Opioid Replacement Therapy for Adolescents and Young Adults

Adolescent Substance Abuse Program
Center for Adolescent Substance Abuse Research
Children’s Hospital, Boston

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Supplemental Materials

This module is a part of a curriculum designed to introduce clinicians to adolescent Screening, Brief Intervention and Referral to Treatment (SBIRT), and provide them with tools and knowledge to efficiently and effectively address adolescent substance use in the primary-care setting. The curriculum is intended to build upon the core SBIRT Overview module, and includes:

- **SBIRT Overview**
  - Brief Motivational Interviewing
  - Confidentiality
  - Parent Guidance
  - ADHD and Substance Use Disorders
  - Pain and Addiction
  - Drug Testing

- **Buprenorphine Treatment of Opioid Dependence**
  - Club Drugs
  - Infectious Diseases
  - Neurobiology of Alcohol and Marijuana Addiction
  - Smoking Cessation

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Goals

Review
• opioid pharmacology
• epidemiology opioid dependence
• pharmacologic treatments for opioid dependence

Present
• best practices for opioid replacement therapy
The human body produces endorphins which bind the mu-receptor resulting in pleasure, satisfaction, a sense of well-being and pain relief. Naturally occurring opioids found in plants (also called opiates) include morphine, codeine and opium. Heroin, also called di-acetyl morphine a semi-synthetic molecule that crosses the blood-brain barrier and is quickly metabolized to morphine. Synthetic opioids include narcotic pain medications such as oxycodone and hydrocodone.
Opioid receptors are densely located in several locations in the CNS.

- Prefrontal cortex: executive functions
- Limbic system: pleasure and reward; binding here plays a critical role in addiction.
- Brainstem: respiratory control; this is the pharmacologic target for cough suppression, and also responsible for respiratory arrest with overdose.
- Spinal cord, and enteric nervous system: these are the pharmacologic target for relief of pain and diarrhea.
The opioid receptor is physiologically dynamic. Spinal cord receptors become available immediately after acute tissue injury and become the primary binding site.

Injured patients can tolerate high doses of opioids without experiencing a “high” or overdose. The same individual might later overdose on a dose that was well tolerated while in pain. Patients treated for pain who do not experience a “high” are at low risk of becoming addicted to opioids.
Misuse (or non-prescribed use) of narcotic pain medications has increased dramatically in the past 10 years, in conjunction with the development of newer, stronger medications.


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Lifetime Misuse of Opioids Among 12th Graders

Lifetime recreational use of prescription pain medication by 12th graders rose dramatically between 1993 and 2003, and has subsequently leveled off at approximately 13%.

Nearly half of all new recreational users of prescription pain medications are under 18.


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Adolescents surveyed by the Partnership Attitude Tracking Study report reasons for misuse of Rx pain medications as the result of their **Availability**, the **Lack of Consequences** involved with use, and the **Perceived Safety**.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy to get from medicine cabinet</td>
<td>62%</td>
</tr>
<tr>
<td>Available everywhere</td>
<td>52%</td>
</tr>
<tr>
<td>Not illegal</td>
<td>51%</td>
</tr>
<tr>
<td>Easy to get through other people’s prescription</td>
<td>50%</td>
</tr>
<tr>
<td>Can claim to have a prescription if caught</td>
<td>49%</td>
</tr>
<tr>
<td>Cheap</td>
<td>43%</td>
</tr>
<tr>
<td>Safer to use than illegal drugs</td>
<td>35%</td>
</tr>
<tr>
<td>Less shame attached to using</td>
<td>33%</td>
</tr>
<tr>
<td>Easy to purchase over the Internet</td>
<td>32%</td>
</tr>
<tr>
<td>Fewer side effects than street drugs</td>
<td>32%</td>
</tr>
<tr>
<td>Parents don’t care as much if you get caught</td>
<td>21%</td>
</tr>
</tbody>
</table>
## Access to Pain Medication

<table>
<thead>
<tr>
<th>% or responders who strongly/somewhat agree</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription drugs are available everywhere</td>
<td>42</td>
<td>55</td>
<td>38</td>
</tr>
<tr>
<td>It is easy to get prescription drugs from parent’s medicine cabinets</td>
<td>56</td>
<td>63</td>
<td>47</td>
</tr>
<tr>
<td>Most teens get prescription drugs from their own family’s medicine cabinets</td>
<td>59</td>
<td>62</td>
<td>51</td>
</tr>
<tr>
<td>Most teens get prescription drugs from their friends</td>
<td>53</td>
<td>62</td>
<td>49</td>
</tr>
</tbody>
</table>

