Brief Overview of Medications for OUD

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How are Drug Use Disorders treated?

Traditional approach:

1. Initiation of abstinence – detoxification
2. Psychosocial treatment
3. Participation in 12 step meetings

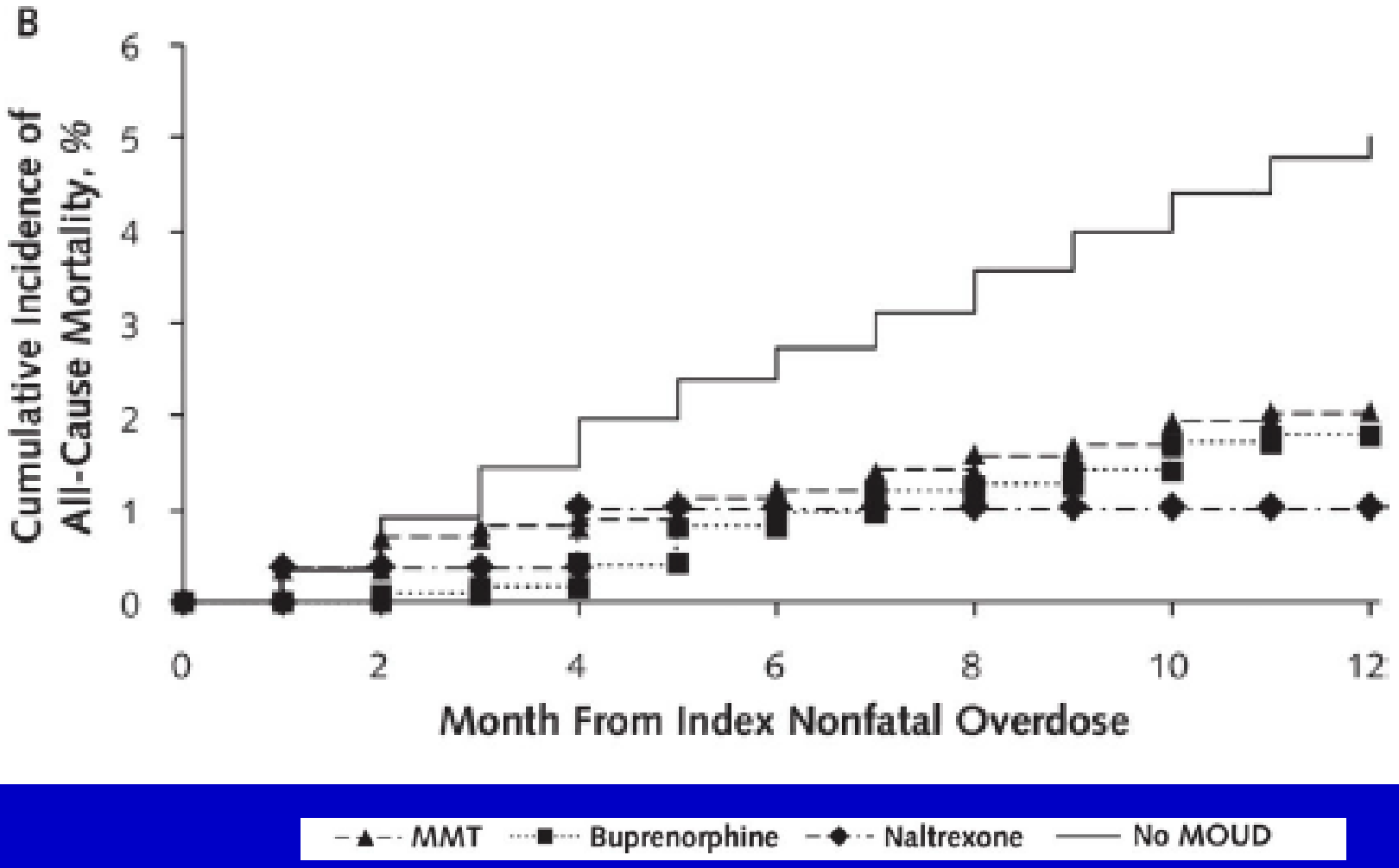
Why do we need medications?

- Detoxification followed by counseling alone results in relapse in an overwhelming number of cases
  - VA trial 112 entered detox 6 were in treatment and opiate free at 90 days (Journal of Addictive Diseases, 2006; 25(4):27-35)
  - 516 patients tapered with buprenorphine over 7 or 28 days. Only 18% were opiate free at 1 month follow up and 13% opiate free at 3 months (Addiction 2009; 104(2): 256-65)

Why do we need medications?

