage, given their expertise in longitudinal, preventive, and family- and patient-centered care. Growing evidence supports the need for integration of OUD treatment into primary care.

## BURDEN OF OPIOID USE AMONG YOUTH

Although much of the current public health crisis in the United States focuses on adult populations using opioids,[1] 1 in 10 adolescents and young adults (15 to 24 years of age) who died in 2016 died of opioid-related causes. These exponential increases in opioid-related morbidity and mortality support the need to identify opioid use early, intervene with effective therapies, prevent escalation of risky use, and reduce opioid-related harms.

Opioid exposure is common among adolescents and young adults (collectively referred to as "youth" hereinafter), with nearly 1 in 4 reporting some type of opioid use, including medical prescriptions.[2] Problematic opioid use includes a range of behaviors, from opioid misuse (defined as taking a prescription opioid in ways not prescribed by a physician) to using illicit opioids (such as heroin) or synthetic opioids (such as fentanyl). It has been estimated that ~891 000 (3.6%) of adolescents <18 years of age misuse prescription opioids, and 2.5 million (7.3%) young adults 18 to 25 years of age misuse opioids annually.[3] In recent estimates, it is reported that ~14% of high school seniors have ever misused prescription opioids,[4] and >150 000 adolescents <18 years of age and ~392 000 young adults 18 to 25 years of age met diagnostic criteria for an opioid use disorder (OUD) in 2016.[3]

Initiation of opioid misuse commonly occurs through the use of prescription opioids. Within the current opioid epidemic, among those with a history of heroin use, most report their first opioid exposure being a prescription opioid.[5,6] Youth usually acquire opioids from family, friends, and personal medical prescriptions.[3] Postdental visits are the leading source of opioid prescriptions to youth, which has been associated with a 6.8% absolute risk increase in persistent opioid use and a 5.4% increase in a subsequent diagnosis of OUD, when compared with those without opioid exposure.[7] Furthermore, the earlier the age of opioid exposure, the greater the vulnerability to developing an OUD.[8]

## IDENTIFYING OPIOID USE IN PRIMARY CARE SETTINGS

Research, expert consensus, and clinical guidelines, including a position statement from the American Academy of Pediatrics, recommend screening, brief intervention, and referral to treatment (SBIRT) as a general strategy and framework for identifying and managing substance use in pediatric primary care during routine health supervision visits.[9] This recommendation resulted, in part, because of the efficacy of SBIRT for unhealthy alcohol use among adults[10,11] as well as studies that show pediatricians often underestimate substance use and fail to identify risky use in youth when assessments of risk are based solely on clinical impressions. For example, in a study by Wilson et al,[12] clinical impressions among pediatricians of their patients' alcohol or drug use had a low sensitivity of 0.63 for identifying use. Additionally, sensitivity was even lower for correctly identifying problematic use at 0.14, whereas no pediatricians correctly identified those youth with substance use dependence. These findings support the need for the use of validated screening tools.[12]

There are numerous validated structured tools that have been used to screen youth for substance use as part of the SBIRT model (see Table 1). Studies have shown that

administering the selected screening tool via computer self-administration or pediatrician interview is equally valid; however, computer self-administration screening is more time efficient, especially for youth reporting any use in the past year.[13] Furthermore, studies have found less than half of pediatricians seeing youth use validated screening tools to screen for substance use.[14] Thus, the intent of using a strategy such as SBIRT is to increase the use of structured screening tools to improve identification of youth substance use, including opioid use.

