

Treatment for Opioid Dependence in Adolescents and Young Adults

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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



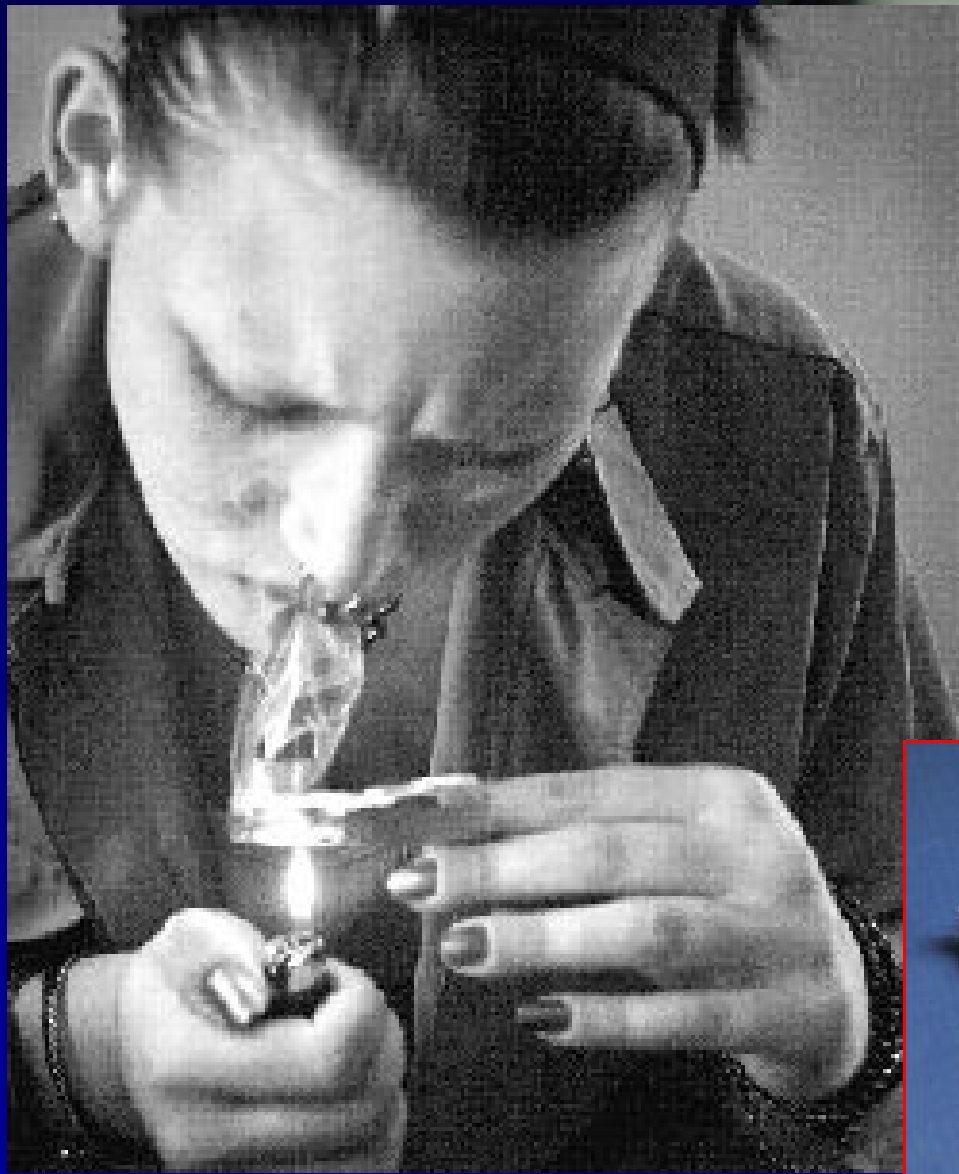
ELIXIR No. 61

TERPIN HYDRATE
AND
DIACETYL-MORPHINE

Frosst

Each fluidounce contains
Terpin Hydrate..... 1.00
Diacetyl Morphine..... 1.00
The above is the composition of every fluid ounce of this elixir. It is intended to substitute this preparation for a most useful form of opium. It contains the same amount of opium as is contained in the same amount of the latter.

Charles E. Frosst & Co.
MONTREAL - CANADA



Opioids: Prescription analgesics



C-III ABBOTT LABORATORIES



10 mg/660 mg

Vicodin HP®
(hydrocodone bitartrate/
acetaminophen tablets, USP)

C-II PURDUE PHARMA L.P.



10 mg

20 mg

40 mg

80 mg

160 mg
Controlled-Release Tablets

OxyContin®
(oxycodone HCl)

C-II ENDO PHARMACEUTICALS



2.5 mg/325 mg

5 mg/325 mg

7.5 mg/325 mg

7.5 mg/500 mg

10 mg/325 mg

10 mg/650 mg

Percocet®
(oxycodone HCl/acetaminophen, USP)

Access



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Valium
Fioricet (generic)
Soma (Cansoprodol)

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Access

- NEW PRODUCTS
- WEIGHT LOSS
- MUSCLE RELAXANTS
- ANTI DEPRESANTS
- SLEEPING AID
- PAIN RELIEF
- MENS HEALTH
- WOMENS HEALTH
- SEXUAL HEALTH
- STOP SMOKING

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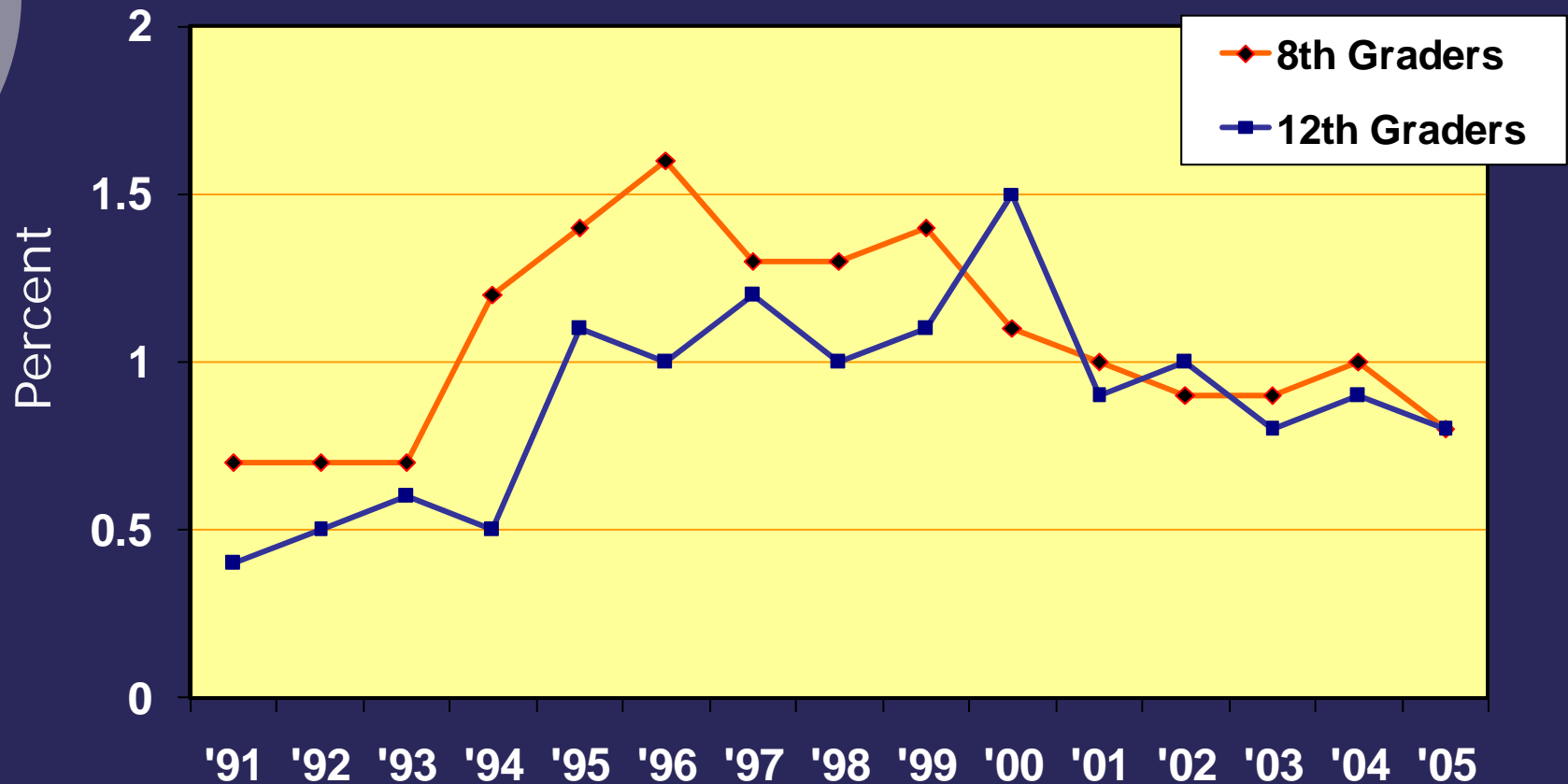
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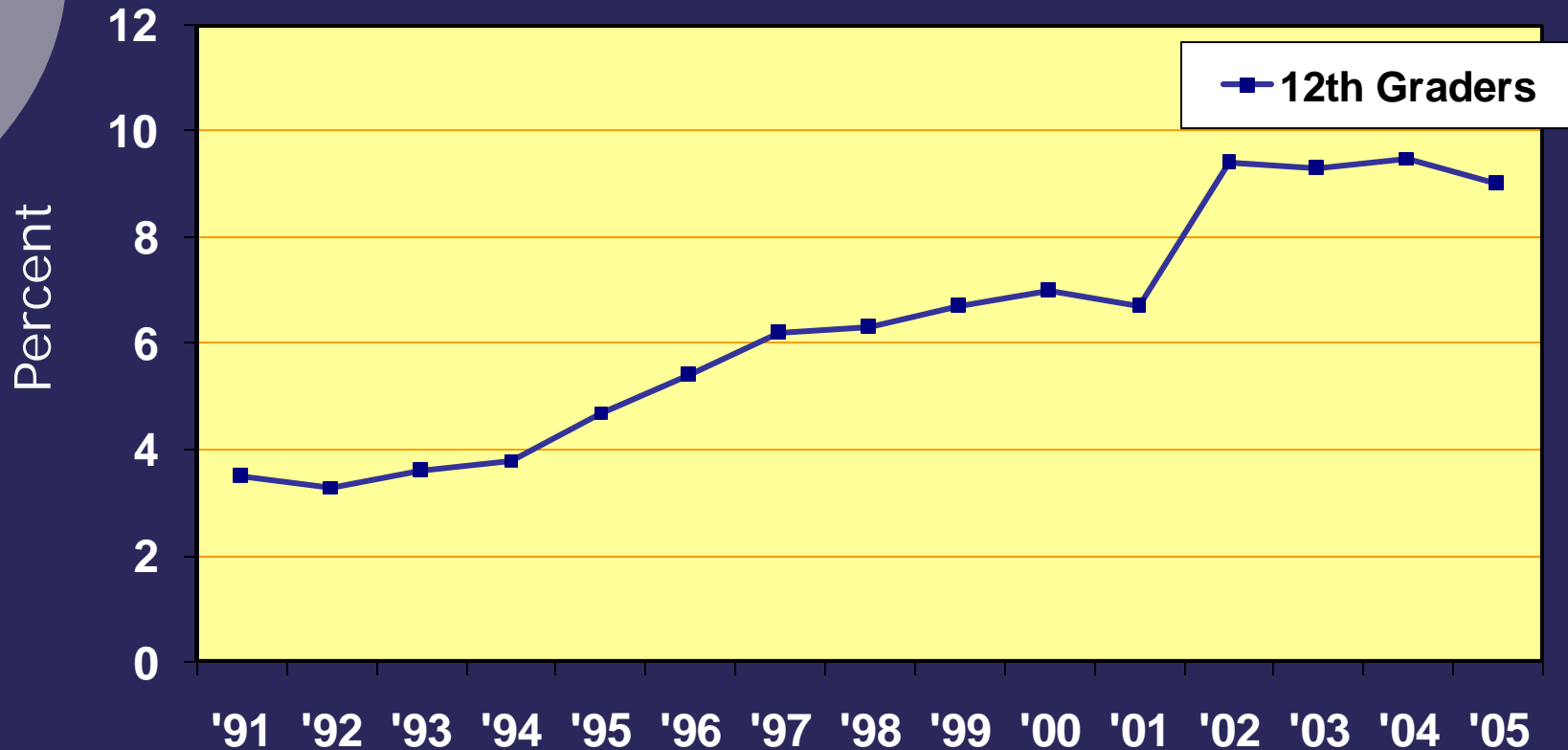
Heroin Use From 1991-2005 (MTF)