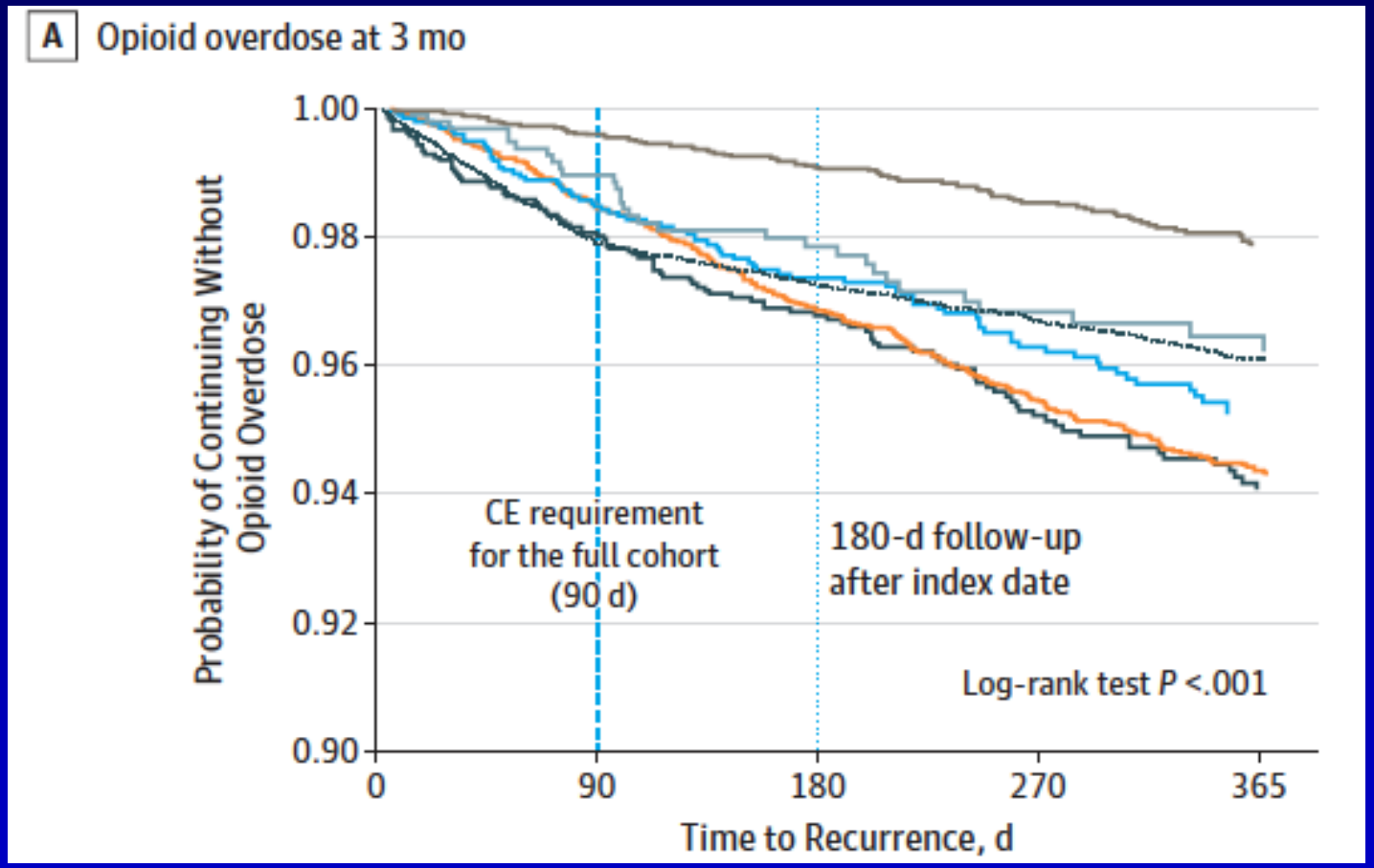
- Detoxification followed by counseling alone increases the risk for overdose and death
  - 276 opiate addicted patients entered rehab, 24 overdosed and died over an 8 year follow up, 6 in the first 4 weeks (Drug Alcohol depend 2010; 108: 65-69)
  - 137 detoxified opiate addicted patients were followed, 5 died within a year of discharge from rehab, 3 within the first 4 months (BMJ2003; 326:959-60)

MOUD reduces mortality after non-fatal overdose



Ann Intern Med. 2018 Aug 7;169(3):137-145

MOUD with methadone or buprenorphine reduced overdose



JAMA Netw Open. 2020 Feb 5;3(2):e1920622.

What do we want a medication to do?

The Ideal Medication

- Stops withdrawal
- Reduces craving
- Blocks the high from abused drugs

Methadone maintenance for OUD

- **Methadone is long acting opiate agonist – it attaches itself to the mu opiate receptor and activates it.**
- **It is very effective at alleviating opiate withdrawal and craving**
- **At low doses it will not block an opiate high, however, if the dose is gradually increased it will confer enough tolerance to prevent patients from experiencing pleasurable effects of heroin or abused prescription opiates.**
- **Methadone is highly effective (Cochrane Database Syst Rev. 2009 Jul 8;(3))**
- **Methadone is dispensed exclusively at opiate treatment programs (OTP) under strict rules**
  - **Sometimes inconvenient**
  - **Exposes patients to conditioned reminders of drug use, causing craving**
  - **Dangerous itself in overdose**