## MANAGING OUD IN PRIMARY CARE SETTINGS

Strategies for managing OUD in the primary care setting include delivering brief interventions via the SBIRT model, providing referrals, and/or prescribing medications. Evidence for the efficacy of SBIRT for youth, especially in the primary care setting, is ongoing.[19] Although evidence has been inconsistent on whether SBIRT improves outcomes for youth, one particular short-term benefit that SBIRT has shown is reducing risky alcohol use among young adults.[20–22] Moreover, the use of motivational interviewing as a technique to deliver the brief intervention to youth has shown promising, but modest findings related to reducing risky use, such as driving while intoxicated and increasing intentions of engaging in treatment.[23–25] Overall, preliminary evidence shows positive short-term effects from integration of SBIRT into clinical settings catered toward youth, although these have mainly been focused on alcohol use; evidence for efficacy for drug use is still accumulating.[25–28] Disappointingly, for youth, there are fewer high-quality clinical trials demonstrating both accuracy of screening tools and evidence of long-term benefits from early detection and intervention, compared with studies with adults. Nevertheless, although there is adequate evidence for substance use screening and intervention for populations >18 years of age, there is insufficient evidence to recommend routine screening for youth from the United States Preventive Services Task Force.[29] Thus, there is a strong and immediate need for additional research on how best to screen, implement, and/or integrate SBIRT into clinical practice focusing on youth. On the basis of the best available evidence, guidance from experts, and the rising mortality and morbidity associated with untreated OUD, we recommend that pediatricians use the SBIRT framework specifically for opioid use. This framework should be focused on brief interventions to reduce risks associated with ongoing opioid use (eg, reducing risk for fatal overdose or use of safe injection practices to decrease risk for infections), while using motivational interviewing techniques to engage youth in treatment of OUD.

Treatment of OUD with medications, behavioral interventions, and referrals can occur in the pediatric primary care setting,[13,28,30,31] as well as in specialty treatment referral programs.[32,33] Pediatricians should engage families of youth in the treatment plan, as this has demonstrated improved rates of treatment adherence and completion, longer duration of abstinence from substance use, and fewer relapses for youth.[34–36] When involving parents, it is important to recognize that confidentiality and minor consent laws vary by state.[37] The typical focus of management is identifying the least restrictive treatment setting needed for success, although youth often move between multiple levels of care during a single treatment episode.[9] Despite high rates of mental health comorbidity, a substantial treatment gap exists, with only 4.6% of youth receiving comprehensive dual diagnosis care (eg, care

for both a substance use disorder and a mental health condition).[3] Thus, it is essential for pediatricians to evaluate for other co-occurring illnesses that might complicate access to or engagement in treatment.

## REDUCING OPIOID-RELATED RISKS IN PRIMARY CARE SETTINGS

Harm reduction in the primary care setting incorporates practical and evidence-based strategies that are intended to reduce negative consequences associated with drug use, while also promoting health and well-being.[38–40] Harm reduction education is particularly important for youth misusing opioids because they tend to have riskier use and/or injection practices compared with older populations.[41] They are often less aware of the dangers associated with injection and less knowledgeable about how to reduce risk for infectious complications.[42] Needle and syringe programs have decreased HIV transmission and risky injection behaviors among young adults and older adults and can also provide linkage to treatment services.[39,43] Supeivised injection sites that have been used by young adults and older adults outside of the United States have been found to decrease mortality without increasing drug use or crime.[44,45] However, substantial evidence supporting the specific harm reduction practices that have the best improvement in outcomes for youth is lacking.

Because fatal opioid overdose remains a major cause of opioid-related mortality, and youth are generally uninformed about overdose risk,[42] it is also crucial to deliver overdose education as part of any visit in which a youth endorses opioid use. Comprehensive overdose prevention education should include counseling on strategies for reducing overdose risk, recognizing signs of overdose, and responding to an overdose. This curriculum has been used in training nonmedical persons for fatal overdose prevention, and those that underwent training were able to successfully use naloxone for overdose reversal.[46] In addition to providing overdose prevention education, pediatricians should prescribe naloxone for opioid overdose reversal to youth and their families for all youth using opioids. Naloxone administration by lay people has been shown to be feasible, safe, and effective in reversing opioid overdose.[46–49] It is important to educate and train both the youth and someone close to the youth on how to administer naloxone in the event of an overdose.

