Medication Assisted Treatment for Opioid Use Disorders and Veteran Populations

Kamala Greene-Genece, Ph.D.
VP, Clinical Director
Phoenix Houses of New York

Benjamin R. Nordstrom, M.D., Ph.D.
President and CEO
Phoenix House

Learning Objectives

- Understand how veteran populations are vulnerable to Opioid Use Disorders (OUDs)
- Understand the mechanisms of action buprenorphine, methadone and naltrexone
- Understand the advantages and disadvantages of each medication discussed.

Veterans and Mental Health

- 22 million veterans in the US population
- Vets make up 8.5% of the US population but account for 18% of suicides[1]
- 22 vets die from suicide each day[2]
- Rate of Post Traumatic Stress Disorder (PTSD) in current and former service members is 8%, and 9.2% of all VA users[3]
- PTSD increases the risk of Substance Use Disorders by 3-4 x [4]
- PTSD increases the risk of substance relapse [5]

Veterans and Pain

- High rates of PTSD and pain are common
- True for pre-9/11 vets
- Also true for OIF/OEF vets
- Veterans are more likely than civilian counterparts to have chronic pain[6]
  - 60% recent vets
  - 50% vets overall
  - c/w 30% civilian population with CP

Veterans and Opioids

- Opioid Rxs increased 270% over 12 years[7]
- OUDs in vets increased 55% [8]
- Vets are 2x likely to become addicted to opioids compared to the civilian population
- Vets are 2x likely to die of overdose compared to the civilian population[9]
- Vets getting opioids 233% more likely to have adverse clinical outcomes[10]

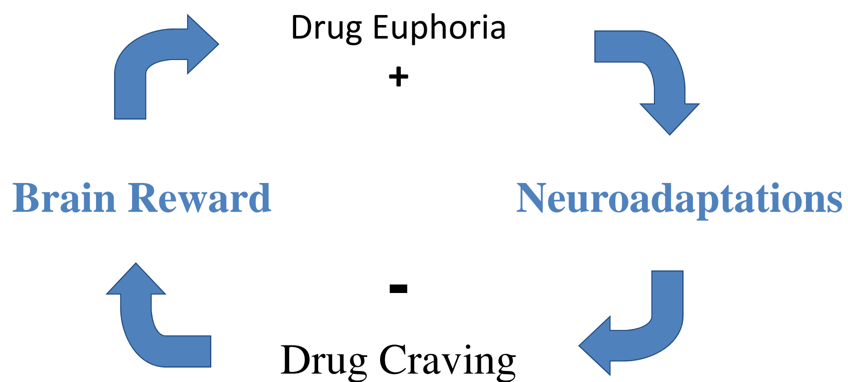
Veterans and Opioids

- Vets with PTSD and pain[10]
  - 260% more likely to get opioids
  - 42% more likely to get high dose
  - 87% more likely to get $\geq$ 2 opioids concurrently
  - 546% more likely to get sedatives concurrently
  - 64% more likely to get early refills

Opioid addiction

- Tolerance develops quickly
- Use gets perpetuated by….
- Positive reinforcement
  - Get euphoria (high)
- Negative reinforcement
  - Get withdrawal when wears off
  - Withdrawal is pretty unpleasant

