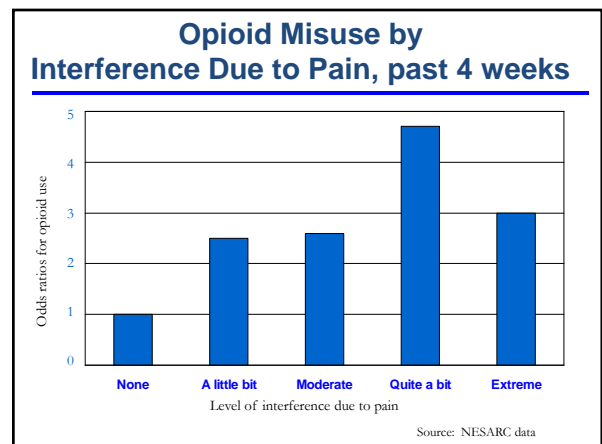
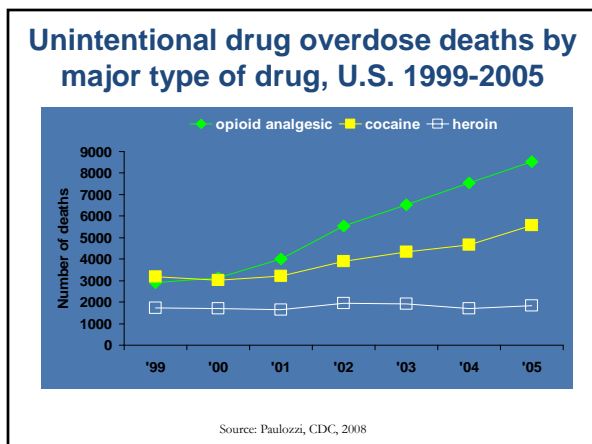
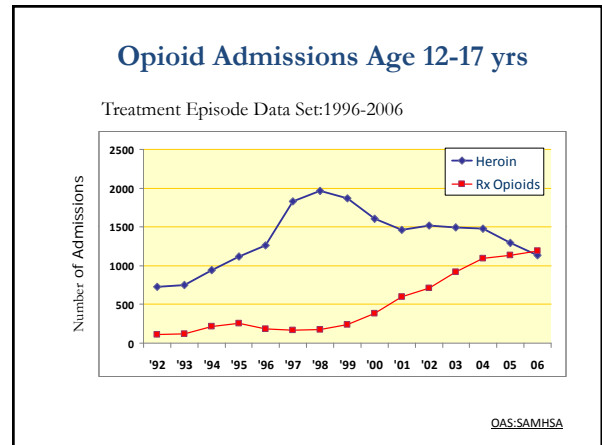
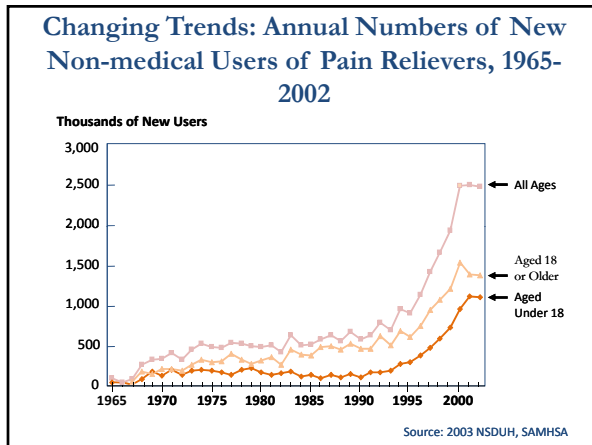
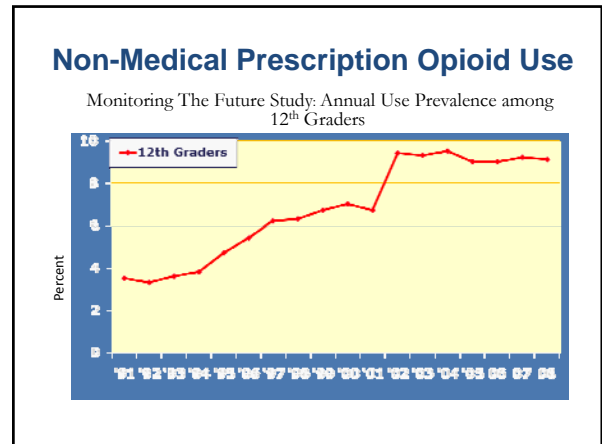


  
**The National Drug Abuse Treatment  
 Clinical Trials Network  
 Prescription Opioid Addiction Treatment Study**  
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 April 22, 2010



### Previous Research on Treatment of Opioid Dependence

- Most studies examine heroin addicts receiving methadone maintenance treatment; favor maintenance pharmacotherapy and more counseling
- Findings from **counseling research** in methadone treatment programs may not generalize to office-based buprenorphine treatment
- Findings regarding **length of pharmacotherapy** for heroin addiction may not generalize to prescription opioid addiction.