For youth that are injecting opioids and still precontemplative about entering into treatment or cessation of injection drug use, safe injection practices and needle or syringe exchanges should be considered to reduce complications from injection drug use. Youth are less likely to be connected with traditional harm reduction networks than adults[50] and may need additional resources from their pediatricians on how to access services at needle and syringe exchanges. Safe injection education may include choosing a safer place to inject (eg, access to clean water, someone nearby in case of overdose, naloxone available), safer materials (eg, use of smaller needles to decrease the size of the puncture wound to reduce infection risk, sterile water, only using new needles and syringes), safer injection sites (eg, forearms are better sites to inject than legs, whereas neck and groin should never be used for injection), and reducing exposure to contaminated products (eg, avoid sharing of needles, syringes, cookers, spoons, cottons, or other equipment).[51]

# TREATMENT WITH MEDICATIONS FOR OUD IN PRIMARY CARE SETTINGS

It is crucial that youth be offered treatment at the time of an OUD diagnosis, including medications, behavioral interventions (see Table 2), and referral to mutual support groups (including traditional 12-step programs like Narcotics Anonymous and youth-oriented organizations like a collegiate recovery community).[52–55] In 2016, the American Academy of Pediatrics released a policy statement recommending that pediatricians offer medication for the treatment of severe OUD.[56] There are currently 3 medications used in the treatment of OUD in youth: extended-release naltrexone, buprenorphine, and rarely methadone. Although data from large, randomized control trials regarding the efficacy of pharmacotherapy for youth with an OUD are lacking,[53] small youth-focused studies and evidence extrapolated from adult data support the use of medications in the treatment of an OUD for youth as the gold standard (see Table 3).[57–61] Treatment protocols with medications have been suggested in a previous review and described in detail in clinical guidelines elsewhere.[62–64] However, in general, there are a lack of studies on the long-term efficacy of these medications as well as a lack of comparative effectiveness trials in youth suggesting optimal treatment regimens and optimal treatment duration.

## Buprenorphine

Several observational cohort studies and small randomized control trials show promising support for the use of buprenorphine in youth with OUD.[70–72] Youth prescribed buprenorphine for OUD are more likely to be retained in treatment and have lower rates of illicit opioid use while taking buprenorphine.[71,72,78] Specifically, Woody et al[71] compared 2 different regimens among 152 youth 15 to 21 years of age with opioid dependence and found that those youth receiving buprenorphine for 12 weeks (8 weeks of maintenance dosing with a 4-week taper off) reported less opioid use at 4 and 8 weeks, less injection drug use, and demonstrated retention in treatment compared with youth receiving a 14-day taper of buprenorphine.[71] In a smaller study, researchers found similar results with youth receiving a 56-day buprenorphine taper, demonstrating greater treatment retention and a significantly higher percentage of opioid-negative urine test results compared with youth who only received a 28-day taper (35% vs 17%).[72] These authors also found that a 2- to 3-times-weekly attendance requirement was associated with better short-term outcomes when compared with a daily attendance requirement. There has been one study in which researchers assessed efficacy of a 28-day buprenorphine taper when compared with a 28-day clonidine taper (used to treat opioid withdrawal symptoms) in a purely adolescent group (13–18 years of age), which showed that buprenorphine was superior to clonidine in retention and reduction of opioid use.[70] Similarly, data in adult populations demonstrate improved retention in treatment of individuals at any buprenorphine dose and improved abstinence from illicit opioids when receiving buprenorphine at 16-mg or higher doses.[61] In addition, receipt of buprenorphine after an opioid overdose was associated with decreased all-cause mortality and opioid-related mortality.[79] These small youth-focused studies mostly assess retention in treatment as the primary outcome of interest, with fewer studies assessing long-term outcomes related to reduced use or mortality. However, Borodovsky et al[78] found overall sufficient evidence for using buprenorphine as a long-term strategy to treat OUD in youth, although they highlighted a need for effective treatment delivery models targeted to

the unique needs of youth. Importantly, detoxification with buprenorphine or methadone has not been shown to be effective in adults or youth in promoting abstinence beyond initial stabilization; thus, maintenance with medications is the recommended approach.[57,70,71]

