Addressing Opioid Overdose and Opioid Use Disorder:
Medication-Based Treatment Approaches

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MAT Commission
Thursday, January 24, 2019

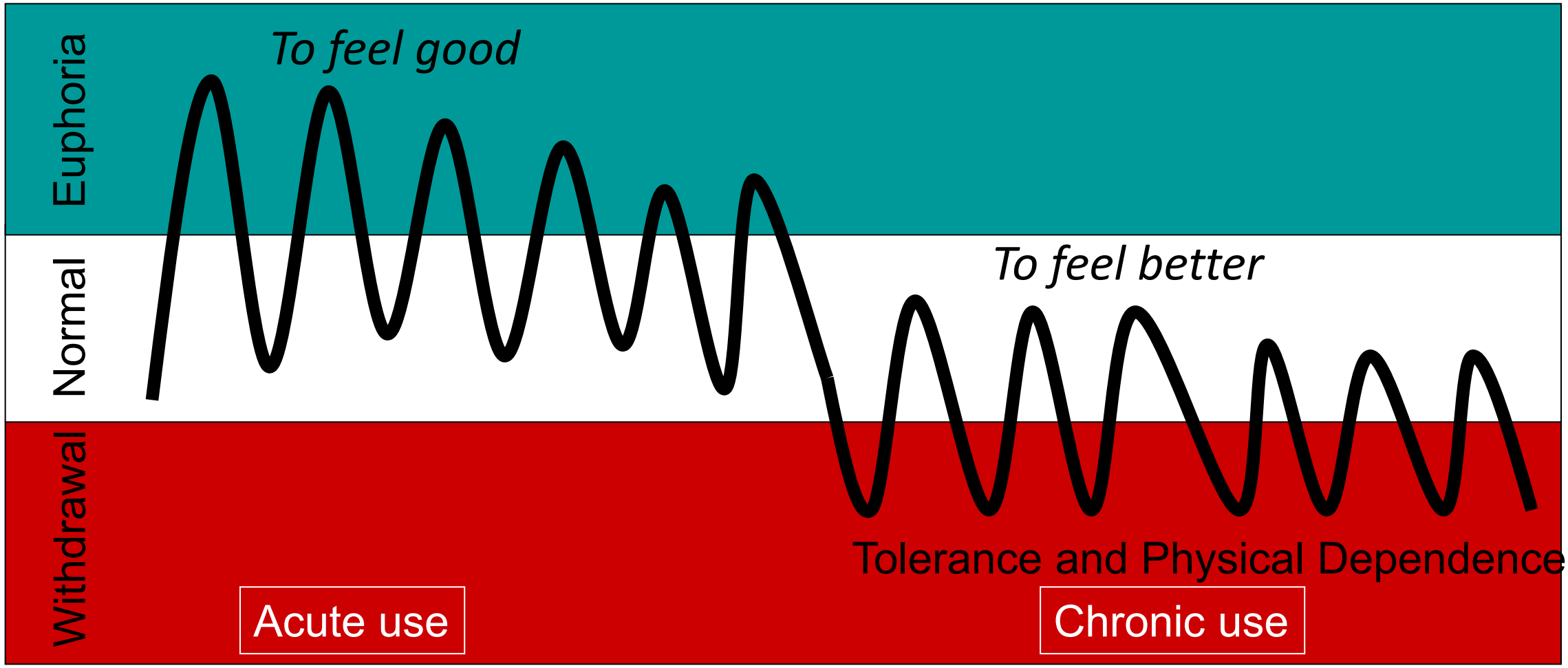
Objectives

Review how medication for opioid use disorder (MOUD) works

Review outcomes

Opportunities for delivering MOUD to high risk patient populations

Why do people use opioids?



