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Medication Treatment of Adolescent Opioid Use Disorder in Primary Care

Brittany L. Carney, MS¹, Scott E. Hadland, MD, MPH, MS^{1,2}, and Sarah M. Bagley, MD^{1,2}

Brittany L. Carney: bcarney@bu.edu; Scott E. Hadland: scott.hadland@bmc.org; Sarah M. Bagley: sarah.bagley@bmc.org

¹Boston Medical Center, General Internal Medicine/Pediatrics, Boston, MA

²Boston University School of Medicine, Department of Pediatrics, Boston, MA

Since 2000, a three-fold increase in unintentional opioid poisonings among adolescents has followed a dramatic increase in adult opioid-related deaths. In 2016, 1 in 13 high school seniors reported past year non-prescription use of opioids. Despite these increases, only 8.5% of adolescents received addiction treatment.

In September 2016, the American Academy of Pediatrics (AAP) released a policy statement recommending that pediatricians offer medication for treatment of severe opioid use disorder (OUD). There are three medications approved for OUD treatment: buprenorphine, naltrexone and methadone. Buprenorphine and methadone are opioid agonists that decrease cravings for opioids and treat withdrawal symptoms. Additionally, both provide “opioid blockade”, which means if an individual uses another opioid after taking their medication, euphoric effects are blocked. Naltrexone, an opioid antagonist, blocks the opioid receptor preventing the effects of opioid use. It may also reduce cravings for opioids. Head-to-head clinical trials of these medications in adolescents are lacking; observational data among adults suggest that among these medications, methadone may be the most effective for retention in treatment.

Medications

Buprenorphine is taken daily via sublingual tablets or films and can be prescribed in pediatric primary care. The film is a dissolving strip absorbed through the buccal mucosa or tongue. Buprenorphine has 2 formulations: (i) combined with naloxone (buprenorphine/naloxone) and (ii) a formulation without naloxone. Pediatricians should prescribe the combined formulation. Naloxone is not absorbed systemically, but if misused and injected, naloxone binds to block the opioid receptor, triggering uncomfortable withdrawal symptoms that discourages misuse. Pregnant females are generally prescribed buprenorphine-only due to concerns about fetal naloxone exposure. Per federal regulations, providers must complete an 8-hour online or in-person course to receive a US Drug Enforcement Agency waiver prior to prescribe buprenorphine. As of 2016, nurse practitioners and physician assistants can also

obtain waivers. Multiple organizations including the AAP have endorsed an adolescent-focused version of the course for pediatricians (www.aap.org/mat).

Naltrexone is available in a daily oral tablet or a monthly depot injection. No special certification is required to prescribe naltrexone. Many practitioners initially prescribe tablets for one week to ensure tolerability before transitioning to monthly injection. Since naltrexone is an opioid antagonist, it can precipitate sudden withdrawal symptoms in a patient who recently used opioids. Therefore, clinicians should only administer naltrexone 3-6 days after the most recent use of short-acting opioids (*e.g.*, most short-acting prescription opioids or heroin), and 7-10 days after the most recent use of long-acting opioids (*e.g.*, most long-acting prescription opioids, buprenorphine, or methadone). It is important to check a urine drug test (UDT) before starting naltrexone and observe the first oral dose in clinic to monitor (~60 minutes) for signs of withdrawal. Generally, naltrexone is not used in pregnant women and if a patient on naltrexone becomes pregnant, an addiction specialist should be consulted.

Methadone is a full opioid agonist. US federal regulations mandate dispensing methadone in federally certified opioid treatment programs; and there are strict guidelines about when a minor can qualify for treatment. As a result, it is uncommonly used to treat adolescent patients in the US.

Treatment Protocol

Amidst a shortage of treatment options for adolescents in many settings (*e.g.*, rural settings), pediatric primary care practices can provide effective care even without extensive resources. Due to strict federal regulations about methadone dispensing, pediatricians will generally be restricted to prescribing buprenorphine, buprenorphine/naloxone, and naltrexone in their practice which are the treatment models that we further describe. At a minimum, practices should establish a clinical model that includes a pediatrician who prescribes medication and monitors treatment, and a mental health practitioner who provides behavioral therapy.