Cycle of Addiction

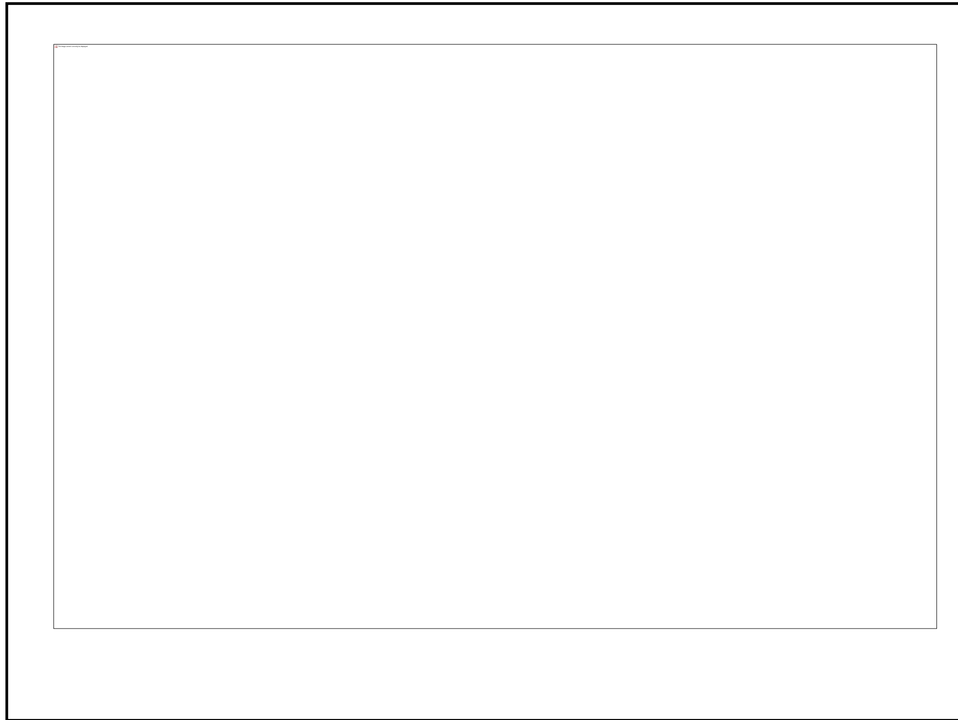


Medication Assisted Treatment

- Reduce opioid use
- Increase retention in treatment
- Reduce HIV risk behaviors
- Reduce overdose deaths

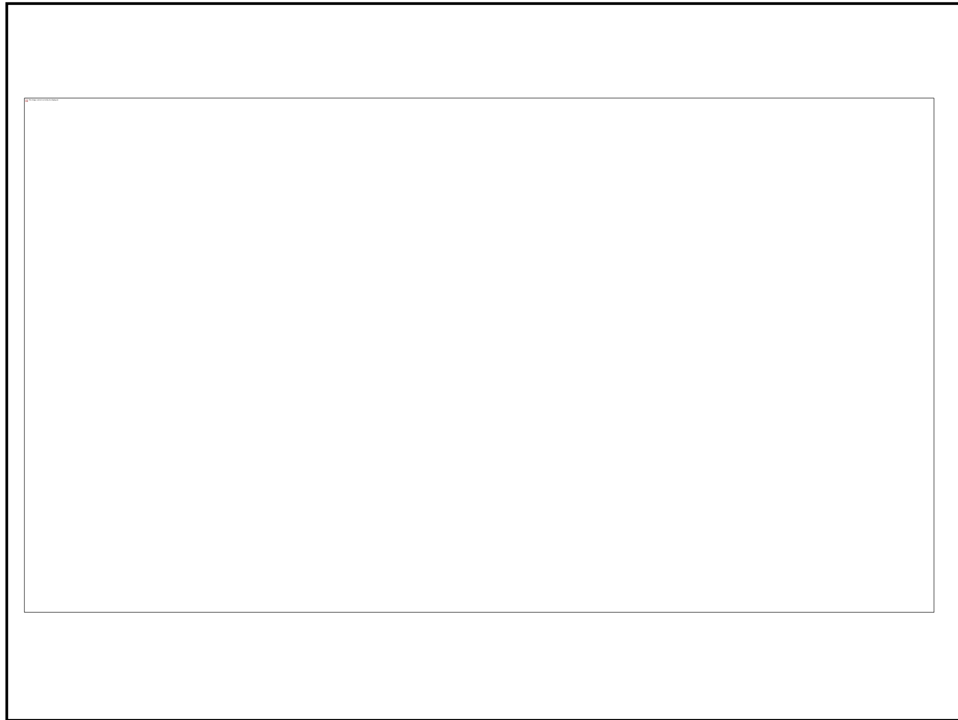
General Opioid Pharmacology

- Full agonists
  - Bind to the receptor and activate the receptor
  - Increasing doses of the drug produce increasing effects until a maximum effect is achieved (receptor is fully activated)
  - Most abused opioids are full agonists



