Advances in Clinical Research for Prescription Opioid Dependence

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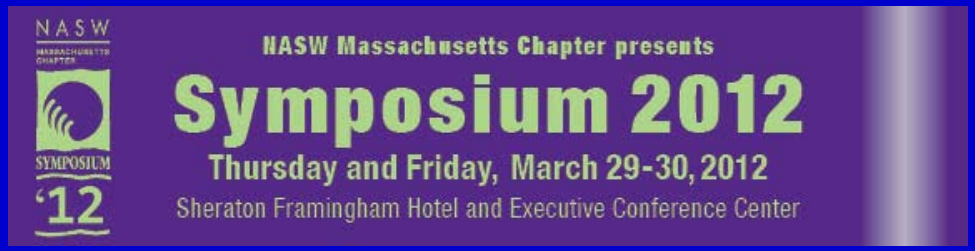


Objectives

To learn about:

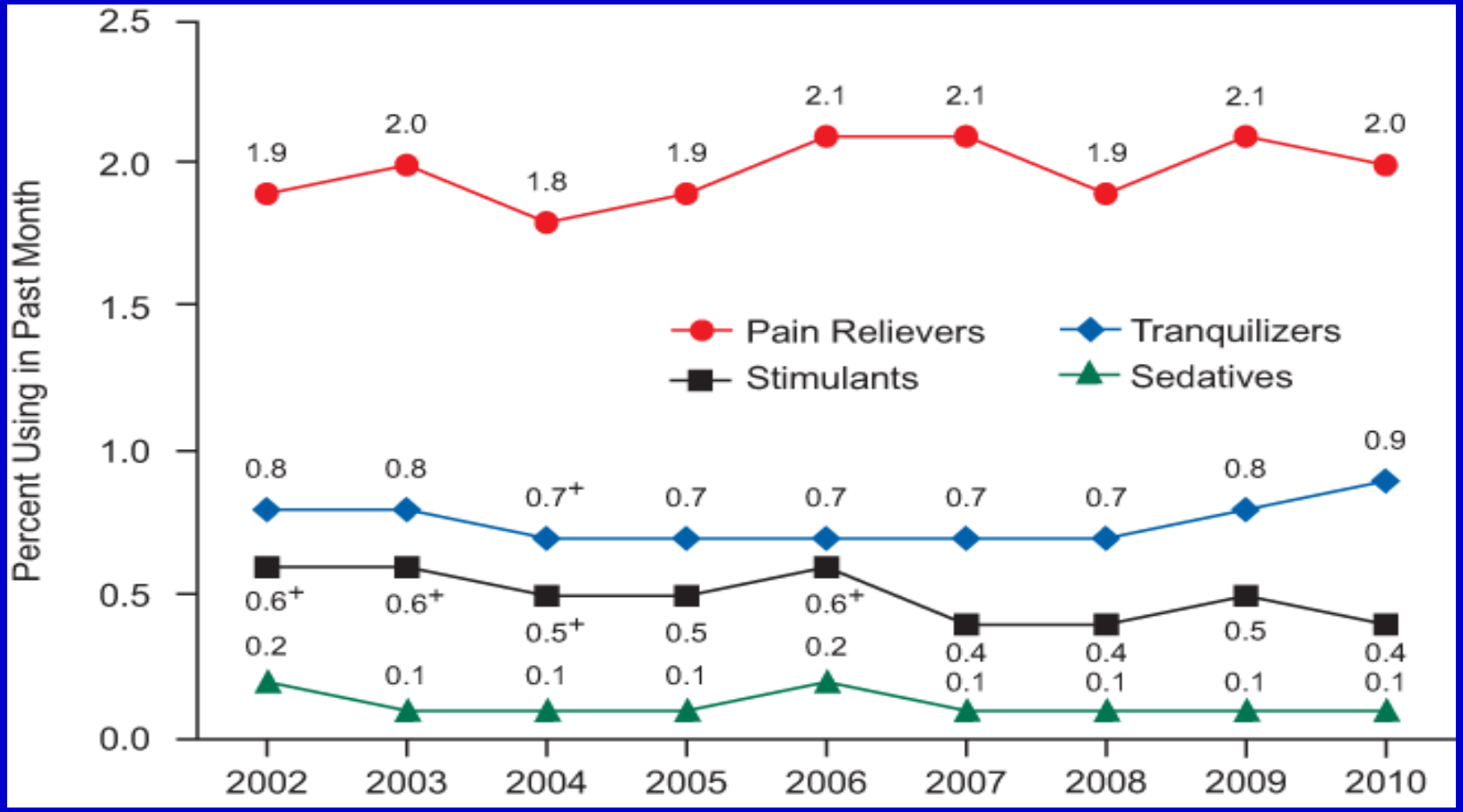
1. the prevalence of prescription opioid dependence and the societal/public health consequences of prescription opioid dependence
2. the design and methodology involved in the NIDA CTN Prescription Opioid Addiction Treatment Study
3. primary outcome results from the NIDA CTN Prescription Opioid Addiction Treatment Study and the implications for social work

Prescription Opioid Dependence: Magnitude of the Problem

- In 2010, 5.1 million ≥ 12 year olds used prescription opioids non-medically in the past month (1.7% of the population)
- 2.0 million were new users of Rx opioids
- Among new users of illicit substances, this was the second largest number of past year initiates second only to marijuana by about 400,000 people in 2010

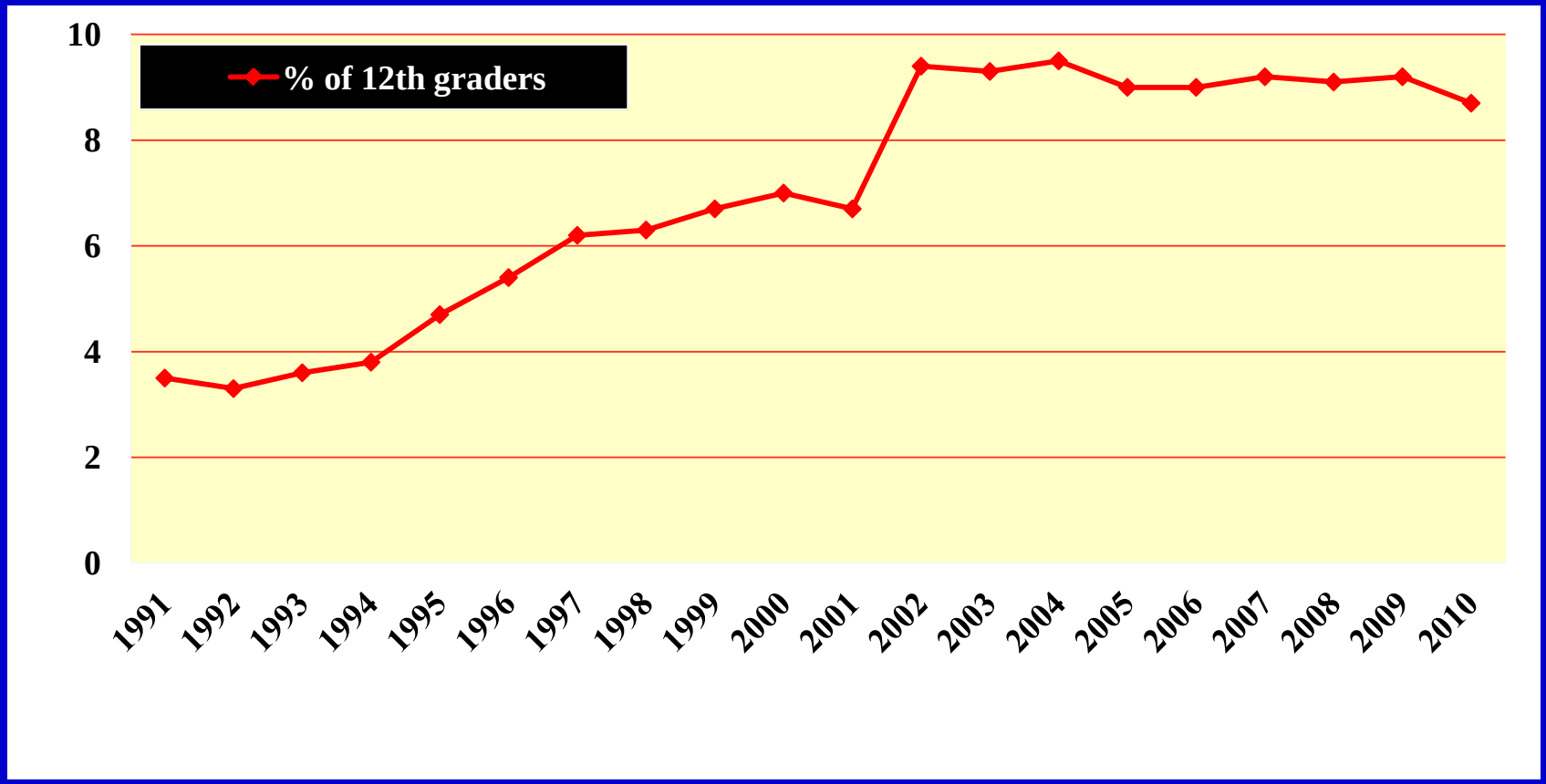
Source: SAMHSA, 2010 National Survey on Drug Use and Health

