Medication Assisted Therapies:
Using Medications for Treatment of Opioid and alcohol Disorders

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Study Drug Support
• Alkermes (Vivitrol)  
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No paid roles w Industry (advising, speaking)
The opioid epidemic and Criminal Justice Systems (CJS)

Opioid misuse has increased in US, 1995-2015

- Prevalence of prescription opioid misuse
- ‘modernization’ of heroin markets
- Increase in opioid-related overdose deaths
- Now a public health and political crisis

CJS systems need to deal with:

- Detox at arrest/incarceration
- Treatment during incarceration
- Treatment during community supervision
- Recidivism, OD death, drop outs
**Drug Poisoning Deaths Involving Opioid Analgesics, Cocaine and Heroin: United States, 1999–2011**

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<tr>
<th>Year</th>
<th>Opioid Analgesics</th>
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<th>Heroin*</th>
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<td>16,917</td>
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**Note:** Not all drug poisoning deaths specify the drug(s) involved, and a death may involve more than one specific substance. The rise in 2005-2006 in opioid deaths is related to non-pharmaceutical fentanyl (see [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5729a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5729a1.htm)). *Heroin includes opium.

**Source:** National Center for Health Statistics/CDC, *National Vital Statistics Report*, Final death data for each calendar year (June 2014).
MAT (Methadone, Buprenorphine, Naltrexone) Works

*Figure 1. Mortality Rates of MMT Treated and Untreated Heroin Users in Australia (Caplehorn et al. 1996, N = 296)*

*Methadone maintenance therapy versus no opioid replacement therapy, Cochrane Reviews, 2009*
Despite the Evidence Supporting MAT…

Community Treatment does not offer enough MAT…

• 2012: only 27.6 percent of heroin users undergoing treatment in the US received some form of MAT

*(SAMHSA/TEDS: Treatment Episode Dataset, 2012)

…CJS offers even less

• 0% < Probation/Parole/Drug Court < 28% *(Matusow, 2014)
In a recent NYC jail study, 88% of persons not on a medication relapsed to heroin use post-release (LeeJD, 2015, Addiction).
Relapse leads to very high rates of Overdose Death following incarceration.

SOURCE:
Binswanger et al, NEJM 2007;356:157-165
Summary of CJS methadone and buprenorphine: impact on mortality post-release

- Pre- and post-release MAT lowered mortality (“Full OST” – Opioid Substitution Therapy)
- Pre-release MAT only still lowered mortality by reducing overdose in Week 1

Addiction
Volume 109, Issue 8, pages 1306-1317, 14 APR 2014 DOI: 10.1111/add.12536
Review: very high rates of relapse (50-90%) occurred after typical detox episodes, despite on-going counseling.

STUDY #2

Krupitsky E et al, Lancet, 2011

Response Profile
Cumulative % of Participants at Each Rate of Opioid Negative Urine Tests: XR-NTX 380 mg vs. Placebo

- Total abstinence (100% opioid-free weeks) during Weeks 5-24 was reported in 45 (35.7%) of subjects in the XR-NTX group versus 28 (22.6%) subjects in placebo group (P=0.0224).

Following inpatient detox, persons not on a medication were again using opioids on average 65% of the time.
Why use Methadone, Buprenorphine, or Naltrexone vs. ‘drug-free’ counseling alone?

WeissRD et al, Arch Gen Psyche, 2011

In this outpatient study, relapse after brief detox w buprenorphine was 90%
Addiction: ‘A Brain Disease’

Addicted brain primarily responding to impulse and cravings
Addiction Treatment: Healing ‘A Brain Disease’

- **Do we do something directly to the brain?**
  - *Medications*
- Do we isolate the patient away from drugs/alcohol?
  - Residential treatment settings, incarceration
- Can the patient re-learn healthy, avoid unhealthy behaviors?
  - Behavioral therapy
Natural Rewards Elevate Dopamine Levels

Food

Sex

% of Basal DA Output

DA Concentration (% Baseline)

Sample Number

Time (min)

Female Present

NAc shell

Empty

Food Sex

Box Feeding

Sample 1 2 3 4 5 6 7 8

Female Present

Sample 1 2 3 4 5 6 7 8

Female Present
cocaine
Effects of Drugs on Dopamine Release

Amphetamine

Cocaine

Nicotine

Morphine

Di Chiara and Imperato, PNAS, 1988

Effects of Drugs on Dopamine Release
But Dopamine is only **Part** of the Story

Scientific research has shown that other neurotransmitter systems are also affected:

- **Serotonin**
  - Regulates mood, sleep, etc.

