



Published in final edited form as:

Curr Pediatr Rep. 2018 June ; 6(2): 99–106. doi:10.1007/s40124-018-0161-z.

Opioid Use Disorders in Adolescents—Updates in Assessment and Management

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Abstract

Purpose of review: To review information specific to adolescents regarding trends in opioid use, risk factors for opioid misuse, medical co-morbidity, and treatment updates.

Recent findings: Although opioid misuse in adolescents is uncommon, it is associated with morbidity and mortality such as hepatitis C and overdose. Adolescents commonly start with prescription opioid misuse before transitioning to heroin use. The existing literature supports the use of buprenorphine/naloxone for the treatment of adolescent opioid use disorders. Safe medication storage and disposal is important to decrease adolescent prescription opioid misuse.

Summary: Opioid misuse occurs in adolescents and pediatric providers need to remain up to date.

Keywords

adolescent; opioid use disorder; prescription opioid misuse; heroin; medication

Introduction

Over the past fifteen years, there has been a marked and steady increase in drug overdose deaths in the United States. In 2016 an estimated 64,000 individuals died of a drug overdose [1]. The rise in overdose deaths has been attributed to an increase in the use of prescription opioids for the management of chronic non-cancer pain [2]. In 2015, over 63% of fatal overdoses involved opioids [3]. In parallel to sales of prescription opioids and drug overdose deaths, there has been an increase in admissions for the treatment of opioid use disorders [3]. While the majority of overdoses occur in adults, 772 adolescents between the ages of 15 and 19 years died from a drug overdose in 2015 [4]. Additionally, drug use disorders begin in adolescence with symptom onset by 18 years of age in 50% of individuals, and by 24 years

of age in 80% of individuals with a lifetime history of a drug use disorder [5]. Pediatricians need to remain up to date in the midst of this public health emergency that is related to an adolescent onset disorder. We review new information specific to youth regarding the prevalence of opioid use, risk factors associated with opioid misuse, risks associated with opioid use, treatment of opioid use disorders, and strategies for prevention and harm reduction.

Prevalence

In 2016, 3.6% of adolescents ages 12 to 17 years and 7.3% of emerging adults ages 18 to 25 years misused an opioid in the United States [6]. Prescription opioids, including oxycodone, codeine, hydromorphone, and morphine, are the most commonly misused opioids [6]. In 2016, 3.5% of adolescents and 7.1% of emerging adults reported past year prescription opioid misuse, while 0.1% of adolescents and 3.5% of emerging adults reported past year heroin misuse. Though the prevalence of past year prescription opioid misuse in youth has been declining since it peaked in 2008, an opposite trend has been observed with past year heroin use which has been increasing since 2012 [7]. In accordance with changing patterns of use among young people, the primary type of opioid misused by adolescents seeking treatment for an opioid use disorder between 2010 and 2015 changed from predominantly prescription opioids to heroin [8]. A total of 153,000 adolescents (0.6%) and 392,000 emerging adults (1.1%) met criteria for an opioid use disorder in 2016 [6].

Risks Factors Associated with Opioid Misuse

History of medical use of a prescription opioid, i.e. an opioid was prescribed and the individual took the medication as prescribed, is a risk factor for later prescription opioid misuse that has been replicated in studies [9–12]. It is estimated that youth who are prescribed an opioid for any reason before high school graduation are at 33% increased risk for prescription opioid misuse before the age of 23 years relative to youth with no history of an opioid prescription [12]. Many youth with a history of medical use and prescription opioid misuse, 80% in one study, misuse prescription opioids that were prescribed to them [11]. Among adolescents with prescription opioid misuse generally, e.g. individuals with and without a history of medical use of a prescription opioid, prescription opioids were most commonly accessed for free from a friend (49%), from their own prescription (35%), or bought from a friend (32%)[13]. It is not surprising that youth are able to access prescription opioids for free since one study of 8th and 9th graders found 74% of adolescents prescribed a medication with potential for misuse had unsupervised access to the medication [14].

Several psychosocial risk factors were recently found to be associated with prescription opioid misuse. Adolescents with a history of a depressive episode when compared to those without a depressive episode had a 1.5 times increased risk for prescription opioid misuse, and a 2.2 times increased risk for an opioid use disorder among adolescents with a history of prescription opioid misuse [15]. Another study also found adolescents who endorsed prescription opioid misuse with the goal to get high had increased symptoms of an affective disorder in addition to increased symptoms of anxiety, somatic, attention, and conduct disorders when compared to adolescents with no opioid use [16]. Furthermore, a history of

childhood emotional or physical abuse has been associated with recent prescription opioid misuse in early adulthood [17]. An association between abuse and prescription opioid misuse is supported by research by Stein and colleagues who found higher scores on the Adverse Childhood Experience questionnaire were associated with a younger age of first opioid misuse among adults entering an inpatient opioid detoxification unit [18].