Past Month Nonmedical Use of Types of Psychotherapeutic Drugs among Persons Aged 12 or Older: 2002-2010



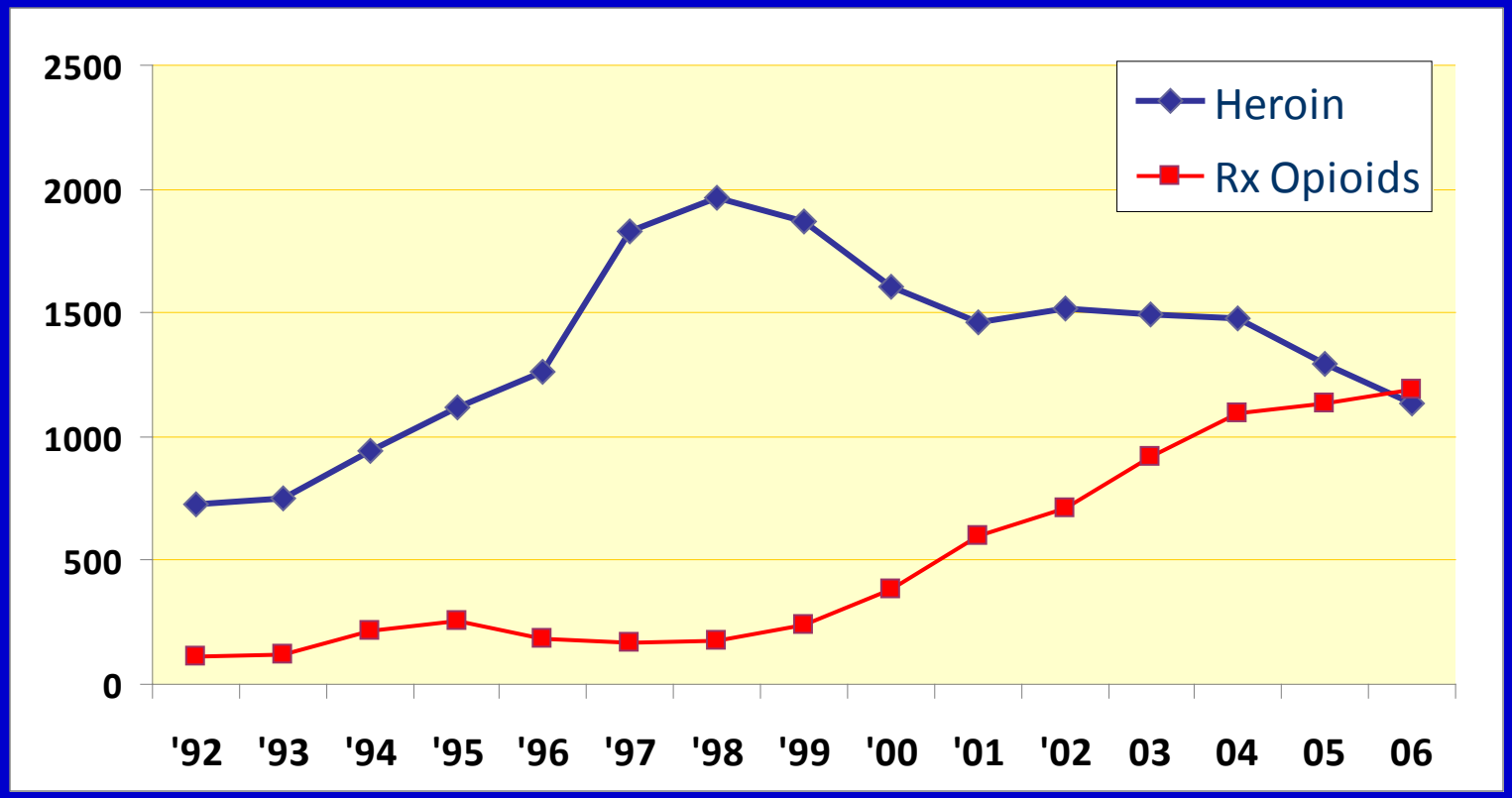
Source: SAMHSA, 2010 National Survey on Drug Use and Health

Trends in Annual Prevalence of Non-Medical Prescription Opioid Use Among 12th graders

