



XR-Naltrexone Engagement and Retention: Best Practices

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Learning Objectives

How XR-Naltrexone Differs from Other Medical Treatments such as Buprenorphine (Suboxone) or Methadone



How to Engage and Retain Patients in Treatment (BRENDA Approach)



How to Address Common Clinical Concerns with XR-Naltrexone Treatment

Introduction



Opioid Epidemic: Serious Public Health Concern



Standard Detoxification and Rehabilitation Programs Not Very Effective



Use of Medications can Improve Treatment Outcomes

Opioid Epidemic at a Glance

Opioid Use Disorder

2,000,000

Heroin Use Disorder

648,000

Opioid Overdose Deaths

60,000

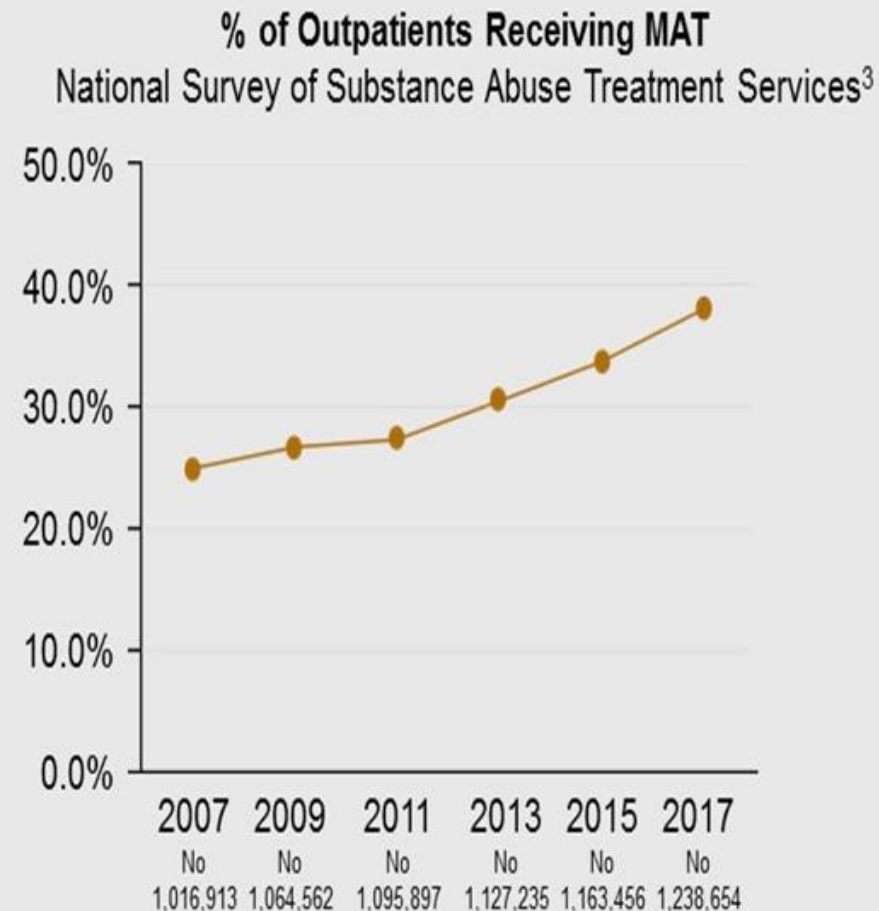
Medications for Opioid Addiction Treatment are Underutilized

US Surgeon General, *Spotlight on Opioids* (2018)¹

Access to FDA-approved medications is a recommended component of opioid dependence treatment programs

SAMHSA TIP #63, 2018²

“...medications reduce illicit opioid use, retain people in treatment...better than treatment with placebo or no medication”



How XR-Naltrexone Differs from Other Medical Treatments such as Buprenorphine or Methadone



Three Very Different Medication Approaches for Opioid Addiction

	Methadone	Buprenorphine	Naltrexone
Activates mu receptor	Yes	Partial	No
Administration	Daily oral	Daily Sublingual or buccal film, 6-month implant, or extended-release injection	Daily oral or monthly injection
Setting	Certified Ambulatory Settings	Physician's Office	Physician's Office
DEA Schedule	Scheduled II Controlled	Scheduled III Controlled	Not Scheduled
Initial Dose Can Precipitate Withdrawal Symptoms	No	Yes	Yes
Can Relieve Withdrawal Symptoms	Yes	Yes	No
Potential for Abuse and Diversion	Yes	Yes	No
Physical Dependence	Yes	Yes	No

Naltrexone is Unique Among Medications to Treat Opioid Addiction



Naltrexone (Oral and Extended Release) is the only pharmacotherapy approved by the FDA to prevent relapse to opioid addiction following opioid detoxification.

