Treatment for Opioid Dependence in Adolescents and Young Adults

Marc Fishman MD
Johns Hopkins University Dept of Psychiatry
Mountain Manor Treatment Center, Baltimore MD

CSAM
10/9/09
Disclosure

• Maryland Treatment Centers: Equity interest, Salary
• International Center for Health Concerns: Consultant
• Center for Substance Abuse Treatment: Treatment Grant
• National Institute on Drug Abuse; Research Grant
Outline

• Background - prevalence and scope of the problem
• Previous experience: high severity and relapse
• Pharmacotherapy
  – Detoxification
  – Buprenorphine
  – Extended release naltrexone
• Program model: Integrating pharmacotherapy and counseling
What we’re up against -
The common view of our patients

- Bad Kids
- Derelicts
- Thugs
- Little monsters
- Incurables and hopeless cases
- Therapeutic nihilism is the rule

We have an (almost) impossible job, but who would do anything else?
What we’re up against - The culture

Drug dealing just to get by
Stack your money till it gets sky high
Kids sing, kids sing
We weren’t supposed to make it past 25
Joke’s on you we’re still alive
Throw your hands up in the air, and say
We don’t care what people say…

- Kanye West
Background - Prevalence and Scope of the Problem
Opioids: Prescription analgesics
Access

Why not try us now?
Try our special offers!

Valium
Prescribed For - Anxiety.
buy now

Xanax
Prescribed For - Anxiety.
buy now

Soma
Muscle Relaxer/Pain Reliever.
buy now

Darvocet
Prescribed For Pain relief.
buy now

Ultrace
Prescribed For Pain relief.
buy now

Why not try NOW?

Absolutely No Doctor's Appointments Needed!
ALL Meds are dispensed from Licensed Pharmacy.
All Prescriptions are filed by Licensed Pharmacists!

Need prescription medication without a prior prescription? We ship quality medications overnight to your door.
Lowest prices on brand name and generic drugs. Order from the convenience of your own home immediately, discreetly and hassle free. Try us Today!

GrandRX is your online pharmacy for drugs through online consultation, specializing in the EXTREMELY POPULAR, yet hard to find High Level Muscle Relaxers, Pain Relief, and prescription Sleeping Aids such as SOMA. Fioricet, Ambien, Cymbalta, and MORE

Join tens of thousands of customers who safely, conveniently, and discreetly order prescription medication including weight loss/diet pill medications, skin care, birth control, muscle relaxants, high level pain relief, anxiety, prescription sleeping aids, anti-depressant medications and more.
Heroin Use From 1991-2005 (MTF)

Annual Use Prevalence: 8th and 12th Graders

Non-Medical Prescription Opioid Use


Past Year Non-Medical Use of Prescription Opioids By Age (NSDUH)

Source: 2002-2004 NSDUH
New Non-Medical Users of Prescription Opioids, By Age of Initiation (NSDUH)

Source: 2002 NSDUH
Opioid dependence in adolescents and young adults, previous experience: High severity and relapse
Adolescent opioid users previous clinical experience

- Higher severity and worse outcomes than non opioid using counterparts
- High rates of AMA from residential
- Alarmingly low rates of continuing care in outpatient
- Relapse and *drop out* as the rule
Past 90 Day $ Spent on alcohol and drugs

- Alcohol or Marijuana problem only
- Opioid problem

- How much did you spend on alcohol? $32
- How much did you spend on drugs? $181
- Total spent on drugs: $626

Courtesy Dennis and Ives: Derived from 2006 CSAT AT dataset
Quarterly cost to society: 2006 $

- No opioid use: $3,191
- Opioid dep/abuse or weekly use: $6,311

Courtesy Dennis and Ives: 2006 dollars New French estimates
ATM Baltimore Site
Heroin Users vs Others

Substance using Days, Past 90

Heroin Users

Other

Baseline 3 Mos. 6 Mos. 9 Mos. 12 Mos.
Days Drug Use Interfered With Responsibilities