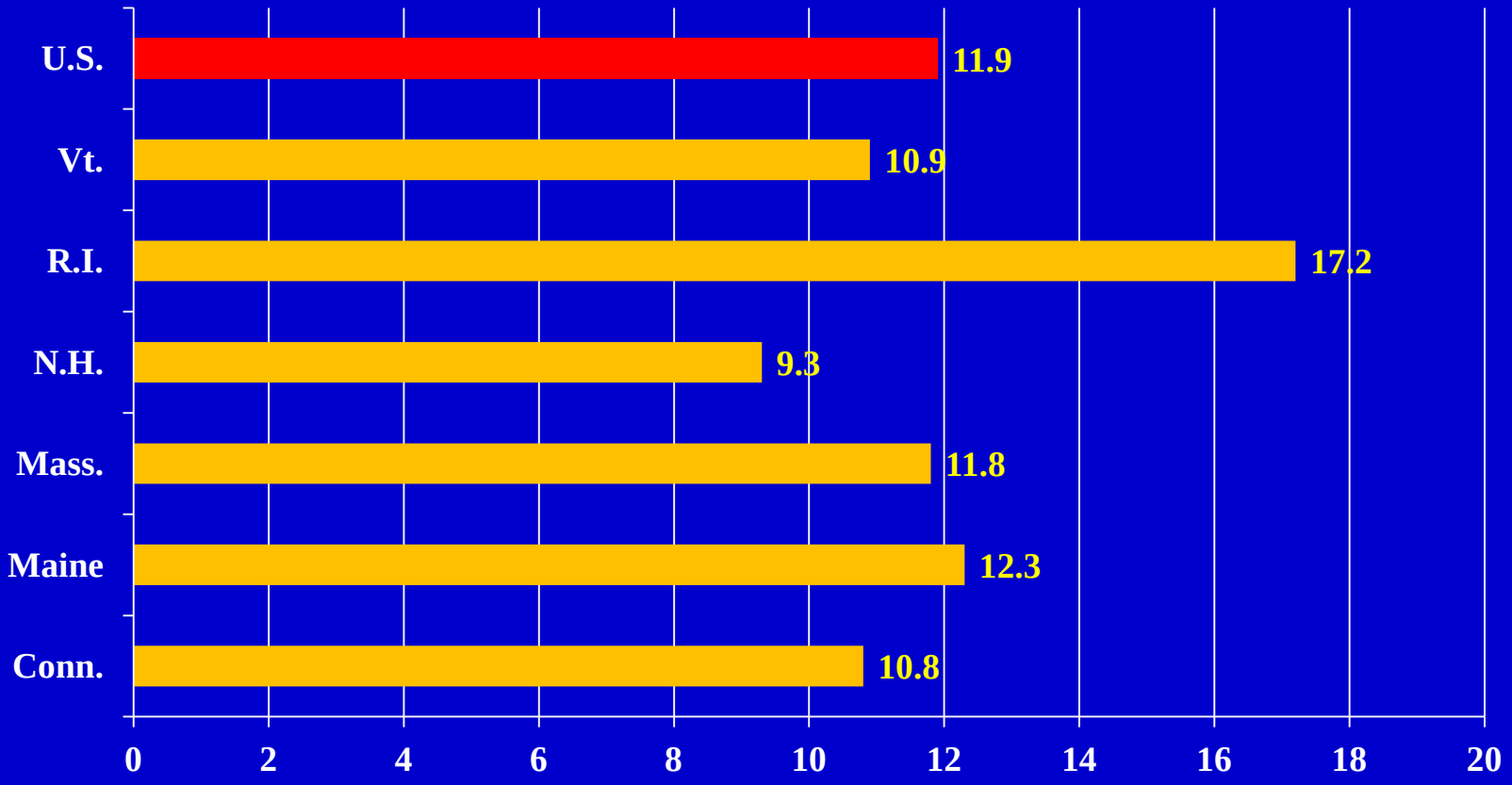


Source: 2010 Monitoring the Future Survey

Opioid Admissions Age 12-17 yrs

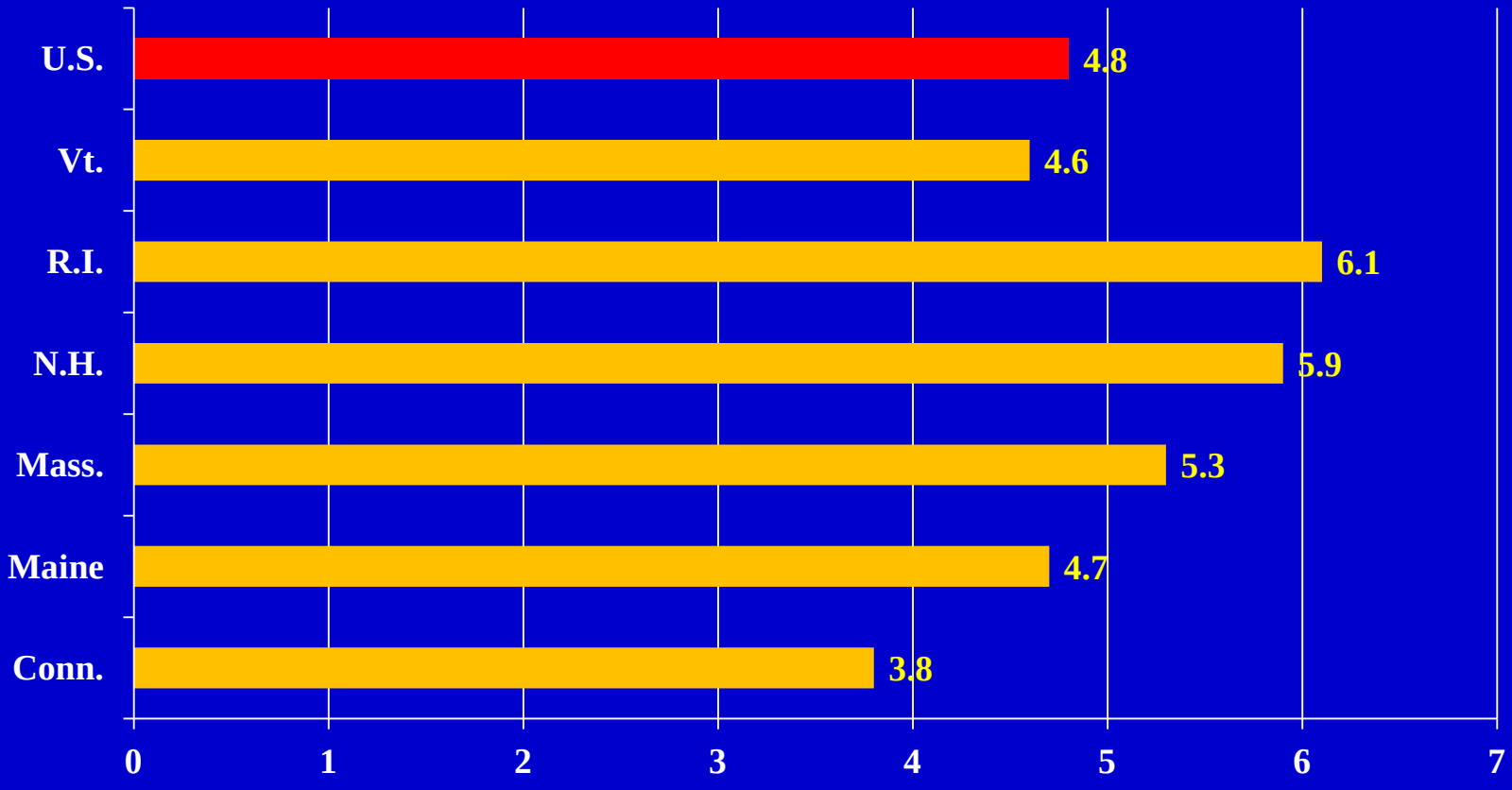


Rate of Deaths from Drug Overdose, per 100,000 people, 2008 (N.E.)