Advantages and Disadvantages of XR- Naltrexone

ADVANTAGES	DISADVANTAGES
No abuse or diversion	Not effective as a detox agent
Not a controlled substance	Must be opioid free before initiating treatment
No physical dependence/withdrawal	Must be ordered through specialty pharmacies
Improved clinical outcomes	Cost of medication and effort to administer injection

X-BOT: A Recent Clinical Study

Comparing Vivitrol and Buprenorphine

X-BOT TRIAL

A six month multicentered study comparing subjects selected for either XR-Naltrexone or buprenorphine treatment

DESIGN

To start the study subjects had to be opioid-free to receive XR-Naltrexone or successfully be induced on buprenorphine

INITIATION

Was more difficult to initiate treatment with XR-Naltrexone than buprenorphine

Of the 283 subjects assigned to the XR-Naltrexone group only 204 (72%) received the first injection

Of the 287 subjects assigned to the buprenorphine group 270 (94%) were inducted to start buprenorphine treatment

RESULTS

No differences between XR-Naltrexone and buprenorphine treatment in relapse rates or treatment retention

For XR-Naltrexone subjects, 96 of 204 (47%) remained active in treatment at 6 months

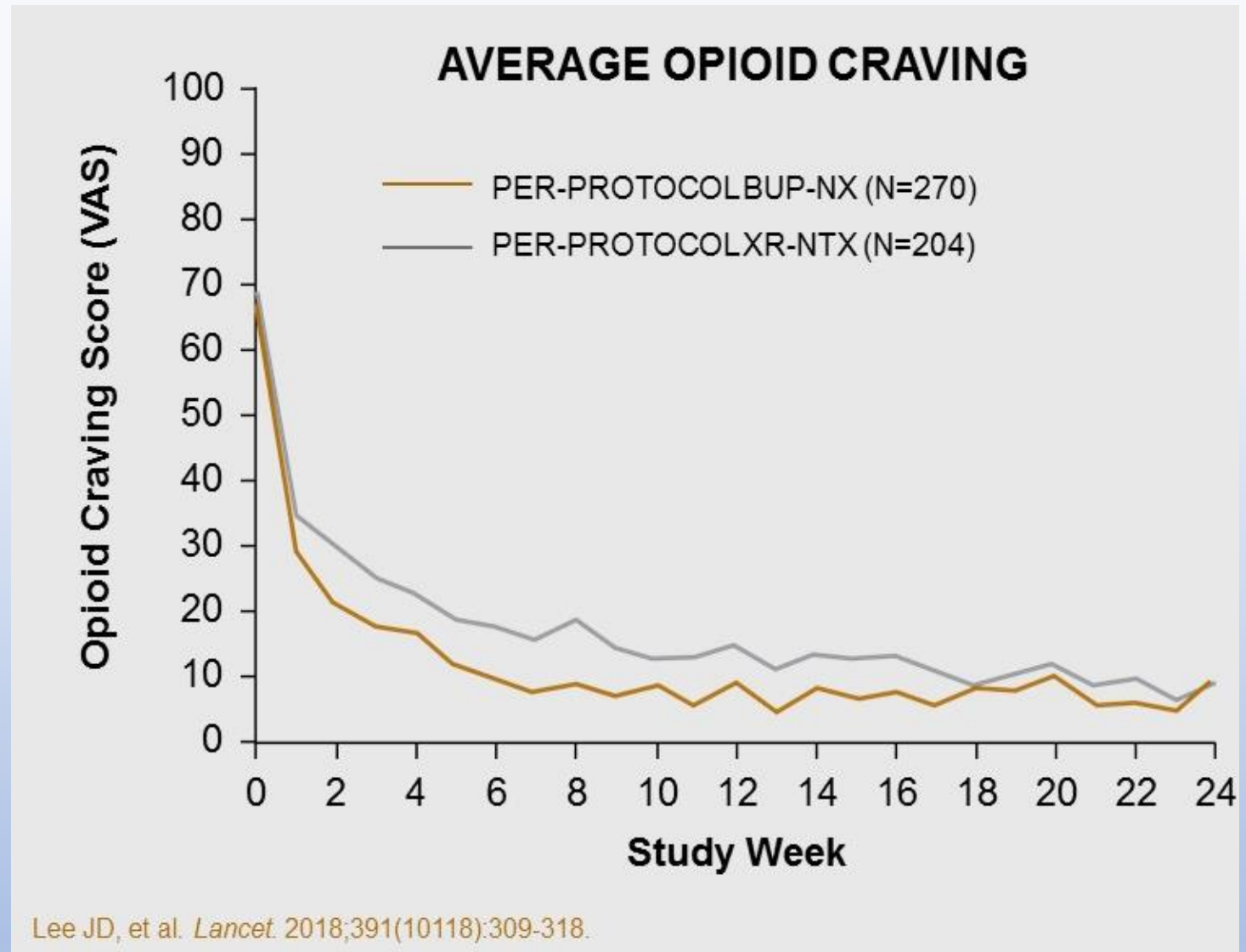
For buprenorphine subjects, 115 of 270 (43%) remained active in treatment at 6 months