Buprenorphine for OUD

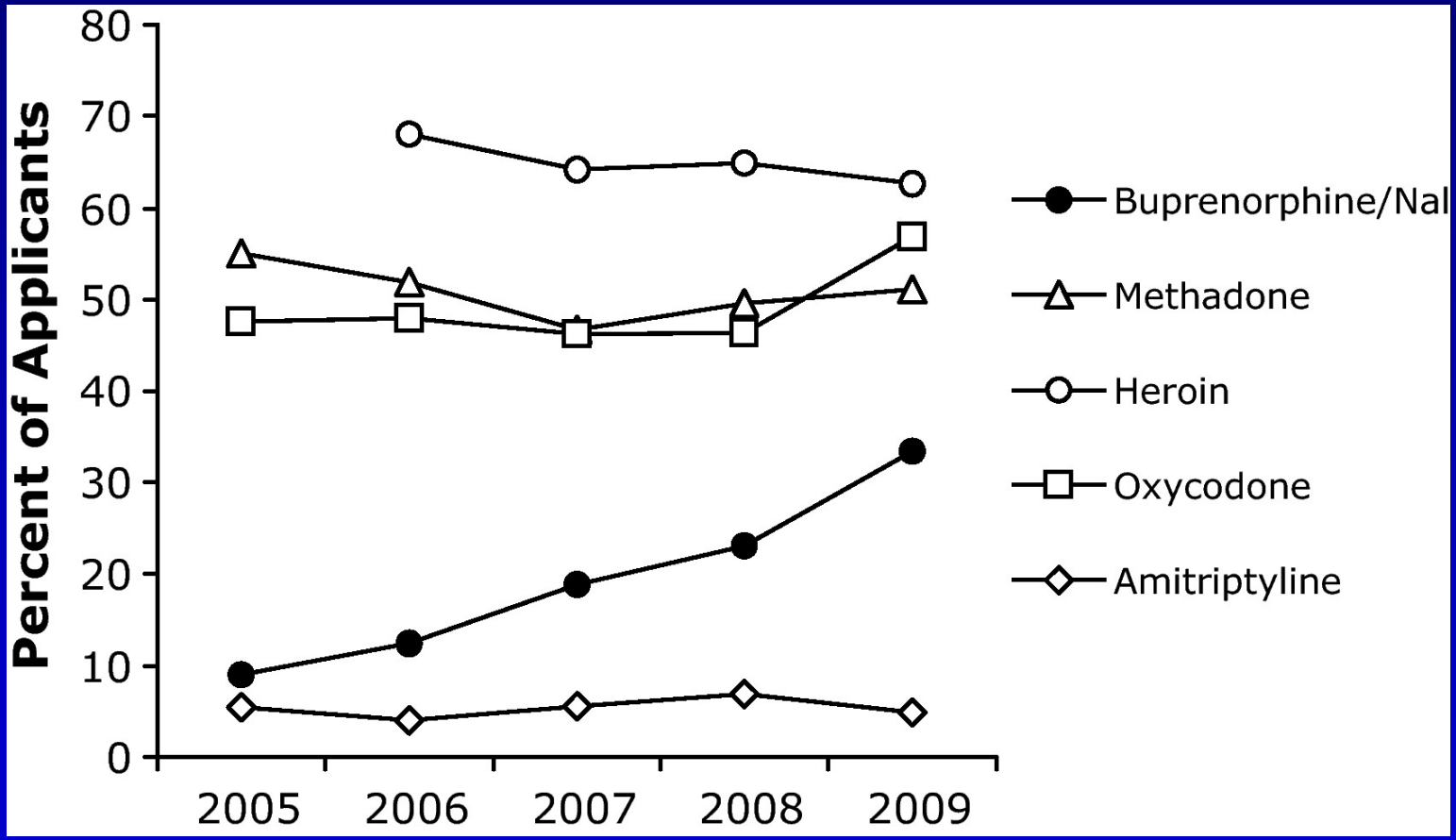
- Mu opiate partial agonist with a higher affinity for the mu opiate receptor than heroin and abused prescription opioids
- Effectively reduces withdrawal and craving
- Blocks opiate high effectively
- Safer to use than methadone, difficult to overdose and can be prescribed at a physicians office
  - More available than methadone
  - Less exposure to conditioned reminders of drug use so less craving
  - Daily dosing not required
- Effective (Drug Alcohol Depend. 2010 Jan 1;106(1):56-60)
- Requires specialized training and a waiver from DEA
- Prone to diversion and abuse
  - Implantable forms available
  - Injectables being tested

Buprenorphine adherence is often poor

Adequate Adherence in Less Than 50% of Patients

- In a trial involving subjects with opioid use disorder participating in office based buprenorphine treatment, it was found that only 48% of the subjects were adherent to the medication as defined as having 80% or more of their visits associated with a positive UDS for buprenorphine. (Am. J. Addict., 2016, 25, 110–117)
- In an examination of medical and pharmacy claims data over a year, only 32% of patients participating in office based buprenorphine treatment took buprenorphine on 80% or more days. (J. Subst. Abuse Treat., 2014, 46, 456–462)

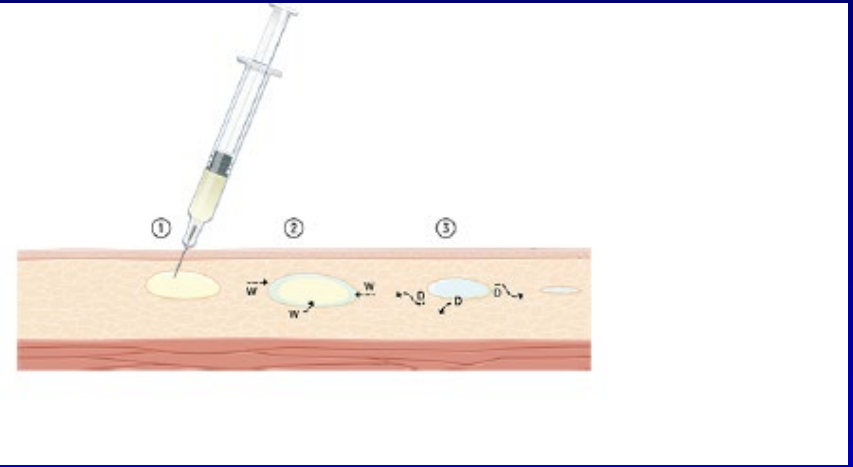
Buprenorphine Sold on the Street



Drug Alcohol Depend. 2012; 120:190-195

Injectable buprenorphine improves adherence

Two different Technologies Similar Results



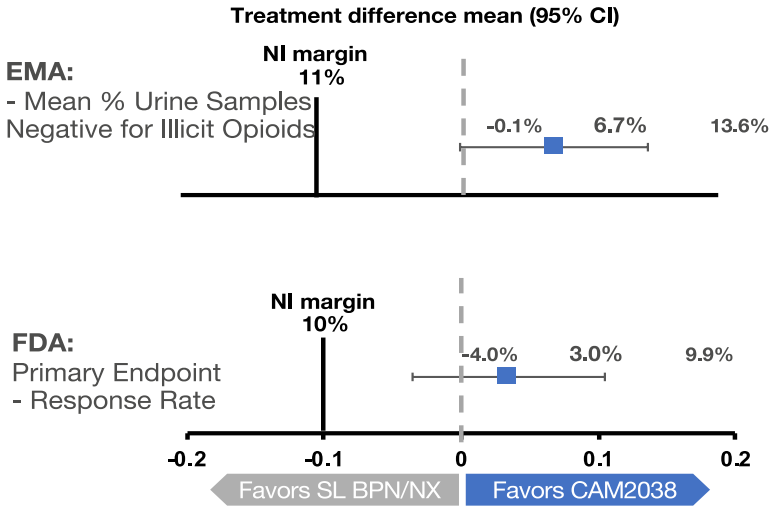
Sublocade™
(buprenorphine extended-release)
injection for subcutaneous use ©
100mg-300mg

