Demystifying Buprenorphine Prescribing for Youth With Opioid Use Disorders
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National Institute on Drug Abuse
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Providers’ Clinical Support System – Opioid Therapies (PCSSO)
- Grant funded by SAMHSA
- Coalition of professional organizations
- Overarching goal: To offer evidence-based trainings on the safe and effective prescribing of opioid medications in the treatment of pain and/or opioid addiction.
- AAP = 2 Webinars per grant year (6 total)
- www.pcss-o.org

CME
CME credit is available for this Webinar upon completion of an evaluation.

More information will be provided near the end of this presentation.
The speaker has no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity. Dr Subramaniam does intend to discuss an unapproved/investigative use of a commercial product/device in this presentation.

Educational Objectives

At the conclusion of this activity participants should be able to:

- Describe the risk factors for and consequences of non-medical use of opioid medication in the pediatric population.
- Describe current treatment options for opioid use disorder (OUD).
- Learn the approach to office-based treatment with buprenorphine for detoxification and maintenance of remission for adolescent OUD.
- Implement an office-based treatment regimen with buprenorphine for adolescent OUD.
- List factors that impact treatment retention and effectiveness in these patients.
- Review the current training and DEA requirements for prescription of buprenorphine.

First Some Basics

- **Terminology**: Opium, opiate, opioid
- **3 OP Receptors**: Mu (MOP), Kappa (KOP) & Delta (DOP)
- **Types**:
  - Natural: morphine, codeine
  - Semi-synthetic: oxycodone, hydrocodone, heroin, buprenorphine
  - Synthetic: methadone, Fentanyl
**Adolescent Brain Development**

- Brain size peaks at 14-15y
- Increase in white matter (connectivity)
- Brain blood/oxygen flow in adolescence decreases into adulthood (i.e. the system is getting more energy efficient)

Adapted from slide by James Bjork, PhD


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**During Adolescence:**

**Brain Structures Governing Cognitive Control and Reward Behavior Are still Developing**

- Maturation/thinning of frontal cortex is last/delayed relative to other cortical areas

Adapted from slide by James Bjork, PhD

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**Drugs of Abuse Interfere with the Brain’s Natural Learning Circuits**

- Addiction could result from the “hijacking” of learning circuitry
- Drugs may cause the brain to artificially remember (learn) the high too strongly—people may then “want” the drug even though they no longer like the way it makes them feel.

Slide adapted from James Bjork, PhD

### Monitoring the Future (MTF) Study

#### Heroin Admissions in 2015:
by gender, age and ethnicity

<table>
<thead>
<tr>
<th>Year</th>
<th>Male</th>
<th>Female</th>
<th>% Male</th>
<th>% Female</th>
<th>% Male</th>
<th>% Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>2.4</td>
<td>2.6</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>2014</td>
<td>1.8</td>
<td>1.6</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
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<tr>
<td>2013</td>
<td>1.4</td>
<td>1.3</td>
<td>1.6</td>
<td>1.6</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>2012</td>
<td>1.2</td>
<td>1.3</td>
<td>1.4</td>
<td>1.4</td>
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**Note:** Data source: Johnston LD, et al., Monitoring the Future – National Results on Adolescent Drug Use: Overview of Key Findings, 2016.
Non-Heroin Opioid Admissions 2015: by gender, age and ethnicity

Age of First Use of Opioids

Treatment Episode Dataset (TEDS): 1992-2010
(youth treatment admissions for primary Opioid problem)

Percentage

11 and <11y 12-14y 15-17y 18-20y
4.8 32 53.2 12.2 51.4 33.2

Self-reported “Drug of First Choice”

Rx Opioid Users
Other Alcohol Marijuana Cocaine Rx Opioids Heroin

Heron Users
Subramaniam and Stitzer-Drug Alcohol Depend (2009)
What are the Characteristics of Youth With Opioid Use Disorder Presenting to Treatment?

