



Efficacy of Buprenorphine for Prescription Opioid Addiction

Roger D. Weiss, M.D.

Chief, Division of Alcohol and Drug Abuse,

McLean Hospital, Belmont, MA

& Professor of Psychiatry,

Harvard Medical School, Boston, MA

June 9, 2011

The Prescription Opioid Addiction Treatment Study (POATS)

- Compared treatments for rx opioid dependence
 - buprenorphine-naloxone of varying durations
 - counseling of varying intensities
- Conducted as part of NIDA Clinical Trials Network (CTN) at 10 participating U.S. sites
- Largest study ever conducted for rx opioid dependence
- 653 participants enrolled
- Study began 6/06 & last visit in 7/09

The Prescription Opioid Addiction Treatment Study (POATS): Design

2-phase adaptive treatment research design

Phase 1

- Randomly assigned to
 - Standard Medical Management (SMM) or
 - SMM + individual Opioid Drug Counseling (SMM + ODC)
- 2-week stabilization with buprenorphine-naloxone (bup-nx)
- Then a 2-week taper
- 2-month follow-up

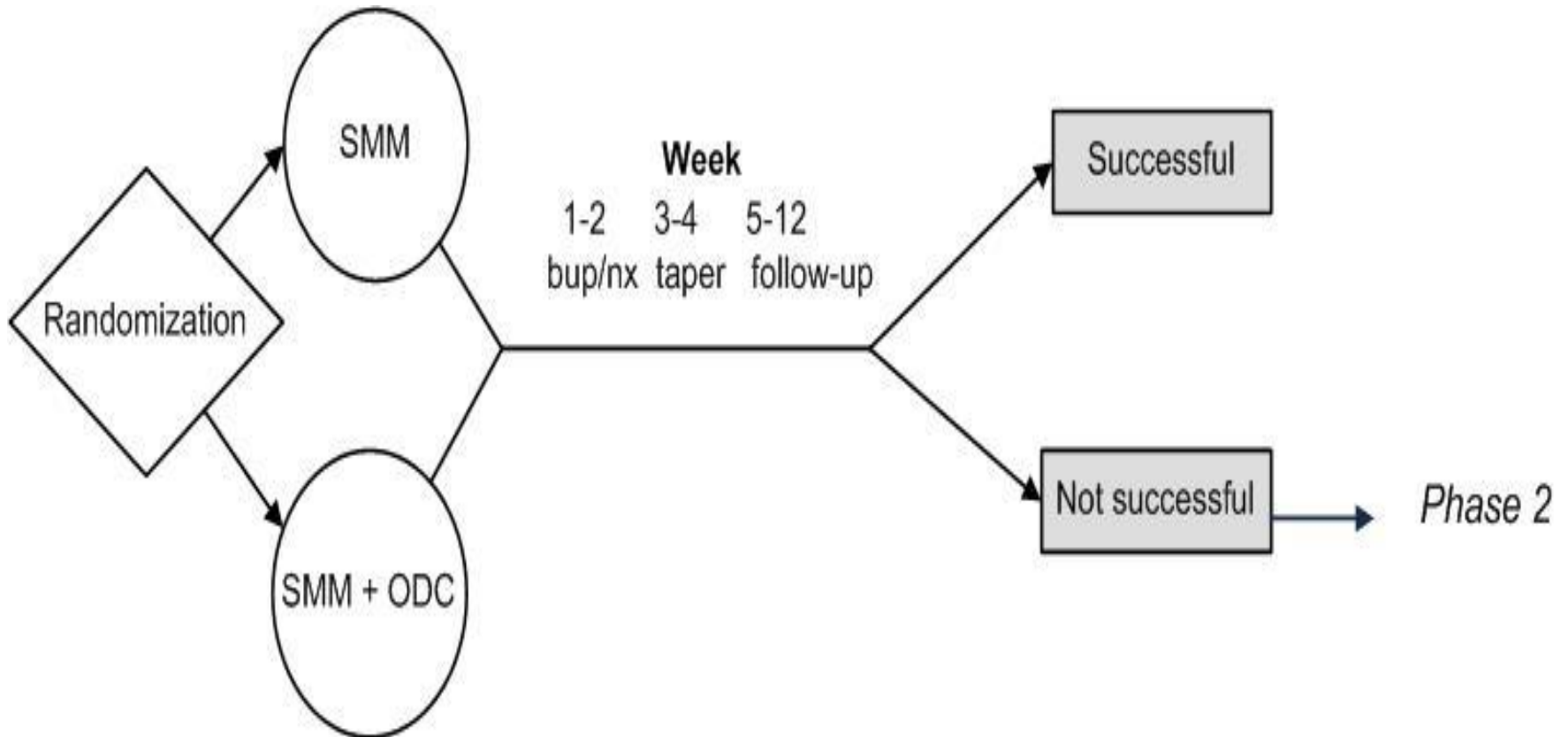
POATS Design (cont'd)