The Partnership for a Drug-Free America: The Partnership Attitude Tracking Study (PATS) 2010. N= 2,544; grades 7th to 12th

Following a sharp rise between 2008 and 2009, the perceived availability of Rx drugs with abuse potential has declined substantially. Still, nearly half of 7th through 12th graders report that Rx drugs are easily obtained from friends and at home.
Heroin

- Heroin is the most powerful opioid because it rapidly crosses the blood-brain barrier resulting in rapid delivery of morphine.
- Increased purity of heroin since the 1990’s has made snorting or smoking practical alternatives to injecting and lowering the barrier to initiate use.
- Use of any opioid results in tolerance, requiring users to increase the dose to maintain effect. Because heroin is much cheaper than pain medication, many users switch when they can no longer afford other opioids.


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Between the periods of 2002-2005 and 2009-2011, the average annual number of heroin users has increased 1.6-fold. The average number of heroin dependent young adults has more than doubled.
# Overview of Treatment for Opioid Dependence

<table>
<thead>
<tr>
<th>Non-pharmacologic</th>
<th>Pharmacologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residential treatment</td>
<td><strong>Detox</strong> methadone, buprenorphine, clonidine,</td>
</tr>
<tr>
<td></td>
<td>“comfort meds”</td>
</tr>
<tr>
<td>Intensive outpatient/partial</td>
<td><strong>Opioid antagonism</strong> naltrexone PO or IM</td>
</tr>
<tr>
<td>12 step fellowships</td>
<td></td>
</tr>
<tr>
<td>Individual or group therapy</td>
<td><strong>Replacement therapy</strong> methadone, buprenorphine</td>
</tr>
<tr>
<td>Family therapy</td>
<td></td>
</tr>
<tr>
<td>Therapeutic school/community</td>
<td></td>
</tr>
</tbody>
</table>

Opioid dependence is a chronic, relapsing neurological condition in which patients develop an uncontrollable compulsions. Patients can recover but as with other chronic conditions, to do well they should remain in long term treatment. Supportive therapy combined with pharmacologic treatment seems to produce the best outcomes.
Pharmacologic treatment options

- **Detoxification**: eases discomfort associated with withdrawal. Includes “comfort medications” such as ibuprofen, trazodone and clonidine for symptomatic relief.

- **Opioid antagonism**: “blocks” opioid receptor so patients cannot get high. Naltrexone used for long term treatment can be given PO or IM.

- **Opioid Replacement therapy**: long term treatment aimed at quelling cravings, improving functioning and reducing relapse rates. Options include methadone (full agonist) and buprenorphine (partial agonist).
Buprenorphine binds the mu-opioid receptor and has action in-between full agonists (such as heroin) and complete antagonists (such as naloxone or naltrexone). Buprenorphine also has greater receptor affinity (binds more tightly) than most full agonists. In patients who recently used a full agonist opioid, buprenorphine administration may precipitate a painful and uncomfortable withdrawal.


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Naltrexone

• Decrease risk of overdose/death
• Decrease IV drug use
• Improve functional status
• Block euphoric effect of exogenous opioids
• Suppress cravings

In 2010 Naltrexone was approved by the FDA for treatment of opioid dependence. The main mechanism of action is blockade of the mu-receptor, though data have shown that naltrexone also suppresses cravings. Naltrexone may be a particularly good option for individuals who have used buprenorphine for euphoria. The intra-muscular option limits diversion and requires less supervision. The main risks include liver toxicity and accidental overdose if a patient tries to overcome the blockade with large opiate dose.

