

# Clinical Decision-Making in OUD Management: Treatment Selection and Implementation

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## Disclosures



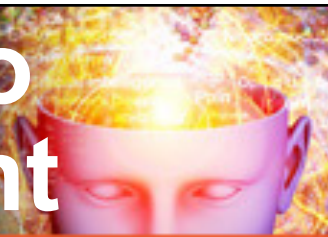
- ***Consultant:*** ADAPT Pharma (Dublin, Ireland)

# Learning Objective 1

Analyze the latest clinical evidence on the use of MOUD, and its various formulations and routes of delivery, to promote long-term recovery and relapse prevention.



# Greater Attention Must Be Made to Link People with OUD to Treatment



- Medication for OUD (MOUD) is effective, improves mortality, treatment retention, and remission, but most people with OUD remain untreated
- Many parts of the country lack access and few addiction treatment centers offer OUD
- Lack of access has resulted in a gap of an estimated 1 million people with OUD untreated each year



# Comparative Effectiveness of Different Treatment Pathways for OUD

- In a national cohort of 40,885 individuals with OUD between 2015-2017, treatment with buprenorphine or methadone was associated
  - 76% reduction in overdose at 3 months
  - 59% reduction in overdose at 12 months
  - 32% relative reduction in serious opioid-related acute care at 3 months and 25% reduction at 12 months compared to no treatment
- Despite the known benefit, only 12.5% initiated treatment
- Retention in care in patients on buprenorphine or methadone for longer than 6 months experienced less overdose and opioid-related acute care

# FDA-Approved Medications to Treat OUD

Medication	Receptor Pharmacology	Formulation	Dosing Frequency
Methadone	Full mu opioid agonist	<ul style="list-style-type: none"> <li>• Oral solution, liquid concentrate, tablet/diskette, powder</li> </ul>	<ul style="list-style-type: none"> <li>• Daily</li> </ul>
Buprenorphine	Partial mu opioid agonist	<ul style="list-style-type: none"> <li>• Sublingual tablet</li> </ul>	<ul style="list-style-type: none"> <li>• Daily</li> </ul>
		<ul style="list-style-type: none"> <li>• Implant</li> </ul>	<ul style="list-style-type: none"> <li>• Every 6 months</li> </ul>
		<ul style="list-style-type: none"> <li>• Extended-release injection for subcutaneous use</li> </ul>	<ul style="list-style-type: none"> <li>• Monthly</li> </ul>
		<ul style="list-style-type: none"> <li>• Extended-release injection*</li> </ul>	<ul style="list-style-type: none"> <li>• Weekly and monthly</li> </ul>
Buprenorphine-naloxone	Partial mu opioid agonist - mu antagonist	<ul style="list-style-type: none"> <li>• Sublingual film</li> <li>• Buccal film</li> <li>• Sublingual tablet</li> </ul>	<ul style="list-style-type: none"> <li>• Daily</li> </ul>
Naltrexone	Mu opioid antagonist	<ul style="list-style-type: none"> <li>• Extended-release injectable suspension</li> </ul>	<ul style="list-style-type: none"> <li>• Every 4 weeks or once a month</li> </ul>

\*Tentative FDA approval.  
 [Package Insert]. Drugs@FDA Website.

# Efficacy and Safety of Various MOUD



## ● Efficacy

- Methadone = Buprenorphine<sup>1</sup>
- Naltrexone = Buprenorphine<sup>2,3</sup>

## ● Adverse Effects

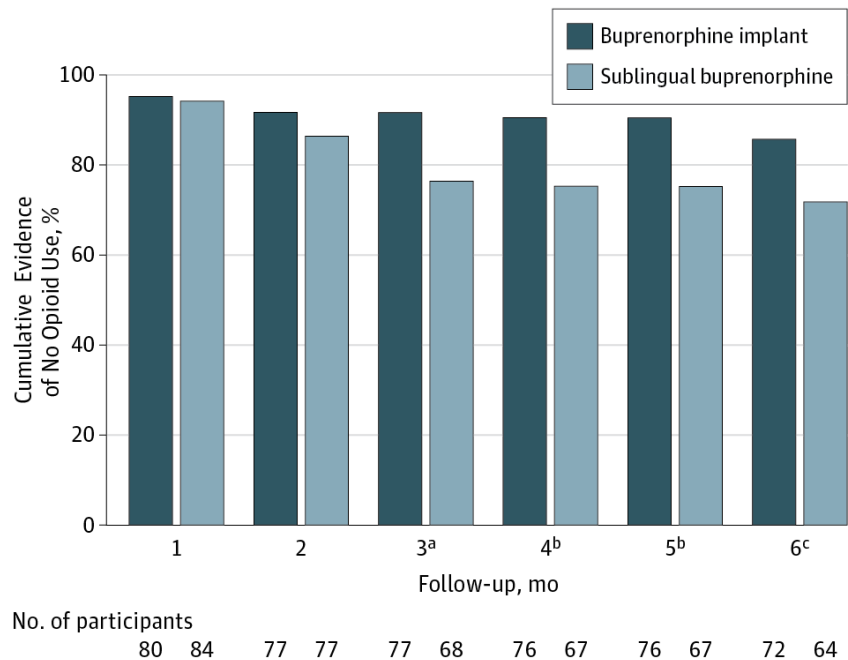
- Methadone has greater AEs than buprenorphine
- Respiratory depression / overdose<sup>4</sup>
- Neonatal abstinence syndrome<sup>5</sup>
- Cognitive, psychomotor dysfunction<sup>6</sup>
- Nonmedical use