Patients who succeed in *Phase 1* are successfully finished with the study

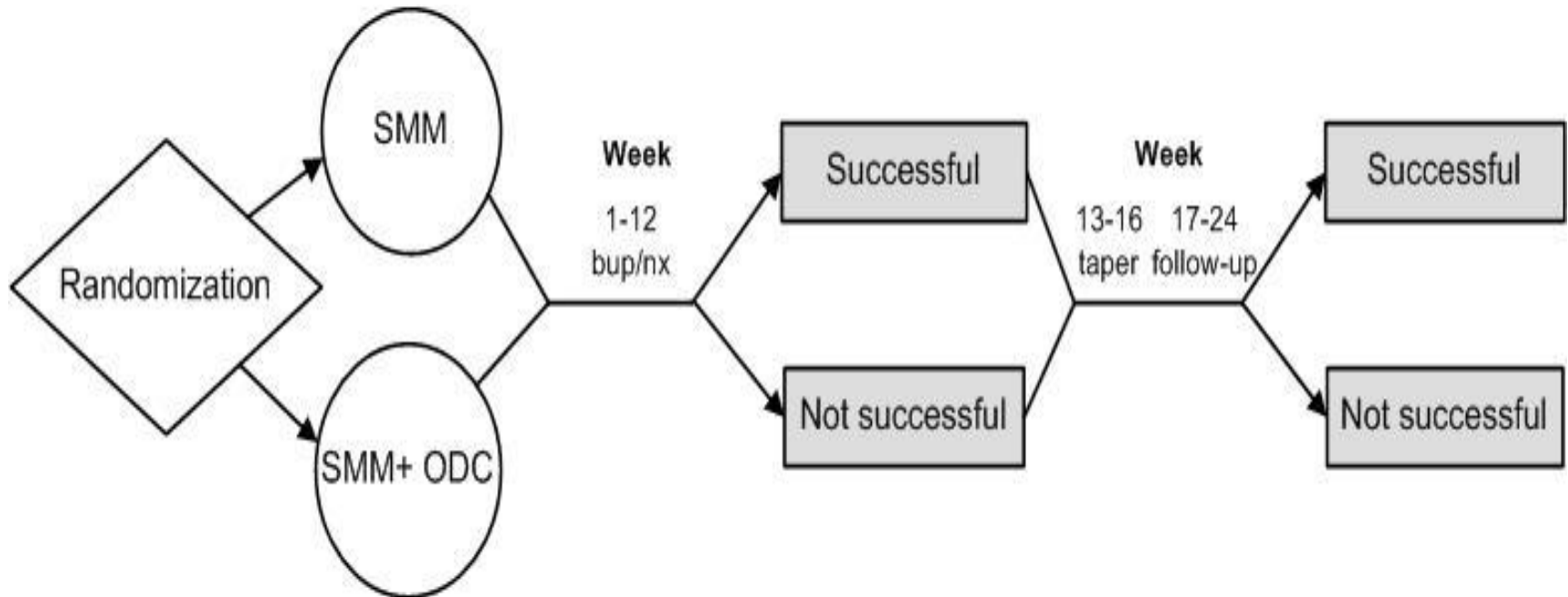
Patients who relapse may go into Phase 2

- Re-randomized to SMM or SMM + ODC
- 6-month study period in Phase 2
 - 3 months of bup-nx stabilization
 - 1- month taper off bup-nx
 - 2 months of follow-up

Phase 1 (up to 12 weeks)



Phase 2 (24 weeks)



POATS Study Questions

- Does adding individual drug counseling to buprenorphine-naloxone (bup-nx) + standard medical management (SMM) improve outcome?
- Optimal length of bup-nx for these patients
 - 1 month? 3 months?
 - Maintenance?
- Does chronic pain affect treatment outcomes?

