Treatments for Adolescents/Young Adults with Opioid Use Disorder

Webinar
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Opioid Pharmaceuticals - Then
Opioid Pharmaceuticals – and Now
Opioids: Heroin
Prevalence
Heroin Use From 1991-2007 (MTF)

Annual Use Prevalence: 8th and 12th Graders

Non-Medical Prescription Opioid Use

MTF: Annual Use Prevalence 12th Graders

New Non-Medical Users of Prescription Opioids, By Age Group: 2002-2007

Source: NSDUH 2003-2007
Opioids and Brain Mechanisms
Opioid Addiction

- Opioids attach to specific receptors - **mu** receptors.
- Activation of these receptors - a **pleasure response**.
- Repeated stimulation of these receptors leads to **tolerance** - requiring more drug for same effect.
Adolescent Brain
Dynamic sequence of gray matter maturation over the cortical surface

Giedd et al., JAACAP 2009
In a developing nervous system

- Difficulty in decision making
- Difficulty understanding consequences of behavior
- More vulnerable to memory and attention problems

*In the Context of Drug Abuse:*

- Less susceptible to intoxication
- Animal studies show greater self-administration, and therefore higher rates of drug dependence
Clinical Characteristics of Adolescents with OUD
Terminology

- Use
- Abuse
- Dependence
- Substance Use Disorder = Abuse or Dependence
## An Overview of Published Studies

<table>
<thead>
<tr>
<th>Samples</th>
<th>Treatment</th>
<th>Community</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of opioid</td>
<td>Heroin</td>
<td>Rx Opioid</td>
</tr>
<tr>
<td>Age</td>
<td>16-22yrs</td>
<td>&gt;16years</td>
</tr>
<tr>
<td>Gender</td>
<td>15-48% Female</td>
<td>More male</td>
</tr>
<tr>
<td>Race</td>
<td>Mostly White</td>
<td>Mostly White</td>
</tr>
<tr>
<td>School</td>
<td>Poor attendance</td>
<td>Lower performance</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>41% clinical Dx</td>
<td>-</td>
</tr>
<tr>
<td>Polysubstance</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Legal Problems</td>
<td>Common</td>
<td>30-87% sold drugs</td>
</tr>
<tr>
<td>% IDU</td>
<td>45-75</td>
<td>5-6</td>
</tr>
</tbody>
</table>

[Hopfer et al., 2000; Clemmey et al., 2004; Gordon et al., 2004; Marsch et al., 2005; Pugatch et al., 2001; McCabe et al., 2005; Sung et al., 2005]
## Demographics & Social Characteristics

<table>
<thead>
<tr>
<th>Matching Criteria:</th>
<th>OUD (94)</th>
<th>Comparison (72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% 18 year-olds</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>% Female</td>
<td>45</td>
<td>35</td>
</tr>
<tr>
<td>% Residential setting</td>
<td>69</td>
<td>76</td>
</tr>
<tr>
<td>% Past 30 D Cocaine use*</td>
<td>46</td>
<td>22</td>
</tr>
<tr>
<td>(50 Cocaine Matched cases)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Caucasian Race*</td>
<td>89</td>
<td>51</td>
</tr>
<tr>
<td>% Baltimore City Residence*</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>% Still in School*</td>
<td>38</td>
<td>60</td>
</tr>
<tr>
<td>% Court Ordered</td>
<td>18</td>
<td>27</td>
</tr>
<tr>
<td>% on Probation</td>
<td>35</td>
<td>44</td>
</tr>
<tr>
<td>% Guardian both parents</td>
<td>19</td>
<td>23</td>
</tr>
</tbody>
</table>

* Denotes statistical significance

Subramaniam et al.-Drug Alcohol Depend (2009)
Meeting DSM-IV Criteria Past Year (Non-nicotine/non-opioid) Substance Use Disorders

Results based on The Composite International Diagnostic Interview (CIDI)
Meeting DSM-IV Criteria for Current Psychiatric Disorders

Results based on The Diagnostic interview for children and adolescents (DICA)
Among OUD Youth: Age of Onset Issues

- Cann/Alc use d/o = 14 y (onset regular use = 12.7-13.5 y)
- OUD = 15.3 y (onset reg. use = 15.1 y)
- Coc use d/o = 15.7 y* (onset reg use = 15.3 y)

- ODD/CD/hypomania/mania = 10.3-11.1 y
- GAD = 11.8 y
- MDE = 13.1 y
- PTSD = 13.9 y