X-BOT Serious Adverse Events

	XR-NTX GROUP	BUP-NX GROUP
Any Treatment-emergent adverse event	111 (54%)	141 (52%)
Study Discontinuation due to adverse event	6	8
Injection site Reaction	46	n/a
Gastrointestinal	34	59
Psychiatric disorders	30	29
Injury, poisoning, and procedural complications	23	25
Infections	22	28
Nervous system disorders	22	28
Number of overdose events ^a	10	9
Fatal overdose events ^a	2	3
^a For patients who received at least one dose of study medication		

X-BOT Opioid Craving

- Craving was self-reported with an opioid craving visual analogue scale (VAS)
- Craving was dramatically reduced during treatment for both XR-Naltrexone and buprenorphine subjects
- XR-Naltrexone reduces craving faster than buprenorphine

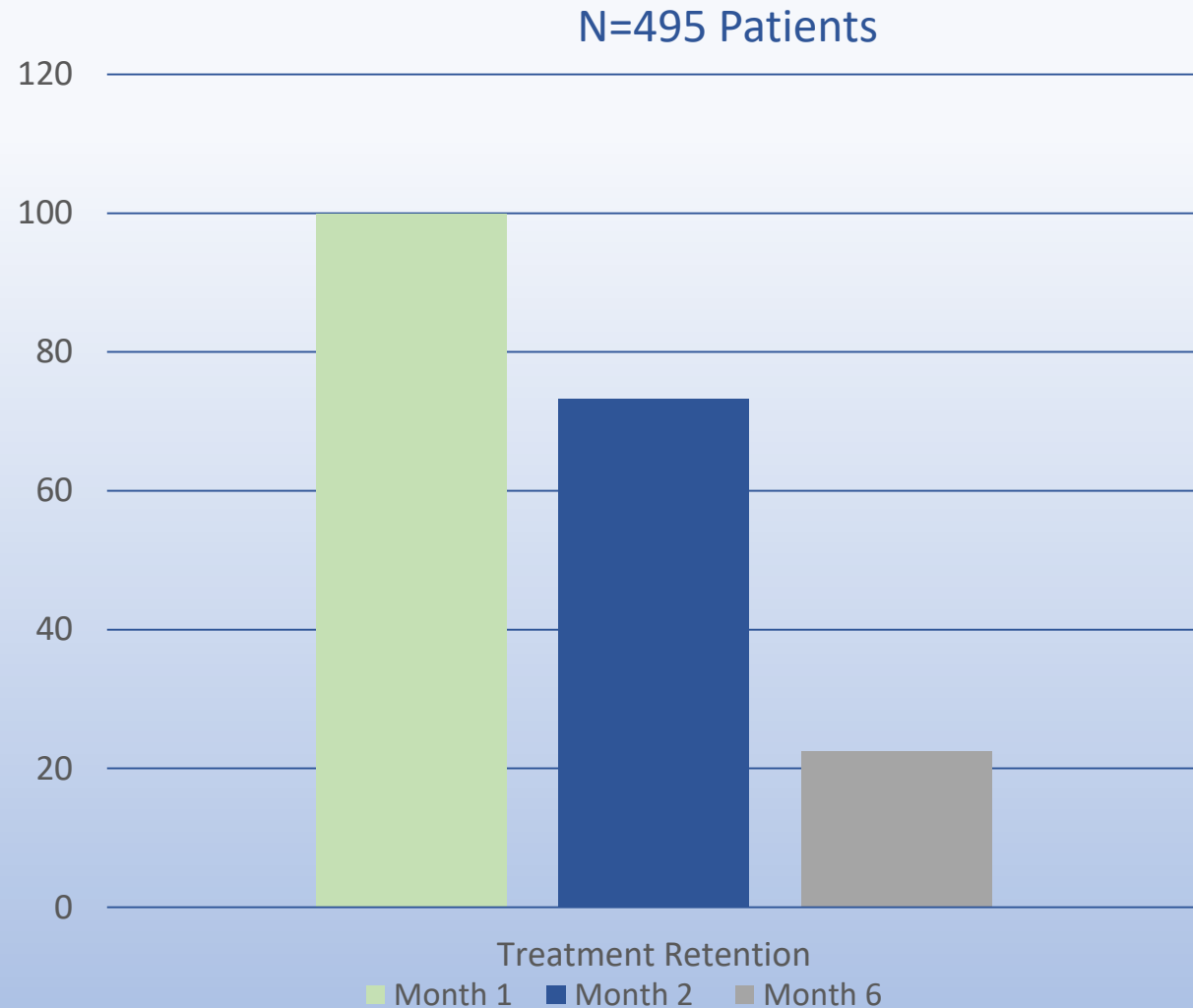


X-BOT Study Conclusions

- ✓ It is easier to initiate treatment with buprenorphine than XR-Naltrexone
- ✓ Once treatment is initiated, both XR-Naltrexone and buprenorphine were safe and effective in reducing drug use and craving
- ✓ Even in this well controlled clinical study, less than half the subjects who started treatment were still in treatment at six months

Treatment Retention on XR-Naltrexone After One and Six Months of Treatment

- For a medication to be effective patients must adhere with taking their medication.
- Treatment retention at 6 months is about 50% in research trials and less than that in real world clinical practice.