Key Eligibility Criteria

- DSM-IV opioid dependence, not just physical dependence
- Little or no heroin use: <4 days in past month, never dependent, & never injected
- Pain only if prescribing MD approves study entry
- Non-psychotic, psychiatrically stable

Weiss et al., Am J Addictions 2010

Results

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

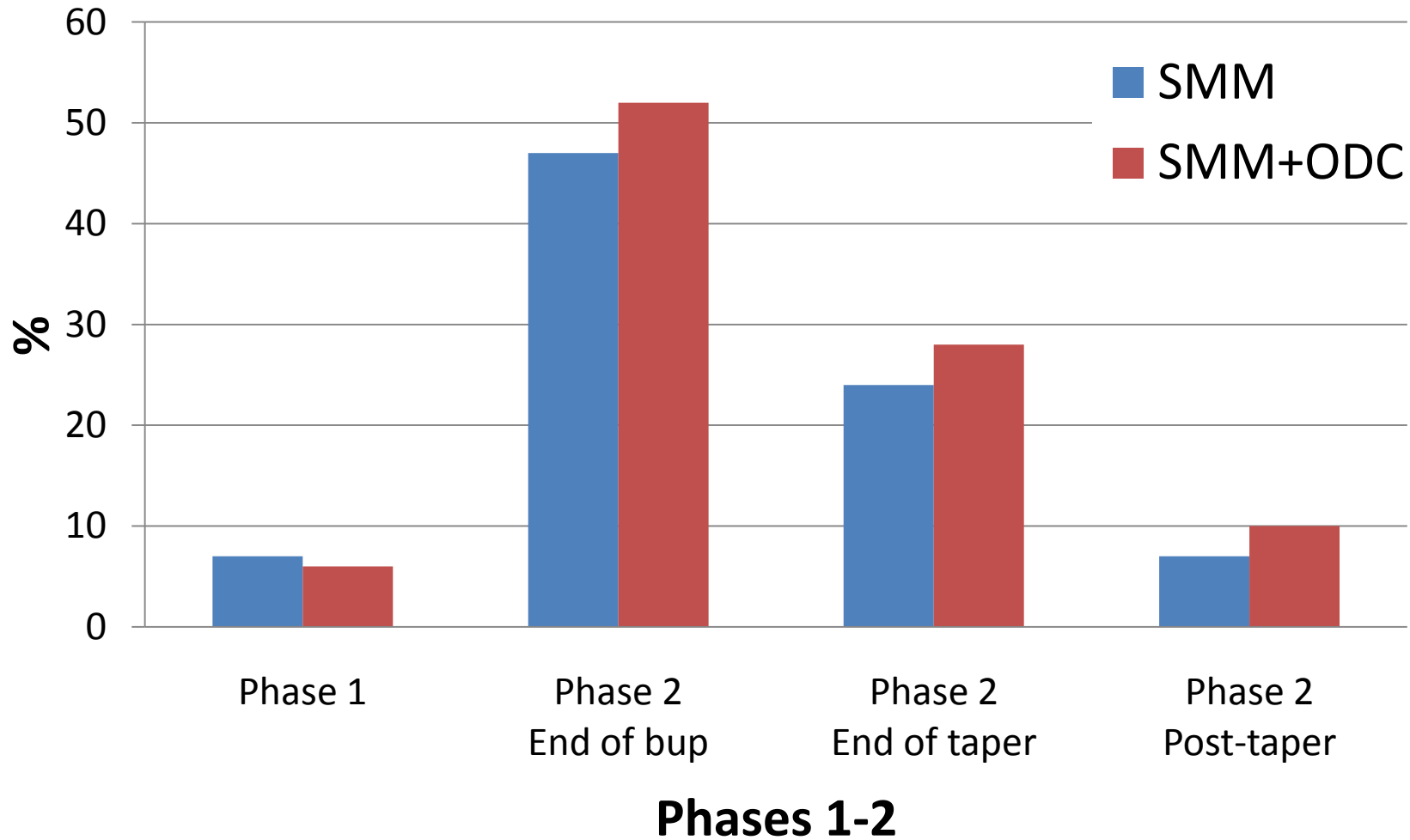
Phase 1 Successful Outcome Criteria (N=653)

