# Medications for Alcohol and Drug Dependence Treatment

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# Medications for Alcohol Dependence Treatment

- Disulfiram (Antabuse®)
- Naltrexone
  - Oral tablets (Revia®)
  - Extended-release injection (Vivitrol®)
- Acamprosate (Campral®)

# Rationale for Using Medications to Treat Alcohol Dependence

- Many patients do not reduce or stop risky drinking with existing psychosocial treatment and AA alone
- Medications can help some patients improve their chances of reducing risky drinking
- These medications exert their effects in different ways

# How Does Disfulfiram Help Reduce Risky Drinking?

- Disfulfiram interferes with the metabolism of alcohol
- Acetaldehyde builds up and causes aversive symptoms including:
  - Dizziness, hypotension, sweating, facial flushing, shortness of breath, nausea, and vomiting

# In What Formulation is Disulfiram available?

Tablet (Antabuse ®)

- FDA-approved for the treatment of alcohol dependence over 50 years ago
- 250 mgs taken orally once per day
- Should not be taken within 12 hours (at least) of any alcohol
- Patient should not drink for up to 2 weeks after last drink
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# What is the Evidence of Disulfiram's Effectiveness?

- 11 Randomized Clinical Trials with a total of 1,527 participants were reviewed (Jorgensen et al., 2011)
- Supervised treatment with disulfiram compared to placebo had some effect on short-term abstinence and days until relapse
- Unsupervised treatment had mixed results

# How Does Naltrexone Help Reduce Risky Drinking?

- Mu opioid receptor activation is in part responsible for the “buzz” from alcohol
- Naltrexone is a mu opioid antagonist (i.e., blocker)
- Patients drinking while taking naltrexone report a reduced “buzz” from alcohol
- There is evidence that a genetic variant of the opioid receptor called OPRM1 may influence the response to naltrexone

# In What Formulation is Naltrexone available?

Tablet (Revia®)

- FDA- approved in 1994 for the treatment of alcohol dependence

Long-acting injection (Vivitrol®)

- FDA-approved in 2006 for the treatment of alcohol dependence
  - Helpful for non-compliant patients
  - Lasts about 30 days
  - Intramuscular injection in the buttock

# What is the Evidence of Naltrexone's Effectiveness?

- 50 Randomized Clinical Trials with 7,793 patients were included in a recent Cochrane Review (Rossner et al., 2010)
- Naltrexone reduced the risk to return to heavy drinking by 83% compared to placebo
- It reduced the number of drinking days by 4%
- It did not reduce the return to any drinking
- Main side effects: GI symptoms & sedation

# How Does Acamprosate Help Reduce Risky Drinking?

- Precise mechanism of action is not known
- Acamprosate acts on the glutamate receptor
  - it inhibits the neurons which may be involved in alcohol craving
- It also may reduce conditioned responses to alcohol-related cues
- These mechanisms may explain acamprosate's ability to reduce the risk of relapse

# In What Formulation is Acamprosate Available?

Tablet (Campral®)

- FDA- approved in 2004 for the maintenance of abstinence in alcohol dependent patients
- 2 tablets (333mg each) three times per day

# What is the Evidence of Acamprosate's Effectiveness?

- 24 Randomized Clinical Trials with 6,915 patients were including in a recent Cochrane Review (Rossner et al., 2011)
- Acamprosate reduced the risk of any drinking after detoxification by 86% compared to placebo
- It increased cumulative abstinence by 11% compared to placebo
- It did not reduce the risk of return to heavy drinking
- Main side effects: Diarrhea

# Medications for Cocaine & Methamphetamine Addiction Treatment

- None are approved by the FDA for cocaine or methamphetamine dependence treatment
- Several have shown promising results
- Several compounds are under development

# Medications for Opioid Dependence Treatment

- Methadone
- Buprenorphine
  - Sublingual mono-product (Subutex®)
  - Sublingual combination product of Buprenorprhine/Naloxone (Suboxone®)
- Naltrexone
  - Oral tablet (Revia)
  - Extended-release injection (Vivitrol)

# FDA-approved Medications for Opioid Addiction Treatment

## Opioid Agonists

1) Full agonist: Methadone (oral)