Annual Use Prevalence: 8th and 12th Graders

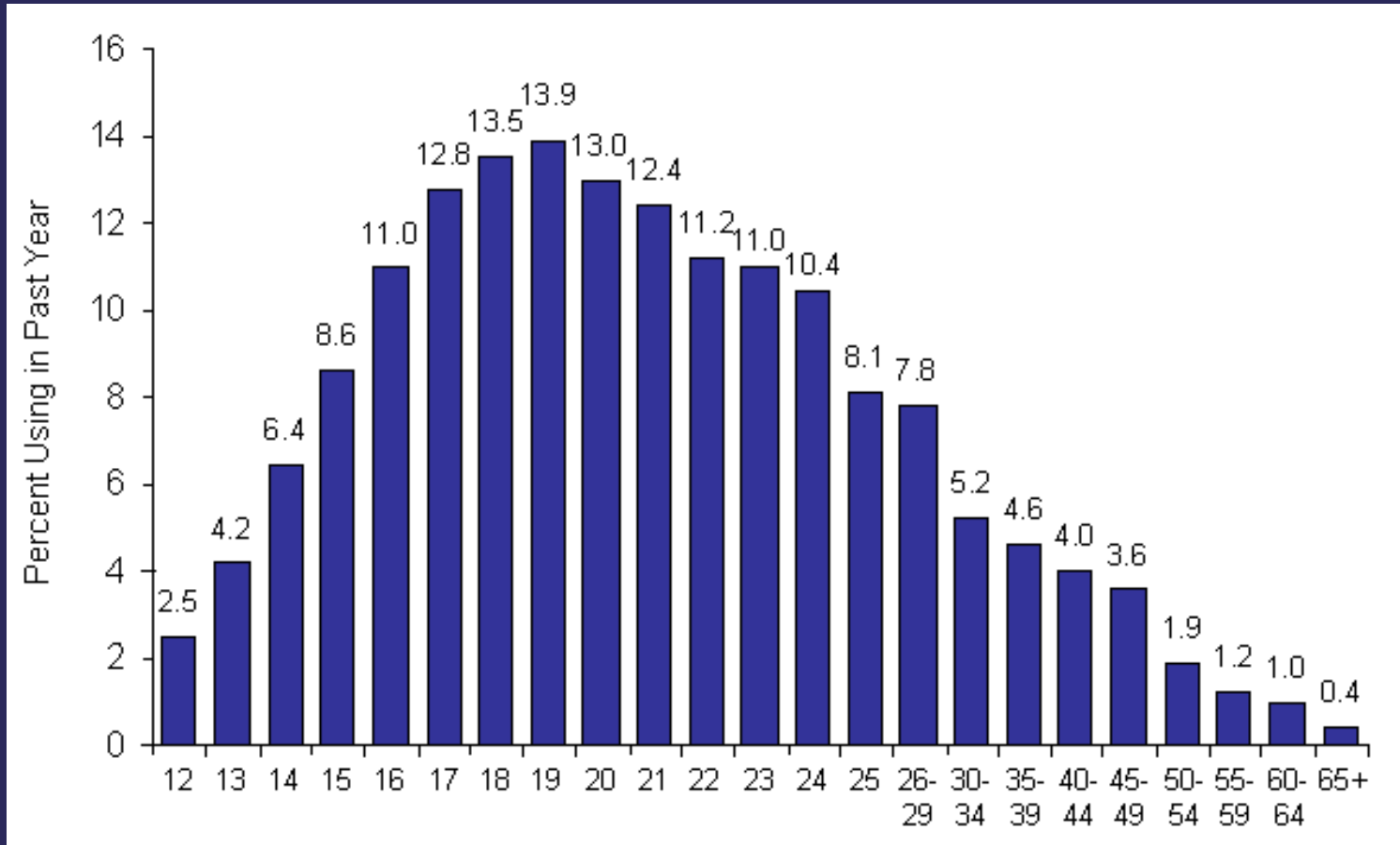


Non-Medical Prescription Opioid Use

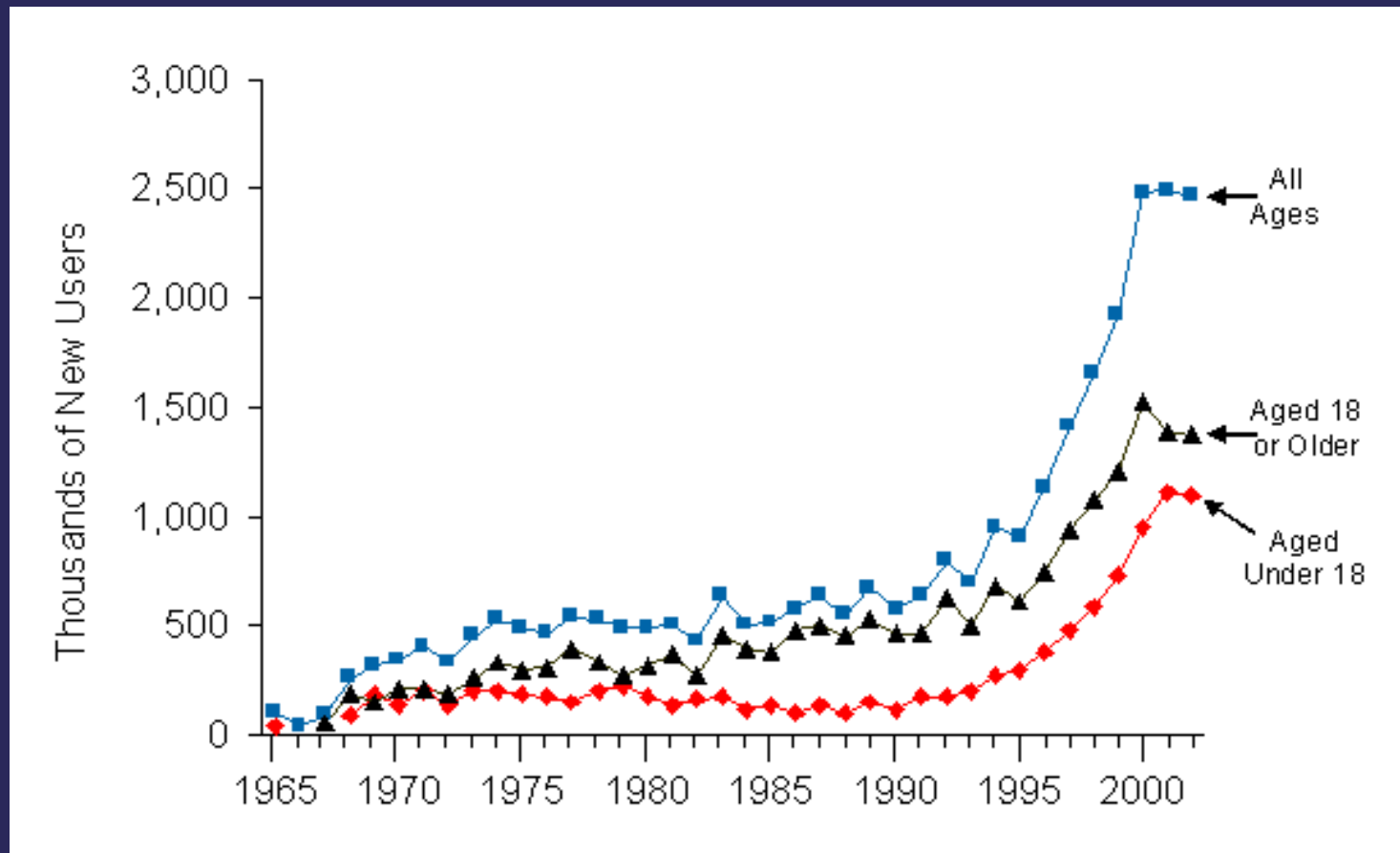
MTF: Annual Use Prevalence 12th Graders,
1991-2005