Methadone was the first medication approved for opioid replacement and has been used successfully since the 1970’s. Most patients remain on methadone replacement for life. Methadone can only be prescribed for opioid replacement through specialized “methadone clinics”, which are often stand-alone and not associated with medical facilities. Patients receive daily observed therapy which improves adherence but can be a barrier to other aspects of daily life. To qualify for methadone a patient must have at least one year history of opioid dependence. Many methadone clinics will not accept minors under age 18.
Buprenorphine

- Decrease risk of overdose/death
- Decrease IV drug use
- Suppress withdrawal and cravings
- Block euphoric effect of exogenous opioids
- Improve functional status

In 2000, the Federal government passed the “Drug Abuse Treatment Act (DATA)” allowing physician’s to prescribe buprenorphine as opioid replacement therapy from their offices after completing 8 hours of specialized training and obtaining a waiver from the DEA. The goal of DATA was to increase access to treatment for opioid dependent individuals, especially those who were not good candidates, or not inclined to use methadone. To date, few pediatricians or child psychiatrists have obtained waivers and access for adolescents remains a problem.
Benefits of Office-Based Treatment

• Confidential, safe & effective treatment provided in a doctor’s office; less exposure to more experienced users
• Fits lifestyle: no daily clinic visits or out-of-town, costly residential treatment
• More time for school, work, family & other activities
• Allows for parental involvement/ support
Suboxone: Buprenorphine/Naloxone

The combination of naloxone with buprenorphine reduces abuse potential. Naloxone is not absorbed when dose is taken sublingually but will be active if snorted or injected.
Buprenorphine formulations in the USA

- “Buprenorphine hydrochloride/Naloxone” combination tablets
  - 2mg (2mg buprenorphine / 0.5mg naloxone)
  - 8mg (8mg buprenorphine / 2mg naloxone)
  - 12mg (12mg buprenorphine / 3mg naloxone)
- “SUBOXONE®” film strips
- “SUBUTEX®” 2mg or 8 mg buprenorphine
NIH consensus statement

• Medical withdrawal is not associated with long term abstinence. Detoxification is considered a preparatory step and NOT a stand alone treatment.

• Opioid replacement therapy is an effective treatment for opioid dependence.

• Buprenorphine is a pharmacologically safer and similarly effective alternative to low-dose methadone. Buprenorphine can be discontinued without significant withdrawal, and patients can be more easily transferred to opioid antagonist treatment.


Published Trial #1
Comparison of Pharmacological Treatments for Opioid-Dependent Adolescents

- Compare relative efficacy of buprenorphine and clonidine for 28- day detoxification of opioid-dependent youth
- Randomized controlled trial; double-blind, double-dummy design
- Participants 13-18 years old, n=36
- All participants received counseling in addition to meds

Behavioral Interventions

- **Individual and family therapy**: based on Community Reinforcement Approach
- **Contingency Management**: incentives based on results of 3x weekly urinalysis & clinic attendance
- **Outreach component**: engage adolescents in recreational & other pro-social activities

Patients who received buprenorphine were significantly more likely to remain in treatment at 4 weeks.


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Patients who received buprenorphine had significantly more opiate negative urines over the course of the 4 week program.

A greater percentage of participants who received buprenorphine initiated naltrexone-HCl treatment after completing the 4 week detoxification trial.

Both groups significantly decreased drug related HIV risk behaviors by the end of the first week of treatment.

Summary of Findings

Compared to clonidine, patients who received 4 weeks of buprenorphine treatment:

- Had fewer positive drug tests
- Stayed in treatment longer
- Were more likely to continue pharmacologic treatment after the 4 week trial period

Published Trial #2
Extended vs. Short-term Buprenorphine-Naloxone for Treatment of Opioid-Addicted Youth

• Randomized-controlled trial
• 2-week detox vs 12-week treatment
• All patients also received 2 counseling sessions (1 individual and 1 group) for 12 weeks
• Participants 15-21 years old, n=156

Opioid-Negative Urine Samples

Percent of opioid (-) urines

Week 4: P<.05
Week 8: P<.05


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Patients in the 12 week group had a lower percentage of opioid-positive urine test results over time though the differences decreased once the buprenorphine taper began at week 8. The 12-week buprenorphine treatment group also had higher retention rates (70%; n=52) than the detox group (20.5%; n=15).


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Summary of Findings

• 12-week treatment with buprenorphine-naloxone improved outcomes compared with 2-week detoxification.

• Further research is necessary to assess the efficacy and safety of longer-term treatment with buprenorphine for adolescents with opioid dependence.