Brixadi

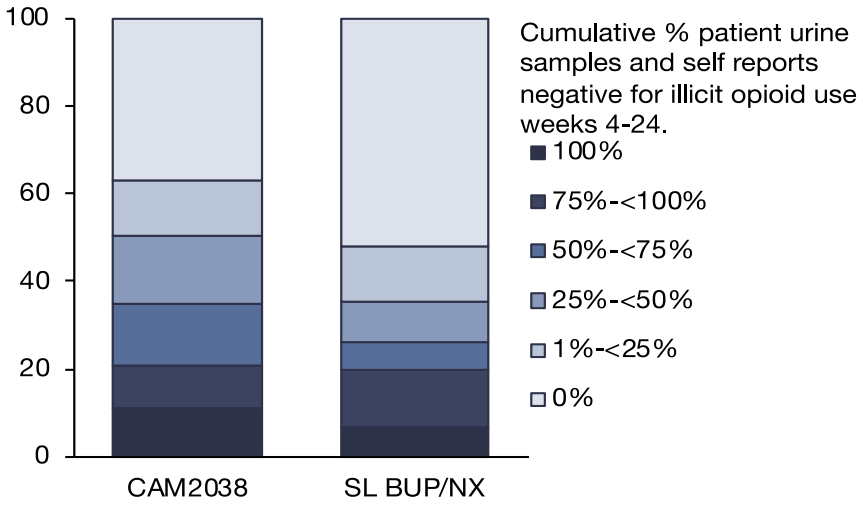
CAM2038 (Brixadi) primary outcomes

CAM2038 met primary and secondary endpoints of noninferiority and superiority versus daily SL BPN/NX

Noninferiority for mean % urines negative for illicit opioids and response rate, P<.001



Superiority demonstrated for first secondary endpoint CDF % illicit opioid-free assessments, P=0.004



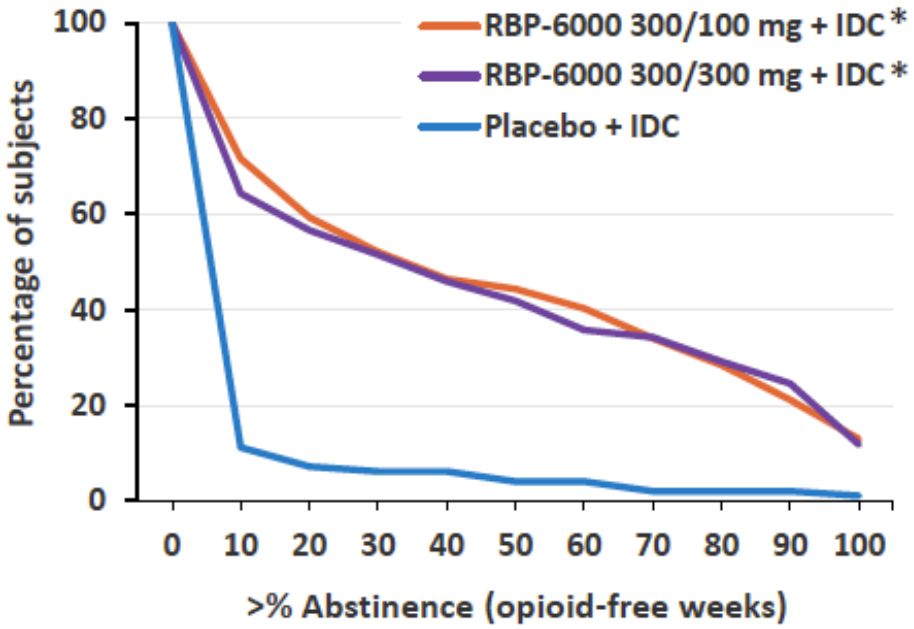
Source: Lofwall MR, et al, JAMA Intern Med. 2018

Sublocade for OUD

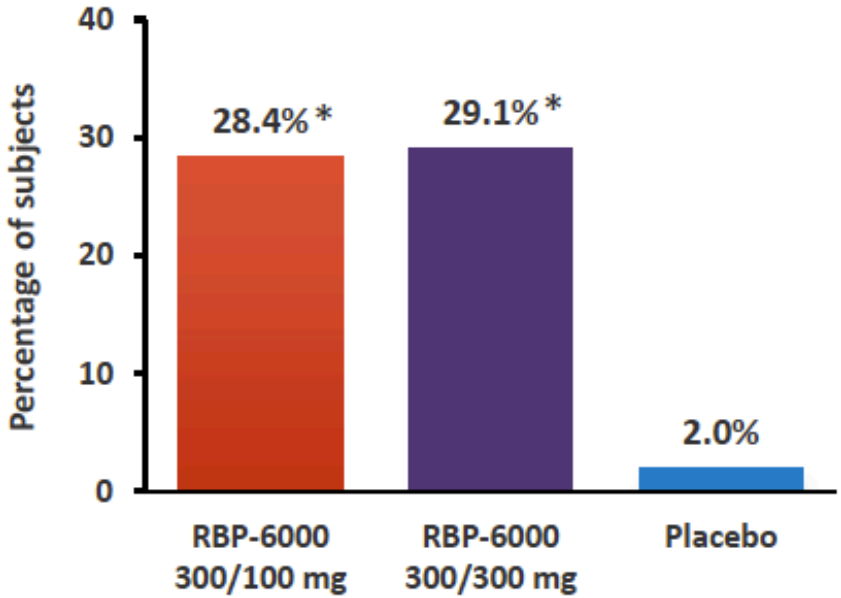
Sublocade Promotes Abstinence from Opioids