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



New Non-Medical Users of Prescription Opioids, By Age of Initiation (NSDUH)

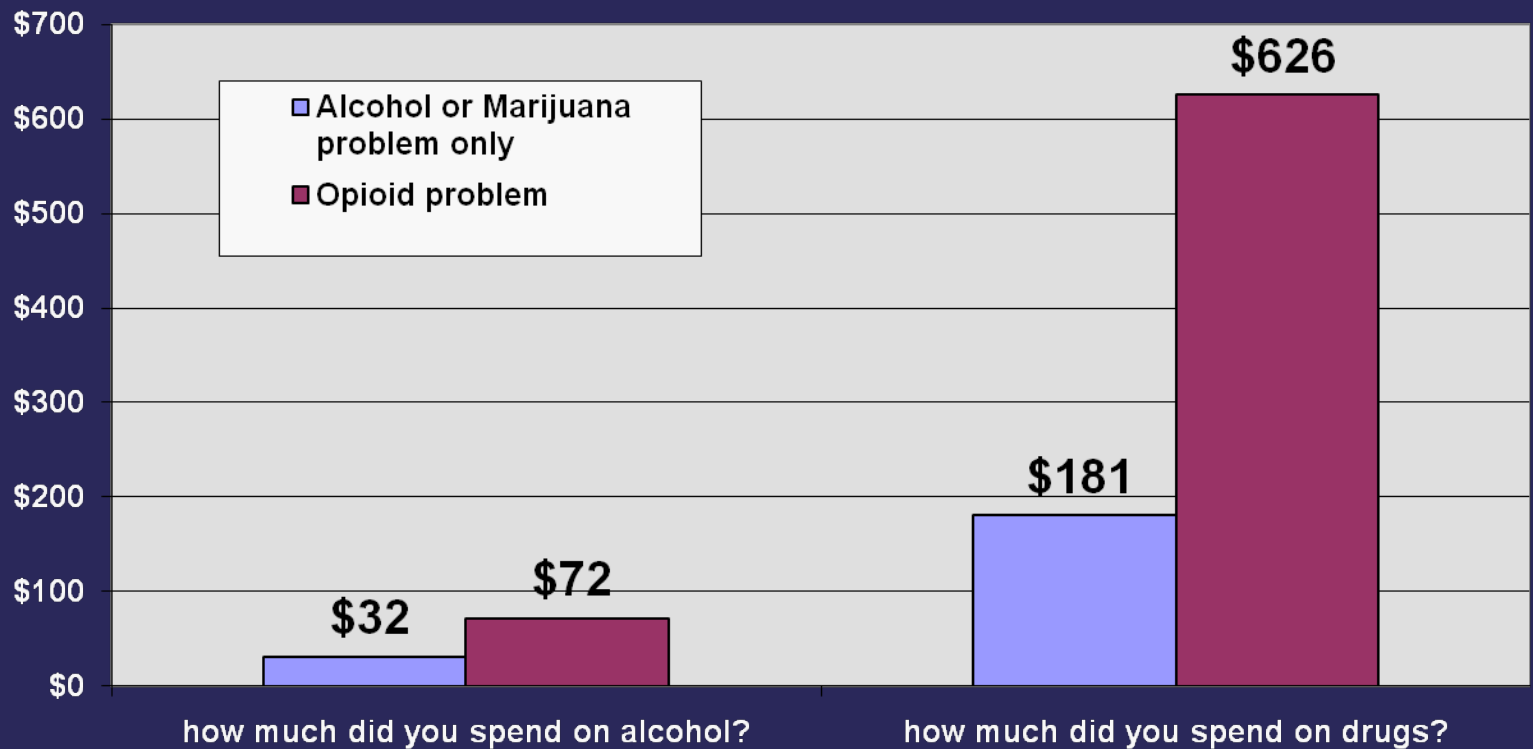


Opioid dependence in
adolescents and young adults,
previous experience:
High severity and relapse

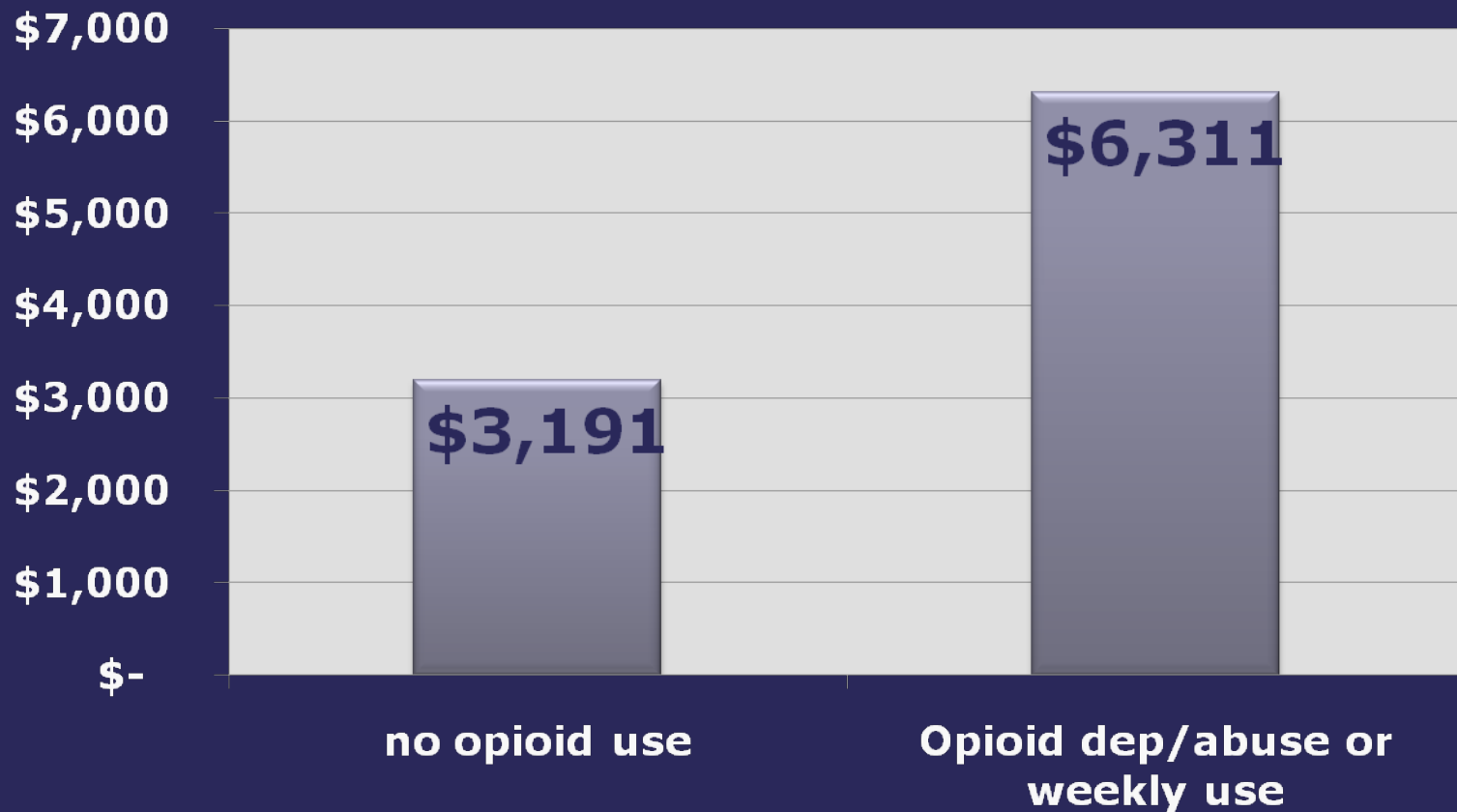
Adolescent opioid users previous clinical experience

- Higher severity and worse outcomes than non opioid using counterparts
- High rates of AMA from residential
- Alarming low rates of continuing care in outpatient
- Relapse and *drop out* as the rule