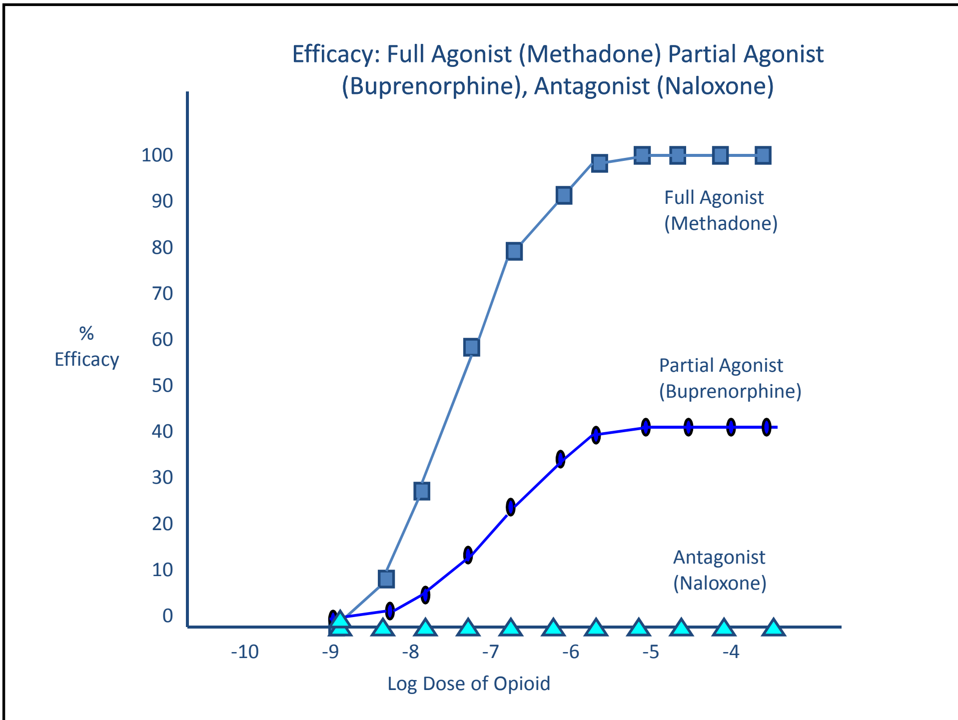
General Opioid Pharmacology

- Partial agonists
  - Bind to the receptor and activate the receptor
  - Increasing the dose does not lead to as great an effect as does increasing the dose of a full agonist- less of a maximal effect is achieved



General Opioid Pharmacology

- Antagonists
  - Bind to the receptor, but don’t activate the receptor
  - Block the receptor from being bound by a full agonist or partial agonist
  - Like putting gum in a lock, or…