Opioids—Prescription Opioids versus Heroin

New research on opioid misuse in youth has primarily focused on prescription opioid misuse relative to heroin use. This likely reflects the recently documented pattern of progression from prescription opioid misuse to heroin use among individuals with opioid use disorders. When Cicero and colleagues examined the first opioid misused by adults entering treatment for a heroin use disorder between 1960 and 2010, they found a clear change from heroin to prescription opioids as the first opioid misused beginning in the early 1990's onwards [19]. Identified reasons for transitioning from prescription opioid misuse to heroin use in this study included easier access to heroin and the cheaper cost of heroin relative to prescription opioids [19]. A similar pattern of a progression from prescription opioid misuse to heroin use has been documented in adolescents [20, 21]. Specifically, in a national sample of adolescents collected between 2002 and 2011 in the United States, youth with a history of prescription opioid misuse were 13 times more likely to initiate heroin use [20]. The highest risk for initiation of heroin use was associated with prescription opioid misuse that started in early adolescence between the ages of 10 and 12 years [20]. The majority of youth with a history of prescription opioid misuse started misusing prescription opioids between the age of 16 to 18 years (45%), followed by 33% between the age of 13 and 15 years, and 11% between the ages of 10 and 12 years. This literature highlights the importance of targeted interventions to prevent prescription opioid misuse and earlier identification of youth with prescription opioid misuse in order to decrease the prevalence of opioid use disorders in youth.

Although research on opioid misuse patterns between 1990 and 2010 clearly documented individuals with new opioid misuse began with prescription opioids and later transitioned to heroin, a newer opioid misuse pattern has been documented in adults that is important for adolescent providers to be aware of. Among adults entering treatment for an opioid use disorder who began using opioids between 2005 and 2015, the percentage of individuals who used heroin as the first opioid misused sharply increased from 8.7% of individuals in 2005 to 33% of individuals in 2015 [22]. Correspondingly, the percentage of these individuals who used oxycodone as the first opioid misused declined from 42% in 2005 to 24% in 2015. The authors speculate that the change in the first type of opioid misused was due to the decreased supply of prescription opioids on the black market. With decreased availability, prescription opioids for misuse increased in cost at roughly the same time that heroin decreased in cost [23]. It is unclear if there has also been a change in the type of opioid first misused by adolescents. Since trends in adolescent opioid misuse generally mirror adult opioid misuse trends, providers should be prepared to assess for heroin use in youth. If adolescents are now beginning to misuse opioids with heroin it is unclear what the clinical implications of this change will be.

Clinically it is very important to identify what type of opioid a patient is using since opioids vary in potency and subsequent risk for overdose. Frequently unbeknownst to the individual misusing opioids, illicit opioids such as heroin have been adulterated with more potent synthetic opioids such as illicitly manufactured fentanyl and carfentanil [24]. Illicitly manufactured fentanyl is approximately 50 to 100 times as potent as morphine, and carfentanil is estimated to be 10,000 times as potent as morphine [25]. These more potent synthetic opioids are thought to be the key factor driving recent drug overdose deaths [26]. One challenge for clinicians and public safety officials in the identification of synthetic opioids is that routine toxicology testing does not commonly test for these substances. Common qualitative urine toxicology screens only test for opiates including heroin, morphine, and codeine [27]. An additional opioid specific panel is needed to detect synthetic opioids including oxycodone, hydrocodone, buprenorphine, and methadone [27]. Fentanyl is not routinely tested for in opioid specific panels but with the rise in use it is increasingly being included. Clinically, it is important to know what substances are included in a test when using toxicology testing to guide assessment and treatment recommendations. Furthermore, there is a role for toxicology testing even when opioid misuse is disclosed since adolescents may be unaware that the opioid they are using has been mixed with more potent opioids such as fentanyl.

Risks associated with opioid use

Much of the medical morbidity and mortality associated with opioid misuse is related to infectious diseases such as hepatitis C and overdose. After a decline in the number of cases of acute hepatitis C in the United States in the early 2000's, the incidence has been steadily increasing since 2011 [28]. The largest increase in rate of hepatitis C occurred among individuals 20 to 29 years of age who also have the highest rate of acute hepatitis C relative to other age groups. In contrast, individuals ages 0 to 19 years of age have the lowest rate of acute hepatitis C. The most common risk behavior reported among individuals with acute hepatitis C was injection drug use [28]. A recent study using national surveillance data found increases in opioid injection mirrored increases in reported cases of acute hepatitis C infection among demographic subgroups suggesting the increases in acute hepatitis C infection were related to opioid injection drug use [29]. It is important to note that Hepatitis C is spread not only through shared syringes, but also through the sharing of other injection paraphernalia such as "cookers" and cotton filters [30]. Since the incidence of acute hepatitis C increases from the lowest rate among children and adolescents to the highest rate among emerging adults, prevention efforts could target youth who are misusing opioids and are not yet injecting drugs. Regardless, since intranasal and injection drug use are not uncommon among youth misusing opioids, all should be tested for hepatitis C [31].