- In eight clinical settings about 75% of patients who receive the first XR-Naltrexone shot receive the second shot and less than 25% are still receiving injections at six months.



From Saxon, in press, 2019

Role of Psychosocial Support

- ✓ To help engage patients into starting treatment
- ✓ To help improve treatment adherence and retention
- ✓ To improve psychosocial functioning

Why BRENDA?

BRENDA is an effective approach for combining psychosocial support with medications in an office setting because:

- It is based on motivational interviewing and is designed to be used with medications for the treatment of addictions
- It is a relatively brief and simple approach that can be administered by nurses or any trained healthcare professional
- The basics of BRENDA are based on strong and growing empirical evidence

Components of the BRENDA Approach

B – Biopsychosocial evaluation

R – Report to the patient on assessment

E – Empathetic understanding of the patient's problem

N – Needs expressed by the patient that should be addressed

D – Direct advice on how to meet those needs

A – Assess responses of the patient to advice and adjusting treatment recommendations

The BRENDA Approach

- Biopsychosocial evaluation
 - Biological and medical assessment
 - Psychological assessment
 - Social assessment

The BRENDA Approach

- Report
 - Formulate patient profile based on evaluation
 - Report evaluation results to patient
 - stick to the facts
 - avoid judgments
 - Assess patient reactions to report; give the patient time to react