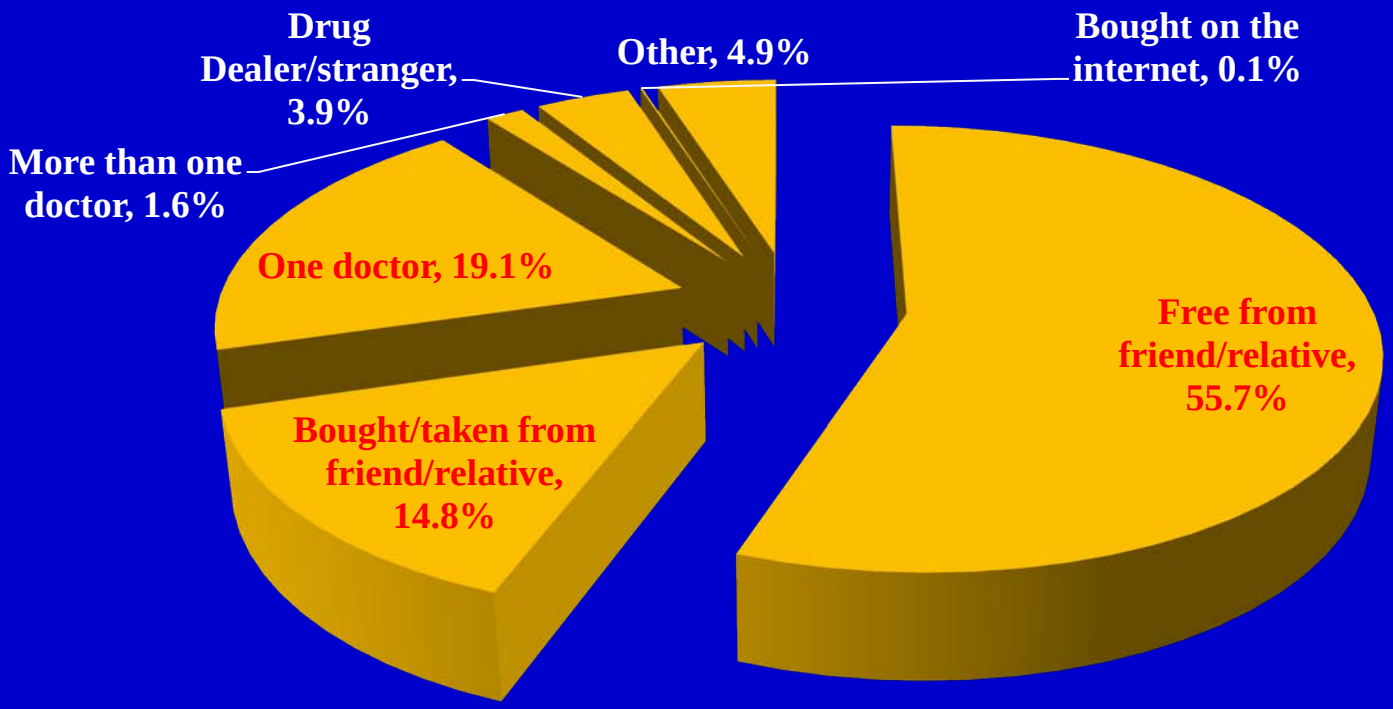
Source: Centers for Disease Control and Prevention, Bureau of Substance Abuse Services [Boston Globe, Nov 14, 2011]

Percentage of people ≥ 12 using opioid pain relievers for non-medical purposes, 2008-2009 (N.E.)

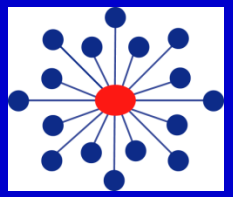


Source: Centers for Disease Control and Prevention, Bureau of Substance Abuse Services [Boston Globe, Nov 14, 2011]

Most recent source of prescription painkillers for non-medical purposes, among users in MA ≥ 12, 2010



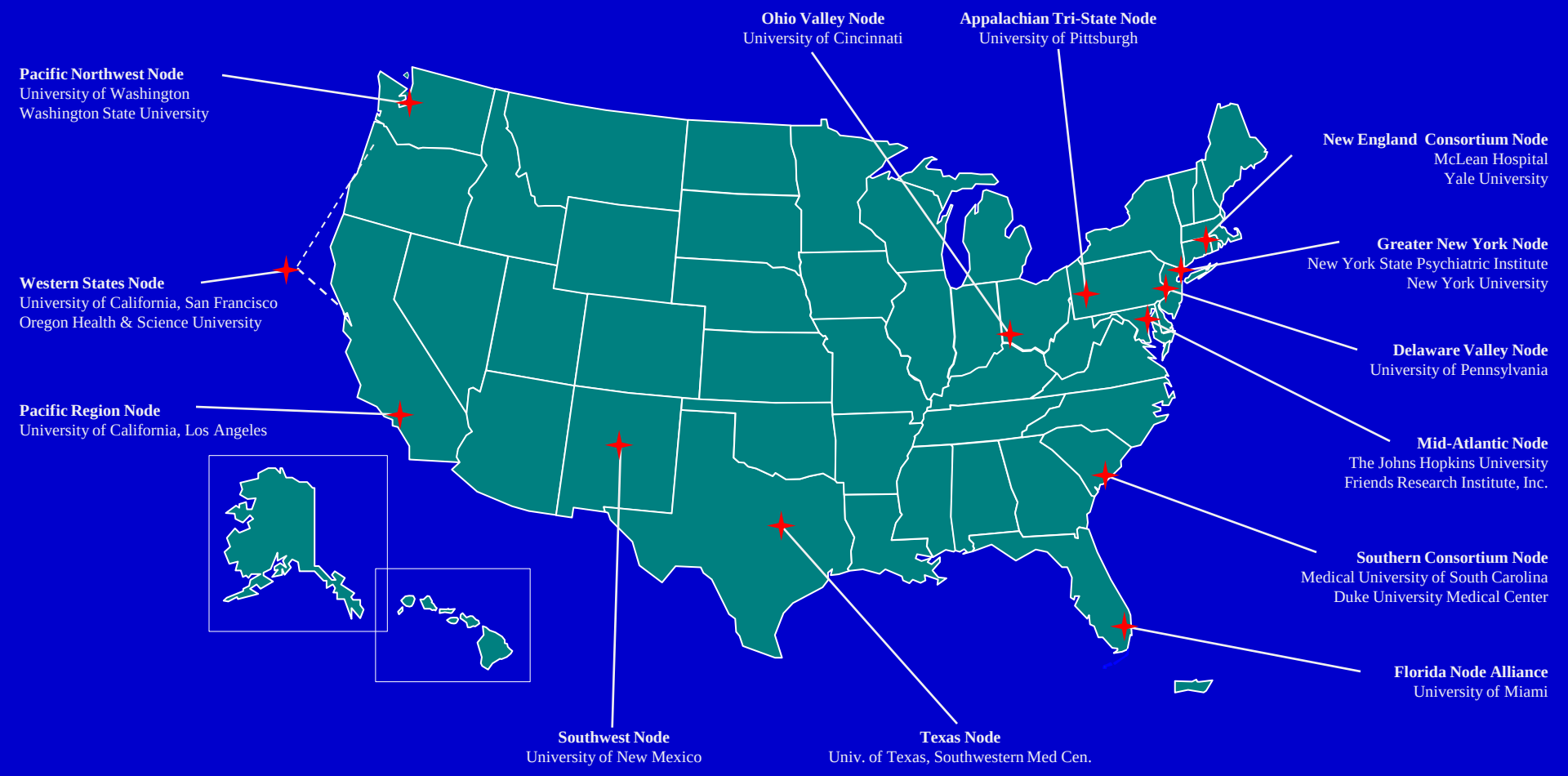
Source: Centers for Disease Control and Prevention, Bureau of Substance Abuse Services [Boston Globe, Nov 14, 2011]



National Institute on Drug Abuse Clinical Trials Network

- A partnership between academic research centers and community drug abuse treatment programs (CTPs) to develop and implement multi-site clinical research studies in CTPs.

National Drug Abuse Treatment Clinical Trials Network



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.