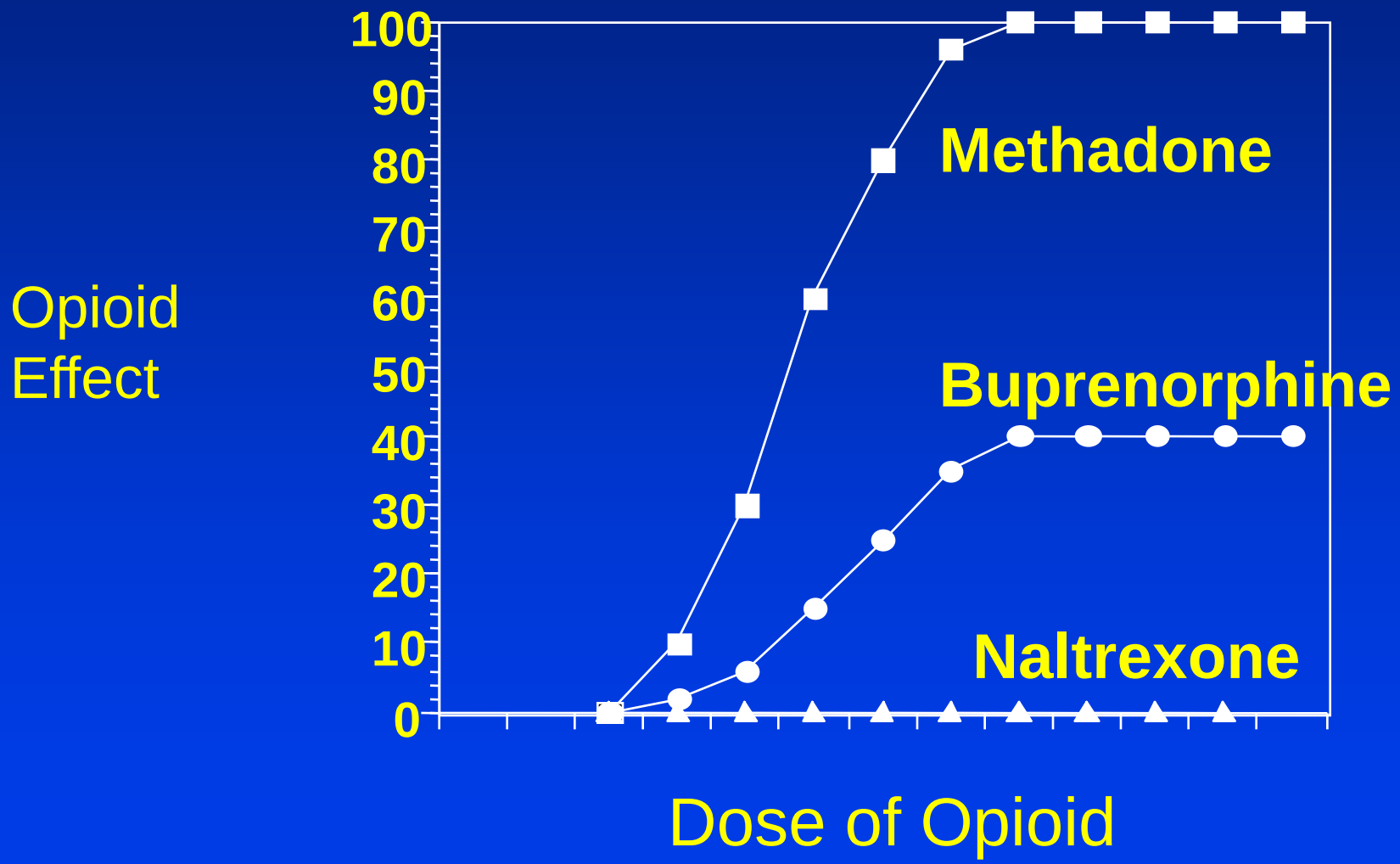
2) Partial agonist: Buprenorphine (sublingual)

## Opioid Antagonist

3) Naltrexone (oral)

4) Naltrexone (extended-release injection)