RBP-6000: Primary & Secondary Endpoints

Primary: CDF of % urine samples negative for opioids + negative self-reports of illicit opioid use (Weeks 5 to 24)



Key secondary: ≥80% of urine samples negative for opioids + negative self-reports of illicit opioid use (Weeks 5 to 24)



*P<0.0001 vs. placebo

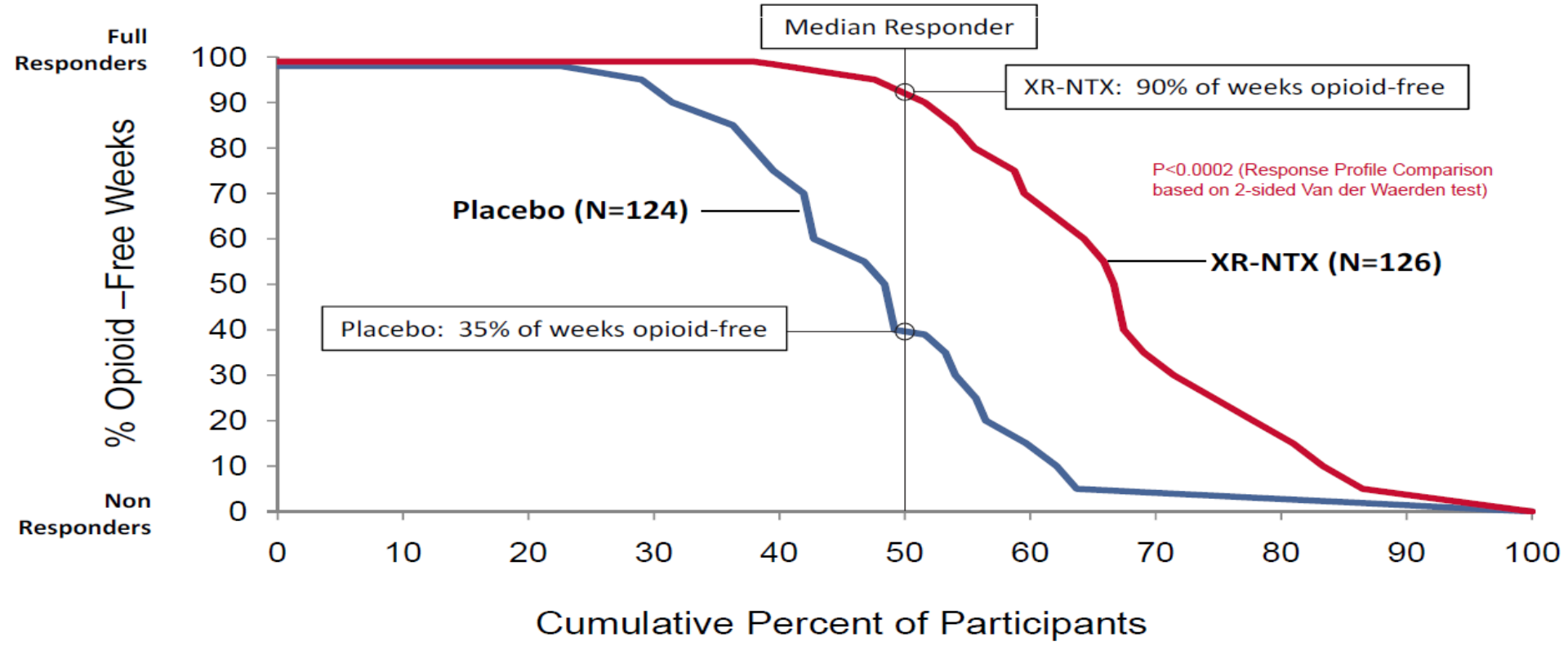
Lancet. 2019 Feb 23;393(10173):778-790.

Naltrexone for OUD

- Opiate antagonist- it blocks the effects of abuse opiates
- Two forms: oral and extended release injectable
  - Oral is generally less effective (Health Technol Assess. 2007 Feb;11(6))
  - Injectable given monthly is effective (Lancet. 2011 Apr 30;377(9776):1506-13.)
- Reduces craving and blocks the high from abused opioids
- No agonist effects and no physical dependence
- Can be given at any physicians office – not limited to OTP
- Does not address withdrawal
- Barriers to treatment- detoxification necessary