Previous Research on Counseling with Buprenorphine

- Most studies have focused on primarily heroin-dependent populations
- *Fiellin et al. (2006):* Only study to examine optimal intensity of counseling for patients receiving office-based buprenorphine treatment.
  - Only 17% of the population dependent on prescription opioids, however.
  - 20-minute vs. 45-minute weekly counseling session
  - No difference in outcomes between counseling groups

Dependence on Heroin vs. Prescription Opioids

- We can't assume that patients with prescription opioid dependence (POD) will have the same course of illness and response to treatment as those dependent on heroin
- Moore et al. (2007): POD patients more likely to
    1. Earn more income
    2. Be hepatitis-C negative
    3. Complete treatment
    4. Have higher % of opioid-negative urines

The Prescription Opioid Addiction Treatment Study (POATS): Design

- Two-phase “adaptive treatment research design”
- Patients begin with 4-week taper of buprenorphine-naloxone (bup/nx)
- Randomly assigned to Standard Medical Management (SMM) or SMM + individual Opioid Drug Counseling (SMM + ODC)

Weiss et al., Contemporary Clinical Trials, 2010

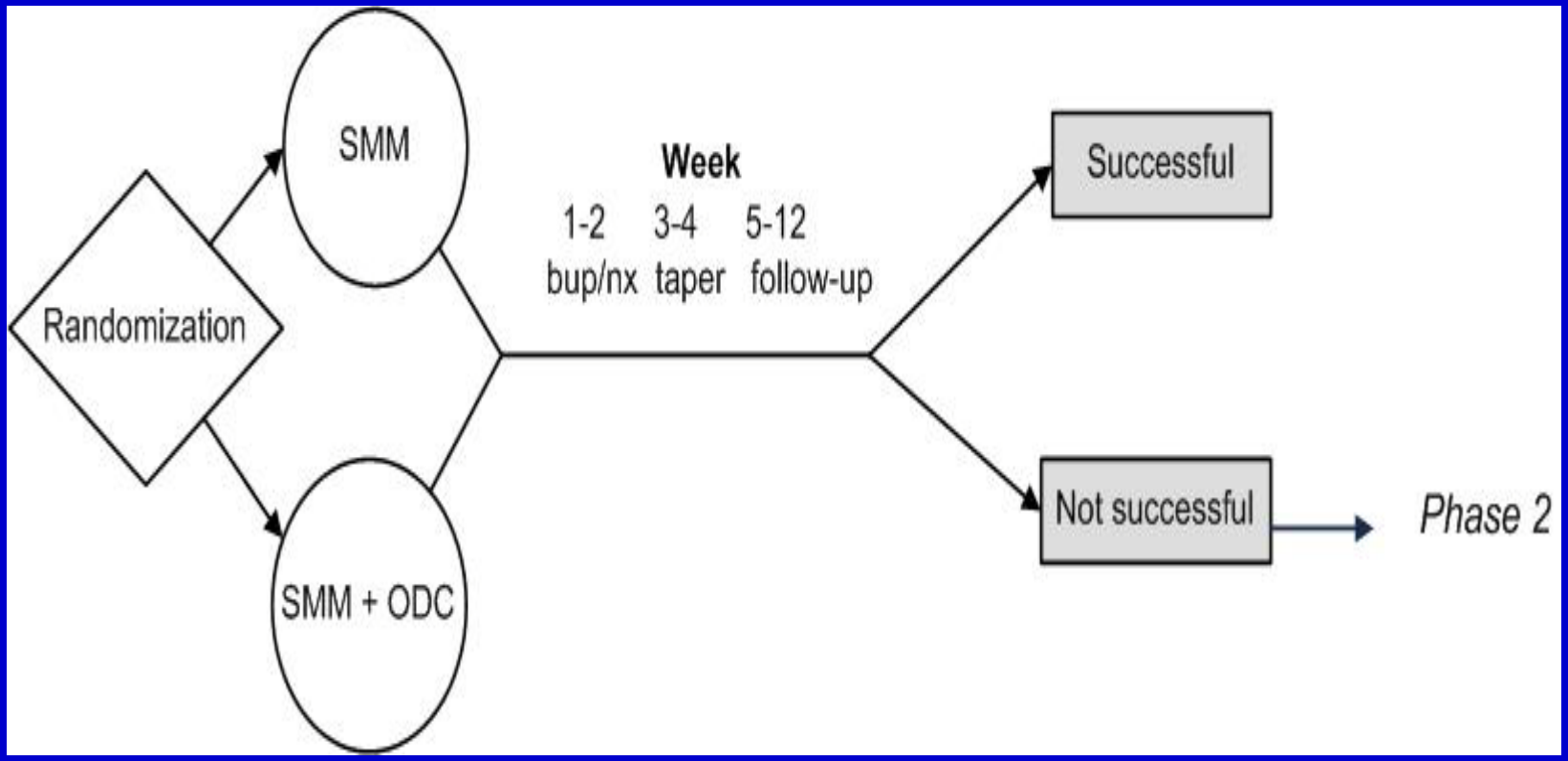
The Prescription Opioid Addiction Treatment Study (POATS): Design

- Patients who succeed in Phase 1 (1-month taper plus 2-month follow-up) are successfully finished with the study
- Patients who relapse may go into Phase 2:
  - 3 months of bup-nx stabilization,
  - 1 month taper off bup-nx
  - 2 months of follow-up
  - Re-randomized to SMM or SMM + ODC in Phase 2