Subramaniam et al.-Drug Alcohol Depend (2009)
<table>
<thead>
<tr>
<th>HIV Risk Behaviors (Past 30 Days)</th>
<th>OUD</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Any Injection Drug Use*</td>
<td>41</td>
<td>01(n=1)</td>
</tr>
<tr>
<td>% Sharing Needles *</td>
<td>51</td>
<td>-</td>
</tr>
<tr>
<td># Times sharing needles *</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>% Sexually active</td>
<td>76</td>
<td>81</td>
</tr>
<tr>
<td>% Always Unprotect. Sex</td>
<td>41</td>
<td>29</td>
</tr>
<tr>
<td>% 2 or &gt; sex partners</td>
<td>38</td>
<td>35</td>
</tr>
</tbody>
</table>

* Denotes statistical significant differences
Study Summary

OUD youth more likely to be
- Caucasian, older teens
- Live outside Baltimore city
- Drop out of school
- Concurrent other SUD and 3 or > SUD
- IDU-related HIV/Hepatitis-C risk
- Rapid progression to OUD

But similar to Cann/Alc use d/o youth
- high rates of psychiatric disorders
- high rates of sexual-risk behaviors
- high rates of illegal behaviors

Subramaniam et al.-Drug Alcohol Depend (2009)
Self-reported “Drug of First Choice”
Treatment Options
Treatment Options for Adolescent OUD

I. Pharmacological:
- Buprenorphine
- Methadone
- Naltrexone

II. Psychosocial:
- Short-term residential treatment (ASAM Level III, non-specific SUD treatment)
- Therapeutic community
- Contingency management
- Individual and group counseling
Short-Term Residential Treatment Outcome (Baltimore Site)

Percent of Days Used Alcohol or Other Drugs

Clemmey et al., 2004: CSAT Adolescent Treatment Models
Medication-assisted Treatments
Full Agonist, Partial Agonist, and Antagonist of Opioids

Intrinsic Activity

Log Dose of Opioid

Full Agonist (Methadone, Heroin, oxycodone)

Partial Agonist (Buprenorphine)

Antagonist (Naltrexone)
Buprenorphine: Preparations and Characteristics

- Buprenorphine combined with naloxone, marketed as Suboxone®,
- Naloxone is not absorbed sublingually/orally but would precipitate withdrawal if injected
- Subutex® - stand alone preparation
- Suboxone®, available in 2mg and 8mg tablets.
- Suboxone is to be placed under the tongue and must be allowed to dissolve sublingually
First Controlled Trial using Buprenorphine for Adolescent OUD

Marsch et al, 2005

- Sample: 38, 13-17 y o.
- Duration: 28-day detox
- Treatment Groups: 6-8mg buprenorphine SL vs. Clonidine 0.1-0.3mg P.O.

Results:
- Greater Treatment retention (Bup vs. clon) (72% vs. 39%)
- > percent of opioid negative urines (64% vs. 32%)
NIDA CTN – Multisite Study Design

Screening (N=236)

Randomization (N=154)

Detox (n=80)

Completed Tx (n=16)

Included in Primary Analysis (n=78)*

*2 excluded (never entered tx)

Withdrew (n=62)

12-Week (n=74)

Completed Tx (n=52)

Included in Primary Analysis (n=74)

Withdrew (n=22)

Woody et al., JAMA 2008
Primary Outcome: Percent of Opioid-Positive Urine Test

![Graph showing observed and missing data imputed for posttreatment phase.](image)

No. of patients
- Detox: 78, 59, 53, 53
- 12-Week: 74, 58, 52, 49

Lessons Learned

- Longer treatment seems to be better.
- Compared to 2-week detox group, the 12-week group showed:
  - Fewer opioid positive urines
  - Greater retention in active treatment phase
  - Lowered use of marijuana and cocaine use and injection drug use
  - Effect only during active treatment with buprenorphine
Buprenorphine Tx – A Flow Diagram

- **Screening**
  - 10 minutes
  - Physician/Other clinician

- **Formal Assessment**
  - 1-3 days
  - Trained professional
  - Co-occurring psychiatric disorder
  - Determine level of care, eligibility

- **Induction**
  - 2-7 days
  - Initial dose finding, counseling optional
  - Benefits authorization

- **Stabilization**
  - 7-90 days
  - Dose adjusted + Counseling
  - Length of treatment is established