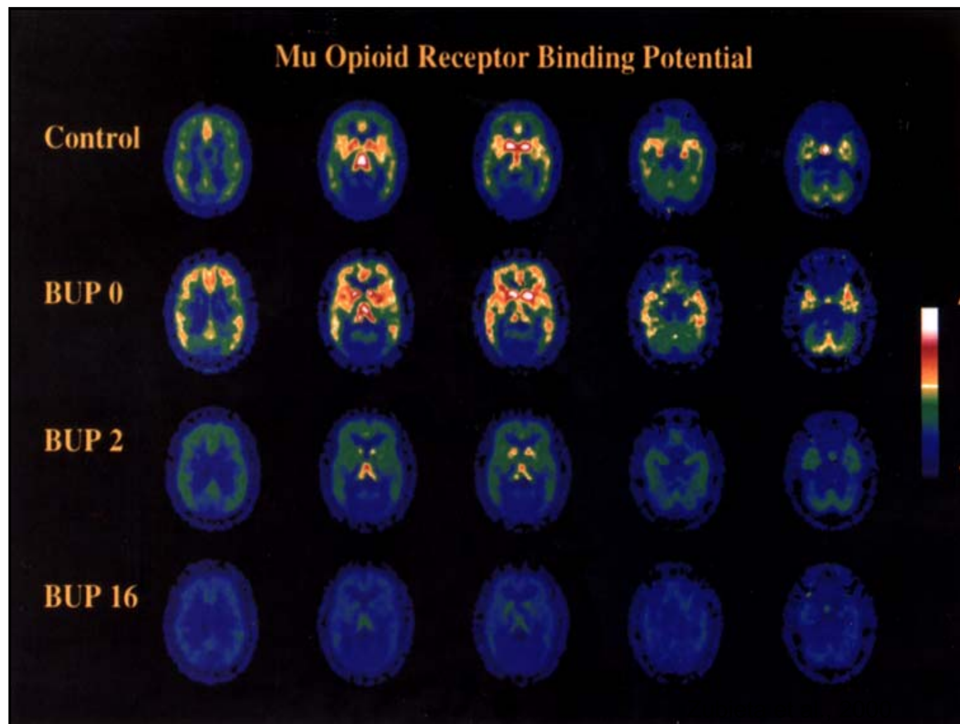

Efficacy: Full Agonist (Methadone) Partial Agonist (Buprenorphine), Antagonist (Naloxone)
100
90
80
70
60
50
40
30
20
10
0
%
Efficacy
Full Agonist
(Methadone)
Partial Agonist
(Buprenorphine)
Antagonist
(Naloxone)
-10
-9
-8
-7
-6
-5
-4
Log Dose of Opioid

Methadone

- Works on the same receptor (mu opioid receptors) as heroin and other abused opioids
- Can use it to taper people down
  - Build a “chemical staircase” for them to walk down
- Can use it to maintain people as well
  - Put on same dose of methadone as heroin
  - Stops withdrawal
  - Ratchet up dose to way past how much heroin they used
  - Price it out of reach
  - Stops positive and negative reinforcement

Buprenorphine

- High affinity for the mu opioid receptor
  - Competes with other opioids and blocks their effects
  - Prevents positive reinforcement
- Slow dissociation from the mu opioid receptor
  - Prolonged therapeutic effect for opioid dependence treatment
  - Long half life (20-44 hours)
  - Prevents negative reinforcement



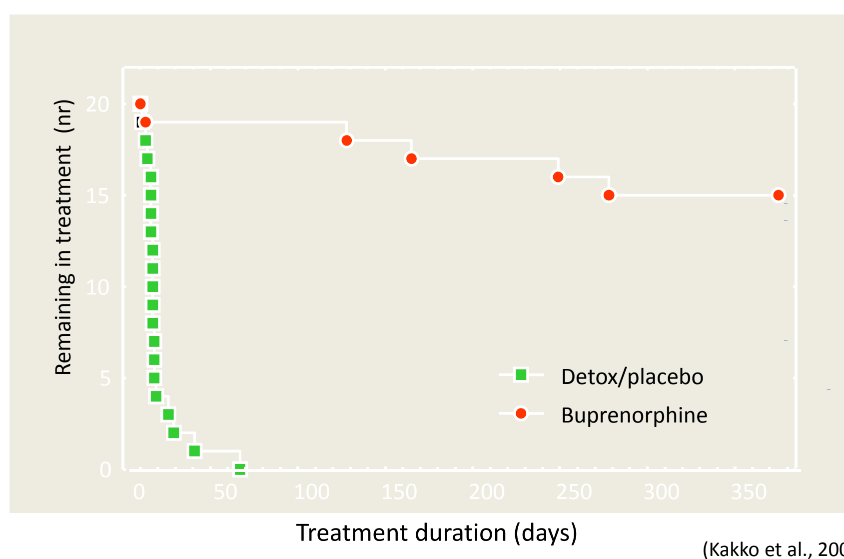
Methadone

- Schedule II
- Dispensed at Opioid Treatment Programs
- Staffing and practices directed by Federal law
  – 42 CFR Part 8
- Compared to psychosocial interventions alone
  – Increased treatment retention
  – Decreased opioid use

Buprenorphine

- Schedule III
- Office-Based Opioid Treatment (OBOT)
- DATA 2000
  - Addiction specialist (3 kinds)
  - 8 hour course
- Compared to psychosocial interventions alone
  - Improve treatment retention
  - Reduce opioid use