- Older teen (> 16 y)
- Mostly male (but high proportion of female)
- Predominantly Caucasian (~ 90%)
- Poor Academic performance, drop out of school
- Reside in non-urban areas
- Higher rates of Multiple Substance use (cannabis most common)
- High rates of Psychiatric Disorders (> 70%)
- High Injection Drug Use among heroin users (40-70%)

Hopfer et al., 2000; Clemmey et al., 2004; Godrie et al., 2004; Marsch et al., 2005; Subramaniam and Atien, 2009; Subramaniam et al., 2009

DSM-5 Criteria for Substance Use Disorder

1. Use in larger amounts or for longer periods of time than intended
2. Unsuccessful efforts to cut down or quit.
3. Excessive time spent taking the drug
4. Failure to fulfill major obligations
5. Continued use despite knowledge of problems
6. Important activities given up
7. Recurrent use in physically hazardous situations
8. Continued use despite social or interpersonal problems
9. Tolerance
10. Withdrawal
11. Craving

Severity is designated according to the number of symptoms endorsed:
- 0 – 1: No diagnosis
- 2 – 3: Mild SUD
- 4 – 5: Moderate SUD
- 6 or more: Severe SUD

Physiologic Adaptations: Tolerance and Withdrawal

- Tolerance is the need for increasing amounts of the substance to achieve the desired effect.
- Withdrawal is a physiological response to a rapid decline in receptor binding, due to either rapidly decreasing concentrations of the opioid, or presence of a blocking agent.

Tolerance and withdrawal alone are not sufficient to make a diagnosis of addiction.
### Opioid Withdrawal Symptoms

<table>
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<tr>
<th>Early – 6 hours</th>
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Typically rated using “Clinical Opioid Withdrawal Scale (COWS)” or similar scale.

### Overview of Treatment for Opioid Use Disorder

<table>
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<th>Pharmacologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residential Treatment</td>
<td>Detoxification, buprenorphine, methadone, clonidine, “comfort meds”</td>
</tr>
<tr>
<td>Intensive Outpatient/Partial</td>
<td></td>
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<tr>
<td>12-Step Fellowships</td>
<td>Maintenance Agonist Therapy</td>
</tr>
<tr>
<td>Individual or Group Therapy</td>
<td>Methadone, buprenorphine (partial)</td>
</tr>
<tr>
<td>Family Therapy</td>
<td>Antagonist Therapy</td>
</tr>
<tr>
<td>Therapeutic School/Community</td>
<td>Naltrexone PO or IM</td>
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Opioid dependence is a chronic, relapsing neurological condition; patients who remain in long-term treatment generally do best. Supportive therapy combined with pharmacologic treatment seems to produce the best outcomes.

Adapted from a slide by Sharon Levy, MD, FAAP.

### Comparison of Receptor Activity Level: Full vs. Partial Agonist vs. Antagonist

Note: partial agonists never fully activate the receptor, even at very high doses.
Role of Pediatrician: Screen, Identify and Intervene

Use validated screening tool to identify risk level and appropriate intervention

- Positive Reinforcement
- Brief Health Advice
- Brief Intervention
- Referral to Treatment

Role of Pediatrician: Educate

- Easy to get from medicine cabinet: 62%
- Available everywhere: 52%
- Not illegal: 51%
- Easy to get through other people’s prescriptions: 50%
- Can claim you have a prescription if caught: 49%
- Cheep: 43%
- Easier to use than illegal drugs: 30%
- Less shame attached to using: 33%
- Easy to purchase over the Internet: 32%
- Fewer side effects than street drugs: 32%
- Parents don’t care as much if you get caught: 21%

AAP Policy

The AAP recommends that pediatricians consider offering pharmacological treatments to their adolescent and young adult patients with moderate/severe opioid use disorders and/or discuss referrals to other providers for this service.
CTN Study: Buprenorphine for Youth OUD
Opioid Positive Urines: 12 weeks Bup vs Detox
(Missing = Positive, N=152)

Drivers of Treatment Success

- **Abstinence from Opioids**: Early abstinence, staying in treatment, receiving additional non-study medications; baseline injection use and having severe medical/psychiatric problems
- **Retention in Treatment**: Early adherence to treatment, early opioid negative urine drug screen, any medication treatment in the month prior to study entry, non-heroin use. Lower retention: Emerging adults (vs. older adults). Daily dosing is associated with lower retention