Naltrexone  
does not have  
these AEs

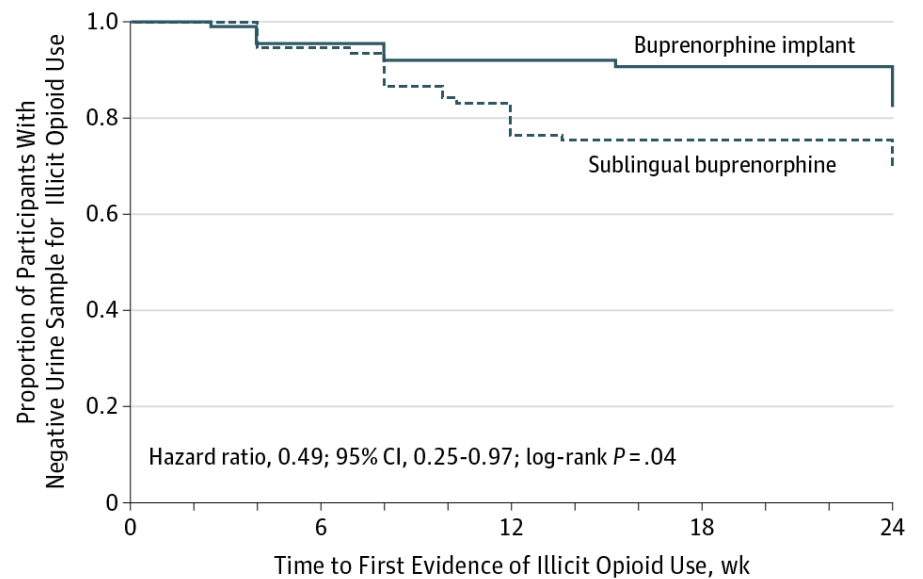
1. Nielsen S, et al. *Cochrane Database Syst Rev.* 2016;9(5):CD011117; 2. Tanum L, et al. *JAMA Psychiatry.* 2017;74(12):1197-1205. 3. Lee JD, et al. *Lancet* 2018;391(10118):309-318; 4. Lee SC, et al. *Drug Alcohol Depend.* 2014;138:118-123; 5. Minozzi S, et al. *Cochrane Database Syst Rev.* 2013;23(12):CD006318; 6. Soyka M. *Pharmacopsychiatry.* 2014;47(1):7-17.