Additionally, there is a promising new formulation of buprenorphine for the treatment of OUD that may benefit youth because it may overcome adherence issues found with sublingual daily dosing: buprenorphine extended-release injection for subcutaneous use. One brand was approved by the US Food and Drug Administration in 2017 and it is in use in the US market, whereas another brand currently has tentative US Food and Drug Administration approval. Both of these formulations have been as efficacious as the sublingual formulation of buprenorphine in adult populations and may have advantages related to adherence and diversion.[80,81] Both products offer a monthly dosing schedule and are subcutaneously placed in the physician's office. In adult trials, reported side effects were similar to side effects reported with sublingual buprenorphine; however, injection site issues can occur. Unfortunately, no youth <18 years of age were enrolled in the human trials for these medications, and thus we lack evidence surrounding safety and/or efficacy for this age group.

### Naltrexone

Although there are only a few case studies on the effectiveness of extended-release naltrexone use in youth for an OUD, they have shown promising results for retention.[33,73] Specifically, in a small case series of 16 youth who received extended-release naltrexone at an outpatient addiction specialty treatment center, 63% were retained in treatment of at least 4 months, and 56% had a "good" outcome (defined as having decreased opioid use, improvement in at least 1 psychosocial domain, or no new problems due to use).[33] A novel pilot administering naltrexone by home delivery to 9 youth connected to a specialty treatment center showed home administration was feasible, acceptable to youth and their families, and that these youth received more doses of naltrexone compared with youth receiving naltrexone in the office.[73] Furthermore, in adult data, it is shown that although it can be more difficult to induct individuals on extended-release naltrexone, once successfully inducted, they do as well as those receiving buprenorphine in achieving opioid abstinence.[77] Monthly naltrexone may be useful for youth without a long history of opioid use and those who are able to abstain from opioids to initiate therapy. Additionally, for youth who have difficulty with daily adherence to oral medication, such as buprenorphine, extended-release naltrexone may be preferred.

### Methadone

Methadone is rarely used as a second-line treatment of an OUD in youth. Methadone access is restricted to licensed opioid treatment programs and is further restricted for youth 16 and 17 years of age. Federal regulations require that methadone clinics receive a special waiver to treat youth.[82] Typically, youth <18 years of age must be pregnant or demonstrate 2 treatment failures of detoxification or psychosocial interventions without pharmacotherapy to be eligible for treatment with methadone.[83] There have been small studies in which researchers assess the effectiveness of methadone for maintenance treatment, mostly among heroin-using youth. In a small retrospective study of 61 youth, methadone was shown to

have better retention rates compared with buprenorphine.[76] This is a similar pattern seen in studies of adult patients; although, at higher doses, both medications performed equally well in suppressing illicit opioid use among adults.[61] However, given the restrictions on availability of methadone and its more-concerning safety profile, it is rarely used in the treatment of OUD among youth.

## TREATMENT MODELS FOR OUD IN THE PRIMARY CARE SETTING

There is a significant gap in research related to best practices for treatment of OUD within pediatric offices. Adult primary care studies and implementation models provide examples that should be tested in pediatric care systems. Multidisciplinary and coordinated care delivery models have been found to be effective strategies in the implementation of OUD treatment into adult clinical settings, although few models included pediatric practices.[84] For example, the Hub-and-Spoke model pioneered in Vermont, Project ECHO (Extension for Community Healthcare Outcomes), and the Massachusetts nurse care manager model are promising models primarily using treatment with buprenorphine and psychosocial services that can be adapted for pediatric and/or adolescent medicine settings.[85] The Hub-and-Spoke model operates with opioid treatment programs called "hubs" that perform the initial induction and then connects the patient with office-based opioid treatment settings called "spokes," such as primary care clinics, to develop a network of expertise, mentorship, referrals, and resources. In Vermont, this model has led to an increase in the number of waivered providers that are able to prescribe buprenorphine as well as a 50% increase in the number of patients being prescribed buprenorphine.[86] A similar model exists in Project ECHO, whereby pediatricians are linked electronically to experts at academic centers via teleconferencing, virtual clinics, Web-based training, and mentorship primarily for buprenorphine prescribing.[87,88] The Massachusetts model uses trained nurse case managers who comprehensively evaluate patients for appropriateness, educate and counsel patients, monitor and manage adherence, evaluate for any need for transition to higher level of care, and communicate with prescribing physicians.[89,90] There are few large-scale clinic models implemented to deliver care to youth with OUD. In a novel clinic model treating youth 14 to 25 years of age with OUD, they found youth could be inducted onto buprenorphine at home by starting dosing 18 to 24 hours after last opioid use.[32] Although youth were successfully inducted on medication for treatment of OUD, only 45% remained in treatment at 60 days, and <1 in 10 were in treatment at 1 year, suggesting long-term retention of youth remains challenging. The likelihood of integrated behavioral health and primary care services for youth to treat OUD is not unprecedented because coordinated care, co-located care, and integrated care models have good efficacy in treatment of youth with depression.[91] Additional research highlighting how best to integrate OUD treatment into a variety of pediatric primary care and subspecialty settings is critically needed.