Buprenorphine Formulations

- **Film Strips**
  - Brand name only.
  - Combination with naloxone
  - **Suboxone®** sublingual film. Available as 2(5.5), 4(1), 8(2) or 12(3) mg
  - **Bunavail®** buccal film. Available as 2.1 (0.3), 4.2 (0.7) or 6.3 (1) mg
  - Dissolve more rapidly than tablets (advantage for observed dosing)
  - Individually wrapped, reduces accidental ingestion by young children

**CAUTION**: Accidental ingestion of buprenorphine by young children may result in over sedation and respiratory depression. Individually wrapped films may reduce accidental ingestion.
Buprenorphine Formulations

- Tablets
  - Available as generic
  - Combo (buprenorphine/naloxone) and mono (buprenorphine) available
  - 2(5.5)/8 (2) mg formulations available
  - Newer 1.4(0.36)/5.7(1.4) menthol-flavored Zubsolv® tablets (combo)
  - Mono-product has higher misuse potential; indicated only in pregnancy.

CAUTION: Accidental ingestion of buprenorphine by young children may result in over sedation and respiratory suppression.

Begin with a Comprehensive Initial Evaluation

- Complete history of substance use, past treatments
- Medical history and review of systems
- Current medications and Allergies
- Brief Psychiatric History - Suicide/Depression/ADHD
- Psychosocial history including psychosocial support
- Physical exam
- OUD Diagnosis – DSM 5 criteria
- Treatment Plan, including medications prescribed
- Plan for Referral - Psychiatric disorders, Hepatitis-C infection, etc.

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Typically rated using “Clinical Opioid Withdrawal Scale (COWS)” or similar scale
Withdrawal Management

Buprenorphine is started when the patient is in active opioid withdrawal:
• Plan in advance as patients must be opioid-free for several hours and present in active withdrawal
• Offer ancillary medications (clonidine, ibuprofen, Pepto-bismol, Bentyl/other meds for stomach cramps)
• Use a treatment contract
• Be available for check-ins and dose adjustments in the first few days of withdrawal management

Sample Buprenorphine Contract

I agree to stop using all drugs, including opioids, alcohol, medications and other street drugs. I will request additional support if I am unable to treat drug abuse on my own.

Induction

• Ensure that young women are not pregnant
• Start medication when a COWS indicates moderate withdrawal (>8). Abstinence prior to starting buprenorphine
  • 12-18 hrs for short-acting opioids (heroin)
  • 24-36 hrs for sustained-release opioid medications
  • 36 hrs for methadone (30mg x 2 weeks; 15mg x 1 day; no methadone x 1 day; then induce on BUP/NX)
• Obtain a baseline urine drug screen
Induction

- Start with 2-4 mg. Observe the first dose (and demonstrate for parents)
- Rescore COWS after 45 min
  - If the score has decreased but still indicates moderate withdrawal, administer a second dose
- Some patients will have withdrawal symptoms controlled with 4 mg; for others consider a second 2-4 mg dose few hours later
- Advise the patient not to change the dose without speaking to a physician.
- Titrate dose to suppress withdrawal symptoms and cravings.

Buprenorphine
Side Effects and Drug Interactions

- Generally well tolerated when used as prescribed.
- Common side effects:
  - Headache
  - Nausea/vomiting
  - Constipation
  - Urinary retention/hesitancy
  - Drowsiness
  - Dry mouth
  - Perspiration
  - Sexual dysfunction/decreased libido
- It is very rare that one has to discontinue meds due to AEs
- Elevations in liver transaminases possible (rare, but patients with Hep C are at higher risk)
- Few clinically significant drug interactions; particularly uncommon in adolescents

Follow-up

- See patients frequently while on medication – weekly until a stable dose is achieved, and then at least monthly after that.
- Ask about medication adherence and side effects
- Evaluate and monitor mental health symptoms.
- Use patient history, parental report and drug testing to monitor sobriety and medication adherence.
- For patients on buprenorphine, titrate the dose to balance craving suppression and side effects.
  - Most adolescents will stabilize on a dose between 4 and 16 mg buprenorphine per day.
AAP Policy

- Urine drug testing may have a role in assessing adolescents for substance use disorders in certain circumstances, and in monitoring adolescents in treatment for an identified substance use disorder.
- Invasive
- Complex – potential for false positive false negative results
- Confidentiality issues
- Never be the sole basis for making a diagnosis

Maintaining and Terminating Medications

- The optimal length of time for medication treatment is not known.
- In adults longer duration of treatment is associated with better abstinence outcomes. There are no long-term studies in youth and the impact of exposure to long term agonists/antagonists on the developing brain are unknown.
- As a clinical rule of thumb, we recommend avoiding changing medications during periods of stress – final exams, summer vacation, high school graduation, etc.
- Patients who discontinue medications should continue in counseling and should be monitored closely for relapse for an extended period of time.