- **Heroin users**
  - Baseline: 55 days
  - 12 Mos.: 14 days

- **Non-Heroin users**
  - Baseline: 23 days
  - 12 Mos.: 3 days
Heroin Users - GAIN General Mental Distress Index

Heroin Users

Other

Baseline 3 Mos. 6 Mos. 9 Mos. 12 Mos.
581 Male Heroin Addicts Followed for 33 Years

Hser et al., 2001
Pharmacological Treatments

- Buprenorphine Detox
- Buprenorphine Maintenance
- Naltrexone
- Extended release naltrexone
Rationale for medication

• Reduce craving
• Impact physiological dependence - both negative and positive reinforcement
• Protect against lapses, which should be expected
• Reduce high rates of relapse
• Improve poor treatment retention
• Improve poor outcomes of current psychosocial treatments
A Brief History of Opioid Treatment

- **1964**: Methadone is approved.
- **1974**: Narcotic Treatment Act limits methadone treatment to specifically licensed Opioid Treatment Programs (OTPs).
- **1984**: Naltrexone is approved.
- **1993**: LAAM is approved. (Low use, not approved for pregnant patients, cardiac adverse effects)
A Brief History of Opioid Treatment (Cont)


- **2002**: FDA approves tablet formulations of buprenorphine (Subutex®) and buprenorphine/naloxone (Suboxone®)

- **2004**: LAAM® is discontinued in the U.S.

- **2006**: 30 patient limit is increased to 100 per physician (on Buprenorphine maintenance)
Detoxification

- ASAM patient placement criteria (PPC2-R) recommends residential setting as standard of care for adolescent detox
- No data to support ambulatory detox as in adults
- Buprenorphine
- Clonidine
- Other symptomatic Rx
# Bupe Detox Protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>Dose (mg)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>8</td>
<td>Divided dose</td>
</tr>
<tr>
<td>Day 2</td>
<td>12</td>
<td>Initiation</td>
</tr>
<tr>
<td>Day 3</td>
<td>12</td>
<td>Dose finding for peak</td>
</tr>
<tr>
<td>Day 4</td>
<td>12</td>
<td>Single dose</td>
</tr>
<tr>
<td>Day 5</td>
<td>8</td>
<td>Stabilization</td>
</tr>
<tr>
<td>Day 6</td>
<td>4</td>
<td>Taper</td>
</tr>
<tr>
<td>Day 7</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
Agonist Maintenance

• Pure agonist
  – Methadone
• Partial agonist
  – Buprenorphine
Problems with methadone for youth

- Restrictions on access
- Lack of developmentally specific treatment elements
- Anticipation of long term commitment
- Culture and setting
Intrinsic Activity

Full Agonist, Partial Agonist, and Antagonist of Opioids

- Full Agonist: Methadone, Heroin, oxycodone
- Partial Agonist: Buprenorphine
- Antagonist: Naloxone

Graph showing the relationship between log dose of medication and intrinsic activity.
DSM-IV Criteria For Substance Dependence

1. Tolerance (increased amounts or diminished effects)
2. Withdrawal (withdrawal syndrome or use to relieve or avoid withdrawal)

(Addictive Behaviors – impairment and loss of control)

3. Efforts or desire to cut down or control use
4. Taken Larger amounts or over a Longer period than intended
5. Social, recreational or occupational activities given up
6. Time spent in activities necessary to obtain the substance
7. Use despite Persistent or recurrent Physical or Psychological problems
Advantages of Buprenorphine

• Partial agonist/antagonist, less reinforcing
• Ceiling effect
• Safety
• Easy detox
• Strong blockade effect
• Long duration
• Low diversion potential, especially when combined with naloxone (Suboxone)
• Ease of office based delivery and integration into treatment program
Clinical Trials Network: Buprenorphine for opioid dependence in adolescents and young adults

RCT: 2 wk detox vs 12 wks bupe
6 sites
N=154
Extended vs Short-term Buprenorphine-Naloxone for Treatment of Opioid-Addicted Youth
A Randomized Trial

George E. Woody, MD
Sahrina A. Poole, MS
Geetha Subramanian, MD
Karen DiGuglielmo, PhD
Michael Bogenschutz, MD
Patrick Abbott, MD
Ashwin Paulkar, MD
Mark Pullensker, MD
Karen McCaine, MSN, FNP
Jennifer Sharpe Potter, PhD, MPH
Robert Forman, PhD
Victoria Vetter, MD
Laura McNicholas, MD, PhD
Jack Blaine, MD
Kevin G. Lynch, PhD
Paul Fudala, PhD

Context The usual treatment for opioid-addicted youth is detoxification and counseling. Extended medication-assisted therapy may be more helpful.