Overdose risk factors specific to youth with substance use disorders have been less well characterized relative to risk factors identified in adult populations. In adults, opioid misuse has been identified as a risk factor for overdose [32–35] in addition to history of overdose, use of benzodiazepines [33, 35], binge drinking [36, 37], cocaine use [38], amphetamine use [39, 40], depression [41], and increased impulsivity [42]. In youth, among an urban sample with a history of prescription opioid or tranquilizer (benzodiazepines, clonidine, quetiapine) misuse, history of intranasal drug use, injection drug use, and psychiatric hospitalization

increased risk for overdose [43]. We recently evaluated risk factors associated with a history of overdose among treatment-seeking youth with substance use disorders [44] and found an association between overdose history and greater lifetime substance use disorder diagnoses, intravenous drug use, and increased psychopathology. These youth specific findings suggest providers need to thoroughly assess for psychopathology in addition to risk factors associated with substance use when evaluating overdose risk in young people.

Adolescent Opioid Use Disorder Treatment

Adolescent substance use disorder treatment can involve several components including medication, therapy, family involvement, and community supports (Table 1). Despite a limited literature, medication is strongly recommended for the treatment of adolescent opioid use disorders [45, 46] due to the chronic course of the illness and the increased risk for overdose and death associated with continued opioid use. Three medications have FDA approval for the treatment of opioid use disorders in adults: buprenorphine/naloxone, naltrexone extended release, and methadone [47]. Randomized controlled trials for medication in adolescents with opioid use disorders have only been conducted for buprenorphine/naloxone [48–50]. Research on naltrexone extended release in adolescents has been limited to case series reports [51, 52]. Methadone is very difficult for adolescents to access in the United States, and no recent research exists on the use of this medication in adolescents.

Buprenorphine/naloxone is a partial μ -opiate receptor agonist that can be prescribed in the outpatient setting by providers who completed additional training to receive a waiver from the DEA. Buprenorphine has been shown to be more effective compared to clonidine, an α_2 adrenergic agonist, for detoxification off of opioids for 35 adolescents with an opioid use disorder [48]. Adolescents randomized to buprenorphine were more likely to have negative urine toxicology tests and more likely to transition to naltrexone for maintenance treatment of their opioid use disorder compared to those randomized to clonidine. A large subsequent study of 152 youth ages 15 to 21 years with opioid dependence found longer treatment with buprenorphine/naloxone was associated with improved outcomes [49]. Specifically, youth randomized to buprenorphine/naloxone stabilization and maintenance for eight weeks with a taper over four weeks compared to those who were detoxified from opioids with buprenorphine/naloxone over two weeks had less opioid use, less injection drug use, and less need for additional substance use disorder treatment outside of the once weekly therapy and medication visits that were part of the study. A recently published study reported on outcomes associated with the duration of the buprenorphine/naloxone taper for youth ages 16 to 24 years with opioid dependence [50]. Youth tapered off buprenorphine/naloxone over fifty-six days were more likely to have opioid negative toxicology tests and remain engaged in treatment for a longer period of time compared to those tapered off buprenorphine/naloxone over twenty-eight days.

The literature on the use of naltrexone extended release in youth with opioid use disorders has been limited to case series reports [51]. Naltrexone extended release is an opioid receptor antagonist that has no DEA restrictions around prescribing, and is administered once monthly with an intragluteal injection. A descriptive study of sixteen youth, mean age

18.5 years, who received naltrexone extended release showed the majority of the sample (56%) substantially reduced their opioid use or were abstinent from opioids at four-month follow-up [51]. A more recent case series reported on the feasibility of home based administration of naltrexone extended release [52]. Fourteen youth, mean age 20.5 years, who initially receive extended release naltrexone in residential treatment were enrolled in a pilot program offering home-based injections. Nine subjects received a home-based injection, one received a clinic-based injection, and four dropped out of care or were admitted to a higher level of care before receiving an injection as an outpatient. Compared to a historical sample treated in this same program that received naltrexone extended release in residential treatment followed by injections in a clinic, subjects in the home-based program received more doses of medication (mean 4.4 doses versus 2.4 doses) and were more likely to be retained in outpatient treatment over four months (64% versus 19%). The drop-off in patient retention after the initial dose of naltrexone-extended release in residential treatment reflects an initial challenge with once monthly medication for high-risk patients. Once monthly medication ensures adherence but the decreased frequency of medication visits relative to buprenorphine/naloxone, which may initially be weekly, can make it difficult to retain high-risk patients in outpatient treatment. More frequent clinical interactions during initial treatment engagement may help increase retention in treatment. Another challenge in the use of an opioid antagonist medication for patients with opioid use disorders is the need for a period of abstinence (e.g. 7 to 10 days) from opioids prior to starting naltrexone to decrease the risk for precipitated opioid withdrawal. In summary, the existing data support the use of medication for adolescents with opioid use disorders until at a minimum the adolescent has stabilized in treatment, has strong relapse prevention skills, and is working on longer term goals such as school or work.

