Latest Research on Addiction and Treatment

Joshua D Lee MD MSc
joshua.lee@nyumc.org / @DrJoshuaDLee
Associate Professor
NYU School of Medicine, Department of Population Health
Disclosures, LeeJD

• Grants:
  – NIDA (U01, U10 (CTN GNYN))
  – NIAAA (R01)

• Study Drug: Alkermes (Vivitrol), Indivior (Suboxone)

• No financial COIs
Core Addiction Medicine Evidence-Based Interventions are all applicable to CJS

1. Smoking screening and smoking cessation medications
2. Screening and Brief Intervention (SBI) for risky alcohol (but not drugs)
3. Medications for alcohol and opioid disorders
4. Acute withdrawal management
5. Overdose prevention w Naloxone
6. Non-judgemental treatment of medical and psyche co-morbidities
7. Evidence-based counseling approaches (CBT, MET, Contingency Mgt, Medical Mgt, 12-step)
West Virginia (52.0), Ohio (39.1), New Hampshire (39.0), and Pennsylvania (37.9) were the four states with the highest observed age-adjusted drug overdose death rates. The District of Columbia had a rate of 38.8 per 100,000.
More Epidemiology: Fentanyl in the US Heroin Supply

O’Donnell, MMWR 2017:

Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016

• Preliminary estimates of U.S. drug overdose deaths exceeded 60,000 in 2016 ... partially driven by a fivefold increase in deaths involving synthetic opioids (excluding methadone), from 3,105 in 2013 to approximately 20,000 in 2016

• OD death July–December 2016 that tested positive for fentanyl, fentanyl analogs, or U-47700 in 10 states

• Fentanyl detected in 56.3% of 5,152 opioid overdose deaths

![Graph showing percentage of opioid overdose deaths involving fentanyl and fentanyl analogs by state for July–December 2016.](image)
AT BASELINE: Typical of Drug SBIRT RCTs, the largest category of MODERATE risk use is Cannabis

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Then, SBIRT has no effect on MODERATE Cannabis risk

A Randomized Study of the Use of Screening, Brief Intervention, and Referral to Treatment (SBIRT) for Drug and Alcohol Use with Jail Inmates

• SBIRT vs. generic education with Jail inmates; outcomes at 12-months

• No significant difference in alcohol or drug use, treatment, arrests, HIV risk behaviors, or quality of life between the two groups
8. Pharmacological Interventions: XR-Naltrexone v BUP-NX (film) for Opioids

LeeJD, The Lancet 2017

**Comparative Effectiveness of Extended-Release Naltrexone versus Buprenorphine-Naloxone for Opioid Relapse Prevention (X:BOT): A Multicentre, Open-label, Randomized Controlled Trial**

- Estimating differences in opioid relapse-free survival between XR-NTX and BUP-NX

- (Intention-to-treat population, n=570) 24 week relapse events were greater for XR-NTX (185 [65%] of 283) than for BUP-NX (163 [57%] of 287; hazard ratio [HR] 1.36, 95% CI 1.10-1.68)

- Most of this difference was early relapse in most (70 [89%] of 79) XR-NTX induction failures

- Among participants successfully inducted (PP) relapse-free survival was similar

- Overdose rates no different
8. Pharmacological Interventions: XR-NTX vs Daily BUP

TanumL, JAMA Psychiatry, 2017:

**Effectiveness of Injectable Extended-Release Naltrexone vs Daily Buprenorphine-Naloxone for Opioid Dependence: A Randomized Clinical Noninferiority Trial**

- Overall, both were equally effective in short-term reduction of heroin, opioid, and other illicit substance use in 12-week clinical trial in Norway

- XR naltrexone group was noninferior to buprenorphine-naloxone group in the following measures:
  - Retention
  - Proportion of total number of opioid-negative urine drug tests

- XR naltrexone was superior to buprenorphine-naloxone group in the following measures:
  - Heroin use
  - Other illicit opioids
8. Pharmacological Interventions: CAM2038

Walsh, JAMA Psychiatry 2017:

Effect of Buprenorphine Weekly Depot (CAM2038) and Hydromorphone Blockade in Individuals With Opioid Use Disorder: A Randomized Clinical Trial

- Sustained release buprenorphine weekly injectable (CAM2038) administered before and after hydromorphone administration to non-treatment seeking individuals with OUD
- Both dose sizes (24 mg, 32 mg) of CAM2038 produced immediate and sustained blockade of hydromorphone effects (measured using subjective response for liking of hydromorphone) and suppression of withdrawal
Buprenorphine extended-release (Sublocade)

Figure 12. Subjects Achieving Varying Percentages of Opioid-Free Weeks

- Sublocade 300mg/300mg + IDC (n=196)
- Sublocade 300mg/100mg + IDC (n=194)
- Placebo + IDC (n=99)

NOW AVAILABLE

Sublocade (buprenorphine extended-release)
Injection for subcutaneous use
100mg-300mg

INDICATION AND USAGE

Sublocade is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days.