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

Phase 2 Successful Outcome Criteria (n=360)

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

Successful outcomes over time



Chronic Pain:

**Patient Characteristics
& Outcomes**

Chronic pain patients (n=274)

	Mean (sd) or %
Pain severity (0-10)	4.4 (2.2)
Pain interference (0-10)	4.2 (2.7)

Course	Constant	43%
	Intermittent	55%

Duration	>1 year	81%
	≥4 years	55%

Chronic pain location

Back	■ Lumbar/sacral	65%
	■ Multiple spinal areas	36%
	■ Cervical	27%
	■ Thoracic	26%
Other	■ Lower extremities	53%
	■ Upper extremities	30%
	■ Head/face	16%
	■ Chest/abdomen	6%

Primary reason for use in CP patients, Past & Present

- Major reason for **1st use**
 - Pain 83%
 - Get high 13%

- Major reason for **current use**
if *1st reason was pain*
 - Avoid withdrawal 56%
 - Pain 23%
 - Get high 14%

Important reasons for using opioids

Past 6 months

0-10 scale

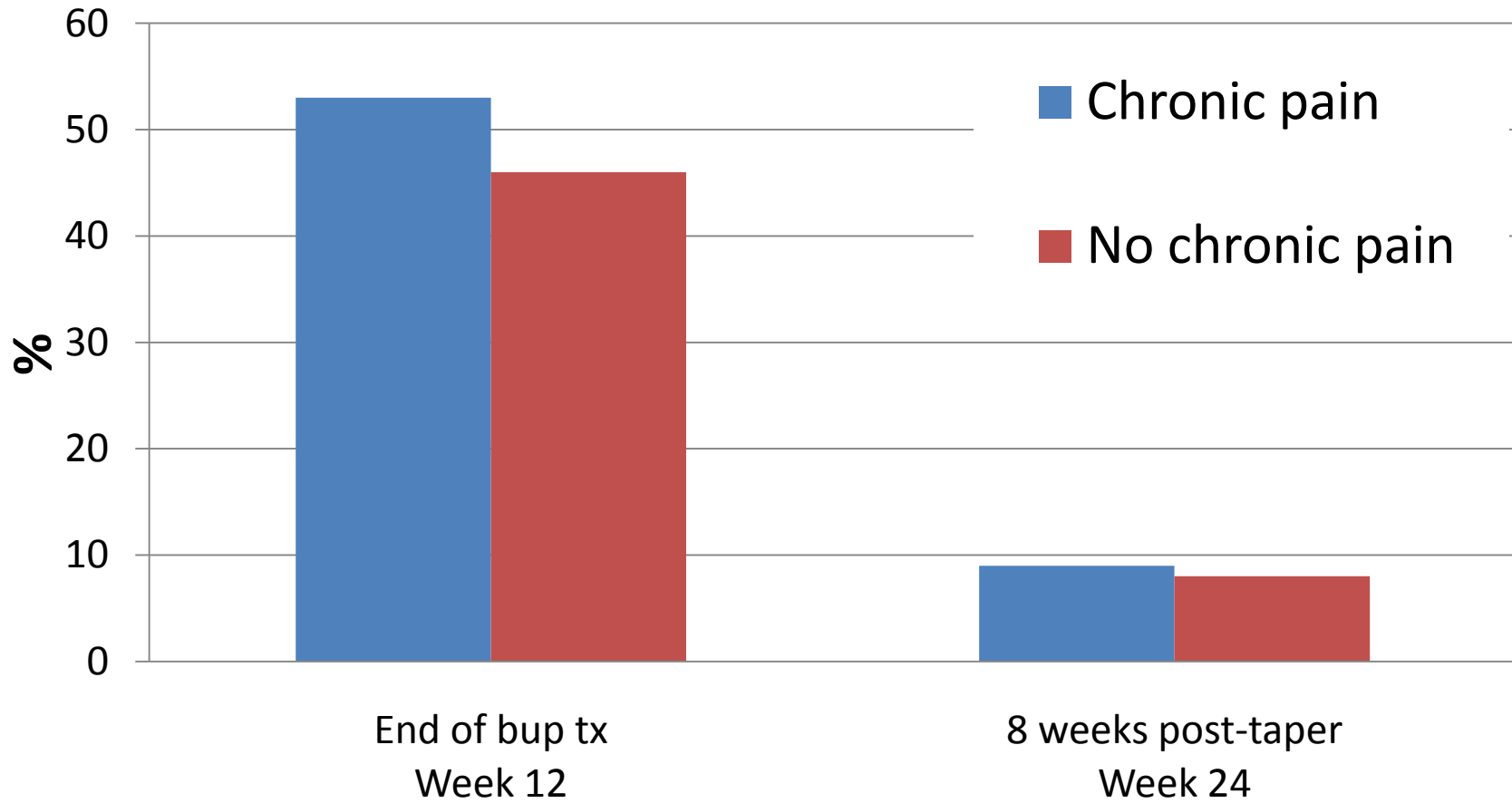
each $p < .02$

	Chronic Pain		No Chronic Pain	
	Mean	(sd)	Mean	(sd)
Non-withdrawal pain	5.7	(3.6)	2.9	(3.2)
Saw OAs & had to give in	4.8	(3.6)	5.7	(3.6)
Good mood & wanted to get high	3.8	(3.4)	5.0	(3.4)
Someone offered OAs	3.5	(3.6)	4.6	(3.7)
With others having a good time	2.8	(3.3)	4.1	(3.6)
Bored	2.8	(3.1)	3.8	(3.2)
Saw others using	2.3	(3.2)	3.0	(3.3)
Tempted out of the blue	1.9	(2.9)	2.5	(3.1)

Important reasons for using opioids, 0-10 scale cont'd

Past 6 months each p>.05	Chronic Pain		No Chronic Pain	
	Mean	(sd)	Mean	(sd)
Ill or in pain from wanting OAs	7.8	(2.7)	8.1	(2.6)
Anxious	4.9	(3.3)	5.2	(3.2)
Sad	3.8	(3.5)	3.8	(3.3)
Angry or frustrated with self	3.5	(3.2)	3.8	(3.2)
Angry or frustrated due to relationship	3.1	(3.5)	3.4	(3.5)
Worried about a relationship	2.9	(3.4)	3.3	(3.4)
Felt others were being critical	2.0	(2.9)	1.9	(2.8)
Wanted to see what would happen	1.1	(2.3)	1.3	(2.3)