### Key Questions Regarding Treatment of Prescription Opioid Dependence

- Length of pharmacotherapy
- Intensity of counseling
- Role of chronic pain

### Prescription Opioid Addiction Treatment Study (POATS) Overview

- NIDA Clinical Trials Network (CTN) study of treatment for prescription opioid dependence, examining
  - Buprenorphine of varying duration
  - Counseling of varying intensity
- Largest treatment study ever conducted for prescription opioid dependence
  - 10 participating CTN sites across U.S.
  - June 2006 - July 2009

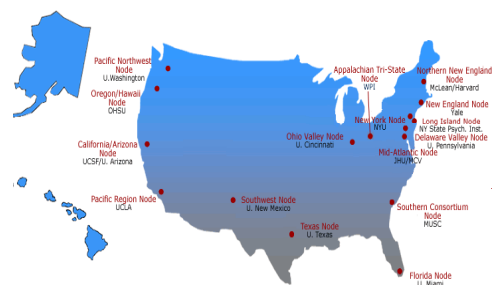
### POATS Study Questions

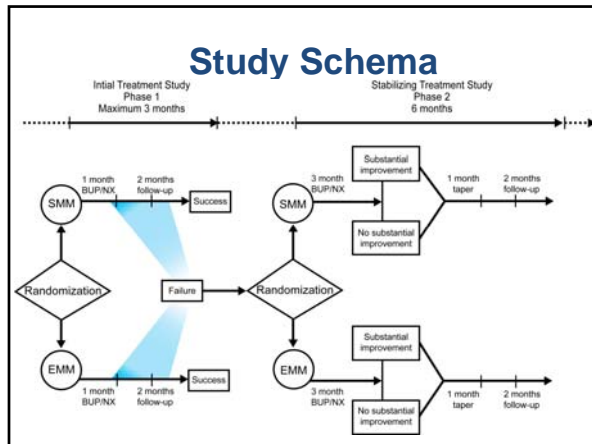
- Does adding individual drug counseling to buprenorphine-naloxone (bup-nx) + standard medical management (SMM) improve outcome?
  - May be a proxy for drug abuse treatment program vs. office-based opioid treatment, using bup-nx
- What length of bup-nx is best for these pts? 1 month? 3 months? Maintenance?
- Do answers vary according to presence or absence of current chronic pain?

### National Institute on Drug Abuse Clinical Trials Network (NIDA CTN)

Partnership between academic research centers and community drug abuse treatment programs (CTPs) to develop and implement multi-site clinical research studies in CTPs to improve drug abuse treatment nationwide

### NIDA Clinical Trials Network (CTN) Nodes





### Key Eligibility Criteria

- DSM-IV opioid dependence, not just physical dependence
- ≥ 20 days opioid use in past 30
- Additional SUDs eligible if not requiring immediate medical treatment
- Non-psychotic, psychiatrically stable

Weiss et al., Am J Addictions 2010

### Heroin-Related Exclusion Criteria

- >4 days of heroin use in past 30 days
- Ever met criteria for opioid dependence as a result of heroin use alone
- Ever injected heroin

Potter et al., Contemporary Clinical Trials, 2010

### Pain-Related Inclusion/Exclusion Criteria

- Pts prescribed opioids for pain were included only if approved by prescribing MD
- Cancer pain excluded
- No traumatic or major pain event within past 6 mos
- Expressed interest in stopping opioids

Weiss et al., Am J Addictions, 2010

## Description of the Study Population

### Baseline Stratification Factors

Lifetime heroin use 23.0%

Current chronic pain 42.0%

- **Chronic pain** defined as self-report of non-withdrawal pain, beyond the usual aches and pains for ≥ 3 months.

### Baseline Sociodemographic Characteristics

<b>Female</b>	<b>40.0%</b>
<b>Caucasian</b>	<b>91.4%</b>
<b>Hispanic</b>	<b>4.7%</b>
<b>Age (mean, SD)</b>	<b>32.7 (10.2)</b>

No observable significant differences between EMM and SMM across baseline characteristics.

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### Baseline Sociodemographic Characteristics (cont.)