Naltrexone is effective

Natrexone Reduced Opioid Use

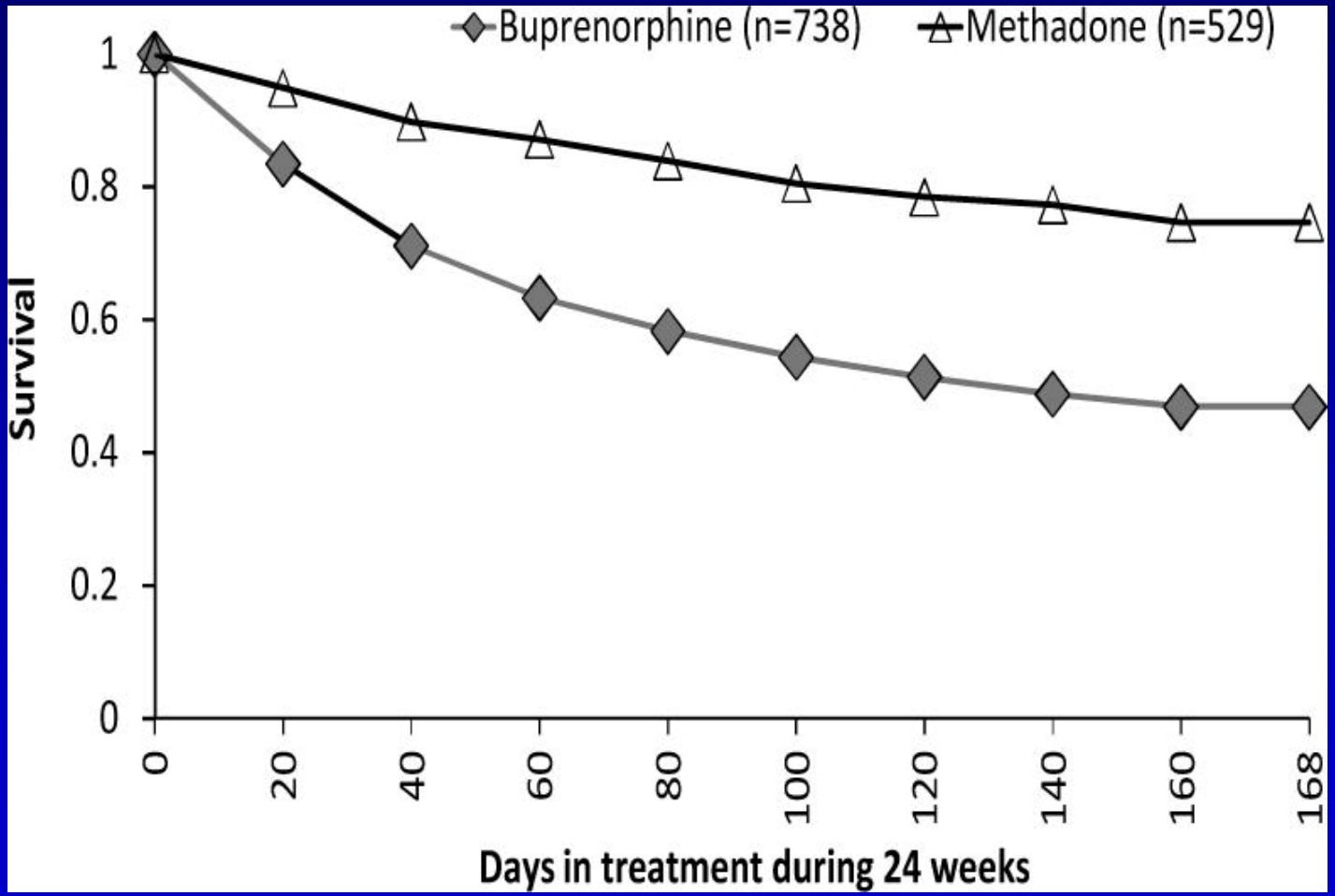


- Total abstinence (100% opioid-free weeks) during Weeks 5-24 was reported in 45 (35.7%) of subjects in the XR-NTX group versus 28 (22.6%) subjects in placebo group (P=0.0224).