Preventing and Managing Relapse

- Encourage patients to remain abstinent from all substances to minimize the chance of a relapse to opioid use.
- Advise patients and parents to plan “structured time”
- If employed, advise parents to monitor income.
- Encourage patients and families to continue monitoring over the summer, as substance use tends to increase when kids are out of school.
- Maintain or increase prosocial/psycho-social activities over the summer: individual counseling, group programs, 12-step meetings, etc.
Psychiatric Care and Psychosocial Support

- Patients should be evaluated and treated concurrently for co-occurring psychiatric disorders. Integrated care or referral to specialty MH care.
- All patients in treatment for OUD should have regular psychosocial support via individual or group counseling with an experienced counselor.
- Behavioral treatment options: Motivational Interviewing/MET, Contingency management, CBT, family therapy, 12-step facilitation.
- 12-step meetings are free and universally available. Another option is SMART recovery.

Treatment of Opioid Overdose

Signs:
- Respiratory depression – usual cause of death
- Coma, pinpoint pupils (may dilate with hypoxia), hypothermia, non-cardiogenic pulmonary edema

Treatment:
- Naloxone (Narcan) nasal or IV, prn
- EVZIO® autoinjector application
- If no response, treat for sedative/hypnotic OD
- Single naloxone dose lasts 1-4 hours
- Naloxone may not work well for buprenorphine because of the higher receptor affinity.

Distribution of intranasal naloxone is a major public health initiative that has reduced mortality from opioid overdose. Patients and parents can fill a prescription for naloxone from the treating physician or receive naloxone and training from a local public health department.

Diversion and PDMP

Diversion refers to giving away or selling or giving a prescribed medication.

- There are 2 main situations in which diversion occurs:
  - Opioid-dependent individuals illegally purchasing buprenorphine to treat their dependence vs. non-opioid dependent individuals using buprenorphine for euphoria.
  - Teens may also sell or trade it for other drugs.

Prescription Drug Monitoring Programs (PDMP): are state-run electronic databases used to track the prescribing and dispensing of controlled prescription drugs to patients.

- Monitor lost prescriptions, requests for early refills or increasing dosage.
Parents

- Are often aware of the teen’s addiction (to opioids)
- Often benefit from education about opioids, complications, treatment options
- Can be encouraged play a supportive role – ensure adherence to medications, treatment, meetings, etc.
- May benefit from guidance on how to provide structure, support and positive reinforcement for success
- Patient confidentiality issues need to be respected
- Educated about overdose (OD) and OD prevention strategies
- May benefit from referral for personal treatment

Documentation
Follow-up Visits (Prescriptions)

- At Follow-up visits:
  - Self-report of substance use, not limited to opioids
  - Reports of medication adherence, side effects, cravings
  - Participation in school and/or work and establish goals
  - Participation in counseling, support groups
  - Urine drug tests and other lab tests, if indicated
  - Collateral report on progress (from parent or guardian) if available
  - Treatment plan including dose/changes to medications prescribed
- Prescribers must keep a record of every prescription written for each patient.
- The DEA periodically audits buprenorphine prescribers to insure best practices are maintained

Confidentiality
Teens Presenting With Parents

- In many cases, especially those with OUD, adolescents will present for treatment with the knowledge, and often with the support, of parents.
- Managing confidentiality is a clinical decision. Consider:
  - Sharing clinical impressions and treatment recommendations.
  - Involve parents if a teen’s behavior puts him/her in acute danger. Parents can be taught to effectively monitor and support recovery.
  - Avoid sharing details that are not directly relevant to treatment.
  - Parents have access to medical records and may seek information if they desire.
Confidentiality Laws

- Rules regarding “emancipation” or “mature minors” which allow children under the age of majority (usually 18y) to obtain medical care are dictated by states. Check with a lawyer or other expert regarding local law.
- In most states, minors can access substance abuse services without parental consent.