- **Glutamate**
  - Regulates learning and memory, etc.
# Addiction Medications:

**All diminish immediate Dopamine-based Reinforcement**

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<th>Category</th>
<th>Type</th>
<th>Example</th>
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<td>Ach/Nicotine receptors</td>
<td>Mixed agonist/antagonist</td>
<td>Varenicline</td>
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<td>Mu Opioid receptors</td>
<td>Agonist</td>
<td>Methadone</td>
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<td></td>
<td>Antagonist treatment</td>
<td>Naltrexone (opioid and alcohol treatment)</td>
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<td></td>
<td>Mixed agonist/antagonist</td>
<td>Buprenorphine</td>
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<td>Glutamate/NMDA, GABA</td>
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<td>Acamprosate</td>
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<td>Topiramate</td>
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Reminder: What is the Difference between Opioid Agonists & Antagonists?
Methadone outcomes, 1965-2015

- Less heroin use
- Less IV use
- Less HIV transmission
- Less overdose death
- Less criminal behavior
  *(harder to show less recidivism)*
- Saves taxpayers money
- Longer lifespan
Methadone prior to prison or jail release is effective.

**Methadone Treatment Pre-and Post-Release Increases Treatment Retention & Reduces Drug Use**

*Findings at 12 Months Post-Release*

- **Methadone Referral only**
  - % in Community-Based Tx: 0
  - % Opioid Test Positive: 17.3
  - % Cocaine Test Positive: 0

- **Methadone Transfer on Release**
  - % in Community-Based Tx: 36.7
  - % Opioid Test Positive: 48.7
  - % Cocaine Test Positive: 25

- **Methadone Pre- & Post-Release**
  - % in Community-Based Tx: 71.9
  - % Opioid Test Positive: 66.6
  - % Cocaine Test Positive: 43.2

Methadone should be continued during incarceration

Josiah D Rich, Michelle McKenzie, Sarah Larney, John B Wong, Liem Tran, Jennifer Clarke, Amanda Noska, Man...

Figure 2 Probability of attending a methadone clinic in (A) the intention-to-treat and (B) the as-treated populations. Data are for 1 month follow-up after participants’ release from incarceration.

Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail: a randomised, open-label trial

The Lancet, 2015
Methadone maintenance treatment may improve completion rates and delay opioid relapse for opioid dependent individuals under community corrections supervision

C. Brendan Clark, Peter S. Hendricks, Peter S. Lane, Lindsay Trent, Karen L. Cropsey

Addictive Behaviors, Volume 39, Issue 12, 2014, 1736–1740

- Methadone treatment in a Birmingham, AL TASC population associated with less relapse and better CJS outcomes
Rikers NYC Jails Key Extended Entry Program (KEEP)

- Current methadone patients (~100/day) & out-of-treatment heroin users (~400/day) offered methadone at arrest
- **All** can access methadone detox
  - Detox from community maintenance dose is slow (weeks)
- Nearly all current MTD patients continue in jail if eligible (no felony)
- Significant exposure of out-of-treatment heroin users to methadone
- Better community retention with higher dose (60-90+ mg/day)
  *Harris, LeeJD, et al, *Substance Abuse*, 2012
Problems: Methadone Clinics and Stigma

- Federally-licensed clinics treating opioid dependence only
  - limited locations
  - limited number of treatment slots
  - may only take insurance
  - daily directly observed therapy (DOT)
- Patients have negative views (sedation, ‘rotting teeth/bones’, forced w/d, ‘handcuffs’)
- Providers have negative views of methadone patients and clinics
Reminder: Buprenorphine & Office-based Treatment

- Medical office visit
- Retail pharmacy
- Chronic treatment

Daily or Thrice-Weekly Buprenorphine Doses Yield Similar Declines in Days of Drug Use

Patients in treatment for opiate addiction received either daily or thrice-weekly doses of buprenorphine. Both groups showed reductions in reported days of heroin use during a 12-week treatment period.
Buprenorphine and Methadone Maintenance in Jail and Post-Release: A Randomized Clinical Trial

Stephen Magura\textsuperscript{a,b,*}, Joshua D. Lee\textsuperscript{c}, Jason Hershberger\textsuperscript{d}, Herman Joseph\textsuperscript{b}, Lisa Marsch\textsuperscript{b}, Carol Shropshire\textsuperscript{e}, and Andrew Rosenblum\textsuperscript{b}


- BUP-NX vs. Methadone at arrest
- N=116, 1:1 randomization
- Results:
  - Higher % on BUP in-jail (82\% vs. 75\%)
    - 10\% vs. 2\% D/C’d meds due to diversion
  - Higher rate of post-release retention if BUP
    - 48\% vs. 23\% (p<0.005)
- BUP appeared feasible and effective
Buprenorphine-Naloxone Maintenance Following Release from Jail


Joshua D. Lee, MD, MSc, Ellie Grossman, MD, MPH, Andrea Truncale, MD, MPH, John Rotrosen, MD, Andrew Rosenblum, PhD, Steven Magura, PhD, and Marc N. Gourevitch, MD, MPH