<b>Employment</b>	Full-time	411 (62.9%)
	Part-time	65 (10.0%)
	Unemployed	82 (12.6%)
<b>Marital status</b>	Never	326 (50.1%)
	Married	180 (27.6%)
	Divorced	101 (15.5%)
<b>Years education (mean, SD)</b>		13.0 (2.2)

No significant differences between EMM and SMM

### Baseline Psychiatric Characteristics

<b>Major Depressive Disorder (CIDI)</b>	Lifetime	41%
	Current	22%
<b>PTSD (CIDI)</b>	Lifetime	18%
	Current	12%
<b>Beck Depression Inventory</b>		22 (12)

No significant differences between EMM and SMM

### Prevalence of Other Substance Use Disorders

		Past Year	Lifetime
<b>Alcohol</b>	Abuse	10%	60%
	Dependence	4%	27%
<b>Cannabis</b>	Abuse	11%	47%
	Dependence	5%	15%
<b>Cocaine</b>	Abuse	6%	32%
	Dependence	3%	18%
<b>Sedative/hypnotic</b>	Abuse	10%	25%
	Dependence	6%	11%
<b>Stimulant</b>	Abuse	3%	22%
	Dependence	2%	11%

Days of use, past 30 days	Mean (SD)
<b>Opioid analgesics</b>	28.2 (3.5)
<b>Cannabis</b>	4.9 (9.4)
<b>Sedatives/hypnotics (not barbiturates)</b>	3.8 (7.9)
<b>Alcohol</b>	3.0 (6.0)
<b>Amphetamine</b>	0.5 (3.3)
<b>Cocaine</b>	0.5 (2.0)
<b>Barbiturates</b>	0.2 (2.0)
<b>Heroin</b>	0.1 (0.6)

### Other Baseline Substance Use Characteristics

Lifetime opioid analgesic injection	1.4%
Current cigarette smoker	70.6%

### Most Frequently Used Opioids in Past 30 Days

Oxycodone (sustained)	35%
Hydrocodone	32%
Oxycodone (immediate)	19%
Methadone	6%
Other	8%

### Opioid Use Disorder Treatment Histories

<b>Any treatment*</b>	<b>210 (30%)</b>
Self-help	124 (59%)
Inpatient/residential	88 (42%)
Outpatient counseling	84 (40%)
Methadone maintenance	64 (31%)
Buprenorphine maintenance	46 (22%)
Medical detoxification	125 (19%)
Intensive outpatient	33 (16%)
Naltrexone	7 (3%)
Other medications	11 (5%)

\*Participants could endorse >1

# Results

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## Session attendance Medication dosing Clinician adherence

### Phase 1 Medical Management Visit Attendance\*

	EMM (n=329)	SMM (n=324)
<b>Overall Mean (SD)</b>	4.4 (1.5)	4.5 (1.5)
<b>Attended ≥ 60% visits</b>	86%	90%
<b>Attended ≥ 80% visits</b>	68%	74%

\*Prior to meeting criteria for failure or success

No differences between EMM and SMM

### Phase 1 Drug Counseling Session Attendance

	EMM	SMM	Overall
<b>Overall Mean (SD)</b>	6.6 (3.5)		
<b>Attended ≥ 60% sessions</b>	71%		
<b>Attended ≥ 80% sessions</b>	49%		

\*Prior to meeting criteria for failure or success

### Phase 2 Medical Management Visit Attendance\*

	EMM (n=180)	SMM (n=180)
<b>Overall Mean (SD)</b>	14.1 (4.4)	13.9 (4.0)
<b>Attended ≥ 60% visits</b>	84%	82%
<b>Attended ≥ 80% visits</b>	77%	73%

\*Maximum: 17 visits

No differences between EMM and SMM

### Phase 2 Drug Counseling Session Attendance\*

	EMM (n=180)	SMM (n=180)
<b>Overall Mean (SD)</b>	11.6 (5.2)	N/A
<b>Attended at least 60%</b>	66%	N/A
<b>Attended at least 80%</b>	34%	N/A

\* Maximum: 18 visits

### Maximum Buprenorphine Dose Prescribed

Phase 1		Phase 2	
8 mg	11%	8 mg	9%
12 mg	23%	12 mg	20%
16 mg	44%	16 mg	38%
20 mg	4%	20 mg	11%
24 mg	11%	24 mg	10%
32 mg	3%	32 mg	5%
Other	3%	Other	8%

### Fidelity and Adherence

<b>EMM</b>	Trained and Certified	42 therapists
	Tapes passed/tapes monitored	176/179 (98%)
	Required additional training	2 clinicians
<b>SMM</b>	Trained and Certified	49 MDs
	Tapes monitored	242/244 (99%)
	Required additional training	2 clinicians

- 99% of sessions were satisfactory
- No clinicians were decertified

**Study Question 1:  
 Does adding drug counseling  
 to bup-nx + Standard Medical  
 Management improve  
 outcome?**

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### Phase 1 Treatment Success (N=653)

EMM	SMM	p
5.8%	7.4%	0.45

**Phase 1 Treatment Success Criteria**

- ≤ 4 days opioid use per month
- No positive urine screens for opioids on 2 consecutive weeks
- No other formal substance abuse treatment
- No injection of opioids