Although the use of medications to treat opioid use disorders has increased over the past ten years in all age groups, adolescents relative to adults are less likely to receive medication. Only 18% of adolescents admitted for treatment due to heroin use in 2015 had a treatment plan that included treatment with buprenorphine/naloxone or methadone compared to 42% of adults aged 45 years and older [8]. A large retrospective cohort study from a national commercial insurance database had similar findings [53]. They found 28% of youth ages 13 to 25 years with an opioid use disorder were started on buprenorphine or naltrexone in 2014 [53]. Within the age range of 13 to 25 years younger individuals were less likely to receive medication. For example only 9.7% of individuals ages 16 to 17 years received medication compared to 31% of those ages 21 to 25 years. Differences in medication receipt based on sex and race also existed. Females relative to males were significantly less likely to receive medication. Non-Hispanic black and Hispanic youth were significantly less likely to receive medication relative to non-Hispanic white youth.

It is important that medication be discussed as part of the treatment plan for youth with opioid use disorders since these medications save lives. A recent meta-analysis in adults with opioid use disorders showed overdose deaths decreased by 70% when individuals were stabilized on buprenorphine/naloxone and 80% when stabilized on methadone [54]. More research is needed to help providers, patients, and families determine which medication is best indicated for the treatment of opioid use disorders in youth, duration of treatment, and barriers to the use of these medications specific to youth.

Behavioral therapy should also be part of the treatment plan for an adolescent with an opioid use disorder. Several behavioral therapies have been shown to be efficacious for adolescents with substance use disorders including motivational enhancement therapy, cognitive behavioral therapy, the adolescent community reinforcement approach, and contingency management [55]. To our knowledge there has been one study to date that focused on the efficacy of behavioral therapy specifically for adolescents with opioid use disorders. In a large community sample of adolescents receiving the adolescent community reinforcement approach, individuals with primary opioid problem use were compared to those with primarily marijuana or alcohol problem use [56]. There were equal rates of treatment initiation, engagement, retention, and satisfaction with treatment between the two groups, and both groups also had decreases in most substance use outcomes. At one-year follow-up however, the adolescents with primary opioid problem use reported higher frequency of substance use and more days of emotional problems and residential treatment, compared to those with primary marijuana or alcohol problem use. This likely reflects the higher severity of illness in the primary opioid problem use group at baseline. It is helpful to know that the adolescent community reinforcement approach is an intervention that can be implemented with young people who have opioid use disorders and is effective for this population. If providers trained in the adolescent community reinforcement approach are available this may be the best type of therapy to use with adolescents with opioid use disorders. Given the limited number of providers trained to work with adolescents with substance use disorders, providers should not feel limited to only refer patients to the adolescent community reinforcement approach until there is greater evidence on the relative efficacy of the different behavioral treatments specific to adolescents with opioid use disorders.

Adolescent caregivers are also an important part of an adolescent's treatment. Youth with opioid use disorders often struggle earlier in their course of illness with low insight into the risks associated with opioid misuse and are subsequently reluctant to change their use and/or engage in treatment. Caregiver involvement is key to facilitate youth engagement in care, provide collateral on the adolescent's functioning at home and school, and monitor medication adherence. The adolescent community reinforcement approach formally includes caregivers in the manualized protocol with two sessions with caregivers only and two sessions with the adolescent and caregiver together to work on positive and effective communication [57]. When adolescents are not ready to engage in treatment, caregivers can learn skills to increase an adolescent's motivation to engage in care through a caregiver focused intervention, the Community Reinforcement and Family Training approach [58]. Community Reinforcement and Family Training has been shown to be effective in motivating youth to engage in care, decreasing their substance use regardless of engagement in care, and improving the lives of caregivers by strengthening their self-care skills [59]. When an adolescent is willing to engage in care, family therapy can be a very effective intervention to decrease adolescent substance use by addressing family risk factors that may be contributing to an adolescent's substance use [60].

Prevention and Harm Reduction

Given the scope of the opioid epidemic there is a need for prevention programs to decrease the risk of opioid use, particularly in adolescence when substance use begins. Promising

results were found in a recent randomized controlled trial of universal prevention interventions implemented during middle school (ref). A significant association was observed between the universal prevention interventions and decreased prescription opioid misuse in late adolescence and young adults.

Providers can help caregivers decrease risk for prescription opioid misuse by discussing safe medication storage and disposal with all families. It is also important for providers to educate patients and families on the importance of taking medication as prescribed, provide clear clinical parameters for when to use a medication “as needed,” and discuss risks associated with diversion. Options for safe medication disposal have been increasing since 2014 when the DEA authorized registrants such as retail pharmacies and hospitals and clinics with on-site pharmacies to become authorized collectors of controlled substances and other prescription drugs [62]. If medication collection sites are not easily accessible the FDA provides guidance on their website on how to safely dispose of medications at home.