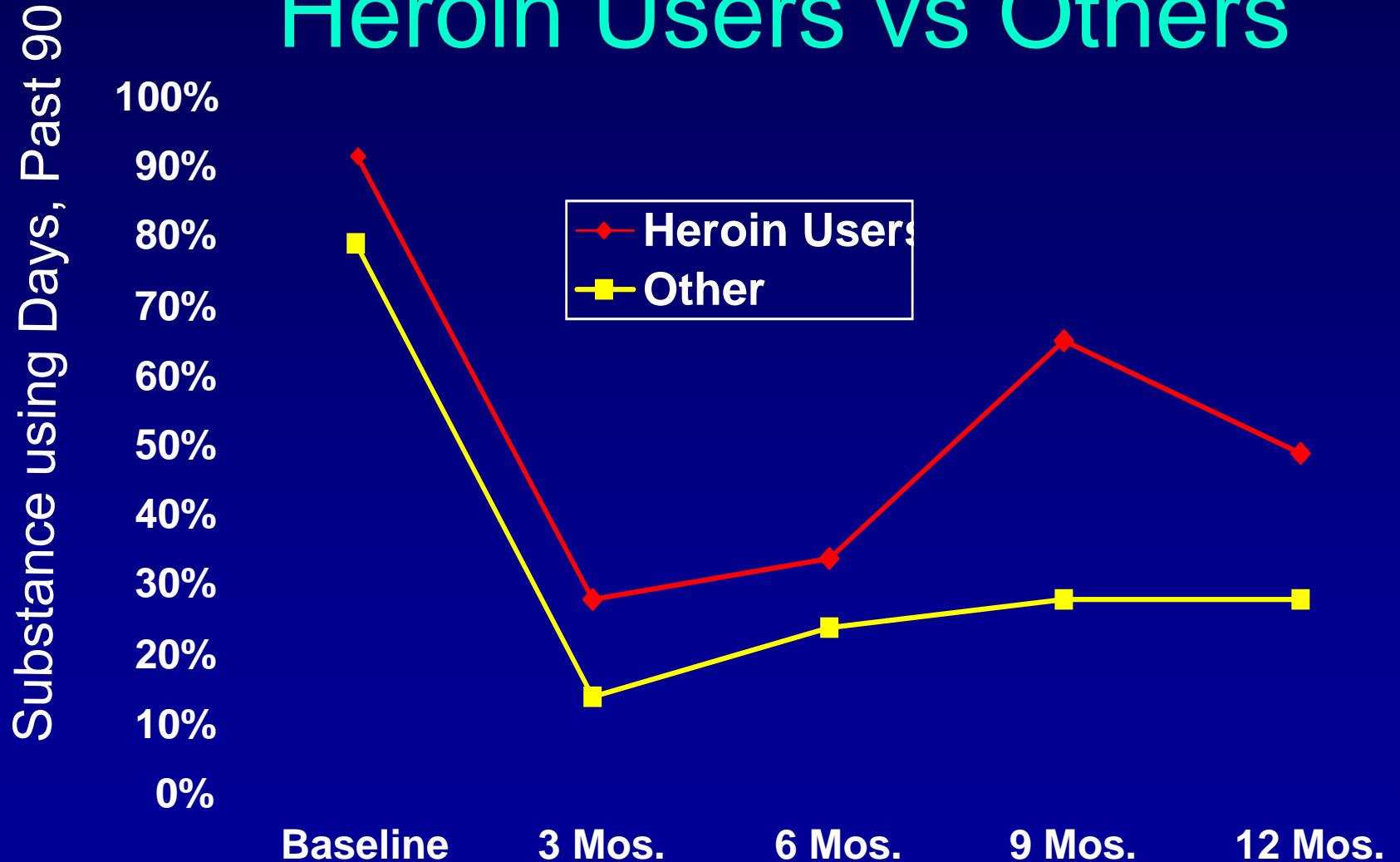
Past 90 Day \$ Spent on alcohol and drugs



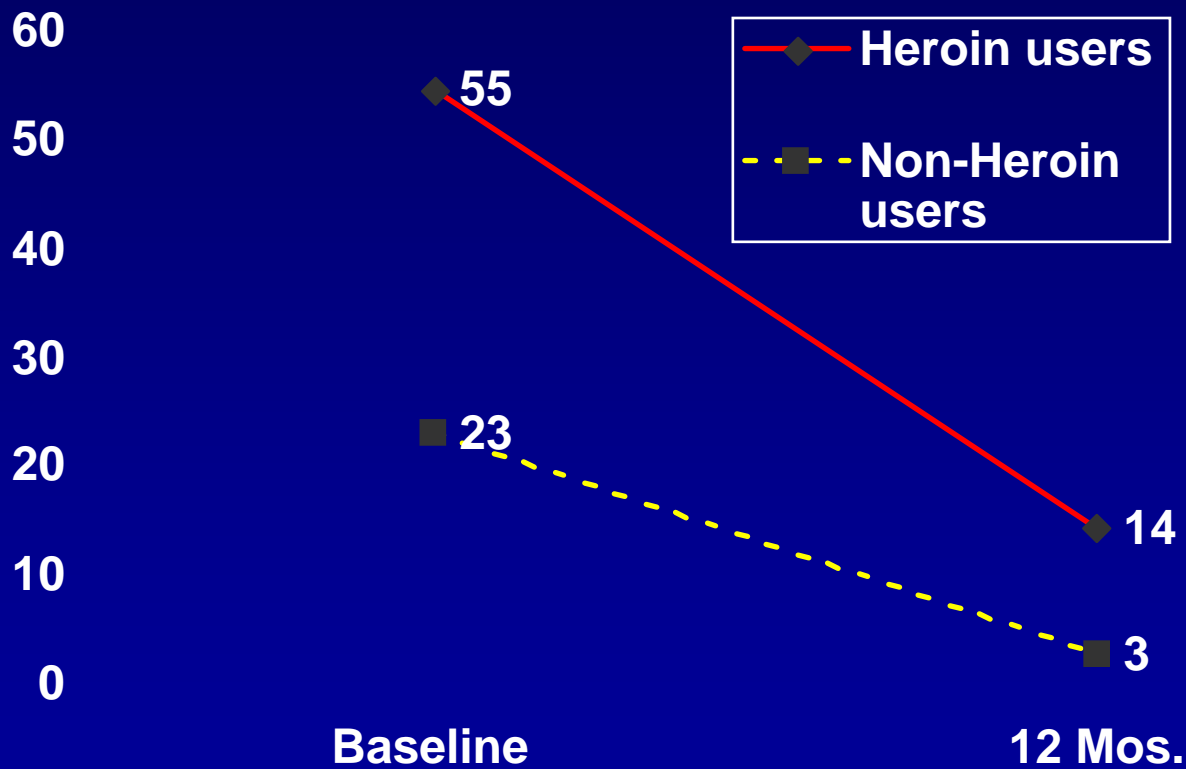
Quarterly cost to society: 2006 \$



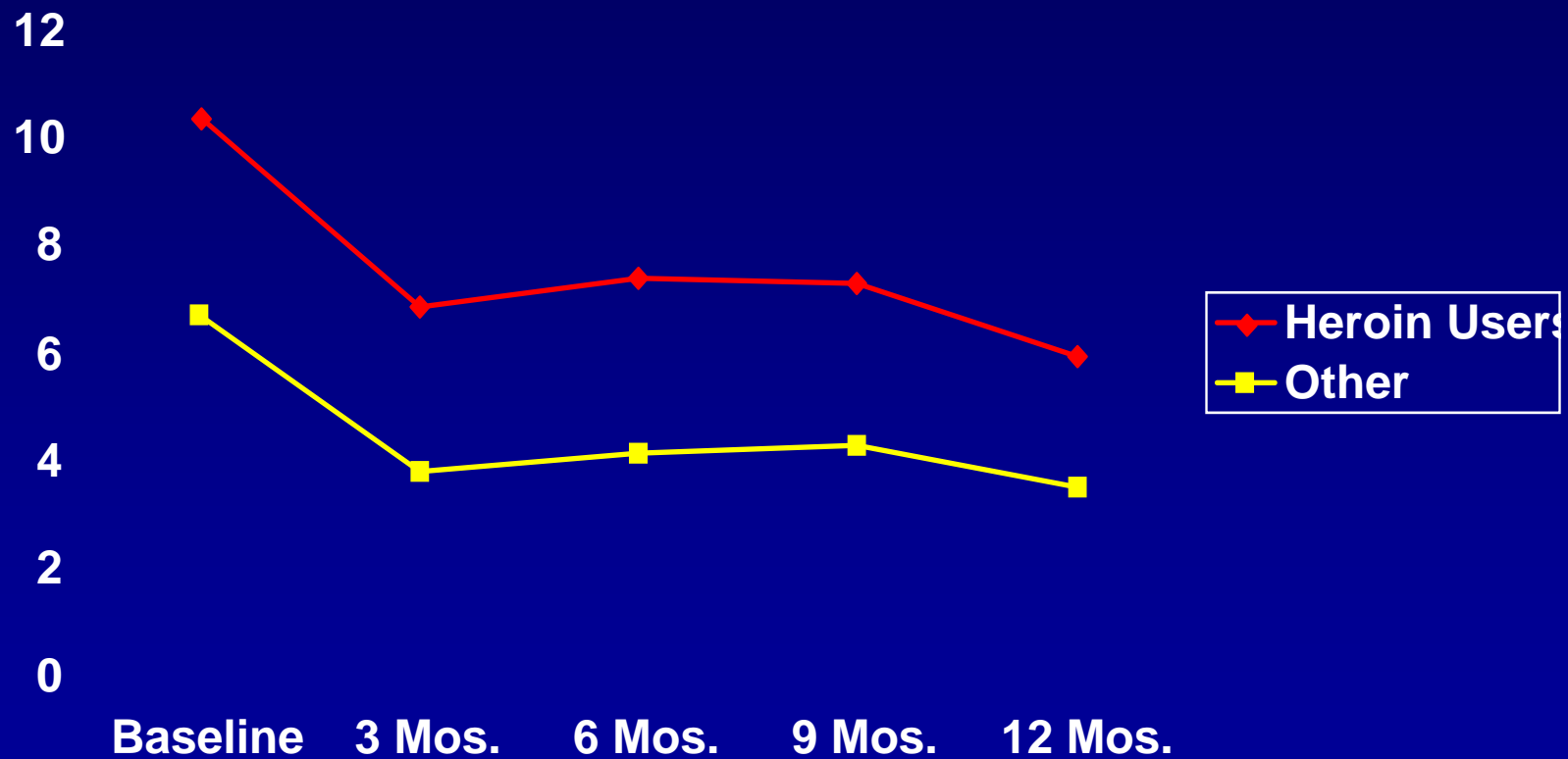
ATM Baltimore Site Heroin Users vs Others