The BRENDA Approach

- Empathy
 - Listen to understand the patient's emotional reaction to report
 - Express understanding of the patient's emotional reaction given his or her assumptions
 - Challenge negative assumptions underlying the patient's distress
 - Collaboration versus confrontation

The BRENDA Approach

- Needs
 - Immediate, basic health and safety needs
 - Elicit patient goals and priorities
 - Explore medication adherence history
 - Needs assessment from collaboration between clinician and patient

The BRENDA Approach

- Direct advice
 - Recommend appropriate medical treatment
 - Explain importance of medication adherence
 - Collaborate in identification of at risk situations
 - Point out how options help achieve patient priorities

The BRENDA Approach

- Assess patient reactions to advice—adjust advice
 - Reassess biopsychosocial status and give positive feedback
 - Compare patient status with patient goal for recovery
 - Assess whether the patient is following up on direct advice and treatment recommendations
 - Link patient actions (inaction) on advice to changes in biopsychosocial status; advise if needed

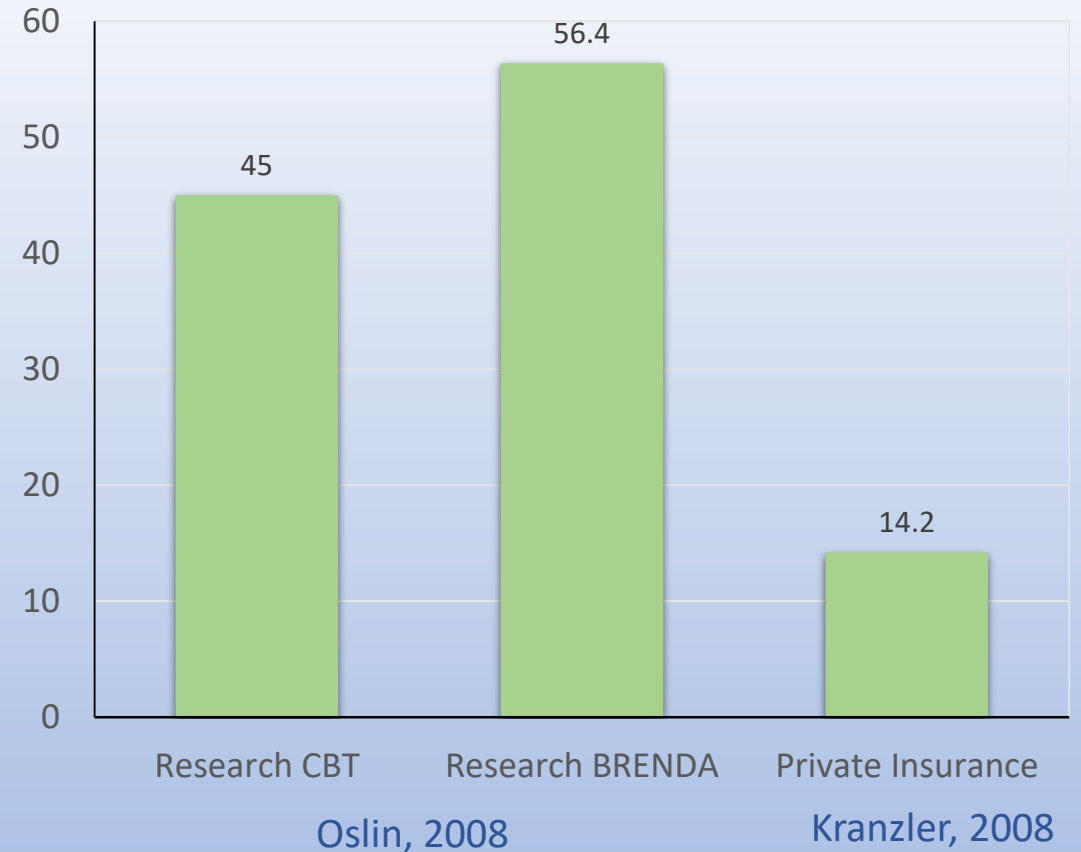
Empirical Support for BRENDA

- Monterosso JR et al. *Am J Addict.* 2001;10:258-268.
- Pettinati HM et al. *J Addict Dis.* 2000;19(1):71-83.
- Garbutt JC et al. *JAMA.* 2005;293(13):1617-1625.
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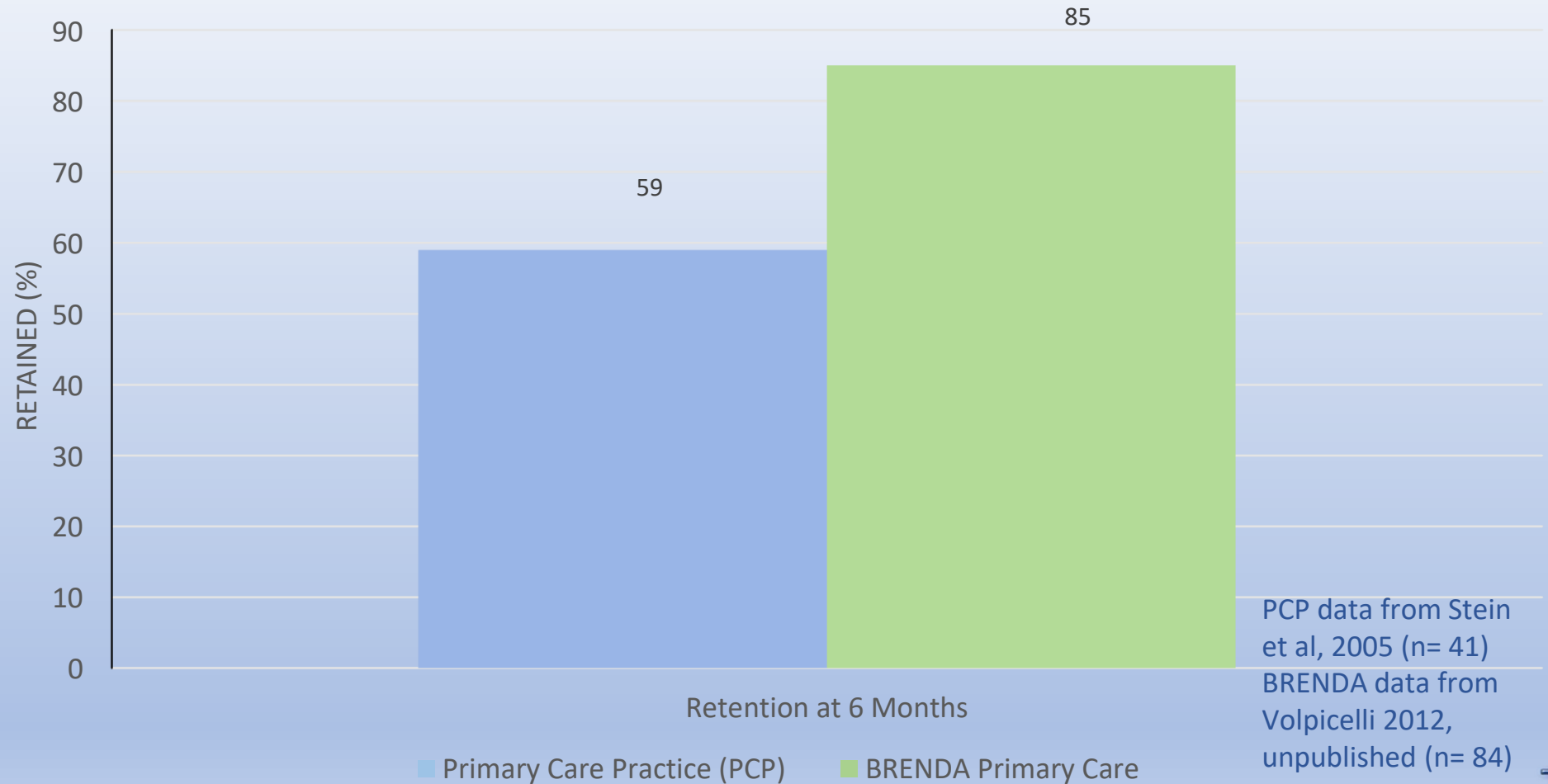
XR-Naltrexone Persistence in Research and Clinical Setting

The percentage of individuals who took XR-Naltrexone (or for private insurance patients, had a filled prescription) for at least 80% of the days during the first six months of treatment.

