

“The Role of Medication”

Evidence-Based Treatment of Opioid Use Disorders: Methadone, Buprenorphine, Naltrexone

Joshua D Lee MD MSc

joshua.lee@nyumc.org @DrJoshuaDLee

Associate Professor

NYU School of Medicine

Department of Population Health

Department of Medicine / DGIMCI

Disclosures

- Grants:
 - NIDA (U01 LeeJD, U10 CTN GNYN)
 - NIAAA (R01 LeeJD),
 - NYC DOHMH/HHC,
 - Alkermes (ISS)
 - NYU SOM
- Study Drug: Alkermes, Reckitt-Benckiser/Indivior
- No financial COIs

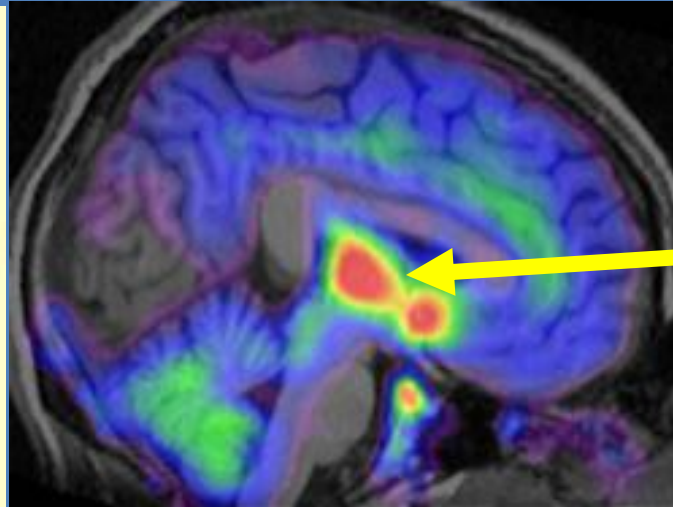
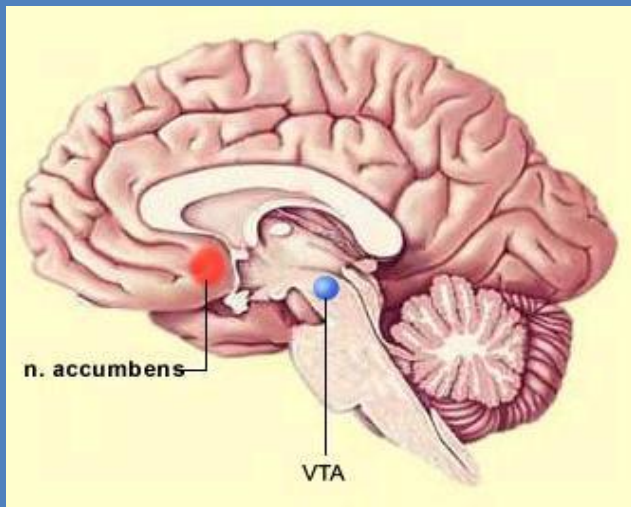
Drug abuse/exposure leads to addiction...

1. Repeated reward seeking – ‘this is fun’
2. Alteration in memory and motivational circuits to favor drug use – ‘learn how, remember how , and prioritize using’
3. Negative re-inforcement of withdrawal effects...‘got to use again so I don’t feel bad’
4. ENDGAME: Repeated, compulsive use of a previously rewarding substance that now may or may not be rewarding and is otherwise harmful

Why opioids, why so much, why now...

1. Opioids are a great high – mellow and euphoric – among those that initially enjoy them
2. Pain, anxiety, depression all get better – initially
3. Widely available after 20+ years of over-prescribing and now 'improved' heroin marketing
4. Tolerance and withdrawal immediately build up in every user – got to keep using to keep from feeling bad
5. **ENDGAME:** A very addictive, deadly, available, and initially beneficial substance that you can't just quit cause you will get really sick

Addiction Treatment: Healing 'A Brain Disease'



Highest concentration of Mu Opioid and Dopamine receptors

- Do we do something directly to the brain?
 - Medications: immediately and long-term: reduce reward, diminish withdrawal, reduce cravings
- Isolate the patient away from drugs/alcohol?
 - Residential treatment, new environment, incarceration
- Re-learn healthy, avoid unhealthy behaviors?
 - Counseling, groups, incentives

Addiction Medications:

All diminish reward effects and normalize motivation

All target discreet neurotransmitter inputs to the reward and motivation centers

Ach/**Nicotine** receptors

Mixed agonist/antagonist

varenicline

Mu Opioid receptors

Agonist

methadone

Mixed agonist/antagonist

buprenorphine

Antagonist

naltrexone

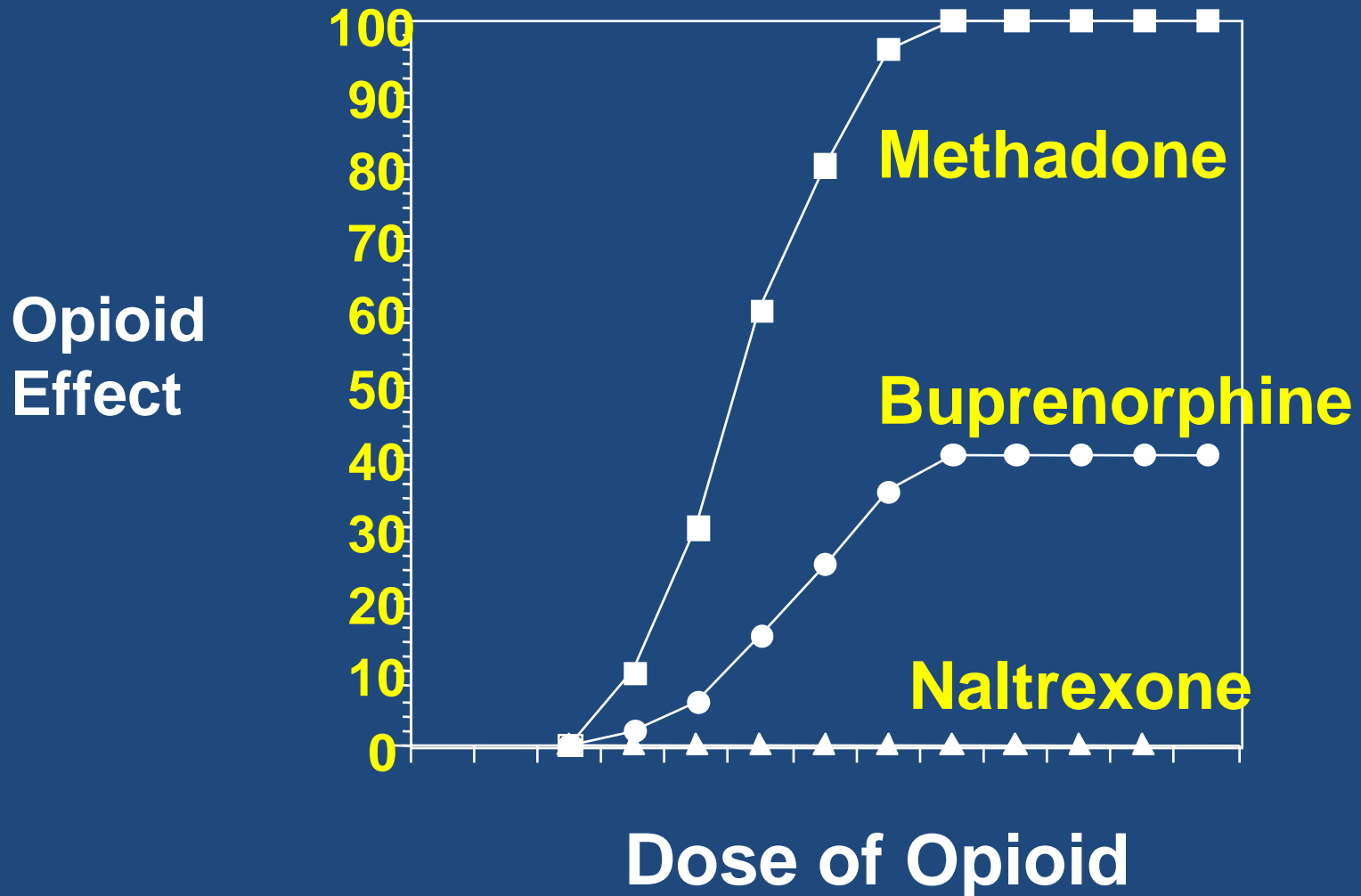
Glutamate/NMDA, GABA receptors

acamprosate