Objective To evaluate the efficacy of continuing buprenorphine-naloxone for 12 weeks vs detoxification for opioid-addicted youth.

Design, Setting, and Patients Clinical trial at 6 community programs from July 2003 to December 2006 including 152 patients aged 15 to 21 years who were randomized to 12 weeks of buprenorphine-naloxone or a 14-day taper (detox).

Interventions Patients in the 12-week buprenorphine-naloxone group were prescribed up to 24 mg per day for 9 weeks and then tapered to week 12. Patients in the detox group were prescribed up to 14 mg per day and then tapered to day 14. All were offered weekly individual and group counseling.

Main Outcome Measure Opioid-positive urine test result at weeks 4, 8, and 12.

Results The number of patients younger than 18 years was too small to analyze separately, but overall, patients in the detox group had higher proportions of opioid-positive urine test results at weeks 4 and 8 but not at week 12 (χ²=4.93, P=.09). At week 4, 49 of 59 detox patients had positive results (82%, 99% confidence interval [CI]=47%–75%) vs 58 of 12-week buprenorphine-naloxone patients (26%; 95% CI=14%–38%). At week 8, 53 detox patients had positive results (54%; 95% CI=38%–70%) vs 52 of 12-week buprenorphine-naloxone patients (23%; 99% CI=11%–39%). At week 12, 53 detox patients had positive results (51%; 95% CI=35%–67%) vs 49 of 12-week buprenorphine-naloxone patients (43%; 95% CI=29%–57%). By week 12, 16 of 78 detox patients (20.5%) remained in treatment vs 52 of 74 of 12-week buprenorphine-naloxone patients (70%; χ²=32.90, P<.001). During weeks 1 through 12, patients in the 12-week buprenorphine-naloxone group reported less opioid use (χ²=18.45, P=.001), less injecting (χ²=6.00, P=.01), and less nonstudy addiction treatment (χ²=25.82, P<.001). High levels of opioid use occurred in both groups at follow-up. Four of 83 patients who tested negative for hepatitis C at baseline were positive for hepatitis C at week 12.

Conclusions Continuing treatment with buprenorphine-naloxone improved outcome compared with short-term detoxification. Further research is necessary to assess the efficacy and safety of longer-term treatment with buprenorphine for young individuals with opioid dependence.

Trial Registration clinicaltrials.gov identifier: NCT00078130

The usual treatment for opioid-addicted youth is short-term detoxification and individual or group therapy in residential or outpatient settings over

For editorial comment see p 2057.

©2008 American Medical Association. All rights reserved.

(Reprinted) JAMA, November 5, 2008—Vol 300, No. 17 2003
Demographics: No Sig Grp Diffs

- **Male**: 90 (58%)
- **Race**
  - Caucasian: 114 (74%)
  - African-American: 3 (2%)
  - Hispanic: 38 (25%)
- **Empl/School (Past 6 months)**
  - School: 28%
  - Working/worked: 72%
- **Hepatitis C + baseline**: 29 (19%)
- **HCV conversion 12 wks**: 5%
CTN Multi-site Buprenorphine study
Retention by Group

- Baseline
- Week 4
- Week 8
- Week 12
CTN Adolescent and Young Adult Buprenorphine Study
Opioid Positive Urines: 12 weeks Bup vs Detox

(Woody et al, JAMA 2008)
Naltrexone for Opioid Dependence
Naltrexone

• Pure competitive antagonist of opioid receptors
• Very effectively prevents and reverses all opioid effects
• FDA approved for
  – Oral NTX for opioid dependence 1984
  – Oral NTX for alcohol dependence 1996
  – Injectable XR-NTX for alcohol dependence 2004
Naltrexone for opioid dependence