### Phase 2 Substantial Improvement (n=360)

	EMM	SMM	p
<b>Week 12 (end of stabilization)</b>	51.7%	46.7%	0.3

**Substantial improvement**

- Abstinent for  $\geq 3$  of final 4 weeks (including final week) of bup-nx stabilization (urine-confirmed self-report)

### Phase 2: Substantial Improvement at End of Taper & at Follow-up

	EMM	SMM	Overall	p
<b>Week 16 (end of taper)</b>	27.8%	24.4%	<b>26.1%</b>	0.4
<b>Week 24 (8 wks post-taper)</b>	10.0%	7.2%	<b>8.6%</b>	0.2

**Study Question 2:**  
 How does length of bup-nx treatment affect outcomes in pts with prescription opioid dependence?

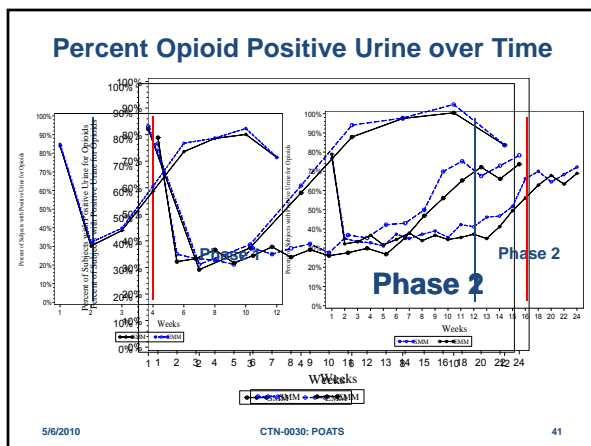
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### Successful Treatment Outcomes at 3 Time Points

	Success
<b>Phase 1</b> 4-week taper + 8 weeks f/u	<b>6.6%</b>
<b>Phase 2</b> Week 12 - End of stabilization	<b>49.2%</b>
Week 24 - 8 weeks post-taper	<b>8.6%</b>

Ph1 vs Ph2 Wk12	<.001
Ph1 vs Ph2 Wk24	0.21
Ph2 Wk12 vs Ph2 Wk24	<.0001



### Interactions and Predictors of Outcome

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### Phase 2 Week 12 Outcome Predictors

		Improved	p
<b>Gender</b>	Male	47.4%	0.48
	Female	51.7%	
<b>Race</b>	White	48.8%	0.56
	Not White	52.9%	
<b>Ethnicity</b>	Hispanic	72.2%	*
	Not Hispanic	48.0%	
<b>Smoking Status</b>	Smokers	47.1%	0.23
	Non-smokers	56.0%	

\*Not tested because of small sample with Spanish origin (5%).

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### Phase 2 Outcome Predictors: Lifetime Heroin Use

Heroin use		Improved	p
<b>Week 12</b> end of stabilization	Yes	37.0%	0.003
	No	53.8%	
<b>Week 24</b> 8 weeks post taper	Yes	5.0%	0.13
	No	10.0%	

### Interactions of Baseline Characteristics x Phase 2 Study Treatment

**No treatment interactions by sex,  
race, ethnicity, or lifetime heroin use**

**No site x treatment interaction**

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### Chronic pain outcomes

Chronic pain definition...

- Pain, beyond usual aches pains, not from withdrawal
- Lasting  $\geq 3$  months or more

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### Chronic pain patients were...

- No more likely to have serious adverse events
- Equally likely to enter Phase 2
- Equally likely to be substantially improved (primary outcome) at Phase 2 week 12 (CP 53% v. no CP 47%,  $p < 0.22$ )
- No CP status x treatment interaction at Phase 2 week 12 ( $p < 0.83$ )

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### % of CP Participants with Clinically Important Reductions in Pain Intensity (0-10)

Reduction at Ph2 wk 12 from baseline	Minimal ( $\geq 10\% \Delta$ )	Moderate ( $\geq 30\% \Delta$ )	Substantial ( $\geq 50\% \Delta$ )
<b>BPI Intensity Scale</b>	69%	51%	35%
<b>Worst pain</b>	66%	51%	34%
<b>Average pain</b>	67%	55%	43%

No difference between treatment groups

### **Caveats**

- Weekly SMM is more intensive than is often provided in the community
- A greater contrast, e.g., between less intensive SMM and more intensive counseling could have resulted in differences between the groups
- It is unclear what length of bup-nx stabilization, if any, could lead to better outcomes after a taper
- Failure criteria in Phases 1 & 2 differed slightly, as did the populations

### **Conclusions**

- Tapering from opioids, whether initially or after a period of substantial improvement, led to nearly universal relapse
- SMM produced outcomes equal to SMM + drug counseling
- Patients with chronic pain did as well as those without chronic pain, & many had significant improvement in their pain