# Sublingual vs. Implant Buprenorphine

Proportion with no evidence of illicit opioid use over 6-mo follow-up



Time to first evidence of illicit opioid use by urine sample

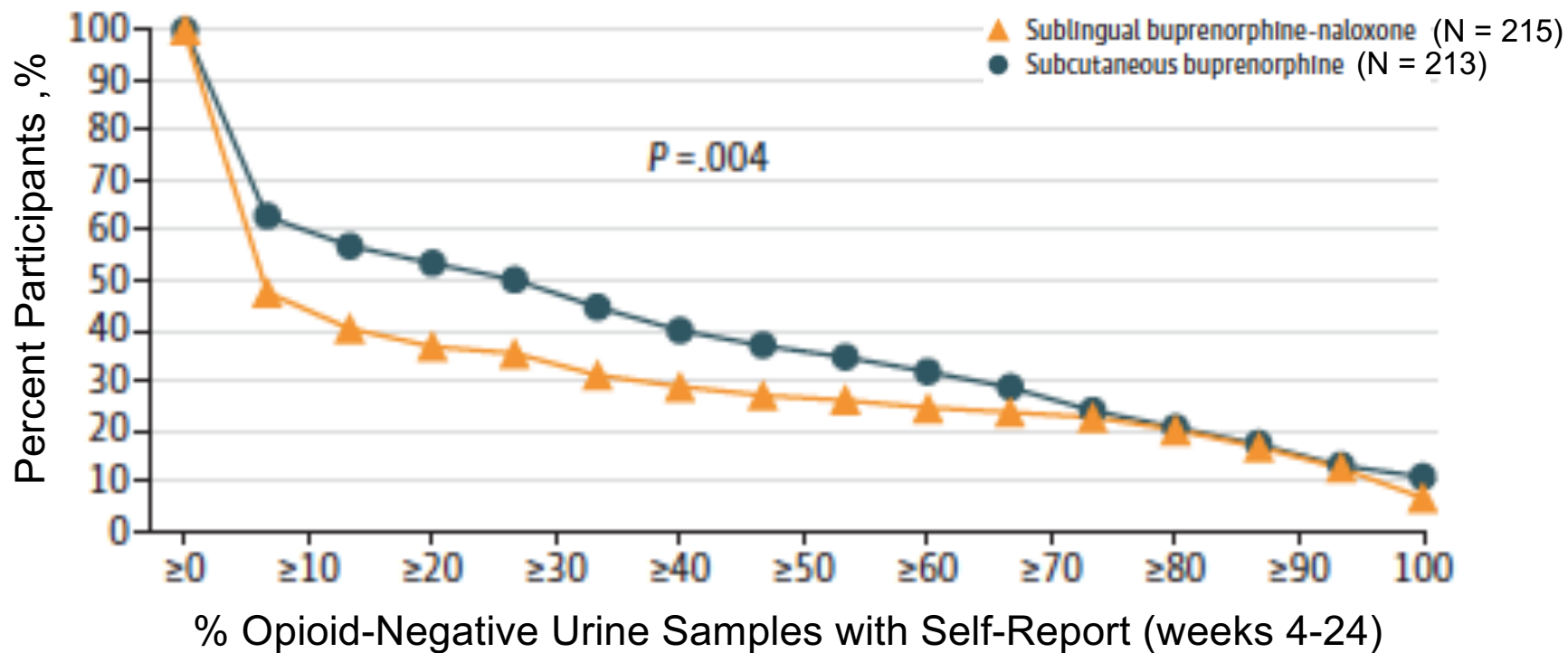
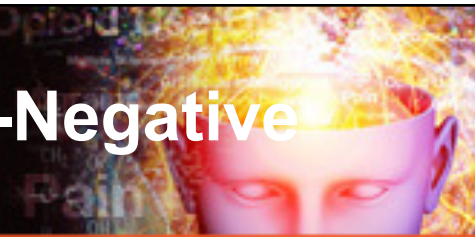


No. of participants

Buprenorphine implant	84	83	79	76	75	75	43
Sublingual buprenorphine	89	89	82	73	66	66	44

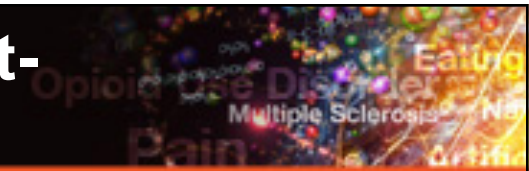


# Subcutaneous Buprenorphine vs. Sublingual Buprenorphine-Naloxone: Percentage Opioid-Negative Urine Samples Over 24 Weeks

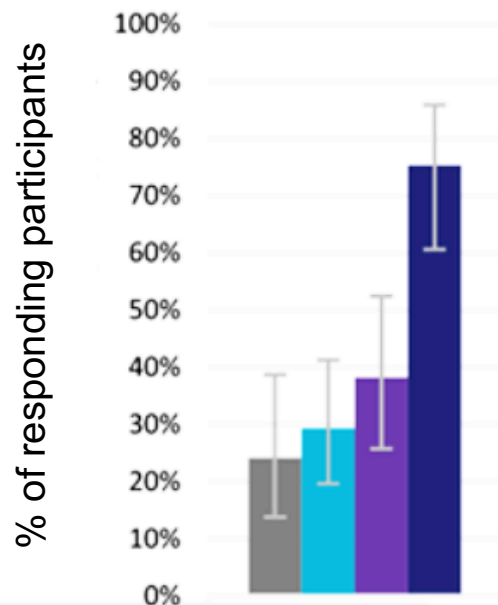


Weeks 1-12: Weekly injections; Weeks 12-24: Monthly injection  
Lofwall MR, et al. *JAMA Intern Med.* 2018;178(6):764-773.