## TREATMENT GAP

There are also a number of gaps in the delivery of the above mentioned medications to youth with OUD, especially for those <18 years of age. For example, only 1 in 4 commercially insured youth with an OUD received any pharmacotherapy to treat their addiction.[92] Specialty treatment programs reported 2.6% of youth 15 to 17 years of age received

medications to treat heroin use disorder, compared with 26% of adults, and only 0.4% of youth received medications to treat prescription OUD compared with 12% of adults.[82] Similarly, <5% of youth <18 years of age and approximately one-quarter of young adults 18 to 22 years of age with Medicaid received medications for OUD within 3 months of diagnosis.[93] Timely receipt of pharmacotherapy to treat OUD has been associated with greater retention in care, compared with youth receiving only behavioral services.[93] Less than 2% of youth between 13 to 22 years of age received medications for OUD within 30 days of a nonfatal opioid-related overdose, whereas 30% received behavioral services.[94] In contrast, 30% of adults received medications for OUD after an overdose.[79] Furthermore, receipt of buprenorphine or methadone was associated with reduced all-cause and opioid-related mortality among adults.[79] Among young adults seeking to enroll in substance use treatment, only 35% successfully linked to treatment because of stigma and/or discrimination, insurance barriers, wait lists, and inability to pay.[95] There are also significant racial and sex disparities, with fewer African American and Hispanic youth as well as females receiving pharmacotherapy compared with white males.[92] Moreover, as only 0.2% of pediatricians have completed the Drug Enforcement Administration waiver process to receive the ability to prescribe buprenorphine, there are only a few pediatricians comfortable and able to treat youth with OUD.[96] Given the above mentioned treatment gaps and significant morbidity and mortality from opioids impacting young people, it is paramount that the pediatric workforce mobilize to screen and treat OUD in youth.

## CONCLUSIONS

Addiction is a pediatric disease that pediatricians are uniquely poised to manage, given their expertise in longitudinal, preventive, and family- and patient-centered care. Opioid use is associated with significant morbidity and mortality, necessitating intervention at the time of diagnosis. For those youth with an OUD, treatment offered at the time of diagnosis with either buprenorphine or naltrexone should become the new standard of care, along with delivery of targeted harm reduction services and linkage to psychosocial supports. However, questions remain unanswered regarding how best to integrate treatment of OUD into clinical practice, including duration and optimal treatment regimens for OUD in youth.

## Acknowledgments

## ABBREVIATIONS

| | |
|---|---|
| **OUD** | opioid use disorder |
| **SBIRT** | screening, brief intervention, and referral to treatment |