topiramate

benzodiazepines

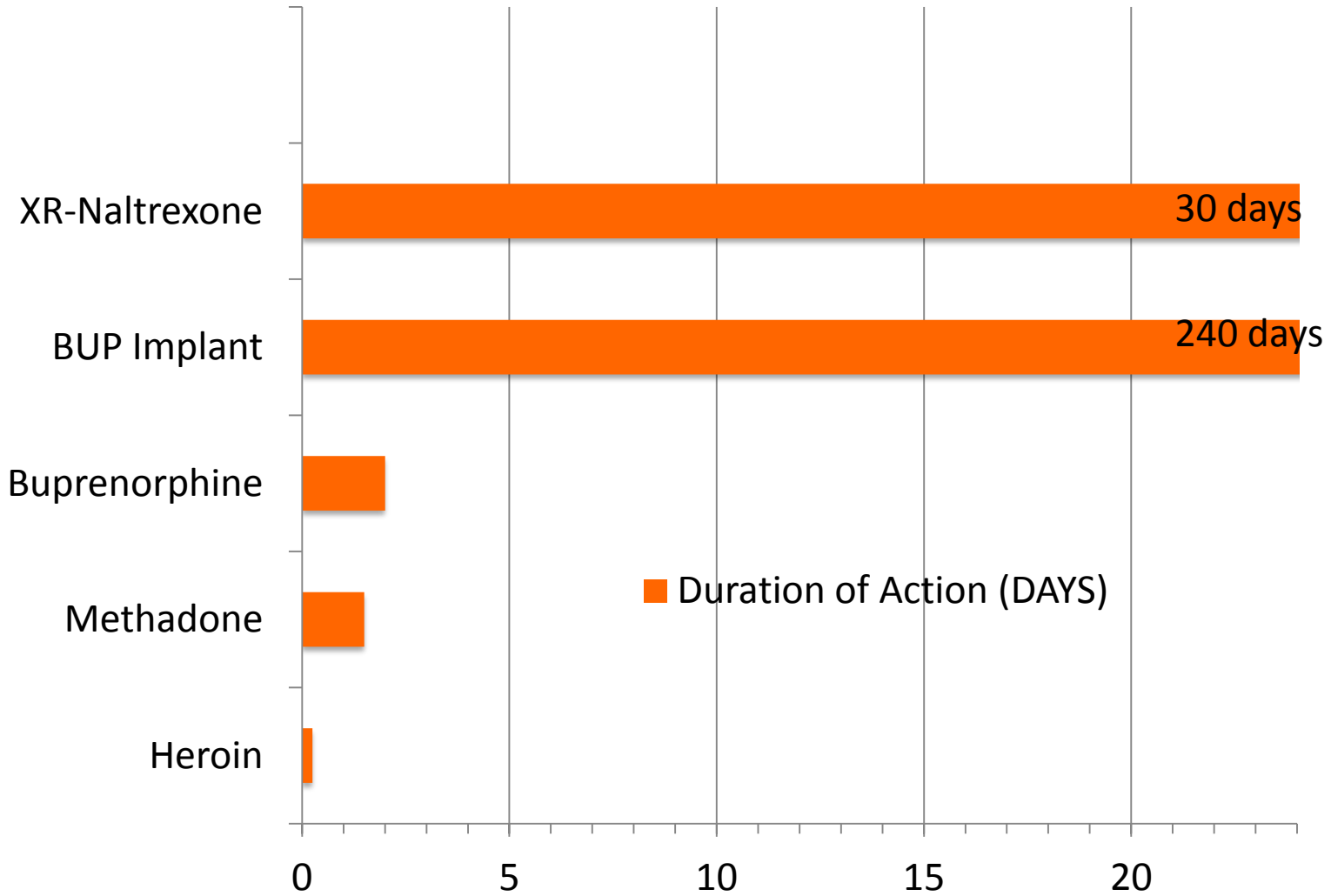
What is the difference between opioid agonists & antagonists?



What makes Opioid Medication 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...they reduce immediate reward effects of heroin
- 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)...less abuse potential
- 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.