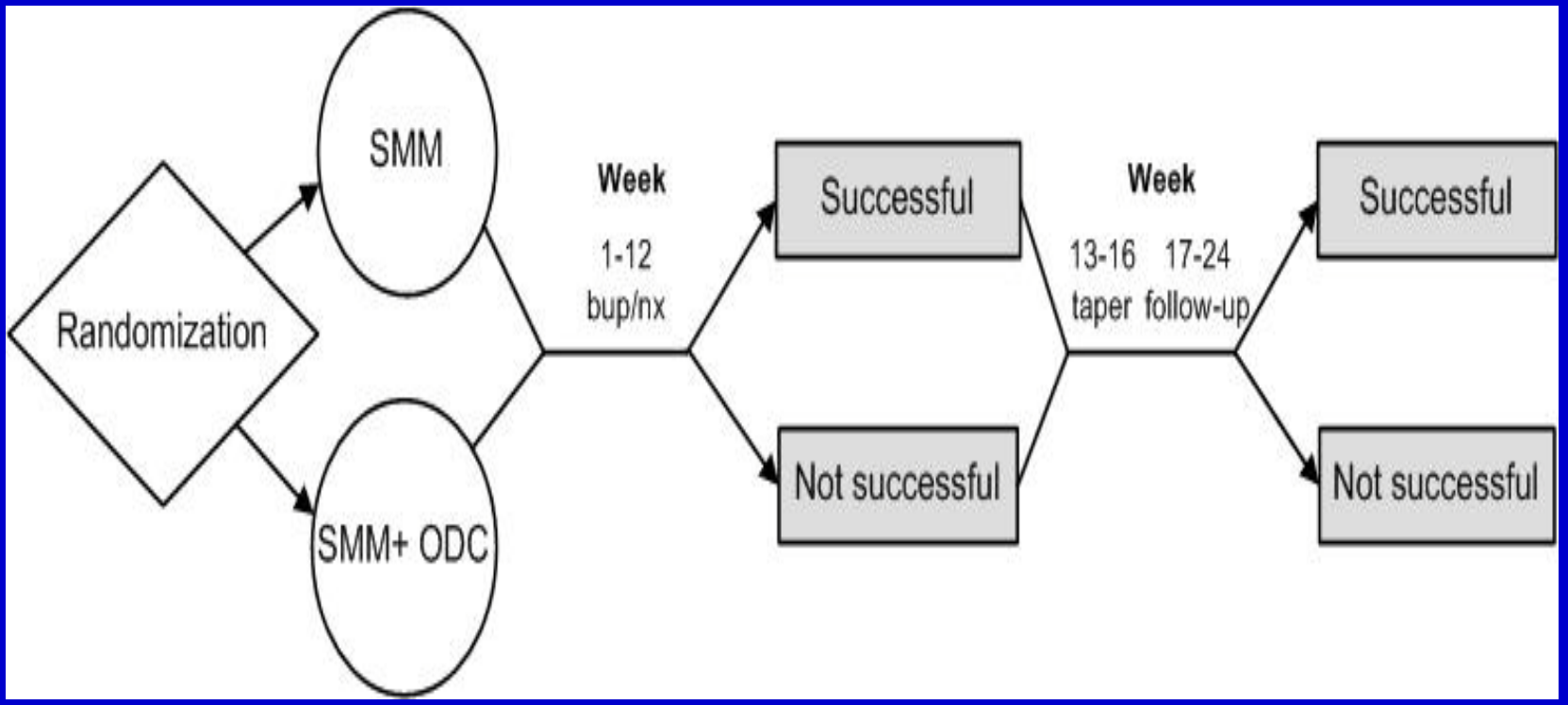
Key Features of POATS Design

- Adaptive treatment research design approximates clinical practice
- Start with a less intensive treatment to see if it works
- Try a more intensive if first treatment doesn't work

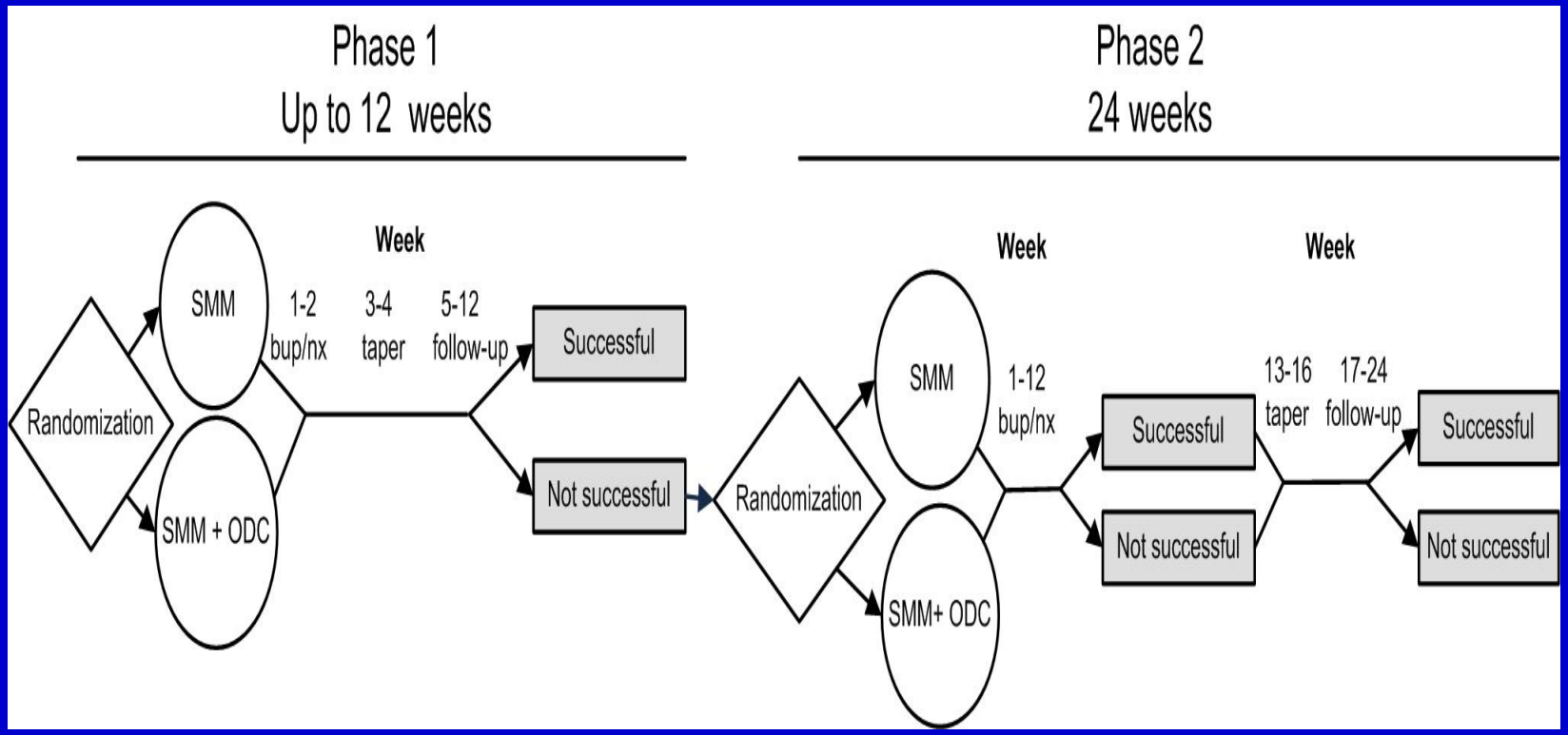
Phase 1 (up to 12 weeks)



Phase 2 (24 weeks)



Study Design



POATS Study Questions

- Does adding individual drug counseling to buprenorphine-naloxone (bup-nx) + standard medical management 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 1) presence of current chronic pain or 2) a lifetime history of any heroin use?

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

Complicating Factors in Defining a Study Population of Subjects with Prescription Opioid Dependence

- Heroin use
- Chronic pain

Heroin Use

- Most previous studies of opioid dependence had included mostly Ss with heroin dependence, with some Ss who had POD
- We wanted to identify a new and distinct population of Ss with POD
- *However*, we wanted the population to be representative of those dependent upon prescription opioids, some of whom also use heroin to varying extent.

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

Chronic Pain

- Many, but not all, patients with POD have been prescribed opioids for pain
- “Prescription” use ≠ pain
- Some people with pain obtain opioids illicitly

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 months
- Had to express interest in stopping opioids

Weiss et al., Am J Addictions, 2010

Heroin and Chronic Pain Design Decisions

- Patients were stratified on the basis of
  - Presence/absence of current chronic pain
  - Lifetime history of heroin use

Treatments

Buprenorphine-Naloxone

- Patients received 8-12 mg on Day 1
- Allowable dose was 8-32 mg/day
- Target dose was 16 mg/day, but flexible dosing allowed
- Once-daily dosing recommended
- Lost prescriptions were not refilled

Standard Medical Management

- Manualized treatment
- Weekly visits with buprenorphine-certified MD
- Initial visit: 45-60': f/u visits: 15-20'
- Assess substance use, craving, medication response
- Recommend abstinence, self-help

Opioid Drug Counseling

- Manualized drug counseling, based on previous successful counseling manuals
- 45-60’ visits
- Phase 1: 2x/wk
- Phase 2: 2x/wk for 6 weeks, 1x/week for 6 weeks

Opioid Drug Counseling (cont.)

- Education about addiction and recovery
- Recommend abstinence
- Recommend self-help
- Skills-based interactive exercises and take-home assignments
- Covers wider range of relapse prevention issues than SMM in greater depth: high-risk situations, managing emotions, dealing with relationships

Description of the Study Population (N = 653 in Phase 1)

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

Female	**40.0%**
Caucasian	**91.4%**
Hispanic	**4.7%**
Age (mean, SD)	**32.7 (10.2)**

No observable significant differences between SMM and SMM + ODC across baseline characteristics.

Baseline Sociodemographic Characteristics (cont.)