Buprenorphine Maintenance/Detoxification: Retention



Treatment duration (days)

(Kakko et al., 2003)

Naltrexone

- Not a controlled substance
- Any licensed provider can Rx
- Oral or long-acting injection
- Compliance is a problem

Naltrexone

- Antagonist therapy based on the behavioral concept of “extinction”
- Euphoric effects of opioids are blocked
- The repeated lack of reinforcement, gradually result in extinction of opioid use

Naltrexone

- Pure opioid antagonist with good oral absorption
- Occupies mu receptors without activating
- Blocks abused agonist opioid drugs
- Duration of action 24-48 hours for oral formulation, one month if IM
- 1984: FDA approved to treat opioid dependence
- Well tolerated and safe

Effectiveness of Naltrexone

Recent Studies:

- Placebo (25.3%) vs. Long-acting injectable naltrexone (61.9%) – negative urine samples after 48 days
- Higher mean days retained in treatment
- Opioid-free weeks from week 5 to 24 were significantly different between treatment groups (90% naltrexone vs. 35% placebo)
- 50% mean reduction in subjective craving

Methadone vs Buprenorphine

- Patient preference typically decides
- Some studies show they are the same
- Some studies show
  - Methadone retains better
  - Buprenorphine reduces opioid use better
- Cochrane meta-analysis:
  - Methadone retains better
  - Equal at reducing opioid use

Naltrexone vs. Buprenorphine

- 2 studies, one Norwegian, one U.S. based
- Found non-inferiority of depot naltrexone
- U.S. study found higher drop outs in the first week for the naltrexone group
- Consider naltrexone for people who present already detoxed (e.g. from correctional settings or post-detox)

How long?

- No solid empirical evidence to answer
- Guidance from TIP 43 is “at least 2 years”
- Stability in multiple domains of life
  - Social
  - Occupational
  - Family

Integration of MAT

- Despite effectiveness of all MAT, NO MEDICATION has been found to change the behaviors associated with illicit drug use
- Thus, behavioral therapies continue to play a critical role in the recovery process:
  - Repairing family and social relationships
  - Finding positing support networks/recreation
  - Obtaining/maintaining fulfilling employment
  - Addressing co-morbid psychiatric/emotional symptoms

MAT in the VAH

- About 53 MMTP in VA system
- Early on, barriers and facilitators to bup were studied (Gordon et al, 2011)
  - Data from 2006-07
  - Lack of perceived need, lack of provider interest and stigma were barriers
  - Need, provider interest, resources were facilitators
- Buprenorphine growing 300 pts at 27 facilities to 6,147 pts at 118 facilities from 2004-2010 (Olivia et al 2013)

VA Response to Opioid Rx

- VA issued prescribing guidelines in 2010
- Between July 2012 and June 2015, reduced the numbers of vets getting opioids by 115,575 people
- Established the Office of Patient-Centered Care, includes non-opioid and alternative approaches to pain

Literature Cited

1. US Dept. VA Office of Suicide Prevention, "Suicide Among Veterans and Other Americans 2001-2014. August 3, 2016.

2. VA Suicide Prevention Program, "Facts About Veteran Suicide July 2016"

3. Institute of Medicine, "Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Final Assessment." June 2014

4. Seal et al "Substance use disorders in Iraq and Afghanistan veterans in VA healthcare, 2001-2010: Implications for screening, diagnosis and treatment." Drug and Alcohol Dependence, 116: 93-101, 2011.

5. Norman 2007

6. Carolyn Clancy, MD Interim Undersecretary for Health, before the Committee on Veteran's Affairs, U.S. Senate, March 26 2015

Literature Cited Cont'd

7. The Center for Investigative Reporting, "VA's opiate overload feeds Veterans' adictions, overdose death." September 28, 2013
8. PBS Frontline, "Veterans face greater risk among opioid crisis." March 2, 2016
9. Bohnert et al, "Accidental poisoning mortality among patients in the Department of Veterans Affairs Health System." Med Care 49(4):393-6, 2011
10. Seal et al, "Association of mental health and prescription opioids and high risk opioid use in US veterans of Iraq and Afghanistan." JAMA207(9): 940-947, 2012