No differences vs. non-jail patients in community primary care BUP

Same retention vs. non-jail

Same rates of urine results and self-report of heroin use
Addiction Treatment Dissemination: Pharmacotherapy in Non-specialty Settings

Efficacious Addiction Pharmacotherapy + Medical Management

Effectiveness & Dissemination Research

Primary Care

Criminal Justice Populations
Extended-Release Naltrexone (Vivitrol): opioid antagonist approach

- Monthly intramuscular injection
- Given by nurse, PA, MD, pharmacist
- Non-narcotic, not a controlled substance
- Must detox off opioids first!!
- Jail, prison, detox, rehab, other
- Not for use if:
  - Pregnancy
  - Chronic pain requiring opioids

**Response Profile**
Cumulative % of Participants at Each Rate of Opioid Negative Urine Tests: XR-NTX 380 mg vs. Placebo

- Placebo (N=124) - 35% of weeks opioid-free
- XR-NTX (N=126) - 90% of weeks opioid-free

*Total abstinence (100% opioid-free weeks) during Weeks 5-24 was reported in 45 (35.7%) of subjects in the XR-NTX group versus 28 (22.6%) subjects in placebo group (P=0.0224).*
Less heroin relapse among parolees and probationers: XR-NTX vs. Treatment as Usual, N=308 across 5 US Sites

LeeJD et al, 2014, Poster
Primary Opioid Outcome:
No relapse, weeks abstinent, urines negative

$\text{p}<0.001$ $\text{p}<0.001$ $\text{p}<0.001$
## Long-term Follow-Up (18 Months)

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<th>Urines, 12 &amp; 18 mos</th>
<th>XR-NTX</th>
<th>TAU</th>
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<td>% opioid negative urine, 12 months</td>
<td>49%</td>
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<td>% opioid negative urine, 18 months</td>
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<td>All-case mortality</td>
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## XR-NTX prior to release: Less heroin use after jail

### XRNTX vs. TAU: OPIATE URINE TOXICOLOGY RESULTS PER VISIT

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### XRNTX-GROUP: OPIATE UTOX RESULTS ONLY

- About to leave jail, urine is ‘clean’ = BLUE
- After jail, using heroin = RED

*In a recent NYC jail study, 88% of persons not on a medication relapsed to heroin use post-release (LeeJD, 2014, in review)*
CJS, MAT, Implementation: Data is strong, so onto logistics and local factors

• All 3 medications now have solid evidence supporting effectiveness

• Choice depends on patient, provider, environment
  • Is the patient using and in community? Is detox already complete?
  • Is there a provider accepting CJS referrals? Medicaid? Uninsured patients?
  • How far away is the treatment provider?
  • Insurance status? Reimbursement in your state?
  • What are the patient’s preferences?
Implementation: current treatment realities

Buprenorphine, Buprenorphine-Naloxone (Suboxone, Zubsolv)
- any provider with an ‘X’ DEA#...now 275 patients per experienced MD
- office- or program-based prescribing
- the most common form of opioid medication treatment in US

Methadone
- only available at a licensed Opioid Treatment Program (OTPs)
- more stigma

XR-Naltrexone (Vivitrol)
- only recently FDA approved
- most expensive costs per month
- antagonist requires patient to detox first…the ‘detox hurdle’
Implementation:
Which medications to use? For which patient?

So…

Is there a methadone provider in the county?
Is there a buprenorphine provider? Reimbursement?
Is there coverage/reimbursement for XR-NTX?
What is the patient motivated for?

...any type or choice of MAT will be effective vs. none

There are no well defined criteria dictating which med for which patient beyond availability and patient preference
Implementation: How to improve XR-NTX re-entry outcomes?

- Patient education, patient preference
  - Does the patient really want this treatment?
- Adherence boosters
  - **negative** CJS consequences?
    - parole violation, increased monitoring…
  - **positive** consequences?
    - money, prizes, privileges, etc?
    - social support?
- counseling?
Implementation:
How to improve XR-NTX re-entry outcomes?

- Patient matching
  - We don’t yet know which patients do best
- Adherence boosters
  - CJS mandated treatment is an acceptable approach
  - Incentive Management works with other conditions
- Case Management and Patient Navigation under study
- Psychosocial treatment, meetings, are usual rec’s
Prologue: MAT and CJS

• Community bup-nx and methadone should be continued during incarceration
  • Similar to HIV or MH meds
• Use of MAT (bup-nx, methadone, XR-NTX) is a long-term strategy ("maintenance")
• Any ‘dose’ of counseling goes with MAT
  • All MAT implies significant counseling from a provider
Summary

• Opioid disorders are poorly treated; if undertreated, CJS and health outcomes are poor

• Studies and data support CJS-MAT combinations
  • High quality evidence supporting use of methadone, buprenorphine, XR-NTX in CJS populations (jails, prisons, parole, probation)

• CJS-MAT implementation is on-going
  • Resources and availability varies. Patient enthusiasm and preference should be strongly considered.