- **Ongoing Treatment**
  - Length of treatment variable
  - On-going Medication
  - Counseling as needed
Treatment Phases

- Detoxification
  - Not effective as stand alone (Mattick, 1996)
  - High rates of relapse (Broers 2000, Vaillant, 1988)

- Maintenance

- Medication-free
Future Directions

- Are there differences in Tx outcomes between Rx opioid and heroin users?
- Additional questions regarding buprenorphine Tx - duration, dosing, medication compliance issues, etc.
- Is naltrexone effective for this age group? Will it be better accepted?
- Explore other psychosocial treatments as platform treatments – e.g. CM
- Examine integration of psychiatric and HIV-risk reduction treatments
Online Resources
How Buprenorphine Works

Opioid receptor is empty. As someone becomes tolerant to opioids, they become less sensitive and require more opioids to produce the same effect. Whenever there is an insufficient amount of opioid receptors activated, the patient feels discomfort. This happens in withdrawal.

Opioid receptor filled with a full-agonist. The strong opioid effect of heroin and painkillers can cause euphoria and stop the withdrawal for a period of time (4-24 hours). The brain begins to crave opioids, sometimes to the point of an uncontrollable compulsion (addiction), and the cycle repeats and escalates.

Opioids replaced and blocked by buprenorphine. Buprenorphine competes with the full agonist opioids for the receptor. Since buprenorphine has a higher affinity (stronger binding ability) it expels existing opioids and blocks others from attaching. As a partial agonist, the buprenorphine has a limited opioid effect, enough to stop withdrawal but not enough to cause intense euphoria.

Over time (24-72 hours) buprenorphine dissipates, but still creates a limited opioid effect (enough to prevent withdrawal) and continues to block other opioids from attaching to the opioid receptors.

The above illustrations are for educational purposes and do not accurately represent the true appearance.

The National Alliance of Advocates for Buprenorphine Treatment
naabt.org

naabt.org • naabt.org • naabt.org • naabt.org • naabt.org • naabt.org • naabt.org • naabt.org

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The **CTN DISSEMINATION LIBRARY** is a digital repository of resources created by and about NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN). It provides CTN members and the public with a single point of access to research findings and other materials that are approved for dissemination throughout the CTN and to the larger community of providers, researchers and policy-makers.

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- CTN Nodes & Community Treatment Programs (CTPs)
- NIDA's CTN web site
- CTN Member Directory (2006)

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### New in the Library
**Issues in Designing and Implementing a Spanish-Language Multi-Site Clinical Trial**

**Quality and Performance Improvements: What's a Program to Do?**
by Frank McCorry. (NIDA Science & Practice Perspectives 2007;3(2):37-47.)

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### CTN Meetings
**Steering Committee, Sept 23-28, 2007. Marriott Bethesda North. (North Bethesda, MD).**

**Blending Addiction Science & Practice: Bridges to the Future, October 16-17, 2006, Seattle.**
View the presentation slides.
What is the Physician Clinical Support System? (PCSS)

The SAMHSA-funded PCSS is designed to assist practicing physicians, in accordance with the Drug Addiction Treatment Act of 2000, in incorporating into their practices the treatment of prescription opioid and heroin dependent patients using buprenorphine.

The PCSS service is available, at no cost, to interested physicians and staff, to assist in implementing office-based treatment of opioid dependence with buprenorphine. The essential elements of the PCSS are a national network of trained physician mentors with expertise in buprenorphine treatment and skilled in clinical education, who will be supported by NATIONAL EXPERTS in the use of buprenorphine and a MEDICAL DIRECTOR.

The PCSS MENTORS are members of medical specialty societies and provide mentoring support and educational services based on evidence-based practice guidelines. The efforts of PCSS are coordinated by a STEERING COMMITTEE composed of representatives from the Federal government, the leading addiction medicine societies, along with primary care and psychiatric organizations that represent the target physician populations.

It is estimated that in its first year of operation the PCSS will provide clinical support services to primary care physicians, pain specialists, psychiatrists, and other non-addiction medical practitioners in an effort to increase access to this form of treatment. The PCSS serves to significantly increase access to buprenorphine treatment among the millions of untreated opioid dependent patients.

The PCSS is designed to offer support to clinicians on a number of TOPICS. The PCSS is active in 48 states, Washington DC, and Puerto Rico. Click here or on the image below to see the PCSS ACTIVITIES MAP.