After referral to treatment, the patient should undergo an assessment for OUD based on DSM-V criteria. Whether a teen can consent to their own substance use treatment without a parent differs across states; practitioners should become familiar with regulations in their jurisdictions and adhere to federal statutes. Prior to starting medication, the patient, family, and clinician should also sign a treatment agreement. The agreement outlines expectations related to visit adherence, conduct in clinic, participation in routine UDT and receipt of behavioral health counseling (including, *e.g.*, motivational enhancement therapy, cognitive behavioral therapy, and adolescent community reinforcement approach).

Laboratory tests are ordered and immunizations are reviewed for all patients to ensure receipt of hepatitis A and B vaccines or immunity (Table 1). Naltrexone should not be offered to patients with liver function tests 3 times the upper limit of normal. In those cases, clinicians should monitor liver function tests, determine the etiology of the increase, and reconsider initiating naltrexone at a later date if possible. Safe medication storage is reviewed with patients and caregivers, including encouraging storing medication in a

lockbox. If possible, caregivers should be asked to observe all medication administrations. If there are small children in the home, caregivers should be given additional guidance about avoiding unintentional ingestion, particularly for buprenorphine.

In addition, UDT is implemented: weekly for 6 weeks, then bi-weekly for 6 weeks, and then monthly if the patient is stable. UDTs have two purposes: (1) to monitor for opioid or other polysubstance use, including use of benzodiazepines, which greatly increases the risk of overdose; and (2) to monitor medication adherence with buprenorphine (since buprenorphine and its metabolites can be detected in the urine). Urine drug panels should include testing for opiates, cocaine, amphetamines, benzodiazepines, and barbiturates, as well as expanded panel testing for oxycodone, methadone, buprenorphine and fentanyl opioids.

Providers should also assess for co-occurring disorders and provide behavioral health supports and referrals to psychiatry when needed. Overdose education and a naloxone prescription should be offered to all patients and families.

Generally, reimbursement rates are standard for primary-care based medical visits when treating opioid use disorder. However, insurance companies may cover a limited number of UDT and checking with them regarding coverage is important.

Conclusion

In the midst of an opioid overdose crisis, pediatricians are uniquely positioned to offer early treatment with medications for severe opioid use disorder. Throughout the US (particularly rural settings), subspecialty drug treatment is not available or impractical due to distance for many families; pediatric providers may be the only provider available to offer evidence-based addiction care. Pediatricians' focus on prevention coupled with their longstanding relationships with their patients and families provide the ideal opportunity to intervene, provide treatment and potentially prevent consequences of long-term opioid use disorder.

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TABLE 1.**Medication Initiation Checklist for Treatment of Severe Opioid Use Disorder**

At first visit	<ul style="list-style-type: none"> - Review of confidentiality - Opioid Use Disorder assessment and diagnosis - Assessment of other substance use disorders including tobacco use disorder - Discussion of treatment options - Laboratory tests: <ul style="list-style-type: none"> • CBC • Chemistry • Liver function • HIV • Syphilis • Hepatitis Panel (hepatitis A and C antibodies, hepatitis B surface antibody and surface antigen) • GC/chlamydia - For females: urine pregnancy test - Vaccinations¹ <ul style="list-style-type: none"> • Hepatitis A • Hepatitis B - Sign release of information to obtain information about prior treatment - Prescription for naloxone
If medication indicated, prior to medication initiation	<ul style="list-style-type: none"> - Sign treatment agreement and consent - Assessment for co-occurring mental health disorders - Refer to behavioral health (or offer within program) - Safe medication storage planning - Review urine drug testing expectations and visit frequency

¹: Confirm HBV and HAV immunity before vaccinating