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**TABLE 1**

Substance Use Screening Tools and Diagnostic Accuracy

| Tool | CRAFFT (Car, Relax, Alone, Friends/Family, Forget, Trouble)[15] | S2BI (Screening to Brief Intervention)[16] | BSTAD (Brief Screener for Tobacco, Alcohol, and Other Drugs)[17] | NIAAA Youth Alcohol Screen (Youth Guide)[18] |
|---|---|---|---|---|
| Tool questions | Part A:<br>During the past 12 months, did you:<br>1. Drink any alcohol (more than a few sips)?<br>2. Smoke any marijuana?<br>3. Use anything else to get high?<br>If "no" to all of Part A, then only ask the car question below. If "yes" to any of Part A, ask all 6 CRAFFT below.<br>Part B:<br>• Have you ever ridden in a car driven by someone (including you) who was "high" or had been using alcohol or drugs?<br>• Do you ever use alcohol or drugs to relax, feel better about yourself, or fit in?<br>• Do you ever use alcohol or drugs while you are by yourself or alone?<br>• Do you ever forget things you did while using alcohol or drugs?<br>• Do your family or friends ever tell you that you should cut down on your drinking or drug use?<br>• Have you ever gotten into trouble while you were using alcohol or drugs? | In the past year, how many times have you used:<br>• Tobacco?<br>• Alcohol?<br>• Marijuana?<br>If "ever" to any of the above, then continue with remaining questions:<br>• Prescription drugs that were not prescribed for you (eg, pain medication or Adderall)?<br>• Illegal drugs (eg, cocaine or ecstasy)?<br>• Inhalants (eg, nitrous oxide)?<br>• Herbs or synthetic drugs (eg, salvia, "K2," bath salts)? | Past-year friends' use and personal use of:<br>• Cigarettes or other tobacco products?<br>• Beer, wine, or any drink with alcohol?<br>• Marijuana?<br>If "yes" to any of the above in personal use, then ask about the following:<br>• Cocaine or crack<br>• Heroin<br>• Amphetamines or methamphetamines<br>• Hallucinogens<br>• Inhalants<br>• Prescription pain relievers<br>• Prescription sedatives<br>• Prescription stimulants<br>• Over-the-counter<br>For each substance, ask frequency of use in the past 30 and 90 d and past year | For elementary and middle schoolers: start with asking if friends drink. Then ask about personal use.<br>For high schoolers: start with asking about personal drinking. Then ask about friend's use |
| Diagnostic accuracy | • Tool correctly classified 86% of patients.<br>• Two or more "yes" answers has a sensitivity of 92.3% and specificity of 82.1% for need for treatment | • Sensitivity and specificity were 100% and 84% (95% CI: 76%–89%) for identifying nontobacco substance use, 90% (95% CI: 77%–96%) and 94% (95% CI: 89%–96%) for SUDs, 100% and 94% (95% CI: 90%–96%) for severe SUDs, and 75% (95% CI: 52%–89%) and 98% (95% CI: 95%–100%) for nicotine dependence | • Optimal cut points for past-year frequency of use items to identify SUDs were ≥6 d of tobacco use (sensitivity = 0.95; specificity = 0.97), ≥2 d of alcohol use (sensitivity = 0.96; specificity = 0.85), and ≥2 d of marijuana use (sensitivity = 0.80; specificity = 0.93) | • Tool uses frequency of past-year alcohol use to stratify lower-, moderate-, and highest-risk groups with respect to likelihood of meeting criteria for alcohol dependence on the basis of DSM-IV criteria using age-sensitive cutoff points |

CI, confidence interval; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; NIAAA, National Institute on Alcohol Abuse and Alcoholism; SUD, substance use disorder.

**TABLE 2**

Behavioral Interventions for Youth With OUD

Cognitive behavioral therapy[65]
Teaches youth how to anticipate problems and develop effective coping strategies
Focuses on monitoring feelings and thoughts and recognizing thinking patterns, high-risk situations, and cues that trigger substance use

Contingency management[66]
Youth can earn low-cost incentives such as prizes or cash vouchers in exchange for participating in treatment, achieving important goals of treatment, and/or not using drugs

Motivational enhancement therapy[67]
Counseling approach to resolve ambivalence about engaging in treatment
Follows the principles of motivational interviewing to overcome or reduce this ambivalence

Adolescent community reinforcement approach[68]
Focuses on abstinence from drugs by replacing reinforcing use influences with healthier family, social, and educational or vocational reinforcers
Uses other important individuals in the youth's life

Family-based therapies[69]
Various therapies that engage the youth's family in treatment
Brief strategic family therapy, family behavior therapy, functional family therapy, multidimensional family therapy, and multisystemic therapy
Additionally, addresses a variety of issues including family communication and conflict; other co-occurring behavioral, mental health, and learning disorders; school problems; and peer networks
Shown to be highly efficacious for youth

National Institute on Drug Abuse. Principles of adolescent substance use disorder treatment: a research-based guide. 2014. Available at: https://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/principles-adolescent-substance-use-disorder-treatment.