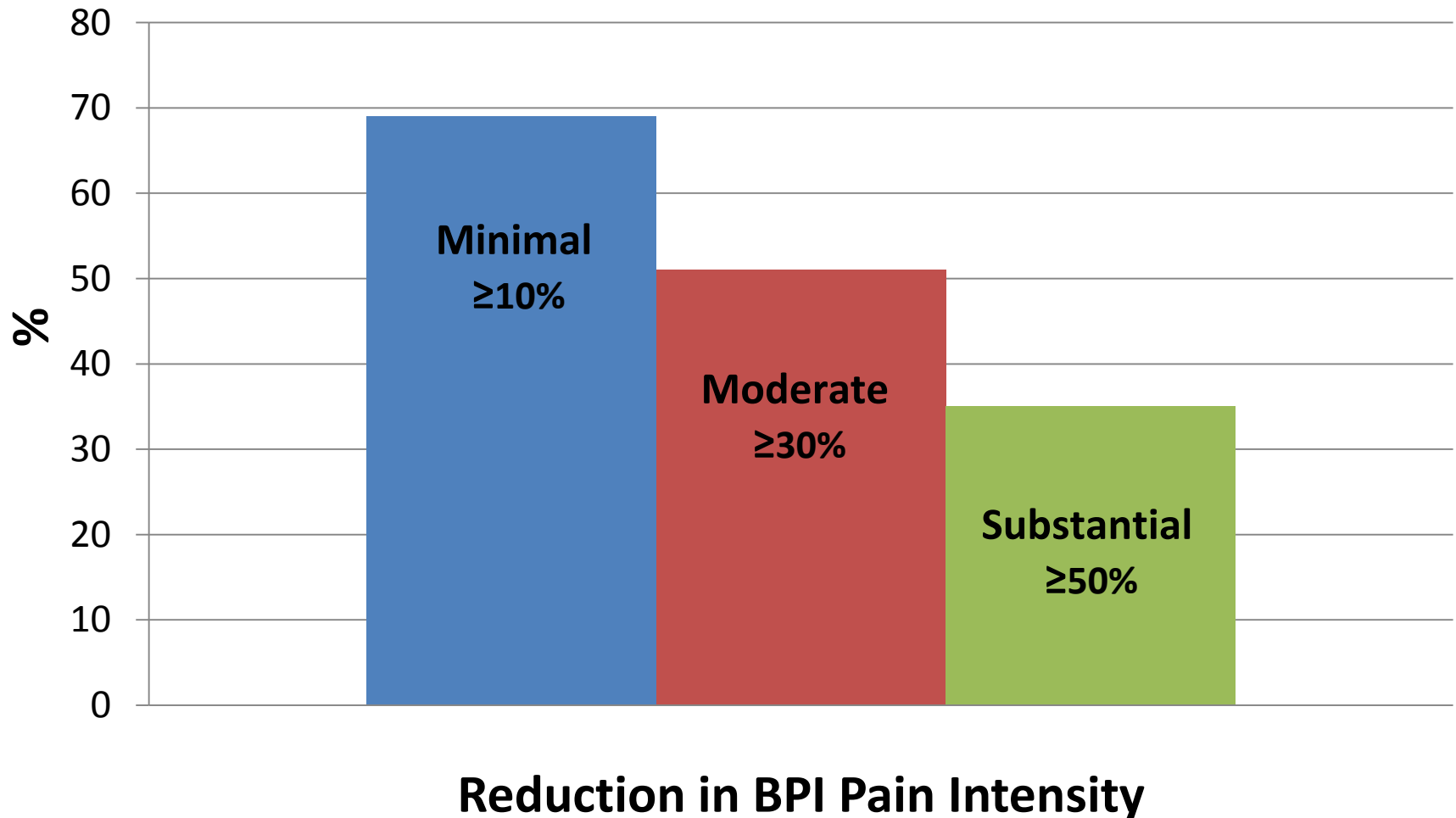
Chronic pain & successful outcomes



Phase 2

Exploratory Results

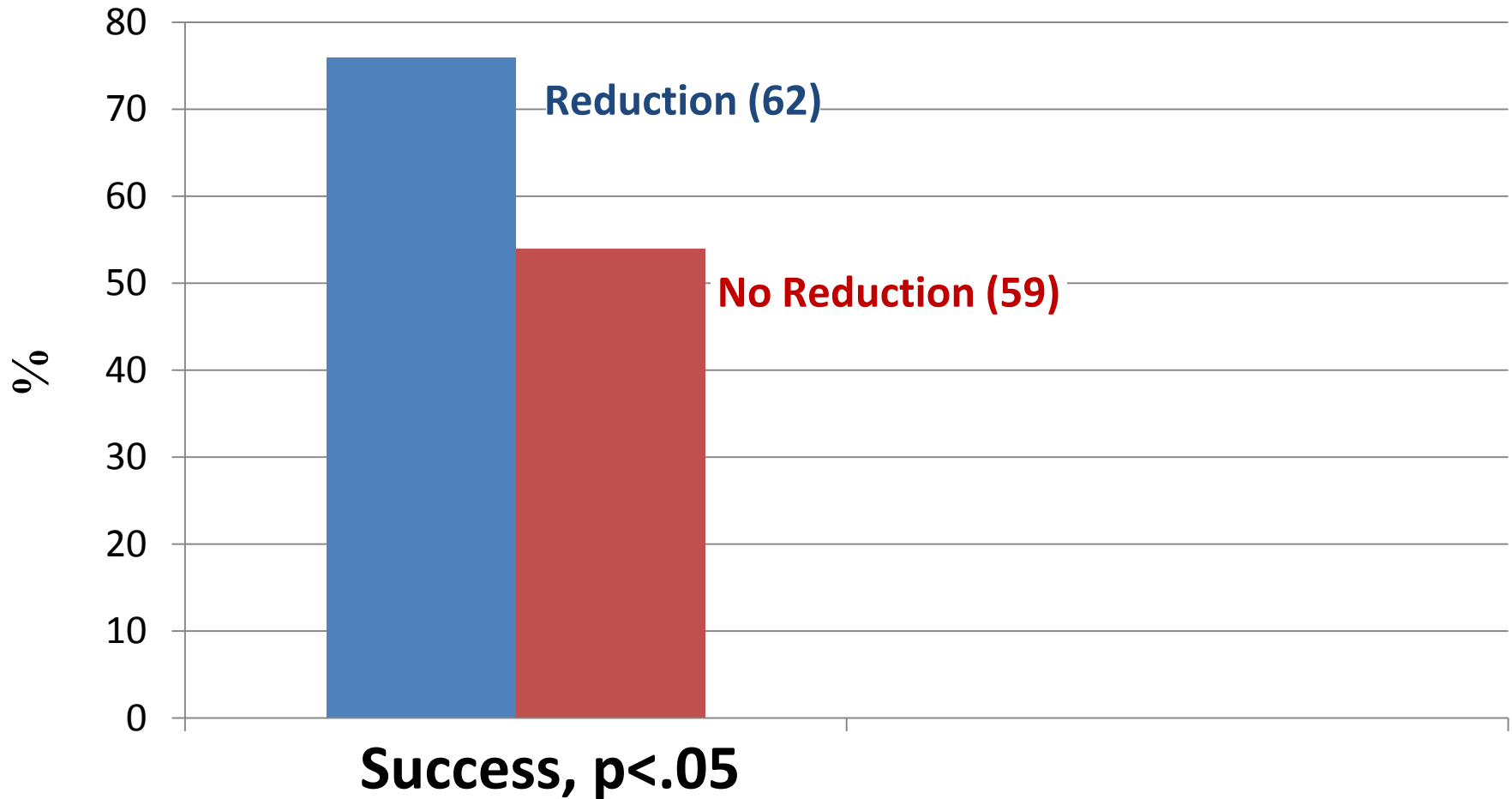
Clinically meaningful pain reduction in CP patients (n=121/149)



Treatment ns

(IMMPACT recommendations, Dworkin et al., Pain, 2008)

Moderate pain reduction ($\geq 30\%$) by Phase 2 successful opioid use outcome



POATS: Overview for chronic pain

Conclusions

- CP patients as likely to succeed as those without CP
- No significant safety concerns observed
- Many had significant pain improvement