# 12-Month Outcomes of Recovery from OUD Post-Buprenorphine-XR Treatment



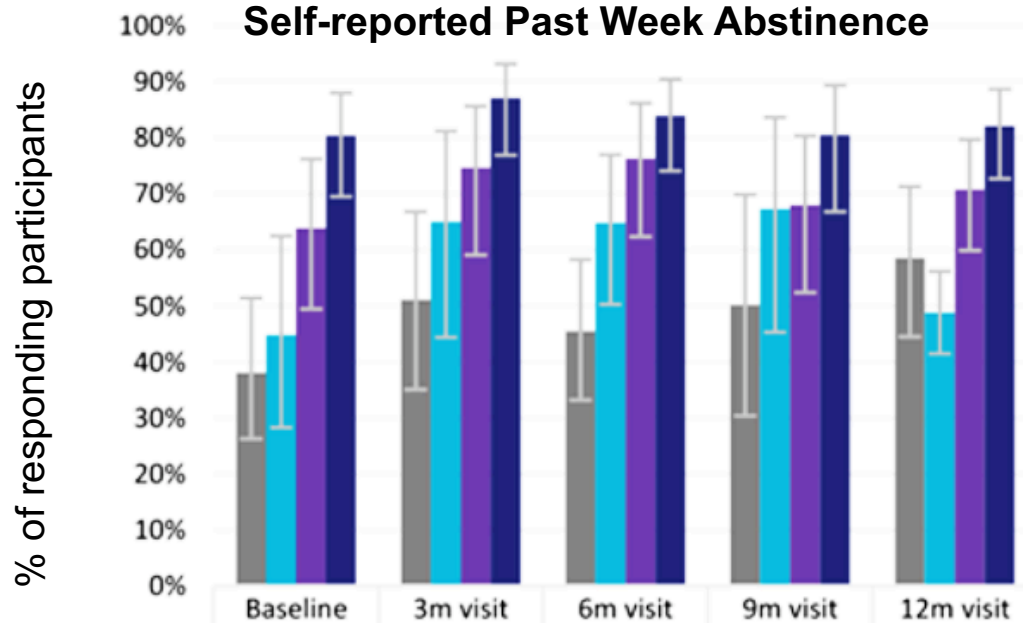
## Sustained Abstinence For Full 12 Mos.



0-2m BUP-XR	24.1%
3-5m BUP-XR	29.3%
6-11m BUP-XR	38.2%
12m BUP-XR	75.3%

BUP-XR = extended-release buprenorphine.  
Peiper NC, et al. *J Addict Med.* 2019;13(3):E1-E42.

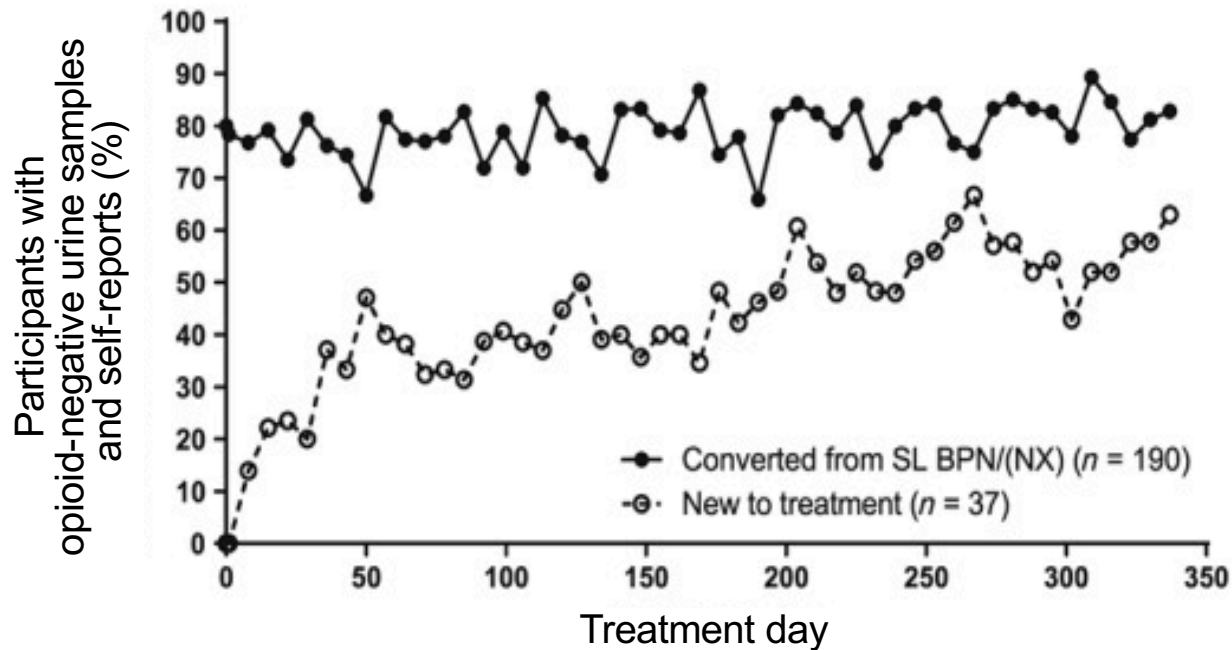
## Self-reported Past Week Abstinence



BUP-XR Group	Baseline	3m visit	6m visit	9m visit	12m visit
0-2m BUP-XR	38.1%	51.1%	45.5%	50.2%	58.6%
3-5m BUP-XR	44.8%	65.0%	64.8%	67.3%	48.8%
6-11m BUP-XR	63.9%	74.7%	76.3%	68.0%	70.8%
12m BUP-XR	80.4%	87.1%	83.9%	80.5%	82.1%