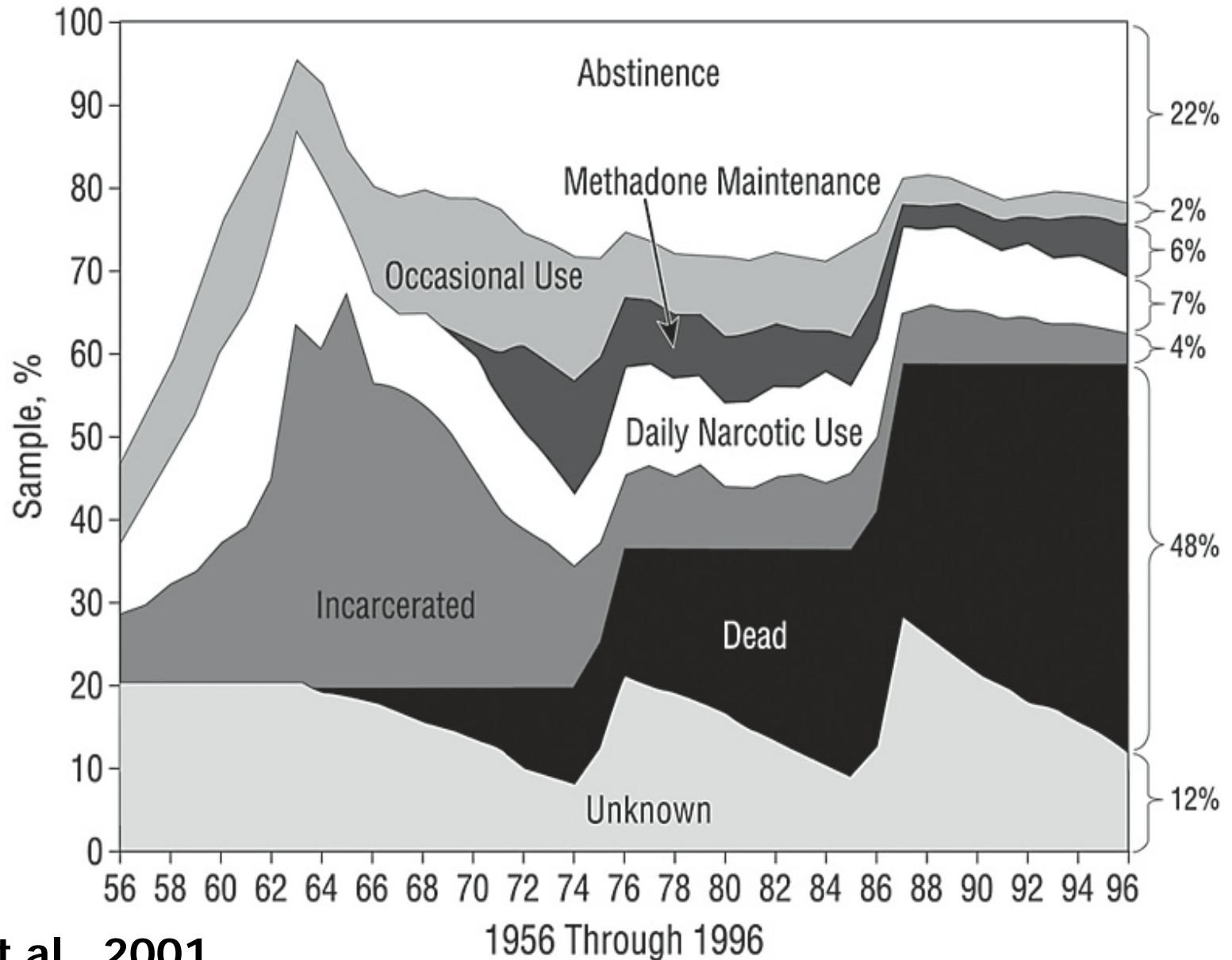
Days Drug Use Interfered With Responsibilities



Heroin Users - GAIN General Mental Distress Index



581 Male Heroin Addicts Followed for 33 Years



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)

- 2000: Drug Addiction Treatment Act of 2000 (**DATA 2000**) expands the clinical context of medication-assisted opioid treatment to offices and OTPs.
- **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

Day 1	8 mg	Divided dose	Initiation
Day 2	12 mg		Dose finding for peak
Day 3	12 mg		Stabilization
Day 4	12 mg		
Day 5	8 mg		
Day 6	4 mg		
Day 7	2 mg	Single dose	Taper

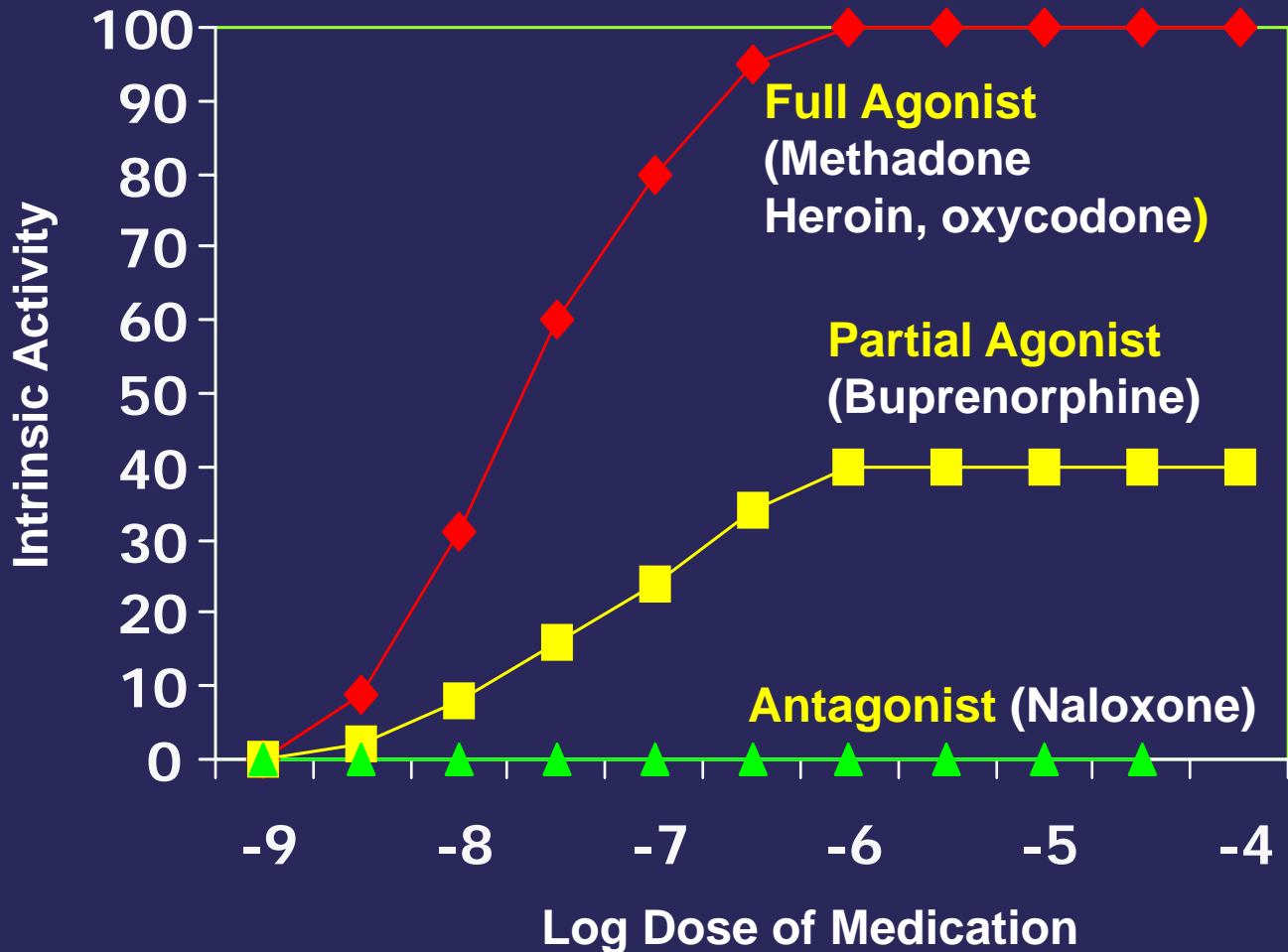
Agonist Maintenance

- 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

Full Agonist, Partial Agonist, and Antagonist of Opioids



DSM-IV Criteria For Substance Dependence

1. **T**olerance (increased amounts or diminished effects)
2. **W**ithdrawal (withdrawal syndrome or use to relieve or avoid withdrawal)

(Addictive Behaviors – impairment and loss of control)

3. **E**fforts or desire to cut down or control use
4. Taken **L**arger amounts or over a **L**onger period than intended
5. **S**ocial, recreational or occupational activities given up
6. **T**ime spent in activities necessary to obtain the substance
7. Use despite **P**ersistent or recurrent **P**hysical or **P**sychological 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

Journal of the American Medical Association, 2008

Extended vs Short-term Buprenorphine-Naloxone for Treatment of Opioid-Addicted Youth A Randomized Trial

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Mark Publicker, MD
Karen McCain, MSN, FNP
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Robert Forman, PhD
Victoria Vetter, MD
Laura McNicholas, MD, PhD
Jack Blaine, MD
Kevin G. Lynch, PhD
Paul Fudala, PhD

RECENT CONCERN HAS FOCUSED on opioid use among youth. For example, the proportion of 12th graders reporting past-year heroin use increased from 0.6% in 1992 to 0.9% in 2006. Similar increases occurred with pharmaceutical opioids—3.3% in 1992 to 9.5% in 2004¹—and recent data show that 13.4% of individuals aged 12 years or older who reported new use of heroin in the past 13 to 24 months meet criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (DSM-IV) for dependence.²

For editorial comment see p 2057.