# What is the difference between opioid agonists & antagonists?

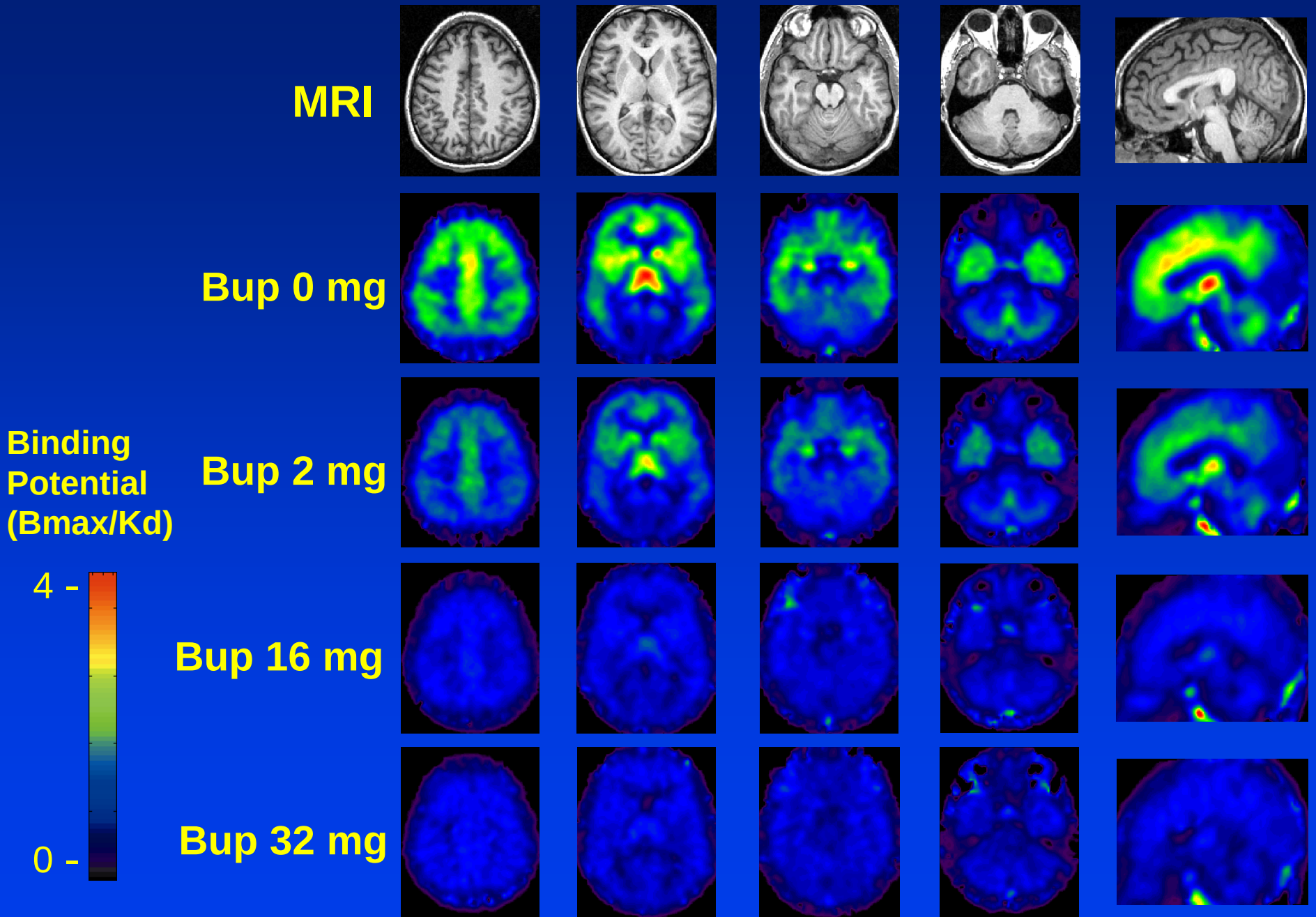


# I. Opioid Agonists

# How Do Methadone and Buprenorphine Reduce Opioid Use?

- Both activate the opioid receptors
- Buprenorphine's (unlike methadone's) effect plateaus at higher doses which accounts for its better safety profile [less likely to cause overdose]
- Reduce heroin craving
- Alleviate withdrawal
- Block heroin's euphoric effects