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

No significant differences between SMM and SMM + ODC

Baseline Psychiatric Characteristics

Major Depressive Disorder (CIDI)	Lifetime	41%
	Current	22%
PTSD (CIDI)	Lifetime	18%
	Current	12%
Beck Depression Inventory mean		22 (12)

No significant differences between SMM and SMM + ODC

Prevalence of Other Substance Use Disorders

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

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

Other Baseline Substance Use Characteristics

Mean years opioid use	4.5
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

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

*Participants could endorse >1

Maximum Buprenorphine Dose Prescribed

Phase 1	
8 mg	11%
12 mg	23%
16 mg	44%
20 mg	4%
24 mg	11%
32 mg	3%
Other	3%

Phase 2	
8 mg	9%
12 mg	20%
16 mg	38%
20 mg	11%
24 mg	10%
32 mg	5%
Other	8%

Results

Weiss RD, et al., *Arch Gen Psychiatry.* 2011;68(12):1238-1246. doi:10.1001/archgenpsychiatry.2011.121

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

Phase 1 Successful Outcome (N=653)

SMM+ ODC	SMM	p
6%	7%	0.45

Phase 1 Successful Outcome 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 Successful Outcome (n=360)

	SMM+ ODC	SMM	p
Week 12 (end of stabilization)	52%	47%	0.3

Phase 2 Successful outcome

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

Phase 2: Successful Outcome at End of Taper & at Follow-up

	SMM+ ODC	SMM	**Overall**	p
Week 16 (end of taper)	28%	24%	26%	0.4
Week 24 (8 wks post-taper)	10%	7%	9%	0.2

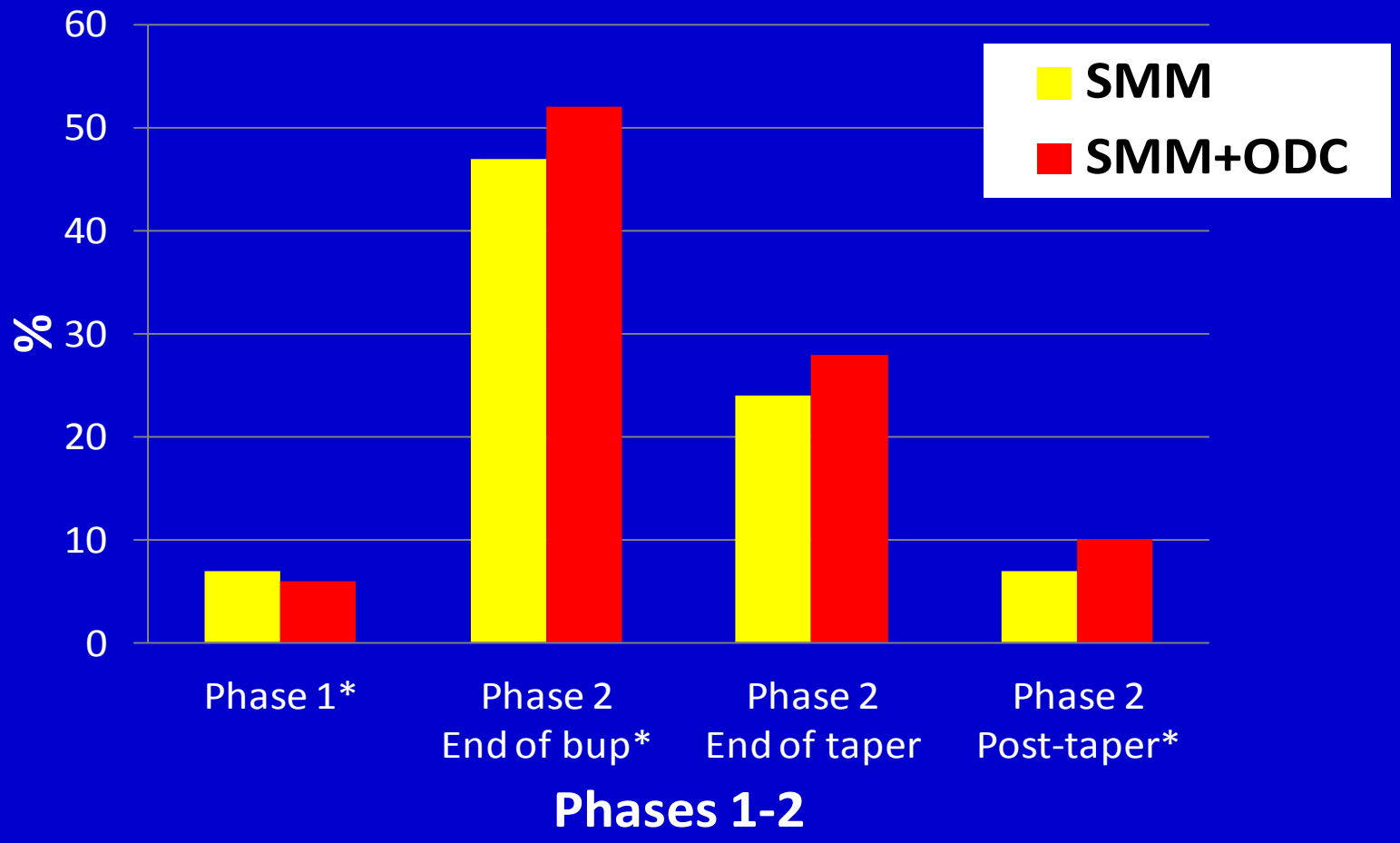
Study Question 2:
How does length of bup-nx treatment affect outcomes in pts with prescription opioid dependence?

Successful Outcomes at 3 Time Points

		Success
Phase 1	4-week taper + 8 weeks f/u	**7%**
Phase 2	Week 12 - End of stabilization	**49%**
	Week 24 - 8 weeks post-taper	**9%**

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

Successful outcomes over time



Weiss et al., Arch of Gen Psych, 2011

Predictors of Outcome

Phase 2 Week 12 Outcome Predictors

		Success	p
Gender	Male	47%	0.48
	Female	52%	
Race	White	49%	0.56
	Not White	53%	
Ethnicity	Hispanic	72%	*
	Not Hispanic	48%	
Smoking Status	Smokers	47%	0.23
	Non-smokers	56%	

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

Phase 2 Outcome Predictors: Lifetime Heroin Use

Heroin use		Success	p
Week 12 end of stabilization	Yes	37%	0.003
	No	54%	
Week 24 8 weeks post-taper	Yes	5%	0.13
	No	10%	

Chronic Pain Participant Outcomes

Chronic pain participants (n=274)

		M (SD) or %
Pain severity (0-10)		4.4 (2.17)
Pain interference (0-10)		4.2 (2.67)
Course	Constant	43.1%
	Intermittent	54.7%
Duration	> 1 year	81.4%
	≥ four years	54.7%

Chronic pain location

Head/face	16.1%
Chest/abdomen	5.5%
Upper extremities	29.6%
Cervical	27.0%
Thoracic	26.3%
Lumbar/sacral	**65.0%**
Lower extremities	52.9%
Multiple spinal areas	36.1%

Chronic Pain (CP) vs no CP: Sociodemographics

	CP (n=274)	No CP (n=379)
Female	42.3%	38.3%
Age (years)**	35.4 (10.3)	30.8 (9.7)
Caucasian (vs not)	91.2%	93.1%
Years of education	12.9(2.3)	13.1 (2.1)

Chronic pain and Outcome

		Success	p
Phase 2 Week 12	Chronic Pain	53.0%	
(end of stabilization)	No	46.5%	0.22
Phase 2 Week 24	Chronic Pain	9.4%	
(8 weeks post-taper)	No	8.1%	0.60

Caveats: Overall Study Findings

- Weekly SMM is more intensive than is often provided in the community; we had no low-intensity MM condition

- A greater contrast, e.g., between less intensive SMM and more intensive counseling could have resulted in differences between groups

Caveats: Overall Study Findings (cont.)