Providers can also reduce harm associated with opioids by encouraging patients and families to access naloxone if anyone in the home is prescribed a prescription opioid or anyone has a history of opioid misuse. Naloxone is a short acting opioid antagonist that can be administered intramuscularly, intranasally, or intravenously to reverse an opioid overdose. Most health insurances cover naloxone, and in some states naloxone can be accessed over the counter in retail pharmacies [63].

Conclusions

Opioid misuse begins in adolescence and the opioid epidemic has not spared youth. Adolescent opioid misuse commonly begins with prescription opioid misuse and can progress to heroin use. It is important to identify what type of opioid an adolescent is using since heroin use relative to prescription opioid misuse can be associated with increased morbidity due to adulterants such as fentanyl. Medication is an important part of the treatment plan for adolescents with opioid use disorders since medications for opioid use disorders decrease overdose mortality. All providers should discuss the importance of safe medication storage and disposal with patients and families to decrease prescription opioid diversion and subsequently decrease the prevalence of prescription opioid misuse in youth.

Acknowledgments

Financial Disclosures:

Amy M. Yule, MD: Dr. Amy Yule received grant support from the Massachusetts General Hospital Louis V. Gerstner III Research Scholar Award from 2014 to 2016. Dr. Yule is currently receiving funding through the AACAP Physician Scientist Program in Substance Abuse 5K12DA000357-17. She was a consultant to Phoenix House from 2015 to 2017 and is currently a consultant to the Gavin Foundation (clinical services).

Timothy E. Wilens, MD: Dr. Timothy Wilens receives or has received grant support from the following sources: NIH(NIDA). Dr. Timothy Wilens is or has been a consultant for: Alcobra, Neurovance/Otsuka, and Ironshore. Dr. Timothy Wilens has a published book: *Straight Talk About Psychiatric Medications for Kids* (Guilford Press); and co/edited books *ADHD in Adults and Children* (Cambridge University Press), *the Massachusetts General Hospital Comprehensive Clinical Psychiatry* (Elsevier) and *Massachusetts General Hospital Psychopharmacology and Neurotherapeutics* (Elsevier). Dr. Wilens is co/owner of a copyrighted diagnostic questionnaire (Before School Functioning Questionnaire) and he has a licensing agreement with Iron shore (BSFQ Questionnaire). Dr. Wilens is Chief, Division of Child and Adolescent Psychiatry and (Co) Director of the Center for Addiction Medicine at

Massachusetts General Hospital. He serves as a consultant to the US National Football League (ERM Associates), U.S. Minor/Major League Baseball, Bay Cove Human Services (Clinical Services), Phoenix/Gavin House and Bay Cove Human Services.

Rachael M. Lyons, BS: Nothing to disclose at this time.

References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

1. Total U.S. Drug Deaths. National Institute on Drug Abuse Advancing Addiction Science: Center For Disease Control WONDER. 2017 More than 64,000 Americans died from drug overdoses in 2016, including illicit drugs and prescription opioids-nearly double in a decade
2. Center for Disease Control. Vital Signs: Overdoses of Prescription Opioid Pain Relievers-United States, 1999–2008. *MMWR Surveill Summ* 2011;60:1–6.
- 3•. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths-United States, 2000–2014. *MMWR Morbidity and mortality weekly report* 2016;64(50–51):1378–82. [PubMed: 26720857] Provides information on the number of drug overdose deaths in 2015 with details on regional changes and the type of synthetic opioids involved.
- 4••. Curtin SC, Tejada-Vera B, Warner M. Drug Overdose Deaths Among Adolescents Aged 15–19 in the United States: 1999–2015. *NCHS data brief* 2017(282):1–8. Provides information on trends in drug overdose deaths in adolescents including details on gender, intentionality of overdose, and substances involved in the overdose.
5. Compton WM, Thomas YF, Stinson FS, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: results from the national epidemiologic survey on alcohol and related conditions. *Arch Gen Psychiatry* 2007;64(5):566–76. [PubMed: 17485608]
6. 2016 National Survey on Drug Use and Health: Detailed Tables Rockville, MD Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality; 2017.
7. Martins SS, Segura LE, Santaella-Tenorio J, Perlmutter A, Fenton MC, Cerda M, et al. Prescription opioid use disorder and heroin use among 12–34 year-olds in the United States from 2002 to 2014. *Addict Behav* 2017;65:236–41. [PubMed: 27614657]
8. Mental Health Annual Report: 2015 Use of Mental Health Services: National Client Level Data Rockville, MD: Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality 2015.
9. McCabe SE, West BT, Veliz P, McCabe VV, Stoddard SA, Boyd CJ. Trends in Medical and Nonmedical Use of Prescription Opioids Among US Adolescents: 1976–2015. *Pediatrics* 2017;139(4).
10. McCabe SE, Veliz P, Schulenberg JE. Adolescent context of exposure to prescription opioids and substance use disorder symptoms at age 35: a national longitudinal study. *Pain* 2016;157(10):2173–8. [PubMed: 27227693]
11. McCabe SE, West BT, Teter CJ, Boyd CJ. Medical and nonmedical use of prescription opioids among high school seniors in the United States. *Arch Pediatr Adolesc Med* 2012;166(9):797–802. [PubMed: 22566521]
- 12•. Miech R, Johnston L, O'Malley PM, Keyes KM, Heard K. Prescription Opioids in Adolescence and Future Opioid Misuse. *Pediatrics* 2015;136(5):e1169–77. [PubMed: 26504126] Reports on risk factors associated with future opioid misuse among a national sample of youth prospectively followed from 12th grade through age 23.
13. Miech RA, Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. Monitoring the Future National Survey Results on Drug Use, 1975–2014: Secondary School Students. Ann Arbor: Institute for Social Research, The University of Michigan; 2015.