- Great lab efficacy, terrible general clinical effectiveness, disappointing because of poor medication compliance and high dropout
- Special population exceptions: highly motivated or with compliance enhancements
  - Physicians
  - Contingency management
  - Maybe parental supervision?
Development of XR-NTX

- Depotrex
- Australian implant
- Russian implant
- Vivitrol
Naltrexone for alcohol dependence

- Reduces cravings, reward for alcohol, no punishing effects
- Moderate effectiveness: reduces relapse to heavy drinking
- Outcomes: decreased rates of relapse to heavy drinking, decreased heavy drinking days, decreased drinking days, not abstinence
- Important addition to repertoire, but disappointing adoption by clinicians
Injectable depot NTX for heroin dependent adults

- Brief (2 month) efficacy trial, RCT: n = 60
- Depotrex: placebo vs 192 mg vs 384 mg
- Residential induction
- Twice weekly outpatient individual counseling
- Improved retention and reduced opioid pos urines in dose dependent fashion

Comer et al 2006
Retention in treatment by study week and treatment group

Percentage of urine samples negative for various drugs of interest

NTX Safety in Opioid Dependence

• Hypothetical concern re overdose by massive overpowering of blockade, but never reported.
• Small Australian adolescent series (n=8) shows OD’s decreased after NTX implant.
• Liver toxicity concerns from previous obesity trial oral NTX 350 mg/d, not seen in trials with lower doses.
• General recommendations:
  – Avoid with severe active liver problems
  – Educate about risk of decreased tolerance with relapse after cessation (no different than post-detox without pharmacological support)
Extended-Release Naltrexone for Opioid Dependence in Adolescents and Young Adults: Mountain Manor Experience and Case Series
XR-NTX Induction Method

- Residential detox using bupe taper
- 7 day abstinence by confinement
- NTX induction with 4 d oral dose titration
- 1st dose injectable XR-NTX prior to residential discharge
- Outpatient maintenance
20 received xr-ntx

3 never came for any OP tx

17 came to ≥ 1 OP session after receiving xr-ntx (following residential discharge)

2 dropped out after only 1 OP tx session

15 came to > 1 OP session

5 dropped out before 4 months

10 were retained in treatment at 4 months
XR-NTX case series summary (n=17)

- Age: Mean 17.8 (range 15-20)
- Gender: 9/17 (53%) F
- Race: 16/17 (94%) W
XR-NTX case series summary (n=17)

- Retained in treatment at 4 months: 10/17 (59%)
- Total time retained in treatment: mean 22 wks (median 19; range 1-53)
- Currently retained in treatment: 3/17
- Abstinent from opioids or only minor lapses through 4 months: 10/17 (59%)
- Avg # doses at 4 months = 2.8
- “Good” outcome at 4 months = 9/17 (53%)
- Received a 2nd dose: 10/17
- If received a 2nd dose
  - Retained at 4 months: 8/10
  - Good outcome: 7/10
Treatment model and program implementation: Integrating pharmacotherapy and counseling
Mountain Manor clinical continuum

- Acute short term residential
- Detoxification
- Partial Hospital Program (PHP)
- Intensive Outpatient Program (IOP)
- Outpatient (OP)
- Mental health clinic
- Special education day school
- Group home for girls
- Medical, psychiatric, nursing staff
- Close affiliation with adolescent medicine clinic
Program refinement
Specialty adolescent / young adult opioid treatment

• Outpatient specialty track
  – Cross-trained counselor specialists
  – Individual manual guided MET/CBT counseling
  – More case management
  – Opioid group
  – Medical visits
  – Team meeting a little more like “rounds”

• Residential intake
  – Identification during detox
  – In-reach by specialty counselors
Elements of treatment model

- Longitudinal engagement and management
- More effective counseling techniques
- Anti-addiction pharmacotherapy (medications)
- Co-occurring (dual diagnosis) treatment
- Refinements in program design
Take the longitudinal view