Lancet 2011; 377: 1506–13

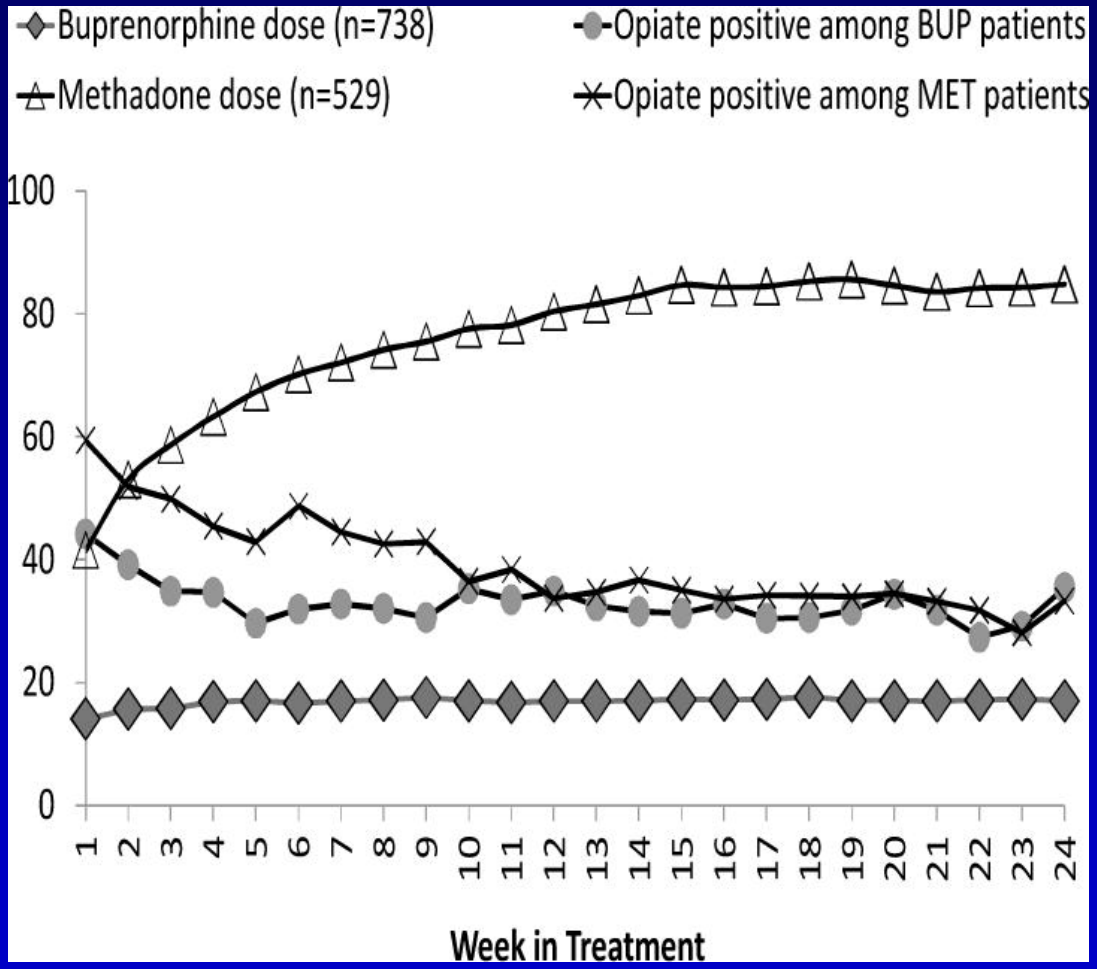
Methadone vs. sublingual buprenorphine

Retention in MMT often Superior to Buprenorphine



Addiction. 2014 109(1);79–87

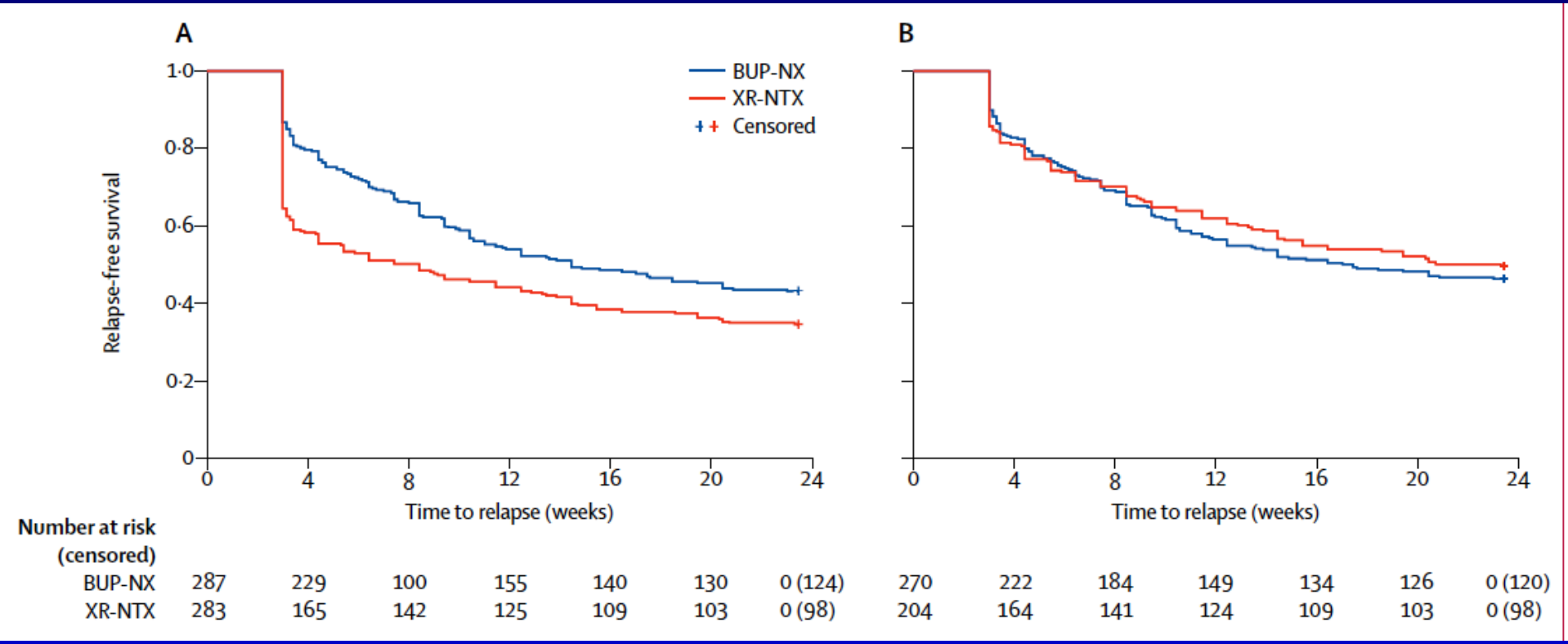
Methadone vs. SL buprenorphine



Addiction. 2014 109(1);79–87

Injected naltrexone vs. sublingual buprenorphine

Relapse-free Survival Over 24 Weeks

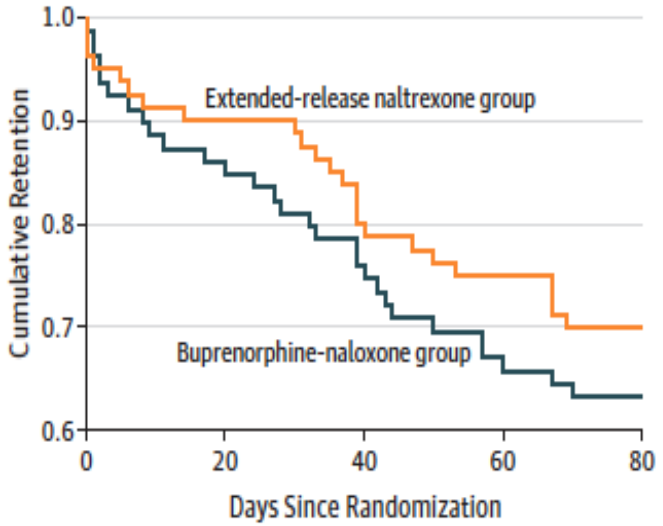


Lancet. 2018 Jan 27;391(10118):309-318.