In research studies about 50% good medication adherence but in clinical practice about 14% showed medication adherence.



Buprenorphine Retention in Primary Care Setting



Program Description

- Initial biopsychosocial assessment
- Ambulatory detoxification (daily)
- Weekly psychosocial (BRENDA) sessions first 3 months
- 2x per month psychosocial sessions for next three months
- Once a month sessions for next 6 months
- Monthly medication checks and XR-Naltrexone injection with Physician, PA, or NP
- Each visit includes UDS, self-report assessments of craving, mood, & cognitive functioning

NTX-XR Persistence in Opioid and Alcohol Patients

(from Volpicelli, 2017 unpublished)



NTX-XR Persistence in Male and Female Patients

(from Volpicelli, 2017 unpublished)



NTX-XR Persistence in Patients Involved with the Criminal Justice System



NTX-XR Persistence in Patients with a Psychiatric Co-Morbidity



NTX-XR Persistence in Insurance or Fee for Service Patients



NTX-XR Persistence in BRENDA vs. Non-BRENDA Patients

(from Volpicelli, 2017 unpublished)



Conclusions

- Emphasis on medication adherence inherent in the BRENDA approach results in improved treatment retention
- Most patients who received XR-Naltrexone combined with psychosocial support remained active in treatment for over six months

Definition of Addiction

Understanding the Nature of Addiction Helps Us
Make Rational Recommendations for Using
Medications in Addiction Treatment

DSM 5 DEFINITION OF ADDICTION:

- Addiction is a **complex condition, a brain disease that is manifested by compulsive substance use despite harmful consequence.**
- People with addiction (severe substance use disorder) have an intense focus on using a certain substance(s), such as alcohol or drugs, to the point that it takes over their life.
- They keep using alcohol or a drug even when they know it will cause problems.
- Yet a number of effective treatments are available, and people can recover from addiction and lead normal, productive lives.

ASAM DEFINITION OF ADDICTION:

- Addiction is a treatable, chronic medical disease involving **complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.**
- People with addiction use substances or engage in **behaviors that become compulsive and often continue despite harmful consequences.**
- Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

OLD JAPANESE PROVERB

- First the man takes a drink
- Then the drink takes a drink
- Then the drink takes the man

To treat addiction, you must break the cycle!



NATURAL VERSUS ADDICTIVE NEEDS

- Natural needs such as hunger are present at birth, reduced by eating, and are stable over time
- Addictive needs such as heroin craving are not present at birth, grow stronger with use, and become all important over time

Buprenorphine versus XR-Naltrexone

- Buprenorphine is like leasing a car, it gets you transportation, but you don't own the car until you pay for it when the lease is up
- NTX-XR is like buying the car outright, its harder in the beginning but then you own the car

How to Address Common Clinical Presentations



26-year-old male
returning to old
neighborhood after 6-
month incarceration, on
probation

- Abstinence 12 step program
- Methadone Treatment program
- Buprenorphine program
- XR-Naltrexone and psychosocial support

31-year-old female who recently OD'ed, not interested in treatment and may want to become pregnant

- Abstinence 12 step program
- Methadone treatment program
- Buprenorphine program
- XR-Naltrexone and psychosocial support

55-year-old female who has just completed her 3rd rehab in past 5 years and is tired of revolving door

- Abstinence 12 step program
- Methadone Treatment program
- Buprenorphine program
- XR-Naltrexone and psychosocial support

45-year-old male who has been taking street buprenorphine and now wants a prescription

- Abstinence 12 step program
- Methadone Treatment program
- Buprenorphine program
- XR-Naltrexone and psychosocial support

Conclusions

- XR-Naltrexone is more difficult than other medications to initiate treatment, but for people who have successfully detoxed from opioids is a safe and effective treatment.
- Agonists medications such as methadone and buprenorphine are effective in reducing harm associated with addiction, but one remains physically dependent on opioids
- XR-Naltrexone combined with psychosocial support can lead to breaking the addictive cycle in a large percentage of patients