• We don’t have a cure - this is not new news
• Ongoing continuing care treatment for remitting and relapsing disorder
• Long term maintenance and monitoring phase
• Relapse prevention is an active treatment
Use the Continuum of Care

- Residential is 1st line initial level of care
- Emphasis on engagement from detox to next level of care (the revolving door should lead somewhere)
- But one size does not fit all: as many doors as possible
- Flexible response with multiple services
- Institutional affiliation
- Expectation of relapsing/remitting course
Opioid culture is different

- Older, more suburban, more Caucasian
- Distinctive subculture doesn’t mix well with non-opioid users
  - Self segregate from other adolescent substance abuse populations
  - Heroin users see non-heroin users as “babies” and not having a “real” drug problem
  - Stigmatized by other adolescent substance abuse populations
  - Non-heroin users see heroin users as “dope fiends” and “junkies”
  - Stigma against injection use
- Crime and risk behaviors related directly to obtaining drugs
- Selfish concern with supply
More adult-like concerns despite immaturity

- Later stage of addiction
- Fewer parental and other supports
- Homelessness
- Working and need for financial independence
Expectation of waxing/waning course

- Expect lapse and relapse
- Expect repeated need for withdrawal management
- Expect disparity of attitude and stage of change
  - “I never want to be that messed up again”
  - “These kids play too much; I need to stop!”
  - “My problem is heroin, weed is no big deal”
  - “I just have to be careful not to get a habit again”
  - “Smoking weed and drinking can’t lead me back to dope”
Post treatment heroin use associated with other substance use

Polysubstance Use

MJ Use

H12 - PolySub
H12 + PolySub

H12 - MJ Use
H12 + MJ Use
Implementation Issues
Counselor cross training

• Withdrawal
• Craving
• Clinical detection of intoxication: pinpoint pupils, scratching, nodding
• Medication tracking and management
• Medication adherence management
• Doctor management
Implementation Issues

- Insurance coverage for medication
- Insurance coverage for inpatient induction - length of stay
- Difficulties of outpatient induction
- Insurance coverage for outpatient induction - staff time
- Coordination of medical care
- Medication choice: NTX vs bupe vs nothing
Attitudes:
Can you be in “recovery” on medicines

- Medicines just a crutch or band-aid
  - *Maybe. Like meetings or group.*
- If the patients like it so much, there must be something wrong.
  - *But if they don’t like it, it doesn’t matter how good it is.*
- If medications are an “easy fix” will patients refuse needed psychosocial treatments and supports.
  - *Actually, they come to psychosocial treatment more.*
- If medications eliminate cravings will patients miss opportunity for needed cravings management?
  - *Academic if they relapse. Postpone until later when stronger. Maybe need later high intensity counseling.*
- Abuse and diversion
  - *Real issue, needs to be managed, but not as problematic as scare stories make it out to be.*
Implementation Issues

- Adherence
- “95% is showing up”
Next steps

- Improve family involvement
- How to manage medication discontinuation
- Broader coverage and reimbursement, including meds
- Improved medication adherence strategies
- Separate strategies for patients in action stage in relation to other substances
- Longer term outcomes
Conclusions

• We are experiencing a serious epidemic of adolescent heroin and diverted prescription opioid use
• Adolescent opioid users represent a subgroup with special characteristics
• Adolescent heroin users have higher severity than other drug-using adolescents, including profiles of substance use and psychosocial impairment
• Psychiatric co-morbidity plays a very prominent role
Conclusions (II)

- Despite high severity, adolescent heroin users do respond to treatment
- Medication support should become more widely adopted: buprenorphine is effective, extended release naltrexone appears promising
- Attention to special population characteristics important
- More work is desperately needed for adolescent opioid dependence
  - Specialized treatment model development
  - Specialized treatment research
Conclusions (III)

- Critical elements of treatment include
  - Specialty counseling techniques
  - Special attention to engagement over time
  - Expectation of relapse and remission
  - Medication assistance
  - Enhancement of medication adherence

- WE NEED MORE TREATMENT!