XR-Naltrexone Engagement and Retention: Best Practices

Joseph R. Volpicelli, M.D., Ph.D.
Institute of Addiction Medicine
Plymouth Meeting, Pennsylvania
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”

---

% of Outpatients Receiving MAT
National Survey of Substance Abuse Treatment Services³

<table>
<thead>
<tr>
<th>Year</th>
<th>Yes</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>1,016,913</td>
<td>17.1%</td>
</tr>
<tr>
<td>2009</td>
<td>1,064,552</td>
<td>18.9%</td>
</tr>
<tr>
<td>2011</td>
<td>1,095,897</td>
<td>19.7%</td>
</tr>
<tr>
<td>2013</td>
<td>1,127,235</td>
<td>20.6%</td>
</tr>
<tr>
<td>2015</td>
<td>1,163,458</td>
<td>22.4%</td>
</tr>
<tr>
<td>2017</td>
<td>1,238,654</td>
<td>24.9%</td>
</tr>
</tbody>
</table>
How XR-Naltrexone Differs from Other Medical Treatments such as Buprenorphine or Methadone
## Three Very Different Medication Approaches for Opioid Addiction

<table>
<thead>
<tr>
<th>Medicaid</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activates mu receptor</td>
<td>Yes</td>
<td>Partial</td>
</tr>
<tr>
<td>Administration</td>
<td>Daily oral</td>
<td>Daily Sublingual or buccal film, 6-month implant, or extended-release injection</td>
</tr>
<tr>
<td>Setting</td>
<td>Certified Ambulatory Settings</td>
<td>Physician’s Office</td>
</tr>
<tr>
<td>DEA Schedule</td>
<td>Scheduled II Controlled</td>
<td>Scheduled III Controlled</td>
</tr>
<tr>
<td>Initial Dose Can Precipitate Withdrawal Symptoms</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Can Relieve Withdrawal Symptoms</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Potential for Abuse and Diversion</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Physical Dependence</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>No abuse or diversion</td>
<td>Not effective as a detox agent</td>
</tr>
<tr>
<td>Not a controlled substance</td>
<td>Must be opioid free before initiating treatment</td>
</tr>
<tr>
<td>No physical dependence/withdrawal</td>
<td>Must be ordered through specialty pharmacies</td>
</tr>
<tr>
<td>Improved clinical outcomes</td>
<td>Cost of medication and effort to administer injection</td>
</tr>
</tbody>
</table>
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 induced 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.
### Serious Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>XR-NTX GROUP</th>
<th>BUP-NX GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Treatment-emergent adverse event</td>
<td>111 (54%)</td>
<td>141 (52%)</td>
</tr>
<tr>
<td>Study Discontinuation due to adverse event</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Injection site Reaction</td>
<td>46</td>
<td>n/a</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>34</td>
<td>59</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>Injury, poisoning, and procedural complications</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Infections</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Number of overdose events a</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Fatal overdose events a</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*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 imitated, 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
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 BRENSDA 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

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.

Oslin, 2008

Kranzler, 2008

Research CBT: 45%
Research BREENDA: 56.4%
Private Insurance: 14.2%
Buprenorphine Retention in Primary Care Setting

Retention at 6 Months

Primary Care Practice (PCP)  BRENDA Primary Care

PCP data from Stein et al, 2005 (n= 41)
BRENDA data from Volpicelli 2012, unpublished (n= 84)
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)

Percent of Patients Who Received Injections

Opioid (n = 161)
Alcohol (n=49)
NTX-XR Persistence in Male and Female Patients
(from Volpicelli, 2017 unpublished)

Graph showing the percent of patients who received an injection over a 6-month period. The graph compares male (n=142) and female (n=68) patients. The percentage decreases over time, with a steeper decline in the first month for both groups, followed by a more gradual decrease in subsequent months.
NTX-XR Persistence in Patients Involved with the Criminal Justice System

Percent of Patients who Receive Injection

- Criminal Justice n=62
- No Criminal Justice (n=147)
NTX-XR Persistence in Patients with a Psychiatric Co-Morbidity
NTX-XR Persistence in Insurance or Fee for Service Patients

<table>
<thead>
<tr>
<th>Month</th>
<th>Insurance (n=78)</th>
<th>Fee for Service (n=132)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 1</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Month 2</td>
<td>0.80</td>
<td>0.60</td>
</tr>
<tr>
<td>Month 3</td>
<td>0.60</td>
<td>0.40</td>
</tr>
<tr>
<td>Month 4</td>
<td>0.40</td>
<td>0.20</td>
</tr>
<tr>
<td>Month 5</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Month 6</td>
<td>0.00</td>
<td></td>
</tr>
</tbody>
</table>
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
• 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
A 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.