Buprenorphine vs. XRNT in Norway

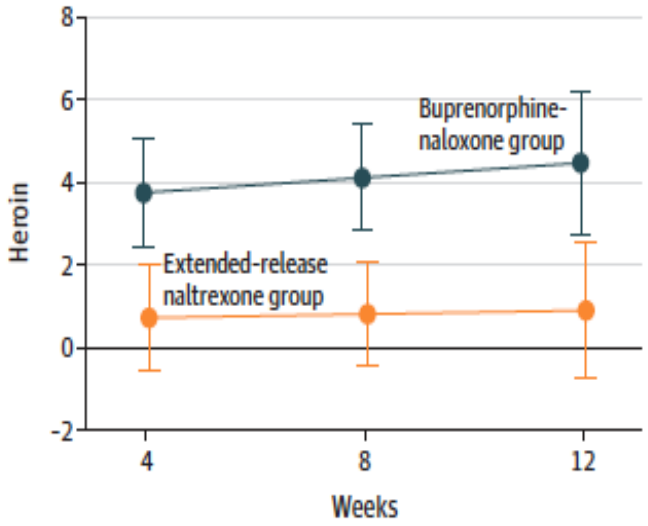
XRNT Superior in Reducing Heroin and other Opioid Use

Figure 2. Survival Curves for Retention in Treatment and Estimated Mean Number of Days for the Use of Heroin, Other Illicit Opioids, and Major Secondary Outcomes



No. at risk

Buprenorphine-naloxone group	78	67	59	52	50
Extended-release naltrexone group	78	73	64	60	56



JAMA Psychiatry. 2017;74(12):1197-1205

Discussion

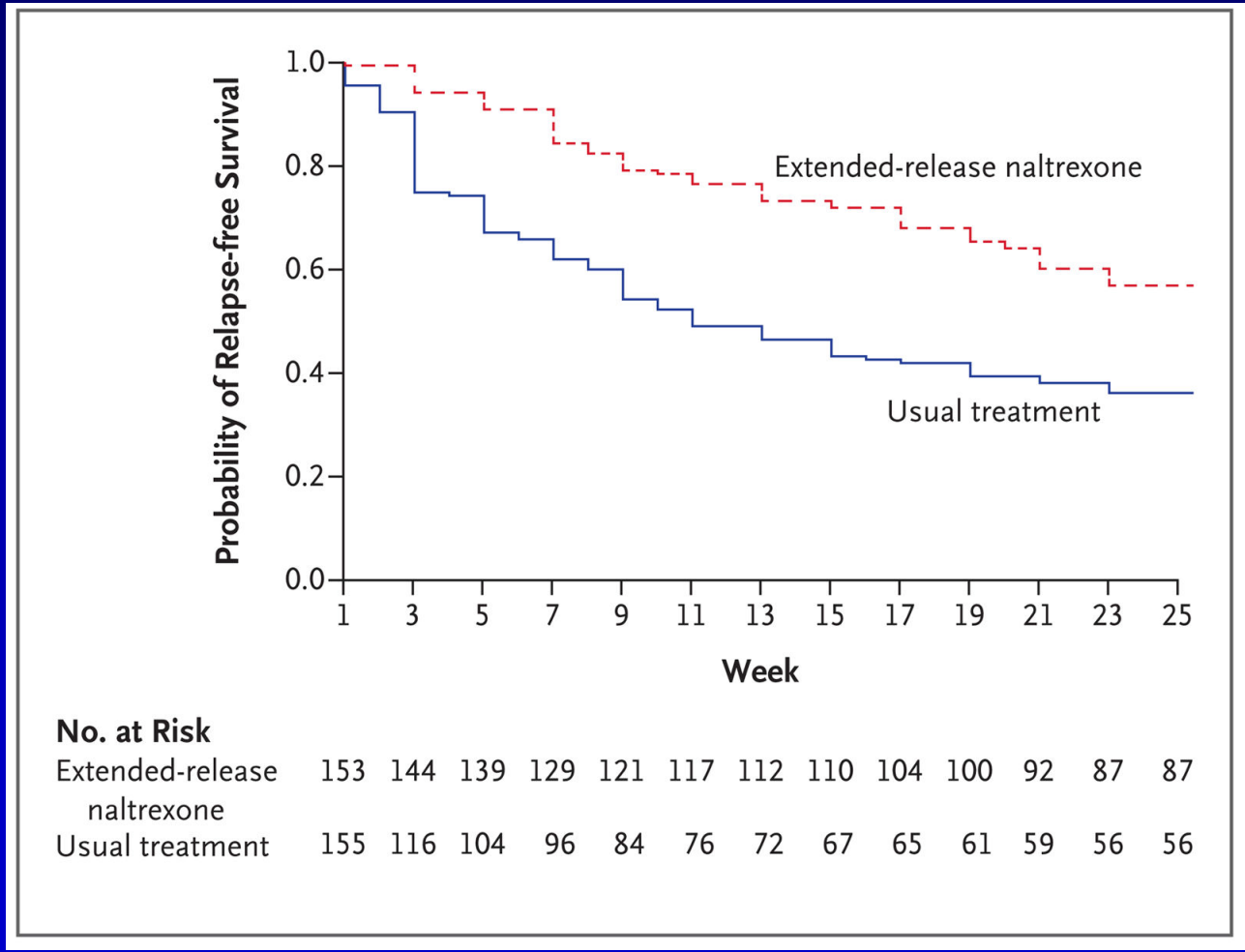
- Detox alone can lead to relapse and death
- Methadone is an effective treatment
  - Inconvenient
  - Poor therapeutic milieu
  - Stigma
- Buprenorphine is effective
  - Diversion poor adherence
  - Injectables may be better
- Naltrexone is effective
  - Detoxification may be a barrier
  - Adherence can be a problem

XRNT for criminal justice offenders

No overdoses in the XRNT group

Seven overdoses in the treatment as usual group

XRNT Reduced Relapse Rates



N Engl J Med. 2016 March 31; 374(13): 1232–1242.