**TABLE 3**

Evidence for Treatment With Medication for OUD

| Study | Study Population | Study Description | Follow-up | Main Outcomes |
|---|---|---|---|---|
| **Buprenorphine** | | | | |
| Marsch et al[70] | Adolescents ages 13–18 y (n = 36) | A double-blind, double-dummy, parallel-groups randomized controlled trial; assigned to a 28-d outpatient detox with buprenorphine or clonidine. Buprenorphine taper: • If ≥70 kg and/or self-reported use >3 bags of heroin or equivalent in opiates, given daily starting dose of 8 mg of buprenorphine; otherwise started on 6 mg • Then tapered down by 2 mg every 7 d | 28-d detox only | 72% of those in buprenorphine group were retained in treatment versus 39% of those in the clonidine group (P < .05). For those in the buprenorphine group, a significantly higher percentage of scheduled urine test results were opiate negative (64% vs 32%; P = .01). |
| Woody et al[71] | Youth ages 15–21 y (n = 152) | Randomized clinical trial at 6 US community programs; assigned to 12 wk of buprenorphine or 14-d taper (detox). Buprenorphine dosing: • 12-wk group: titrated up to max of 24 mg/day with taper starting at week 9 • 14-d detox group: titrated up to max of 14 mg/day and tapered off by day 14. | 12 wk | Those in the detox group had significantly higher proportions of opioid-positive urine test results at weeks 4 and 8 but not at week 12. Those in buprenorphine group had less injection drug use and more remained in treatment versus youth in detox group. |
| Matson et al[32] | Youth ages 14–25 y (n = 103) | Retrospective chart review of clinic patients seen at an adolescent medicine specialty addiction medicine clinic. Buprenorphine dosing: • Home induction based on protocol; majority were on 8 mg twice daily maintenance. | 1 y | Opioid abstinence was high at 85.2% with high adherence at 86.6% during clinic visits; 75% of patients returned for a second visit. Low retention of 45% at 60 d and 9% at 1 y. |
| Marsch et al[72] | Youth ages 16–24 y (n = 53 in total; n = 11 under age 18) | Double-blind, placebo, randomized controlled trial (2 sites); assigned to 28-d taper versus 56-d taper of buprenorphine. Buprenorphine taper: Titrated up to max of 16 mg/day. | 63 d | Those in longer taper group had a significantly higher percentage of opioid-negative urine test results (35% vs 17%, P = .039). |
| **Extended-release naltrexone** | | | | |
| Fishman et al[33] | Youth ages 16–20 y (n = 16) | Case series in a community-based adolescent substance abuse treatment program in Baltimore, Maryland, offering monthly injection of extended-release naltrexone. | 4 mo | 85% (12 out of 14 who came back for a second visit) received at least 2 doses. 63% were retained in treatment of at least 4 mo. 56% had either substantially decreased opioid use, improvement in at least 1 psychosocial domain, or no new problems due to substance use. |
| Vo et al[73] | Youth ages 17–25 y (n = 14 in home-based delivery group; n = 21 in treatment as usual group receiving naltrexone in clinic) | 2-y pilot clinical quality improvement initiative offering home-based delivery of extended-release naltrexone with a convenience sample of youth attending a community-based adolescent substance abuse treatment program in Baltimore, Maryland. Intervention: Naltrexone initially delivered to the treatment center from a pharmacy and then brought to patient's home by a team consisting of a nurse practitioner and a counselor every 3–4 wk. | 16 wk | 64% (9 out of 14) received at least 1 dose of extended-release naltrexone at home. Home delivery group had an average of 3.3 doses of the potential 5 monthly doses (including first inpatient dose) versus 2.0 doses for treatment as usual group. 50% of the home delivery group received all 5 doses versus 9% in the treatment-as-usual group. |