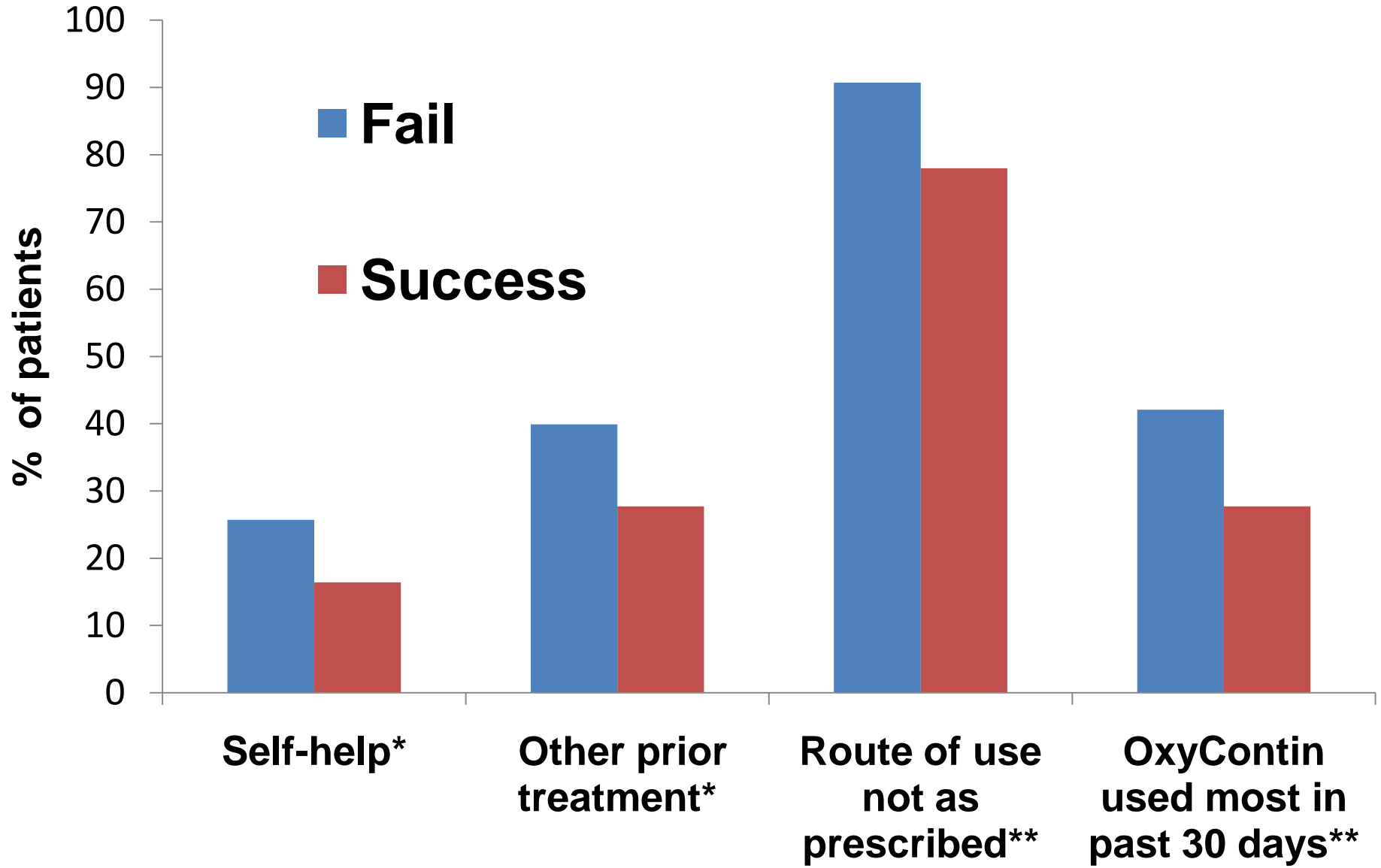
Limitations

- Treatment-seeking for a substance use disorder, **not** pain
- Heterogeneity of chronic pain: location, severity
- No non-treatment control group to compare pain over time

**What Predicts Successful
Outcome in Patients with
Prescription Opioid
Dependence Treated with
Buprenorphine-Naloxone?**

**Patient Predictors of Outcome –
Bivariate Analysis
(N=360;
8/25 tests were significant)**

Significant baseline predictors by outcome



*p < .05 **p < .01

Significant predictors by outcome (cont'd)

Patient characteristics		Failure (n=183)	Successful (n=177)
<u>Sociodemographics</u>			
Age, mean±sd **		31.2 (9.1)	33.9 (10.0)
<u>Substance use history</u>			
1 st source of opioids *	Medical rx	49%	62%
	Dealer	14	6
1 st reason for opioid use*	To relieve physical pain	60	70
	To get high	33	24
<u>Other diagnoses</u>			
Major depression**	Past year	14	26
	Lifetime	27	41

*p<.05 ** p<.01

Results:

Predictors of Outcome

Multivariate Analysis

(N=360)

Final logistic regression models for predictors of success (N=360)

Baseline variables	Odds Ratio
Age, for every +10 years	1.28*
Lifetime depression	1.82*
Prior opioid use disorder treatment	.62*
Lifetime route of use other than oral or sublingual	.51 [^]
Model R ²	9.7%**

[^]p<.052; *p<.05; ** p<.01

Summary of Predictors of Outcome

Successful outcomes associated with

- Older age
- Depression
- No prior opioid use disorder treatment
- Route of use is oral or sublingual only

Implications and Future Directions

- Perhaps there are clinically meaningful subgroups of patients with prescription opioid dependence
- Older, depressed, initiated use medically for pain vs. younger, more “recreational” users?