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 ($\chi^2=4.93$, $P=.09$). At week 4, 59 detox patients had positive results (61%; 95% confidence interval [CI]=47%-75%) vs 58 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 12-week buprenorphine-naloxone patients (23%; 95% CI=11%-35%). At week 12, 53 detox patients had positive results (51%; 95% CI=35%-67%) vs 49 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 12-week buprenorphine-naloxone patients (70%; $\chi^2=32.90$, $P<.001$). During weeks 1 through 12, patients in the 12-week buprenorphine-naloxone group reported less opioid use ($\chi^2=18.45$, $P<.001$), less injecting ($\chi^2=6.00$, $P=.01$), and less nonstudy addiction treatment ($\chi^2=25.82$, $P<.001$). 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

JAMA. 2008;300(17):2003-2011

www.jama.com

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

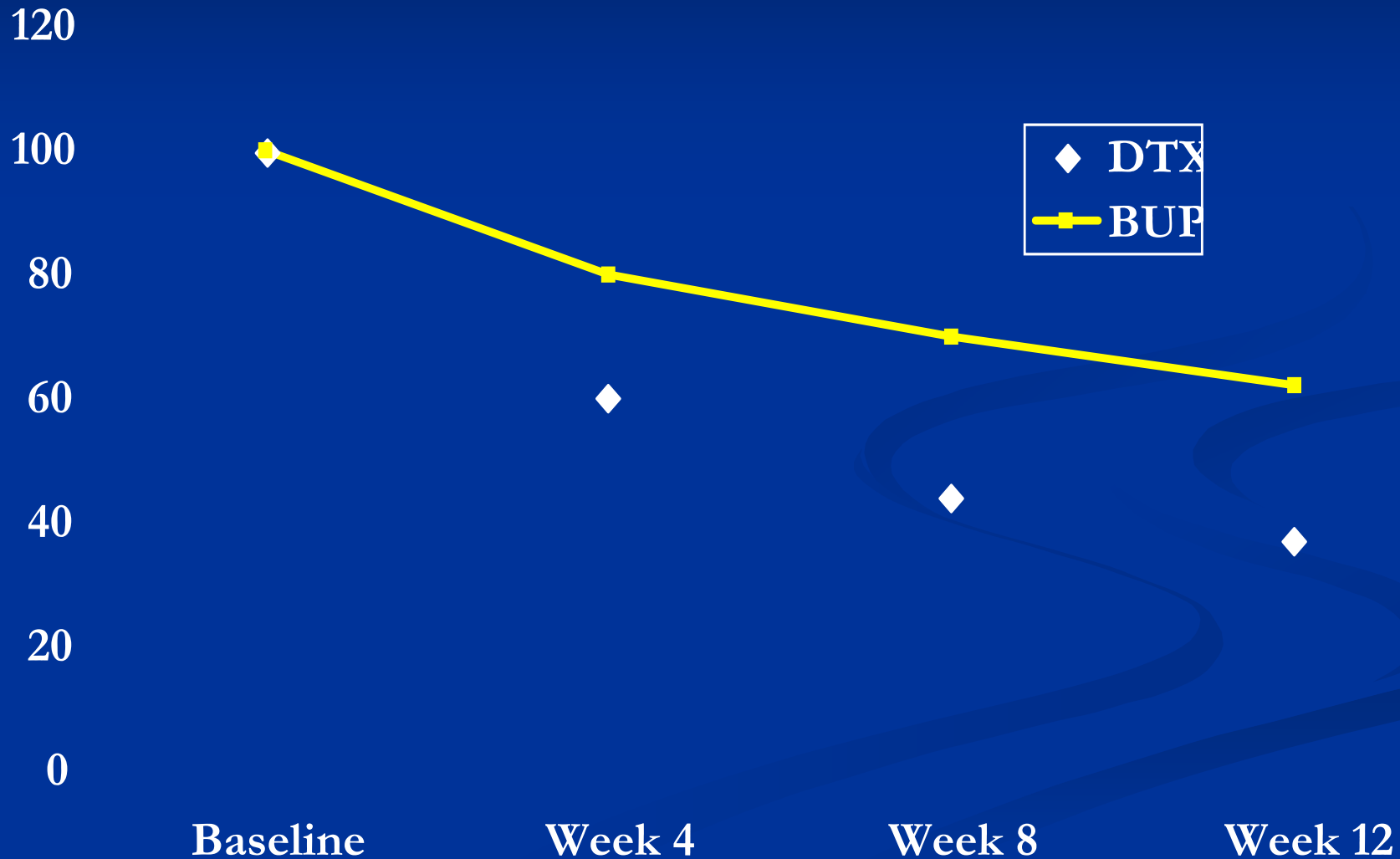
Author Affiliations are listed at the end of this article.
Corresponding Author: George E. Woody, MD, Department of Psychiatry, Treatment Research Institute, University of Pennsylvania, 150 S Independence Mall W, Ste 600, Philadelphia, PA 19106 (woody@research.org).

Demographics: No Sig Grp Dffs

- 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%

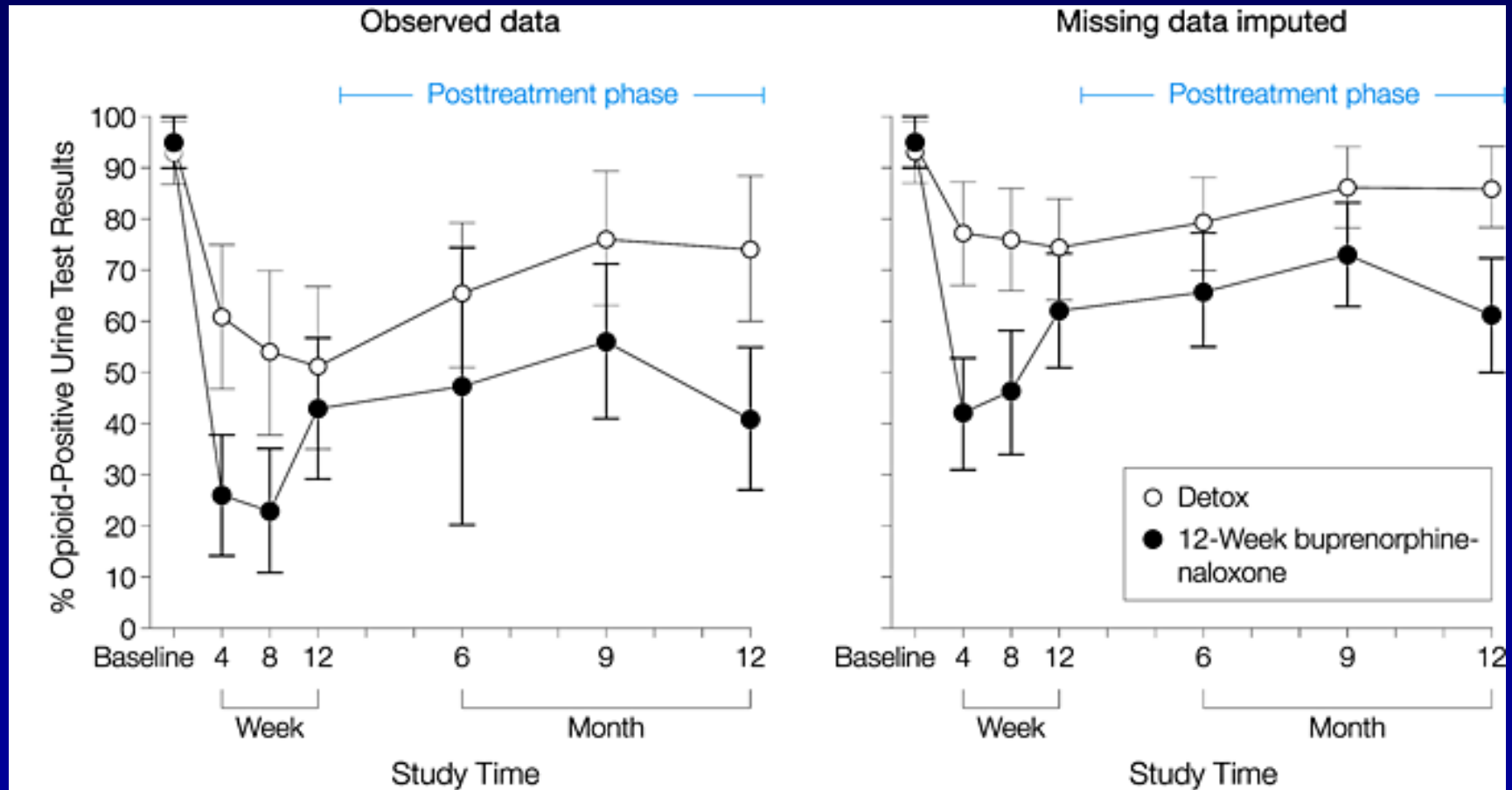
CTN Multi-site Buprenorphine study

Retention by Group



CTN Adolescent and Young Adult Buprenorphine Study

Opioid Positive Urines: 12 weeks Bup vs Detox



No. of patients

Detox	78	59	53	53	46	45	42
12-Week ^a	74	58	52	49	47	45	49

(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?