| Study | Study Population | Study Description | Follow-up | Main Outcomes |
|-------|-----------------|-------------------|-----------|---------------|
| **Methadone** | | | | |
| DeAngelis and Lehmann[74] | Youth using heroin ages 15–24 y ($n = 37$) | Community-based opioid treatment center in Connecticut. Intervention: "low-dose" methadone maintenance regimen based on individual needs for 2–13 wk, followed by a taper off methadone lasting 3–14 wk. | 18 mo | Average methadone dose was 20 mg/day with a range of 10–60 mg/day. Average maintenance phase lasted 7 wk, and average taper phase lasted 7 wk. 35% of youth remained opioid-free and were retained in treatment or were working or in school. |
| Guarino et al[75] | Young adults ages 18–23 y ($n = 22$) | Qualitative study with focus groups consisting of patients ($n = 7$), staff ($n = 6$), n/a and parents ($n = 3$) to better understand components of effective treatment with methadone in a young adult methadone program in New York. Treatment model: outpatient intensive weekly counseling in individual and group settings plus the option of family therapy; patients encouraged to taper off methadone once status is "stabilized." | n/a | The following themes emerged: (1) youth themselves must be motivated for treatment; (2) engagement in treatment is often challenging given youth's limited lifetime history with significant negative consequences due to use; (3) youth-centered treatment is desired with variable treatment options; (4) duration of treatment should be dictated by individual youth's need, goals, and outcomes; (5) effective treatment involves the family of youth; and (6) youth remain hopeful that they will be tapered off methadone. |
| **Comparative effectiveness trials** | | | | |
| Bell and Mutch[76] | Adolescents ages 14–17 y ($n = 61$) | Retrospective chart review of all youth at first presentation for treatment of opioid dependence in an Australian treatment center: 20 youth received methadone, 25 youth received buprenorphine, and 15 youth received symptomatic medication for withdrawal; 1 received no medication. | Variable | Youth receiving methadone had significantly longer retention in the first treatment episode versus those receiving buprenorphine (mean: 354 vs 58 d; $P < .01$) and missed fewer days in the first month (mean: 3 vs 8 d; $P < .05$). However, time to re-entry after first episode of buprenorphine was significantly shorter than after methadone. |
| Mattick et al[61] | Adult patients; 31 trials included ($n = 5430$ total participants with a range of 40–736 participants in each study) | Cochrane Systematic Review comparing buprenorphine to placebo and buprenorphine to methadone for opioid dependence. Quality of evidence varied from high to moderate quality. | Interventions ranged in duration from 2 to 52 wk | High quality of evidence (14 studies) that buprenorphine was superior to placebo in retention of participants at all doses examined (2–16 mg/day). Moderate quality of evidence (3 studies) that high-dose buprenorphine ( 16 mg/day) was more effective than placebo in suppressing illicit opioid use. High quality of evidence (5 studies) that buprenorphine in flexible doses was less effective than methadone in retention; however, no difference was observed in suppression of illicit opioid use with moderate quality of evidence (12 studies). |
| Lee et al[77] | Adults  18 y ($n = 570$) | Open-label, randomized controlled, comparative effectiveness trial at 8 US community-based inpatient programs with follow-up in outpatient program. 283 randomly assigned to extended-release naltrexone versus 287 randomly assigned to buprenorphine. | 24 wk | Extended-release naltrexone had a substantial induction challenge with only 72% of participants successfully initiated versus 94% of participants successfully initiated onto buprenorphine ($P < .0001$). Among those with successful induction, there was no significant difference in 24-wk relapse between the 2 groups ($P = .44$). Among those with successful induction, there was no significant difference in opioid-negative urine test results or opioid-abstinent days between the 2 groups. |

n/a, not applicable.