RECOVER visit

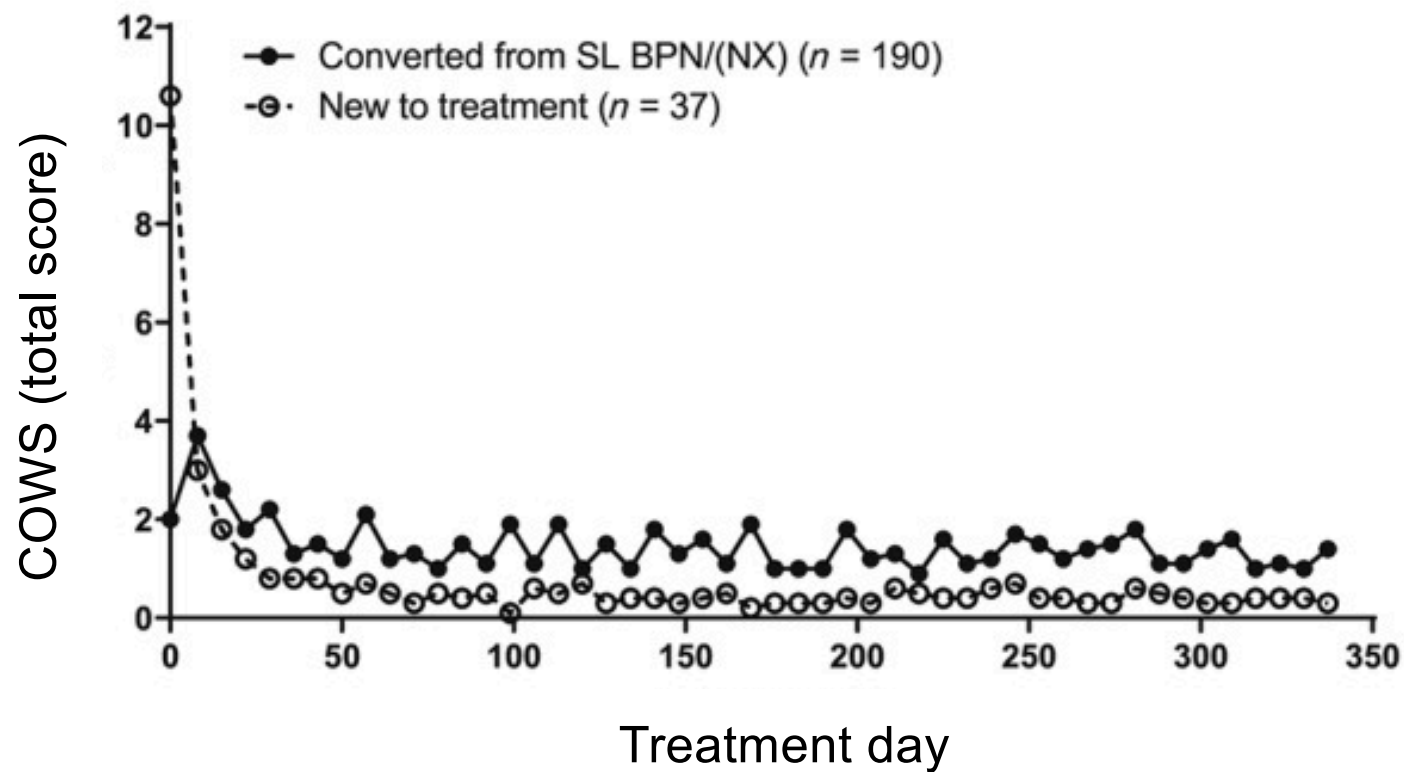
# Efficacy of Weekly and Monthly Buprenorphine Depot (CAM2038) for OUD



Treatment day	1	29	57	85	113	141	169	197	225	253	281	309	337
Converted from SL BPN(NX), n	190	166	142	133	129	118	114	117	112	107	107	103	134
New to treatment, n	37	35	35	35	27	25	26	29	27	25	26	25	27

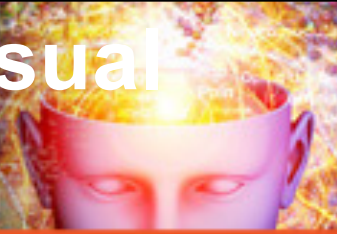
SL BPN/(NX) = sublingual buprenorphine/naloxone.  
 Frost M, et al. *Addiction*. 2019;114(8):1416-1426.

# Efficacy of Weekly and Monthly Buprenorphine Depot (CAM2038) for OUD



COWS = Clinical Opiate Withdrawal Scale.  
Frost M, et al. *Addiction*. 2019;114(8):1416-1426.

# OUD Relapse Rates with Treatment as Usual (TAU) vs XR-NTX at 1 and 6 months



	1 Month			6 Months	
	TAU	XR-NTX		TAU	XR-NTX
Short-term Inpatient (n = 59)	63%	12%		77%	59%
Long-term Inpatient (n = 48)	14%	12%		59%	46%
Outpatient (n = 201)	28%	12%		61%	38%

XR-NTX = extended-release injection naltrexone.