Sublocade should be used as part of a complete treatment plan that includes counseling and psychosocial support.
15. Ethical & Policy Considerations: Overdoses & MAT in CJS

Green, JAMA Psychiatry 2018:
Postincarceration Fatal Overdoses After Implementing Medications for Addiction Treatment in a Statewide Correctional System

- Statewide MAT availability for Rhode Island detainees and jail-released individuals by 2017
- Fatal overdoses of recently released individuals compared from 2016 (pre-MAT) to 2017 (post-MAT)
- 60.5% reduction in fatal OD post-release (26 vs. 9 individuals)
Does exposure to opioid substitution treatment in prison reduce the risk of death after release? A national prospective observational study in England

In a 2017 English national study, prison-based opioid substitution therapy was associated with a 75% reduction in all-cause mortality and an 85% reduction in fatal drug-related poisoning in the first month after release.

Marsden, Addiction, 2017
1-Year Abstinence and Death Rates: No treatment vs. detox-to-abstinence vs. medications

- **Heroin use**
  - Abstinent 0%
  - Using Heroin 100%
  - Deaths/year = 1-2+% 

- **Detox-to-Abstinence**
  - Abstinent 20%
  - Using Heroin 80%
  - Deaths/year = 0.5-1.5%

- **Medications**
  - Methadone
  - Buprenorphine
  - XR-Naltrexone
  - Abstinent 50%
  - Using Heroin 50%
  - Deaths/year = 0.5-0.75%

About half of persons starting meds are in treatment and abstinent at 6-12 months

Mortality is lower among persons on medications
Heroin users usually relapse after jail…less if MAT

In a recent NYC jail study, 88% of persons not on a medication relapsed to heroin use post-release (LeeJD, 2015, Addiction)
Despite the Evidence Supporting MAT…

Communities do 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

• 0-1% of any US jail/prison offers any MAT *(RichJ et al, 2004)*
• 0% < Probation/Parole/Drug Court < 28% *(Matusow, 2014)*
• 28 (55%) state prison systems offer methadone to inmates
• Over 50% of correctional facilities that offer methadone do so exclusively for pregnant women or for chronic pain management.
• 7 states' prison systems (14%) offer buprenorphine to some inmates.
What is the Difference between Opioid Agonists & Antagonists?

Dose of Opioid

Opioid Effect

Methadone

Buprenorphine

Naltrexone
What makes Opioid MAT Rx so ideal?

- **Binding Affinity**: methadone, buprenorphine, and naltrexone all ‘out-compete’ illicit opioids at the mu opioid receptor…they are ‘stickier’ and ‘block’ other opioids

- Agents (all of them) are relatively **long-acting** compared to illicit opioids…daily or less dosing

- Relatively **slow-onset** by oral, SL, or depot routes (vs. inhaling or injecting illicit opioids)

- At stable doses, patients should **feel relatively normal**, can work, study, exercise, etc.

- At stable doses, patient experience **fewer cravings** or urges for illicit opioid use.
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 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
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
Buprenorphine and Methadone Maintenance in Jail and Post-Release: A Randomized Clinical Trial

Stephen Magura\textsuperscript{a,b,\ast}, 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
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
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
Less heroin relapse among parolees and probationers: XR-NTX vs. Treatment as Usual, N=308 across 5 US Sites

LeeJD et al, 2016, NEJM
XR-NTX prior to release: Less heroin use after jail

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**XRNTX-GROUP: OPIATE UTOX RESULTS ONLY**

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**TAU: OPIATE UTOX RESULTS ONLY**

In a recent NYC jail study, 88% of persons not on a medication relapsed to heroin use post-release (LeeJD, 2015, Addiction)
CJS, MAT, Implementation: What do we do now?
Jail incarceration

1. Heroin User
   - jail
   - Begin detox care
   - Offer buprenorphine, methadone, naltrexone
     - Refer back to community treatment

2. Methadone or buprenorphine patient
   - jail
   - No detox
   - Continue methadone/buprenorphine
   - Refer back to community treatment
CJS, MAT, Implementation: What do we do now?
Prison incarceration

Opioid dependent individual

Prison

Detox vs. Maintenance

Pre-release: Offer buprenorphine, methadone, naltrexone

Refer back to community treatment
CJS, MAT, Implementation: What do we do now?
Community Supervision (drug court, probation, parole)

1. Heroin Uuer
   Offer buprenorphine, methadone, naltrexone

2. Methadone or buprenorphine patient
   Continue methadone/buprenorphine
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?  Meds are covered?
  • How far away is the treatment provider?
  • What are the patient’s preferences and motivations?
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 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 and meetings are compatible with all medications
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
Thank You