NOTE: Treating without specific parental consent does not guarantee confidentiality. In fact, protecting confidentiality between adolescent and parent can be particularly difficult. Therefore we recommend involving a parent in treatment whenever possible, though in most cases involving parents is best treated as a treatment goal rather than a requirement.

Confidentiality
HIPPA and Title 42 CFR Part 2

- In a general primary care setting, “HIPPA” rules guide the confidentiality protection of medical records, including information pertaining to substance use.
- Records for treatment of OUD should be handled similarly to other confidential information, such as information about substance use in other patients.
- For substance abuse programs, federal confidentiality regulations (“42 CFR Part 2”) supersede HIPPA. If federal confidentiality rules apply, a minor must sign a consent form for a program to release information to his or her parent or guardian.

DATA 2000

- Waivers to provide office-based opioid dependence treatment (OBOT)
- Any physician eligible to apply for a waiver to prescribe buprenorphine for opioid dependence after completing 8 hours of “waiver” training
- Amendment: Prescribers must limit their practice to the allowable number of buprenorphine patients: up to 30 in the first year, up to 100 after the first year if the provider has obtained a waiver.
- 2016 Comprehensive Addiction and Recovery Act (CARA) extends buprenorphine prescribing privileges to qualifying NPs and PAs who complete 24 hours of specific training and apply for waiver

To date, few pediatricians have obtained waivers. Some teens may get treatment from adult providers, though there is often a gap in treatment services for younger teens.
Ready to Get Waivered? 
Training Opportunities

• Online Training for AAP Members: [www.aap.org/mat](http://www.aap.org/mat)

• Webinar Training: 
  June 28, 2017 5pm-9:30pm Pacific  

• Half & Half Courses (online & in-person) 
  July 18, 2017 1pm-5pm 
  Washington, DC  
  [pcsmat.org/event/half-and-half-pediatric-mat-waiver-training](http://pcsmat.org/event/half-and-half-pediatric-mat-waiver-training)

Or…
Request a Training in Your Community

• The AAP can identify a trainer for you. 
• The AAP can help support room rental and AV needs. 
• Email requests to: 
  [substanceuse@aap.org](mailto:substanceuse@aap.org)

Q & A

• Please use the chat box to submit a question for the speakers. 
• Obtaining CME 
  • After the event, you will receive a link taking you to an evaluation. Upon completion, you will be emailed your CME certification. 
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  • The American Academy of Physician Assistants (AAPA) accepts certificates of participation for educational activities accredited by ACCME. Physician assistants may receive a maximum of 1.0 hours of Category 1 credit for completing this program. 
  • This program is accredited for 1.0 NAPNAP CE contact hours of which 0 contain pharmacology (Rx), 0 related to psychopharmacology, 0 related to controlled substances, and 0 related to other. 
  • For information on how to obtain the National Association of Pediatric Nurse Practitioners (NAPNAP) Continuing Education Substantiated Credit, contact the National Association of Pediatric Nurse Practitioners (NAPNAP) Continuing Education Substantiation.
PCSS-O Colleague Support Program and Listserv

- PCSS-O Colleague Support Program is designed to offer general information to health professionals seeking guidance in their clinical practice in prescribing opioid medications.
- PCSS-O Mentors comprise a national network of trained providers with expertise in addiction medicine/psychiatry and pain management.
- Our mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.
- The mentoring program is available at no cost to providers.

For more information on requesting or becoming a mentor visit: www.pcss-o.org/colleague-support

- Listserv: A resource that provides an “Expert of the Month” who will answer questions about educational content that has been presented through PCSS-O project. To join email: pcss-o@aaap.org

For more information on requesting or becoming a mentor visit: www.pcss-o.org

PCSS-O is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with Addiction Technology Transfer Center (ATTC), American Academy of Neurology (AAN), American Academy of Pain Medicine (AAPM), American Academy of Pediatrics (AAP), American College of Physicians (ACP), American Dental Association (ADA), American Medical Association (AMA), American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA), American Society for Pain Management Nursing (ASPNN), International Nurses Society on Addictions (INNSA), and Southeast Consortium for Substance Abuse Training (SECSAT).

For more information visit: www.pcss-o.org

For questions email: pcss-o@aaap.org

Twitter: @PCSSProjects

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