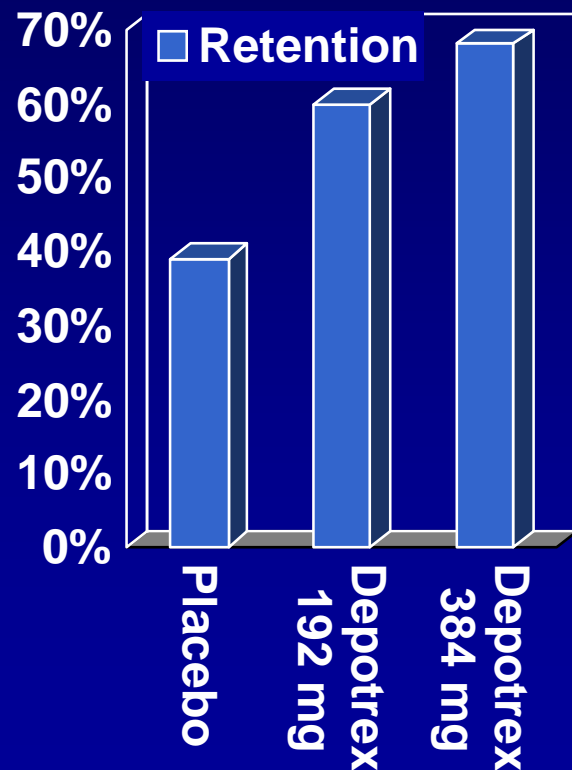
Development of XR-NTX

- Depotrex
- Australian implant
- Russian implant
- Vivitrol

Naltrexone for alcohol dependence

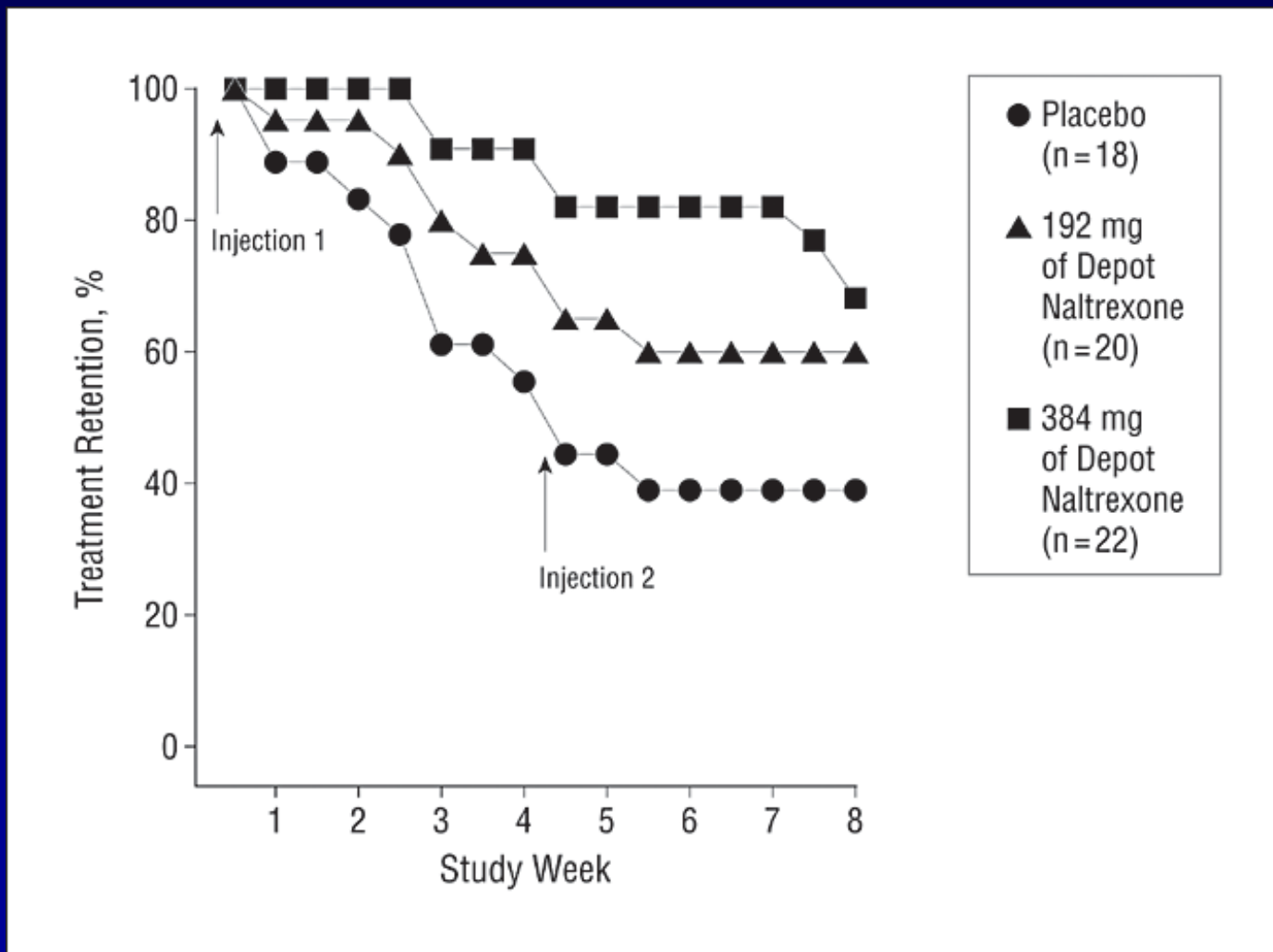
- Reduces cravings, reward for alcohol, no punishing effects
- Moderate effectiveness: reduces relapse to heavy drinking
- Outcomes: decreased rates of relapse to heavy drinking, decreased heavy drinking days, decreased drinking days, not abstinence
- Important addition to repertoire, but disappointing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

Injectable depot NTX for heroin dependent adults



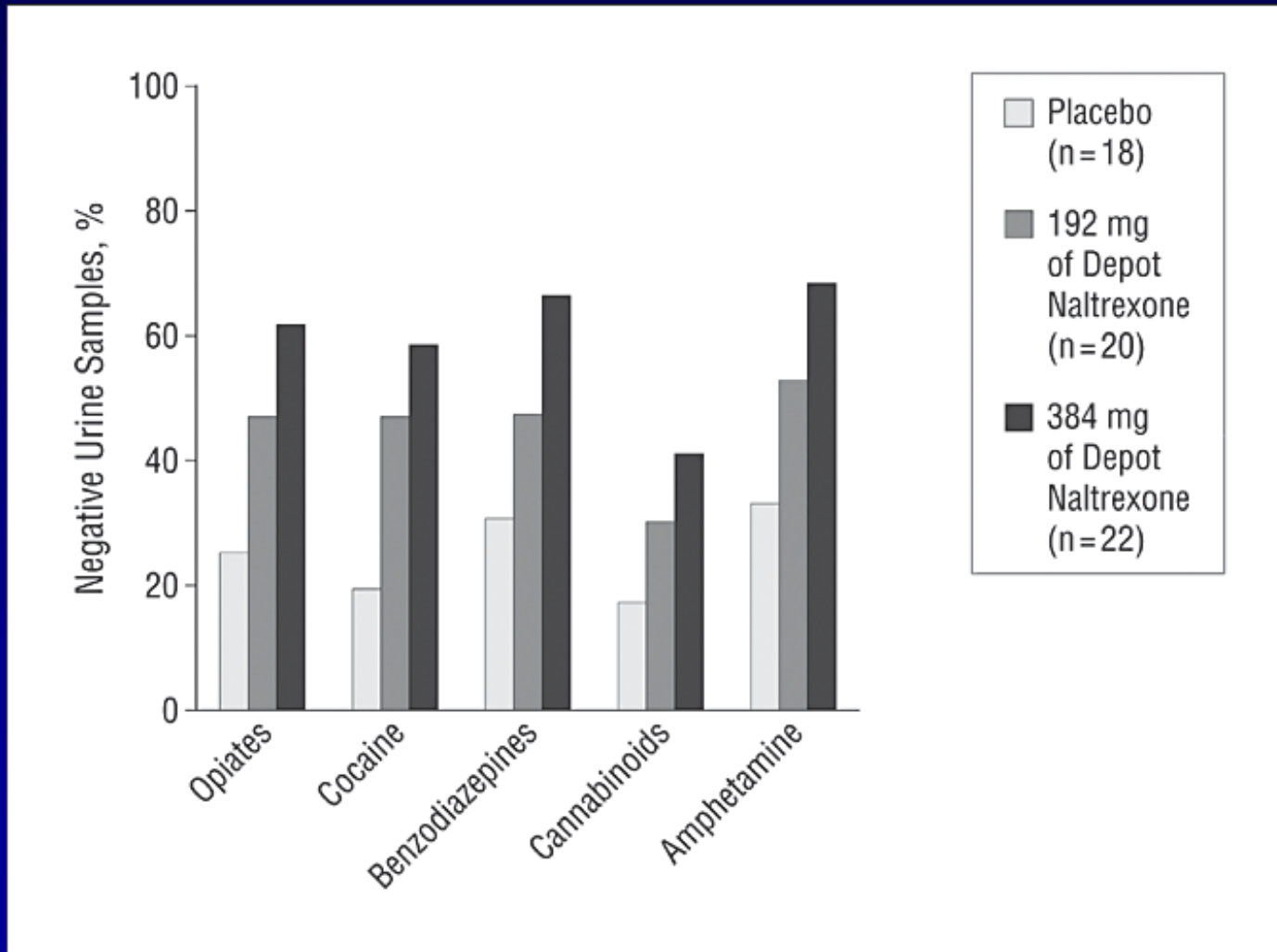
- Brief (2 month) efficacy trial, RCT: n = 60
- Depotrex: placebo vs 192 mg vs 384 mg
- Residential induction
- Twice weekly outpatient individual counseling
- Improved retention and reduced opioid pos urines in dose dependent fashion

Retention in treatment by study week and treatment group



Comer, S. D. et al. Arch Gen Psychiatry 2006;63:210-218.