Kevin

Kevin is a 17 year old boy who is seeking opioid replacement treatment. He does not want his parents to know about his drug problem and has requested confidentiality.
Confidentiality between teen and parent

- Adolescents have the right to request substance abuse treatment without parental knowledge or consent, though teens do better in treatment with family support.
- Ask Kevin reasons for not including his parents in treatment; screen for the possibility of domestic violence if drug use is revealed.
- Set parental involvement as a treatment goal. Offer to help the adolescent give news to parents.
If teen refuses to involve parents

- Remind teens that safety is the limit of confidentiality.
- Tell patients that you cannot lie to their parents.
- Explore plans for keeping treatment hidden.
- Discuss issues of insurance explanation of benefits for office visits and medications if parent provides insurance coverage.
If patient agrees to share information

- Discuss beforehand what and how information will be shared.
- Offer to support teen by being present for the disclosure or initiating it.
Roles for parents in treatment

- Monitor each medication intake (one prescriber, one pharmacy). Consider IM Naltrexone if parent involvement is not possible.
- Support on treatment compliance, including drug testing, clinic visits and psychosocial support.
- Give praise and support for drug-free weeks and remaining in treatment.
Opioid replacement best practices

- Use a treatment contract
- Insist on releases to contact every member of the treatment team
- Encourage patients to work towards abstinence from all substances; warn of the danger of mixing sedatives
- Additional treatment recommended for patients who continue to use substances other than opioids


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Induction

- Start when patient is in withdrawal
- Directly observe the induction
- Use the Clinical Opioid Withdrawal Scale (COWS) to assist in determining dose
- Re-score 45 minutes after each dose. If a score increases after the initial dose of medication stop the induction and refer to detox
- Use the lowest dose that eliminates withdrawal
Maintenance and Monitoring

- Patients should not skip or adjust doses without MD consultation.
- Titrate dose to manage cravings; evaluate at least weekly until a stable dose has been achieved.
- Manage side effects: constipation, urinary retention, nausea, drowsiness, sexual dysfunction.
Monitoring

• Require random drug testing to monitor for compliance and use of illicit drugs
  – Include an opioid panel
  – Include buprenorphine
  – Include ethyl glucuronide to monitor for alcohol use
• Consider missed or adulterated tests positive
Jennifer

• 16 year old girl with one year history of opioid use.
• She was recently caught by her parents who insisted that she go to a detox program. During detox she decided that it was time for her to quit using opioids.
• Presents for an evaluation for opioid replacement therapy.
• Her history is also significant for use of marijuana multiple times a day for the past 4 years.
Encourage Abstinence

- Ask patients to work towards abstinence from all substances.
- Discontinue buprenorphine for patients who cannot quit alcohol or sedative use.
- For other substances continue motivational interviewing. Use “harm reduction” and reduced use as stepping stones.
- Have patients discuss their own contingency plan.
- Add treatment for patients who want to quit other substances but cannot.
- Discuss the importance of abstinence with parents.
- Patients kept on buprenorphine as long as they are not using opioids.

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Tapering

• There is no maximum duration of treatment
• Encourage patients to remain on maintenance for at least one year of sobriety, or explore reasons for tapering
• Taper slowly (over months)
• Continue monitoring and counseling during and after taper
• Encourage patients to remain connected with some form of treatment for life

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Opioid Use During Treatment

This Kaplan-Meyer curve shows decreasing opioid use over time with continued opioid replacement therapy. Daily (purple) and less-than-daily (hash) illicit narcotic use rates decrease through the first 6 years of treatment at which point they appear to stabilize.

The Drug Abuse Reporting Program (DARP) study results show that continued methadone maintenance treatment dramatically decreased use of illicit narcotics and improved behavioral functioning in the first six years of community clinic treatment.

Maintenance and Beyond

• Encourage the patient and family to continue meds until drug-free for at least one year.
• Use a slow taper; involve the patient in deciding when to drop the dose.
• Continue drug testing and follow-up visits after medication has been discontinued.
• Discuss plans for recovery after discharge: AA/12-step, individual counseling, etc.
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PI: Sharon Levy
Adolescent Substance Abuse Program, Division of Developmental Medicine
Boston Children’s Hospital

Module Authors
Sara Forman, Susan Gray, Sion Kim Harris, Marianne Pugatch, Miriam Schizer, Patricia Cintra
Franco Schram

Other Contributors
Kate Ginnis, John Knight, Enrico Mezzacappa, Christina Nordt, Roman Pavlyuk, Lon Sherritt, Shari Van Hook, Zohar Weinstein, Rosemary Ziemnik

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