14. Ross-Durow PL, McCabe SE, Boyd CJ. Adolescents' access to their own prescription medications in the home. *J Adolesc Health* 2013;53(2):260–4. [PubMed: 23683499]
15. Edlund MJ, Forman-Hoffman VL, Winder CR, Heller DC, Kroutil LA, Lipari RN, et al. Opioid abuse and depression in adolescents: Results from the National Survey on Drug Use and Health. *Drug Alcohol Depend* 2015;152:131–8. [PubMed: 25981310]
16. Boyd CJ, Young A, McCabe SE. Psychological and drug abuse symptoms associated with nonmedical use of opioid analgesics among adolescents. *Subst Abus* 2014;35(3):284–9. [PubMed: 24905351]
17. Austin AE, Shanahan ME, Zvara BJ. Association of childhood abuse and prescription opioid use in early adulthood. *Addict Behav* 2018;76:265–9. [PubMed: 28869906]
18. Stein MD, Conti MT, Kenney S, Anderson BJ, Flori JN, Risi MM, et al. Adverse childhood experience effects on opioid use initiation, injection drug use, and overdose among persons with opioid use disorder. *Drug Alcohol Depend* 2017;179:325–9. [PubMed: 28841495]
19. 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):821–6. [PubMed: 24871348]
20. Cerda M, Santaella J, Marshall BD, Kim JH, Martins SS. Nonmedical Prescription Opioid Use in Childhood and Early Adolescence Predicts Transitions to Heroin Use in Young Adulthood: A National Study. *J Pediatr* 2015;167(3):605–12 e1–2. [PubMed: 26054942]
21. Palamar JJ, Shearston JA, Dawson EW, Mateu-Gelabert P, Ompad DC. Nonmedical opioid use and heroin use in a nationally representative sample of us high school seniors. *Drug Alcohol Depend* 2016;158:132–8. [PubMed: 26653341]
- 22•. Cicero TJ, Ellis MS, Kasper ZA. Increased use of heroin as an initiating opioid of abuse. *Addict Behav* 2017;74:63–6. [PubMed: 28582659] Reports on recent trends in first opioid of misuse among adults entering substance use disorder treatment for an opioid use disorder.
23. Rosenblum D, Unick GJ, Ciccarone D. The entry of Colombian-sourced heroin into the US market: the relationship between competition, price, and purity. *The International journal on drug policy* 2014;25(1):88–95. [PubMed: 24211155]
24. O'Donnell JK, Gladden RM, Seth P. Trends in Deaths Involving Heroin and Synthetic Opioids Excluding Methadone, and Law Enforcement Drug Product Reports, by Census Region - United States, 2006–2015. *MMWR Morbidity and mortality weekly report* 2017;66(34):897–903. [PubMed: 28859052]
25. Suzuki J, El-Haddad S. A review: Fentanyl and non-pharmaceutical fentanyls. *Drug Alcohol Depend* 2017;171:107–16. [PubMed: 28068563]
26. Julie K O'Donnell PRMG; Puja Seth. Trends in Deaths Involving Heroin and Synthetic Opioids Excluding Methadone, and Law Enforcement Drug Product Reports, by Census Region — United States, 2006–2015. *Morbidity and Mortality Weekly Report* 2017;66:897–903. [PubMed: 28859052]
- 27•. Hadland SE, Levy S. Objective Testing: Urine and Other Drug Tests. *Child Adolesc Psychiatr Clin N Am* 2016;25(3):549–65. [PubMed: 27338974] Review covering toxicology testing in clinical practice including: types of samples used for testing, indications for testing, and practical concerns associated with testing in adolescents.
28. Viral Hepatitis Surveillance, United States 2015. Center for Disease Control; 2015.
- 29•. Zibbell JE, Asher AK, Patel RC, Kupronis B, Iqbal K, Ward JW, et al. Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014. *Am J Public Health* 2018;108(2):175–81. [PubMed: 29267061] Compares trends in opioid injection with the trends in the incidence of acute hepatitis C virus infection in the United States
30. Thorpe LE, Ouellet LJ, Hershow R, Bailey SL, Williams IT, Williamson J, et al. Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment. *Am J Epidemiol* 2002;155(7):645–53. [PubMed: 11914192]
31. Moyer VA, Force USPST. Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2013;159(5):349–57. [PubMed: 23798026]