- It is unclear what length of bup-nx stabilization, if any, could lead to better outcomes after a taper

- Study was initially designed in 2005, when prescription opioid dependence was seen as perhaps quite different from heroin dependence, with potentially significant differences in response to treatment

Conclusions

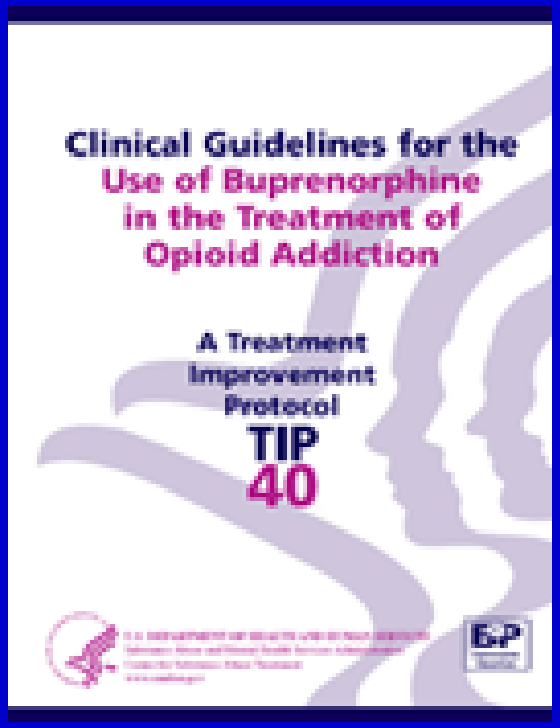
- Tapering from opioids, whether initially or after a period of substantial improvement, led to nearly universal relapse

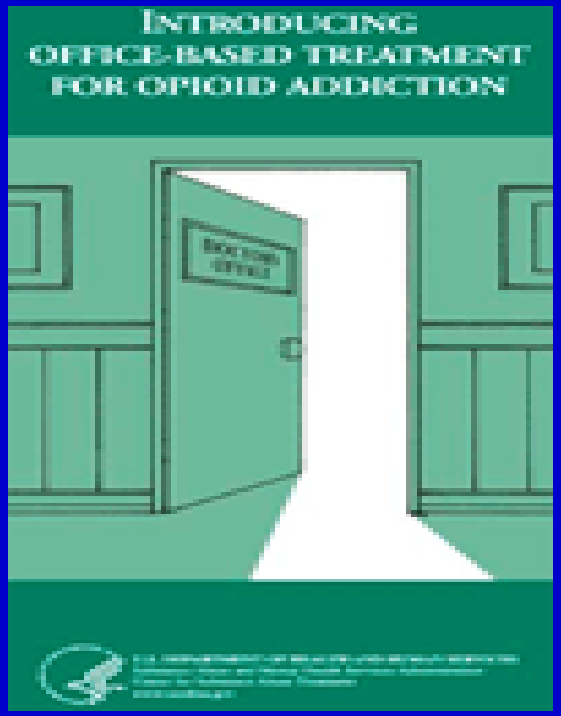
- SMM produced outcomes equal to SMM + drug counseling

Implications for Social Work

- Social workers can play a vital role in the treatment of prescription opioid dependence through:
  - Understanding the population characteristics of prescription opioid dependence, including chronic pain
  - Clinical assessment and collecting thorough case histories
  - Referrals to qualified buprenorphine prescribing MDs

SAMHSA Resources





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SAMHSA

Substance Abuse & Mental Health Services Administration
U.S. Department of Health and Human Services

Buprenorphine
PHYSICIAN & TREATMENT PROGRAM LOCATOR

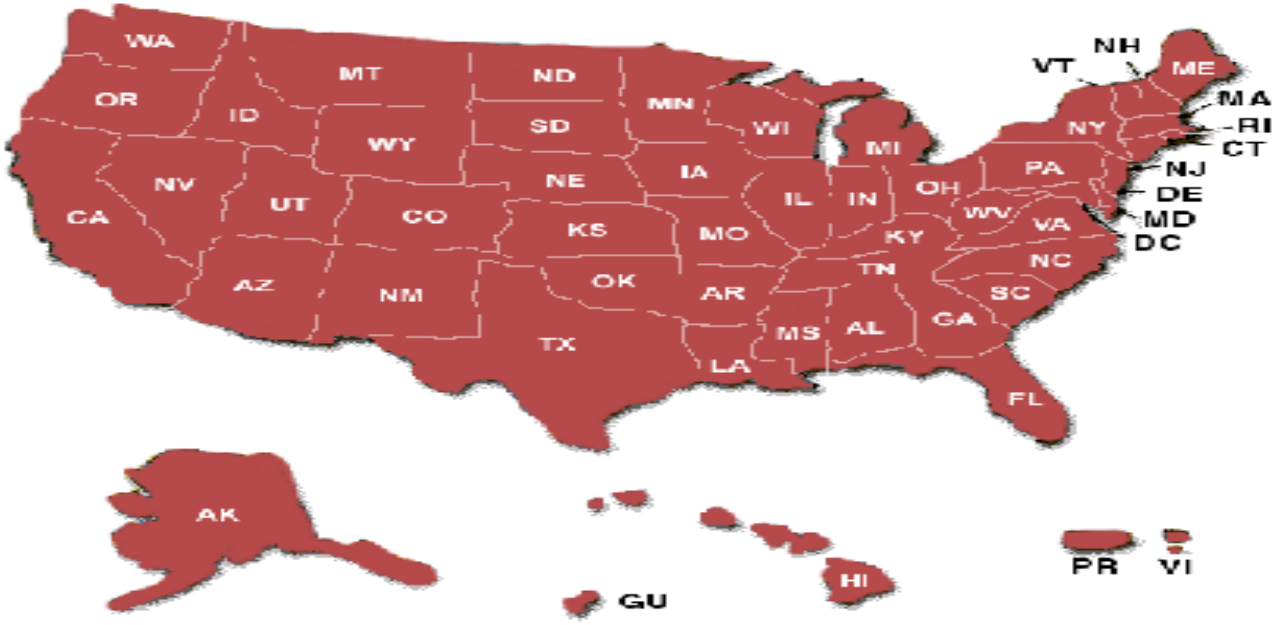
- home
- about the buprenorphine locator
- detailed buprenorphine search
- state substance abuse agencies
- frequently asked questions
- additional resources
- comments or questions
- treatment facility locator

Notice: The maximum number of patients a physician may treat with buprenorphine is limited by law; therefore, some physicians listed on the Locator may not be accepting new patients at this time. If you are unable to find a physician within your area who is accepting new patients, please check our site later, as new physicians are being added weekly.

Treatment programs are authorized under 21 U.S.C. Section 823 (g)(1) to dispense (but not prescribe) opioid treatment medications. Treatment programs registered under 21 U.S.C. Section 823 (g)(1) are not subject to patient limits.

To locate physician(s) and treatment program(s) authorized to treat opioid addiction with Buprenorphine in a particular **State**, select the **State** on the map below or use the **detailed buprenorphine search** tab on the left to search by city, county, or zip code.

Pharmacists: Follow this link to find information on how to verify whether a prescribing physician has a valid DATA waiver.



Additional Resource

Research Funding Support

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