# Effects of Buprenorphine Dose on μ-Opioid Receptor Availability



# What is the difference between heroin addiction and opioid agonist treatment?

| | ***Heroin Addiction*** | ***Opioid Agonist Treatment*** |
|---|---|---|
| **Route** | **Injected or Snorted** | **Oral or Sublingual** |
| **Onset** | **Immediate** | **Slow** |
| **Euphoria** | **Yes** | **No** |
| **Dose** | **Unknown** | **Known** |
| **Cost** | **High** | **Low** |
| **Duration** | **4 hours** | **24 hours** |
| **Legal** | **No** | **Yes** |
| **Lifestyle** | **Chaotic** | **Normal** |

# In What Formulation is Buprenorphine Available?

## Combination of buprenorphine with naloxone (Suboxone®)

- Sublingual buprenorphine is well absorbed
- Naloxone (a potent, short-acting opioid antagonist) is not well absorbed sublingually
- Injection of suboxone will precipitate opioid withdrawal

## Buprenorphine Alone (Subutex®)

- Rare indications for use
- Several generics available at lower price

# What is the Evidence of Methadone's Effectiveness?

- 11 Randomized Clinical Trials with a total of 1,969 participants were included in a Cochrane Review (Mattick et al., 2009)
- Methadone was more effective than placebo in reducing heroin use and in retaining patients in treatment
- There was inadequate evidence that it reduced criminal behavior
  - Although many longitudinal studies show an association between methadone treatment and reduced criminal behavior

# What are the characteristics of effective maintenance treatment?

- **Higher doses (individualized to patients' needs)**
- **Longer time in treatment**
- **Psychosocial services of appropriate intensity & duration**

# What is the Evidence of Buprenorphine's Effectiveness?

- 24 Randomized Clinical Trials with a total of 4,497 participants were included in a Cochrane Review (Mattick et al., 2008)
- Buprenorphine was more effective than placebo in reducing heroin use and in retaining patients in treatment
- Buprenorphine was less effective than medium dose methadone in reducing heroin use

## How are buprenorphine & methadone provided?

Shorter-term: Detoxification

Longer-term: Maintenance

Length of time on these medications should be individually determined by patient and physician together

# Is Opioid Detoxification Effective?

- Effective at reducing withdrawal symptoms
- Helps some patients detoxify
- By itself, it is most often not successful in maintaining abstinence
- Most patients relapse quickly after detoxification
    - 29% success at 2 weeks post-detox (Ling et al, 2009)

# Is Opioid Detoxification Effective?

- Low success rate is true for both inpatient & outpatient detoxification
- Relapse is associated with increased risk of overdose death and recidivism

# Agonist Treatment in Criminal Justice System

- These medications can be used in probation, parole and drug courts
  - Although not uniformly available
- Probationers respond to methadone (Kelly et al., 2013) and to buprenorphine (Mitchell et al., In press) as well as non-probationers
- Agonist treatments often are not continued upon incarceration

# Agonist Treatment in Jails

**Inmates**

- Awaiting trial
- Short sentences (< 1 year)

**Uses of Agonist Treatment**

- Detoxification from heroin (if desired/indicated)
- Initiate in jail and continued upon release
- Continue in jail for arrested patients

# Prisons

Prisoners

- Long sentences (> 1 year)

Treatment Issues

- Initiate treatment for in-prison heroin users
- Initiate treatment for in-prison abstainers who wish to avoid release upon release

# II. Opioid Antagonists

# In What Formulation is Opioid Antagonist Treatment Available?

Oral Naltrexone (Revia ®)

- Highly effective pharmacologically
- Hampered by poor patient adherence
- Useful for highly motivated patients

Injectable formulation (Vivitrol ®)

- FDA-approved for opioid dependence in 2010
- Effective for about 30 days

# Summary

- FDA-approved medications for alcohol and opioid dependence have proven effectiveness
- These medications can reduce the use of alcohol and opioids
- However, the are underutilized in criminal justice settings, presenting an opportunity to improve outcomes by making them more widely available