32. Hakansson A, Schlyter F, Berglund M. Factors associated with history of non-fatal overdose among opioid users in the Swedish criminal justice system. *Drug Alcohol Depend* 2008;94(1–3): 48–55. [PubMed: 18082338]
33. Kerr T, Fairbairn N, Tyndall M, Marsh D, Li K, Montaner J, et al. Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. *Drug Alcohol Depend* 2007;87(1): 39–45. [PubMed: 16959438]
34. Warner M, Chen LH, Makuc DM, Anderson RN, Minino AM. Drug poisoning deaths in the United States, 1980–2008. *NCHS data brief* 2011(81):1–8.
35. Jones CM, McAninch JK. Emergency Department Visits and Overdose Deaths From Combined Use of Opioids and Benzodiazepines. *American journal of preventive medicine* 2015;49(4):493–501. [PubMed: 26143953]
36. Pabayo R, Alcantara C, Kawachi I, Wood E, Kerr T. The role of depression and social support in non-fatal drug overdose among a cohort of injection drug users in a Canadian setting. *Drug Alcohol Depend* 2013;132(3):603–9. [PubMed: 23647731]
37. Seal KH, Kral AH, Gee L, Moore LD, Bluthenthal RN, Lorvick J, et al. Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998–1999. *Am J Public Health* 2001;91(11):1842–6. [PubMed: 11684613]
38. Coffin PO, Tracy M, Bucciarelli A, Ompad D, Vlahov D, Galea S. Identifying injection drug users at risk of nonfatal overdose. *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine* 2007;14(7):616–23. [PubMed: 17554010]
39. Rossow I, Lauritzen G. Balancing on the edge of death: suicide attempts and life-threatening overdoses among drug addicts. *Addiction* 1999;94(2):209–19. [PubMed: 10396789]
40. Gossop M, Stewart D, Treacy S, Marsden J. A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction* 2002;97(1):39–47. [PubMed: 11895269]
41. Bartoli F, Carra G, Brambilla G, Carretta D, Crocamo C, Neufeind J, et al. Association between depression and non-fatal overdoses among drug users: a systematic review and meta-analysis. *Drug Alcohol Depend* 2014;134:12–21. [PubMed: 24210424]
42. Maloney E, Degenhardt L, Darke S, Nelson EC. Are non-fatal opioid overdoses misclassified suicide attempts? Comparing the associated correlates. *Addict Behav* 2009;34(9):723–9. [PubMed: 19447563]
43. Silva K, Schragger SM, Kecojevic A, Lankenau SE. Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs. *Drug Alcohol Depend* 2013;128(1–2):104–10. [PubMed: 22974490]
44. Yule AM, Carrellas NW, Fitzgerald M, McKowen JW, Nargiso JE, Bergman BG, Kelly JF Risk factors for overdose in treatment-seeking youth with substance use disorders during follow-up. *The J Clin Psychiatry* (in Press).
- 45••. Committee On Substance USE, Prevention. Medication-Assisted Treatment of Adolescents With Opioid Use Disorders. *Pediatrics* 2016;138(3).Reviews effective treatment for opioid use disorders in youth and advocates for improving access to medication treatment for opioid use disorders in adolescents and young adults.
- 46••. Chang DC, Klimas J, Wood E, Fairbairn N. Medication-assisted treatment for youth with opioid use disorder: Current dilemmas and remaining questions. *Am J Drug Alcohol Abuse* 2018;44(2): 143–6. [PubMed: 29190156] Commentary on dilemmas and questions regarding the use of medication for opioid use disorders in youth. Recommends buprenorphine/naloxone as first line treatment.
47. Connery HS. Medication-assisted treatment of opioid use disorder: review of the evidence and future directions. *Harv Rev Psychiatry* 2015;23(2):63–75. [PubMed: 25747920]
48. Marsch LA, Bickel WK, Badger GJ, Stothart ME, Quesnel KJ, Stanger C, et al. Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial. *Arch Gen Psychiatry* 2005;62(10):1157–64. [PubMed: 16203961]
49. Woody GE, Poole SA, Subramaniam G, Dugosh K, Bogenschutz M, Abbott P, et al. Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. *JAMA* 2008;300(17):2003–11. [PubMed: 18984887]