Duration of Action (DAYS)



Medication Treatments: Agonists and Antagonists

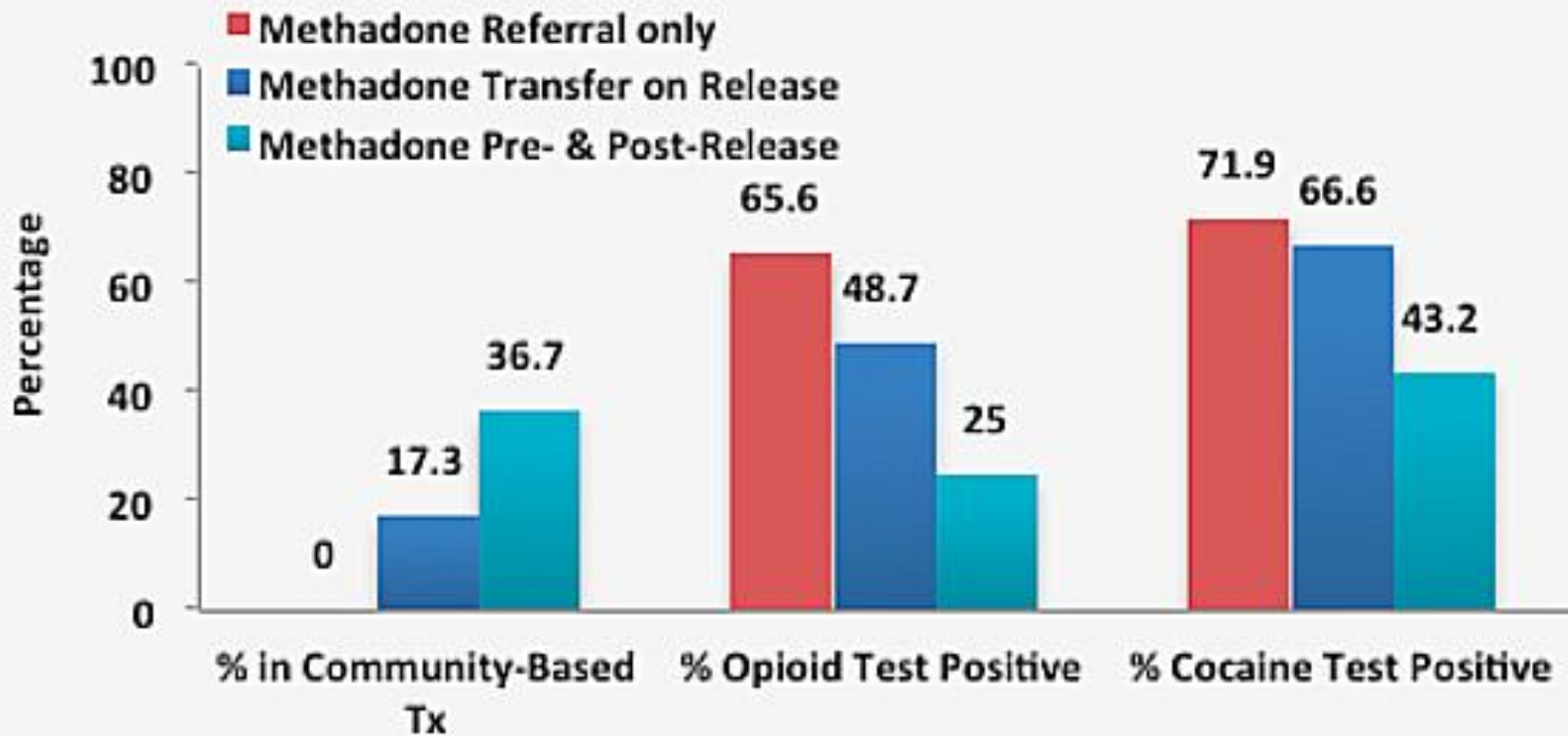
	Agonists: BUP and Methadone	Antagonist: XR-Naltrexone
<i>I need help now, can I use Rx right away?</i>	Yes	No. You need to detox first
<i>I detoxed weeks ago, can I use Rx now and avoid relapse?</i>	Yes (but unusual)	Yes
<i>Will I still be on an opioid?</i>	Yes	No
<i>Will I experience withdrawal if I quit Rx?</i>	Yes	No
<i>Does Rx block heroin use; I can't get as high if I use?</i>	Yes	Yes
<i>Can I get back to work and feel normal on Rx?</i>	Yes	Yes
<i>I have to take it every day?</i>	Yes (unless long-acting BUP)	No (monthly)
<i>Can I sell my Rx; can someone else get high off it?</i>	Yes	No