Nunes EV, et al. *J Subst Abuse Treat.* 2018;85:49-55.



# Extended-Release Naltrexone vs. Sublingual Buprenorphine-Naloxone for Relapse Prevention in OUD



- 12-week multicenter outpatient open-label RCT, N=159
- 5 urban addiction clinics in Norway (2012–2015)
- N = 159
  - Extended-release naltrexone, every 4<sup>th</sup> week for 12 weeks (n = 80)
  - Buprenorphine-naloxone, 4 – 24mg/d daily (n = 79)
- Randomization occurred after detoxification completed
- No significant differences between groups in
  - Proportion total number of days opioid negative urine tests
  - Retention
  - Use of heroin and other illicit opioids
  - Extended-release naltrexone patients reported less heroin craving, more treatment satisfaction

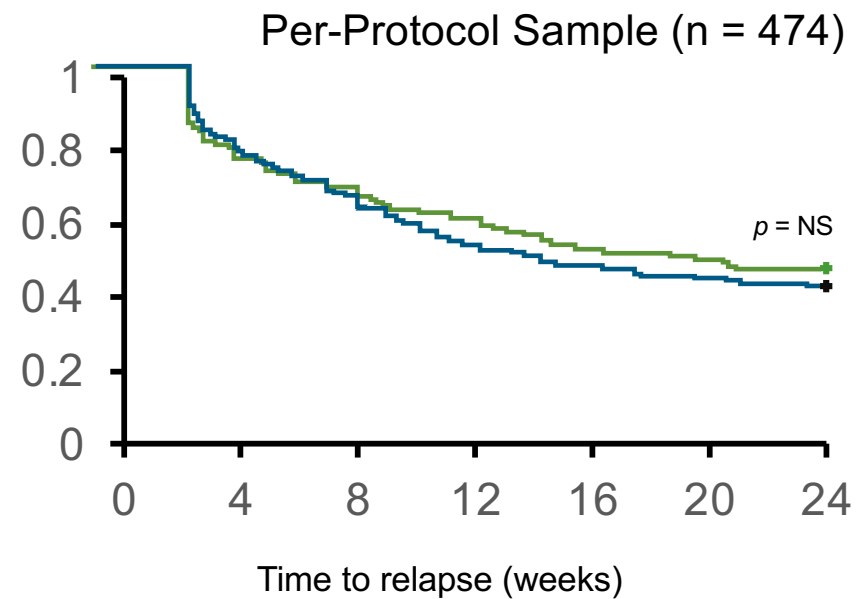
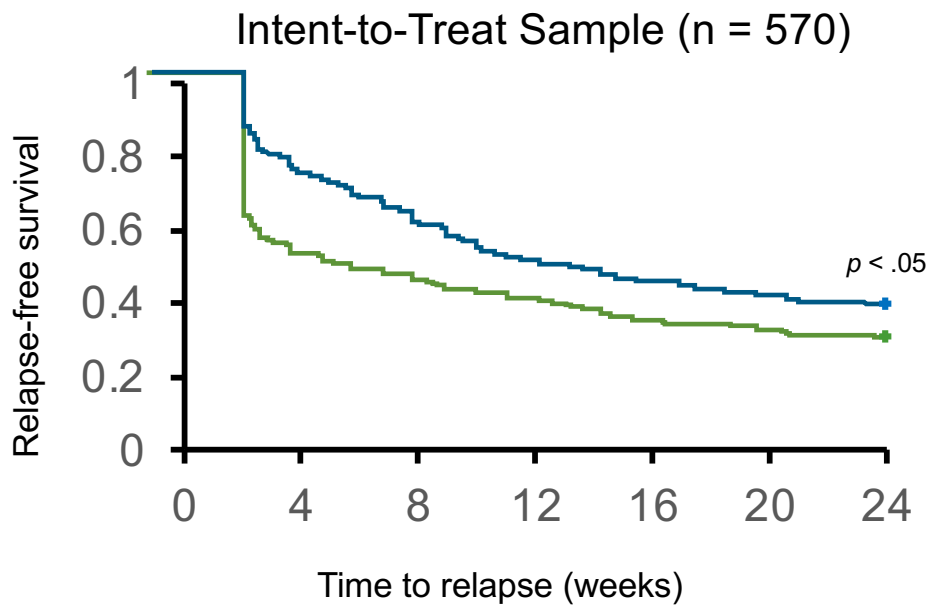
RCT = randomized controlled trial.

Tanum L, et al. *JAMA Psychiatry*. 2017;74(12):1197-1205.