50. Marsch LA, Moore SK, Borodovsky JT, Solhkhah R, Badger GJ, Semino S, et al. A randomized controlled trial of buprenorphine taper duration among opioid-dependent adolescents and young adults. *Addiction* 2016;111(8):1406–15. [PubMed: 26918564]
51. Fishman MJ, Winstanley EL, Curran E, Garrett S, Subramaniam G. Treatment of opioid dependence in adolescents and young adults with extended release naltrexone: preliminary case-series and feasibility. *Addiction* 2010;105(9):1669–76. [PubMed: 20626723]
52. Vo HT, Burgower R, Rozenberg I, Fishman M. Home-based delivery of XR-NTX in youth with opioid addiction. *J Subst Abuse Treat* 2018;85:84–9. [PubMed: 28867062]
53. Hadland SE, Wharam JF, Schuster MA, Zhang F, Samet JH, Larochelle MR. Trends in Receipt of Buprenorphine and Naltrexone for Opioid Use Disorder Among Adolescents and Young Adults, 2001–2014. *JAMA pediatrics* 2017;171(8):747–55. [PubMed: 28628701]
54. Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ* 2017;357:j1550. [PubMed: 28446428]
55. Principles of Drug Addiction Treatment: A Research-Based Guide National Institute on Drug Abuse, National Institutes of Health; 2018.
56. Godley MD, Passetti LL, Subramaniam GA, Funk RR, Smith JE, Meyers RJ. Adolescent Community Reinforcement Approach implementation and treatment outcomes for youth with opioid problem use. *Drug Alcohol Depend* 2017;174:9–16. [PubMed: 28282523] Reports on feasibility, acceptability, and efficacy of the Adolescent Community Reinforcement Approach for youth with primary problem opioid use compared to youth with primary marijuana or alcohol problem use.
57. Godley SH, Meyers RJ, Smith JE, Karvinen T, Titus JC, Godley MD, et al. The Adolescent Community Reinforcement Approach for Adolescent Cannabis Users, Cannabis Youth Treatment (CYT) Substance Abuse and Mental Health Services Administration (DHHS/PHS), Rockville, MD Center for Substance Abuse Treatment 2001.
58. Roozen HG, de Waart R, van der Kroft P. Community reinforcement and family training: an effective option to engage treatment-resistant substance-abusing individuals in treatment. *Addiction* 2010;105(10):1729–38. [PubMed: 20626372]
59. Kirby KC, Versek B, Kerwin ME, Meyers K, Benishek LA, Bresani E, et al. Developing Community Reinforcement and Family Training (CRAFT) for Parents of Treatment-Resistant Adolescents. *Journal of child & adolescent substance abuse* 2015;24(3):155–65. [PubMed: 25883523]
60. Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide National Institute on Drug Abuse (NIDA); 2014.
61. Spoth R, Redmond C, Shin C, Greenberg M, Feinberg M, Schainker L. PROSPER community-university partnership delivery system effects on substance misuse through 6 1/2 years past baseline from a cluster randomized controlled intervention trial. *Prev Med* 2013;56(3–4):190–6. [PubMed: 23276777]
62. DEA and Partners Collect 309 Tons of Pills on Ninth Prescription Drug Take-Back Day 2014 3/8/17.
63. Thompson EL, Rao PSS, Hayes C, Purtil C. Dispensing Naloxone Without a Prescription: Survey Evaluation of Ohio Pharmacists. *Journal of pharmacy practice* 2018;897190018759225.
64. Winters KC, Tanner-Smith EE, Bresani E, Meyers K. Current advances in the treatment of adolescent drug use. *Adolesc Health Med Ther* 2014;5:199–210. [PubMed: 25429247]

Table 1.

Possible components of treatment for adolescents with opioid use disorders [60, 64]

Medication	• Buprenorphine/naloxone (office based, DEA waiver required)
	• Naltrexone extended release (intramuscular injection)
	• Methadone (clinic based, requires special consent)
	• Naloxone (for overdose reversal)
	• Medication for co-occurring psychiatric disorders (e.g. fluoxetine for depression)
Behavioral Therapy	• Motivational Enhancement Therapy (increase engagement and retention in treatment)
	• Cognitive Behavioral Therapy (build coping skills, increase understanding of cues/cravings)
	• Adolescent Community Reinforcement Approach (increase engagement in prosocial substance free activities)
	• Contingency Management (positive feedback/rewards for treatment attendance/abstinence)
Monitor Drug Use	• Toxicology testing—urine or saliva
Medical Treatment	• Assess and treat infectious diseases—Hepatitis C, Human Immunodeficiency Virus, Sexually Transmitted Diseases
Family Involvement	• Caregiver only—Community Reinforcement and Family Training
	• Family Therapy (e.g. Brief Strategic Family Therapy, Family Behavior Therapy, Functional Family Therapy, Multidimensional Family Therapy, Multisystemic Therapy)
Community Recovery Support	• Mutual Help Organizations—Alcoholics Anonymous, Narcotics Anonymous, SMART Recovery
	• Educational Support—Recovery High Schools, Collegiate Recovery Programs
	• Vocational Support