Percentage of urine samples negative for various drugs of interest



Comer, S. D. et al. Arch Gen Psychiatry 2006;63:210-218.

NTX Safety in Opioid Dependence

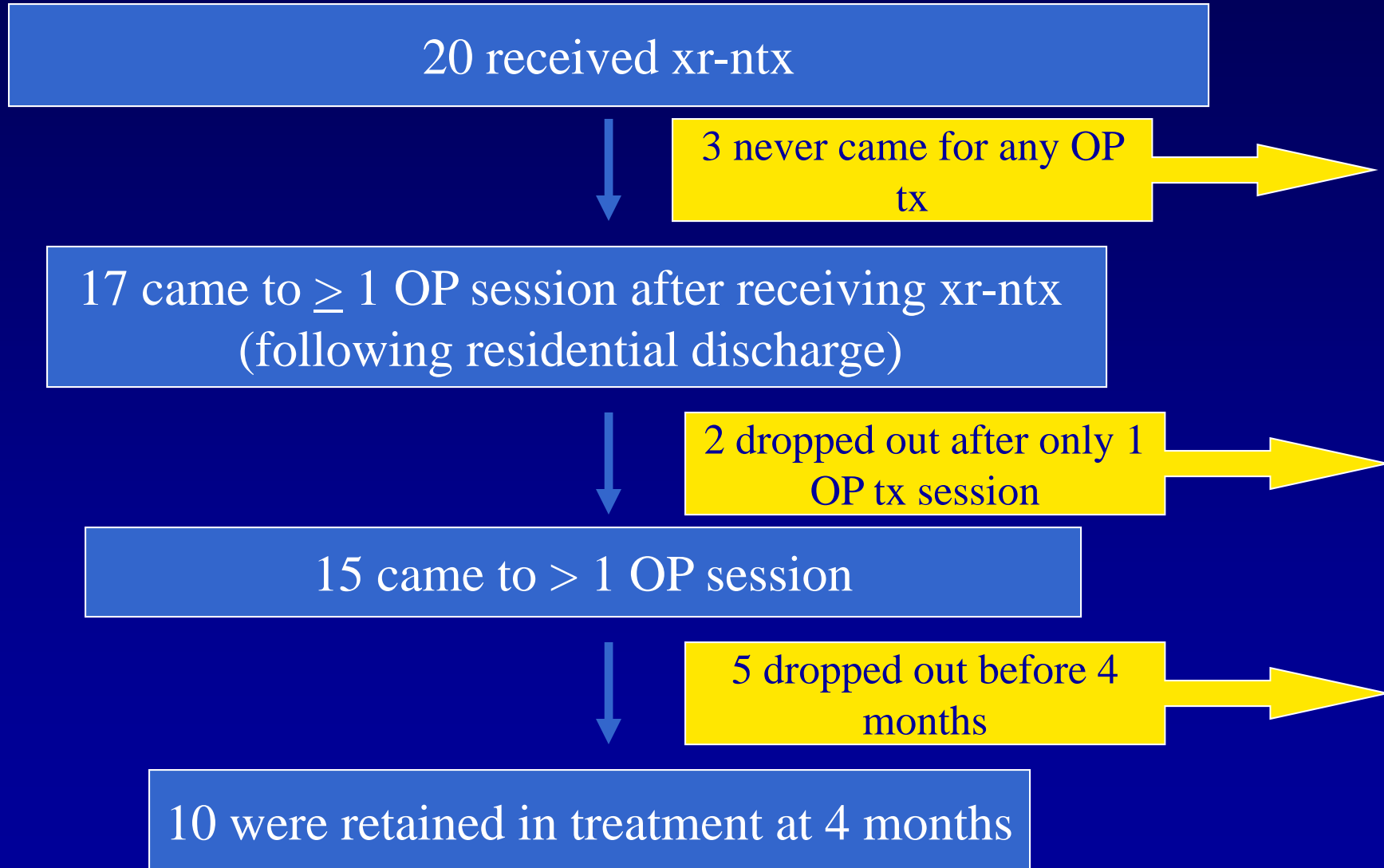
- Hypothetical concern re overdose by massive overpowering of blockade, but never reported
- Small Australian adolescent series (n=8) shows OD's *decreased* after NTX implant
- Liver toxicity concerns from previous obesity trial oral NTX 350 mg/d, not seen in trials with lower doses
- General recommendations:
 - 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

XR-NTX Case Series



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

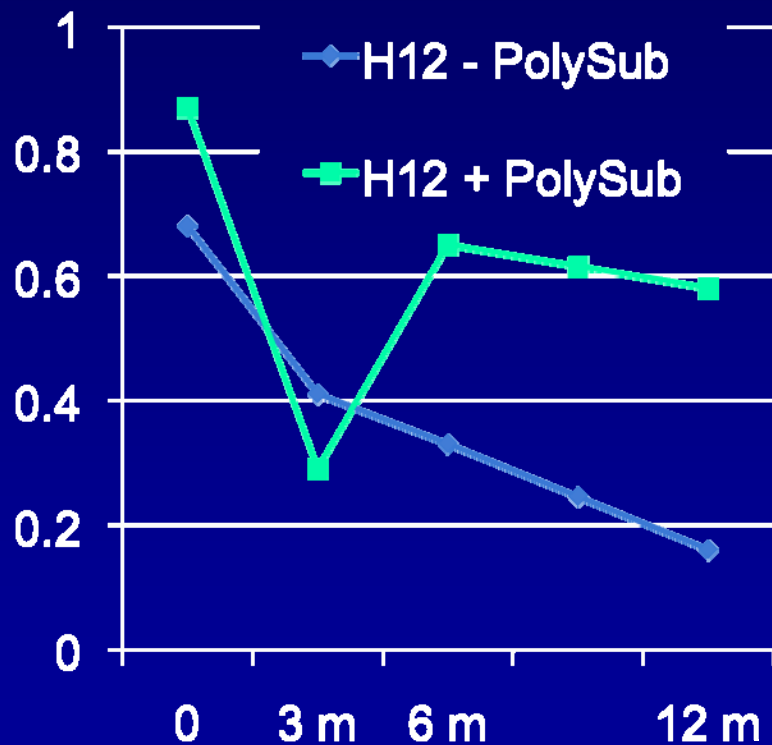
- Later stage of addiction
- Fewer parental and other supports
- Homelessness
- Working and need for financial independence

Expectation of waxing/waning course

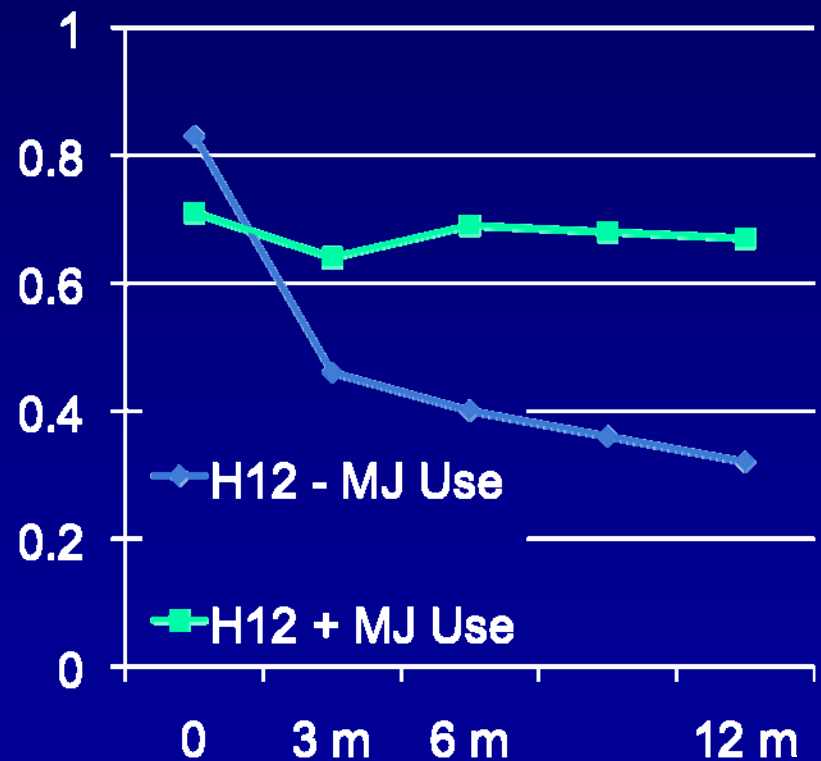
- Expect lapse and relapse
- Expect repeated need for withdrawal management
- Expect disparity of attitude and stage of change
 - “I never want to be that messed up again”
 - “These kids play too much; I need to stop!”
 - “My problem is heroin, weed is no big deal”
 - “I just have to be careful not to 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



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!**