## Comparative Effectiveness of Extended-Release Naltrexone vs Sublingual Buprenorphine for Opioid Relapse Prevention (X:BOT)

- 24 wk, open-label, randomized controlled, comparative effectiveness trial in outpatients after inpatient induction
  - Monthly extended-release naltrexone injections (XR-NTX) vs. daily sublingual buprenorphine (BUP-NX) film
  - Fewer participants successfully initiated XR-NTX than BUP-NX: 72% VS 94%;  $p < .0001$ 
    - At 24 wks, among participants that were successfully initiated, both medications were equally safe and effective
    - Study treatment retention for 24 wks was between 43% and 47%
  - During treatment outcomes were better for BUP-NX than XR-NTX

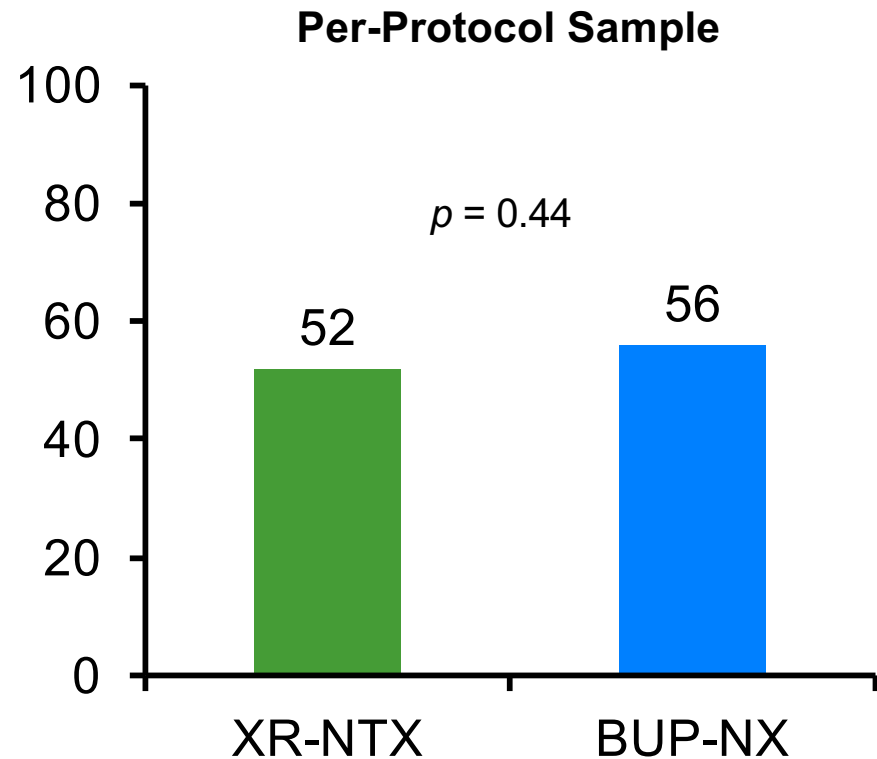
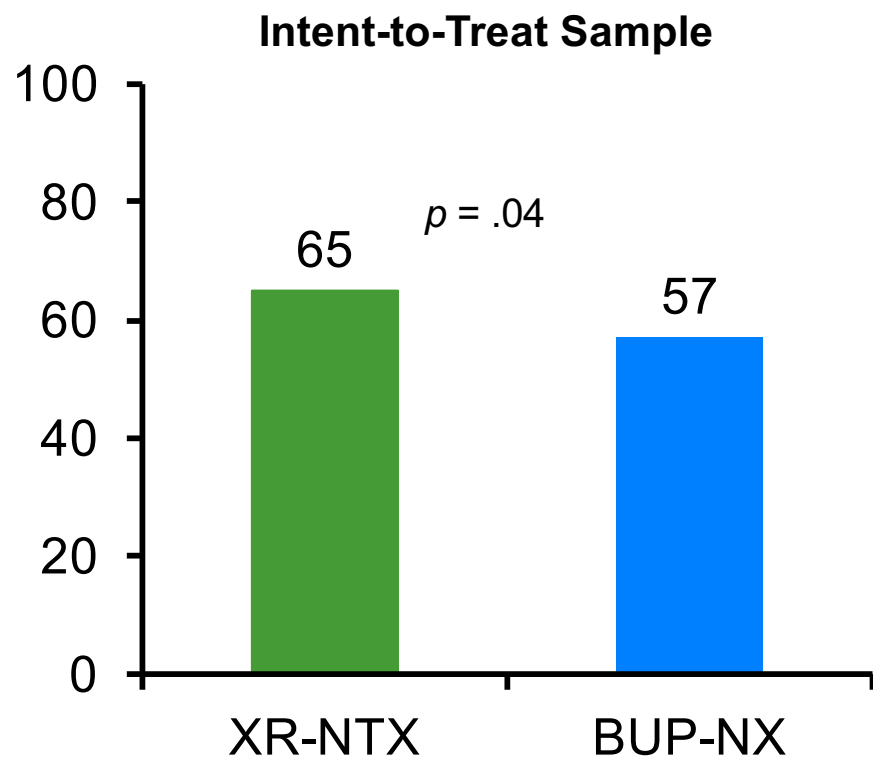
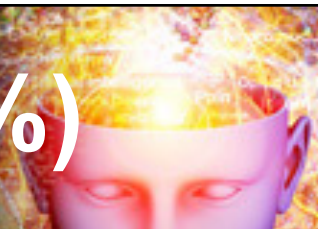
# Comparative Effectiveness of XR-NTX vs. BUP-NX for Opioid Relapse Prevention (X:BOT): Relapse-Free Survival