Opioid Treatments, standards of care

- OTPs and Specialty Treatment
 - Methadone (DOT), buprenorphine, naltrexone
- General Office-Based Care
 - Buprenorphine, naltrexone
- Behavioral Treatments paired with medications
 - CBT, 12-step, Medication Management
- What about in CJS?
(Jail, Prison, Community Supervision)
 - Almost exclusively *no treatment* or counseling-only
 - Any of the three can and should be offered in CJS
 - The more of them the better

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*



Kinlock, Gordon, Schwartz, Fitzgerald, O'Grady (2009). Journal of Substance Abuse Treatment. A Randomized Clinical Trial of Methadone Maintenance for Prisoners

Methadone should be continued during incarceration:

-Rich J, Lancet, 2015

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

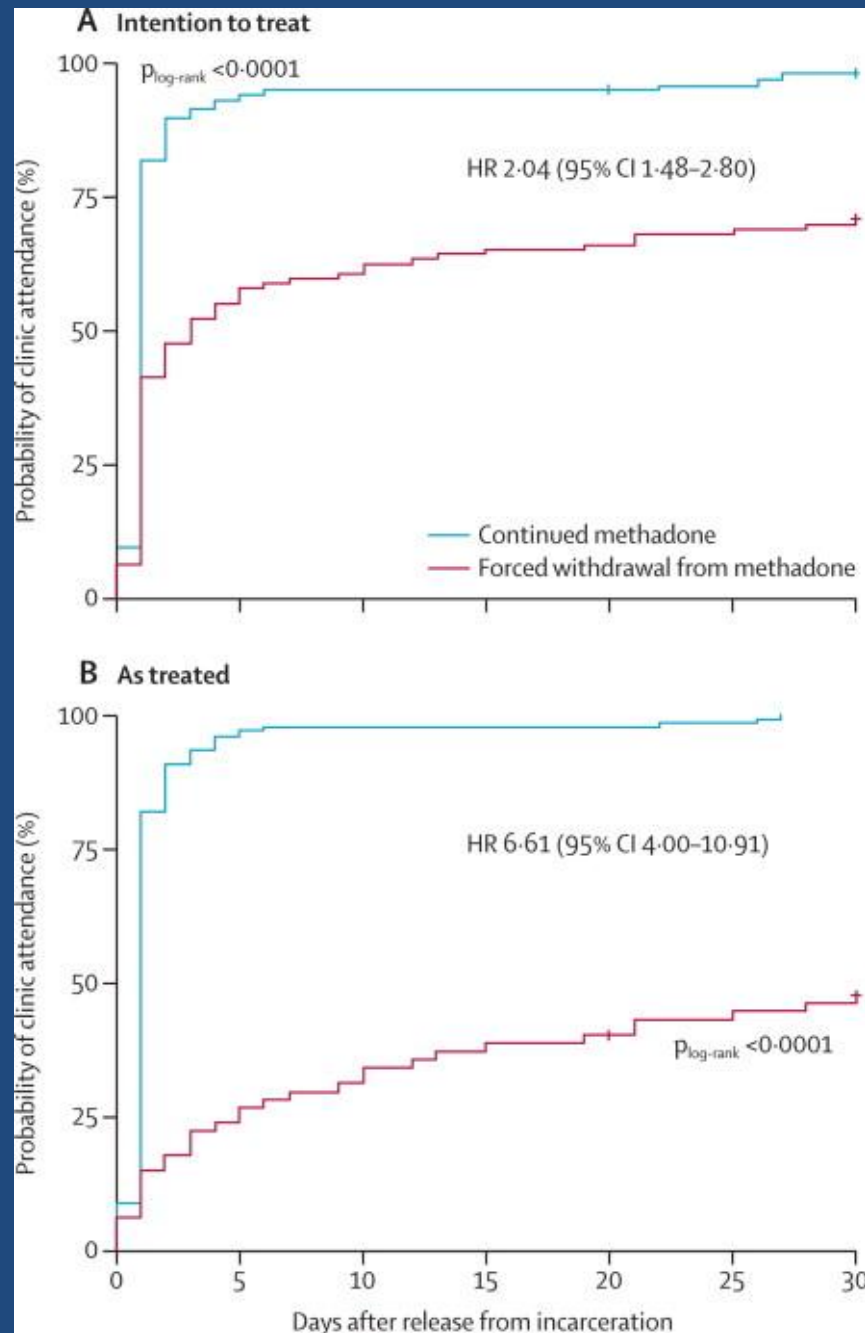
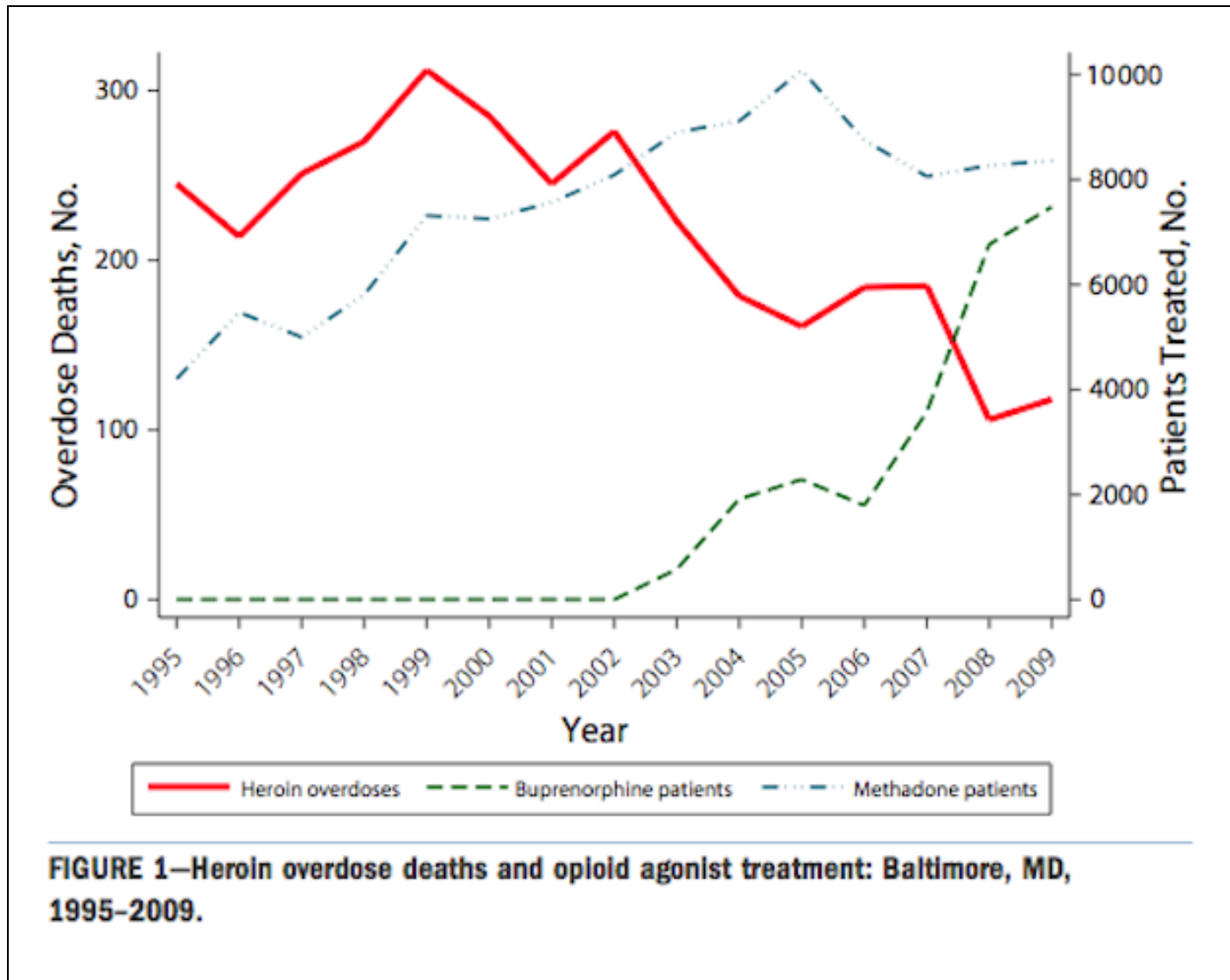