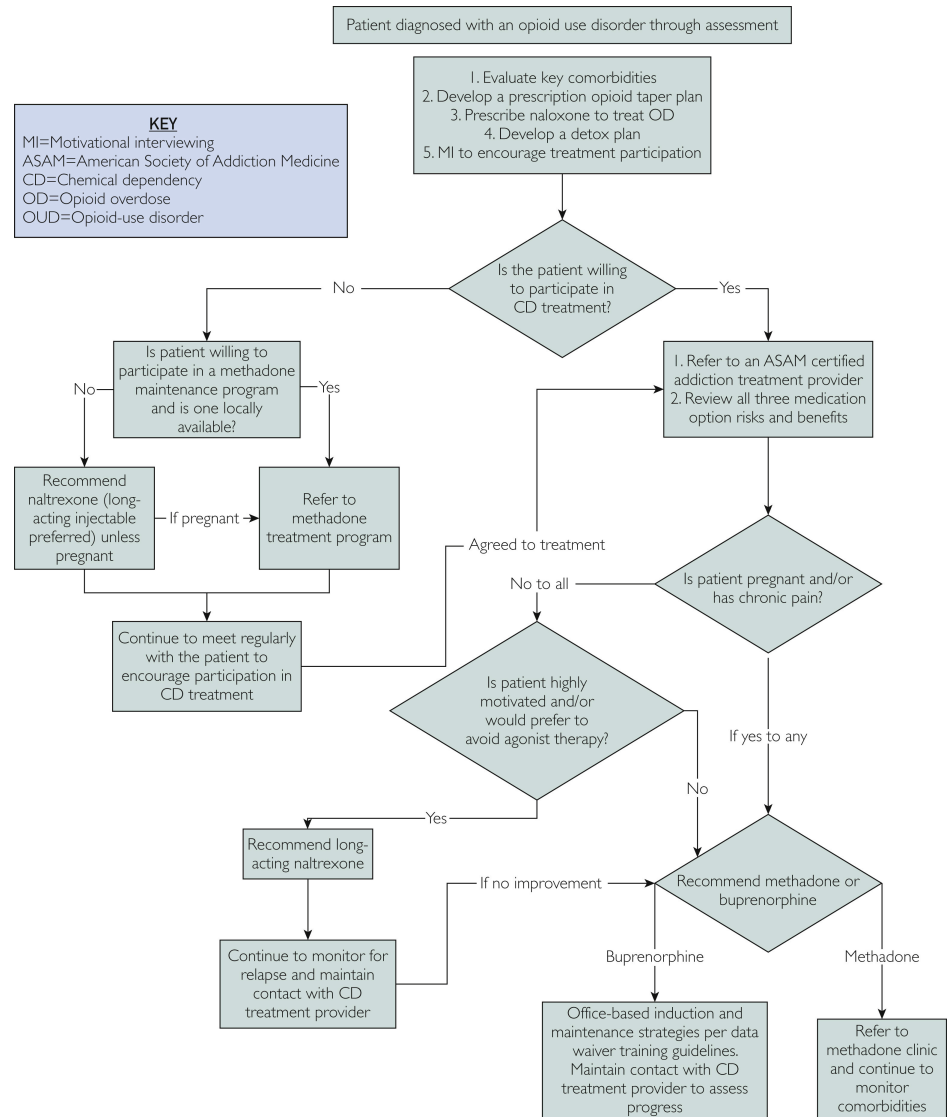
Number at risk (censored)	Time to relapse (weeks)													
	0	4	8	12	16	20	24	0	4	8	12	16	20	24
BUP-NX	287	229	100	155	140	130	0 (124)	270	222	184	149	134	126	0 (120)
XR-NTX	283	165	142	125	109	103	0 (98)	204	164	141	124	109	103	0 (98)

BUP-NX = buprenorphine/naloxone.  
 Lee JD, et al. *Lancet*. 2018;391(10118):309-318.

# X:BOT: 24-Week Relapse Rates (%)



# Algorithm for MOUD





# MOUD Treatment Works



- Comprehensive Opioid Addiction Treatment (COAT) Program
  - Group Based MAT/Medical Management directly followed by Group Therapy
  - Step Based: Advance through 4 treatment phases



[CMEOutfitters.com/Rx4Pain](https://CMEOutfitters.com/Rx4Pain)

# Call to Action



- Medication for OUD (MOUD) is effective, improves mortality, treatment retention, and remission, but most people with OUD remain untreated
- Retention in care is essential to prevention of relapse and overdose

# Questions & Answers

Don't forget to fill out your evaluations to collect your credit.