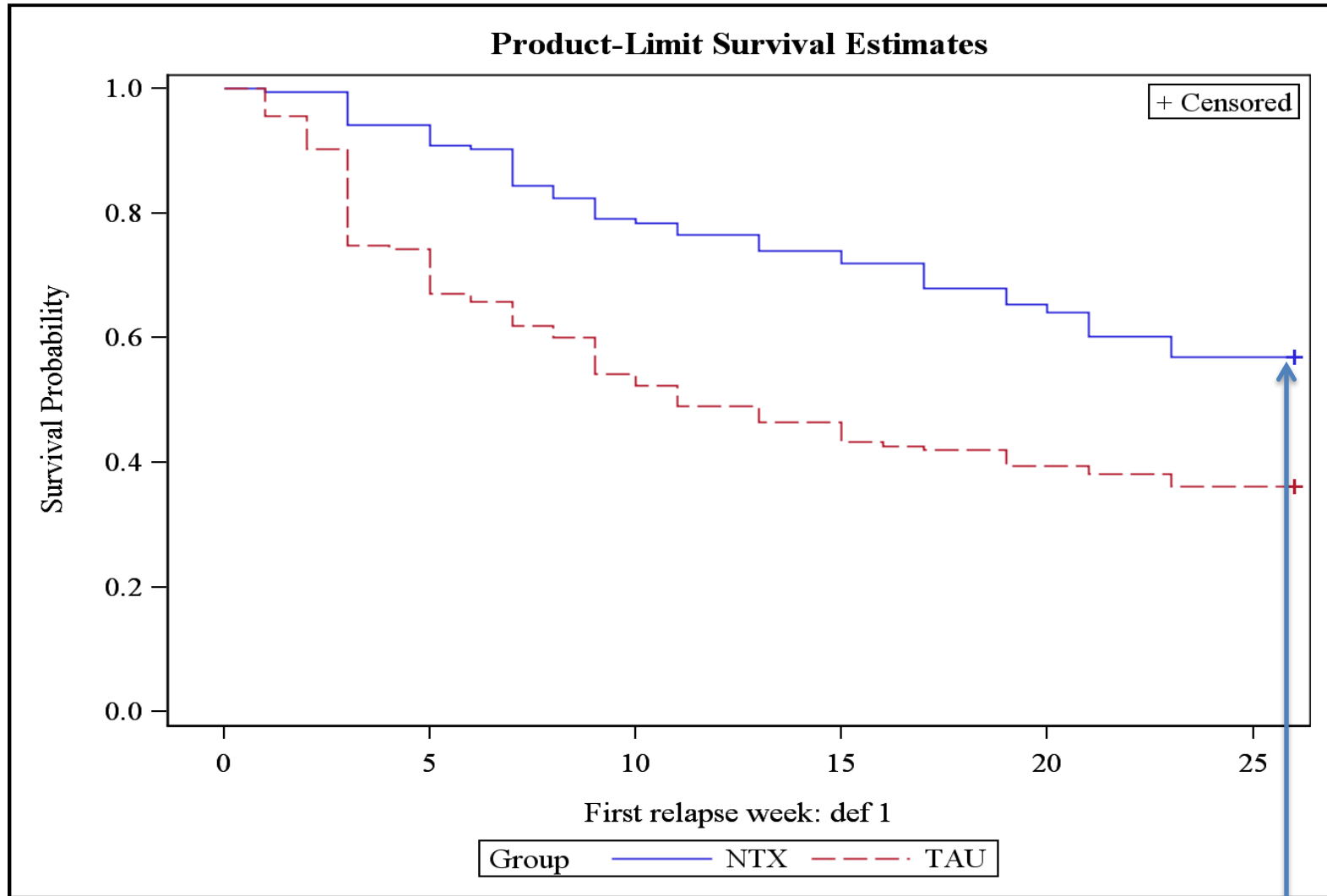
Figure 2 Probability of attending a methadone clinic in (A) the intention-to-treat and (B) the as-treated populations Data are for 1 month follow-up after participants' release from incarceration.

Baltimore, 1995-2010: BUP v ODs



XR-Naltrexone in CJS Community-Dwelling Adults

Time to Relapse: Survival Curve



- Retention on XR-NTX was 61% at 6 months
- 711 of 918 (77%) planned injections given

Summary

- Evidence-based treatment involves one of three medications: methadone, buprenorphine, naltrexone
- **These meds don't guarantee universal good outcomes; they significantly increase the probability of good outcomes occurring**
- Counseling-only or 'more counseling' approaches are on their own ineffective or less effective
- We can do a lot more in addiction specialty care, primary care, and CJS to improve rates of prescribing