Goals of medication for opioid use disorder

Relief of withdrawal symptoms	• Low dose methadone (30-40mg), buprenorphine
Opioid blockade	• High dose methadone (>60mg), buprenorphine, naltrexone
Reduce opioid craving	• High dose methadone (>60mg), buprenorphine, naltrexone
Restoration of reward pathway	• Long term (>6 months) • methadone, buprenorphine, naltrexone

Matching Patients to Medications for Opioid Use Disorder

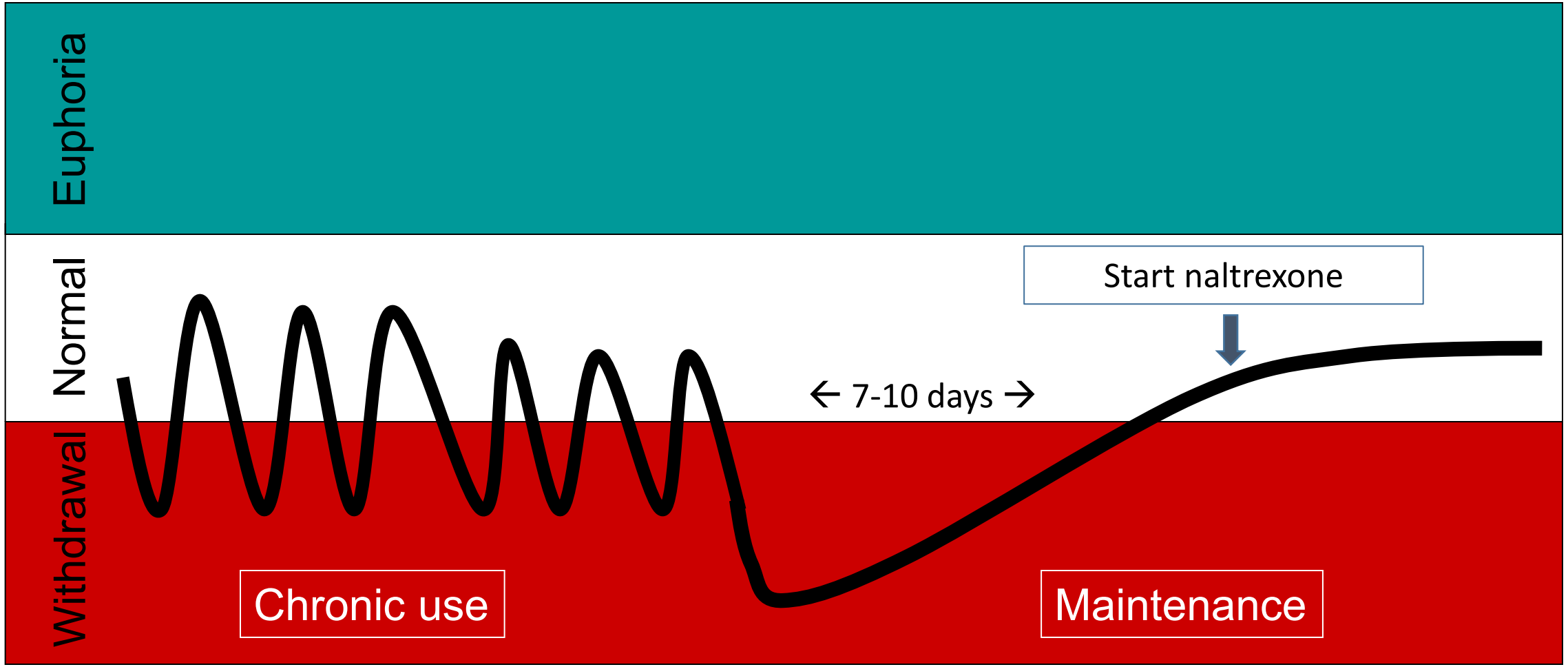
- The choice of methadone, buprenorphine, or naltrexone depends upon:
  - Patient preference
  - Past experience
  - Likelihood of continuing the treatment
  - Access to treatment setting
  - Ability to manage withdrawal (esp for naltrexone)

Matching Patients to Medications for OUD

	Abstinence required?	Dosing schedule	Required Training - Regulation	Retention	Reduce Illicit Opioid Use
Injectable IM Naltrexone	7-10 days	Q28 day provider injection	None	Good - trial Poor - real-world	Excellent
Oral Naltrexone	7-10 days	Daily prescription	None	No better than placebo	Limited due to non-adherence
Buprenorphine	12 hours[1]	Daily prescription	8 hr MD/DO 24 hr NP/PA	Not as good as methadone	Excellent
Methadone	No, BUT start low go slow	Daily clinic administered[2]	Licensed clinic only	Best	Excellent

[1]24-72 hours of abstinence needed when switching from methadone to buprenorphine
[2] Take homes can be earned after 60 days

Maintenance Treatment for Severe Opioid Use Disorder



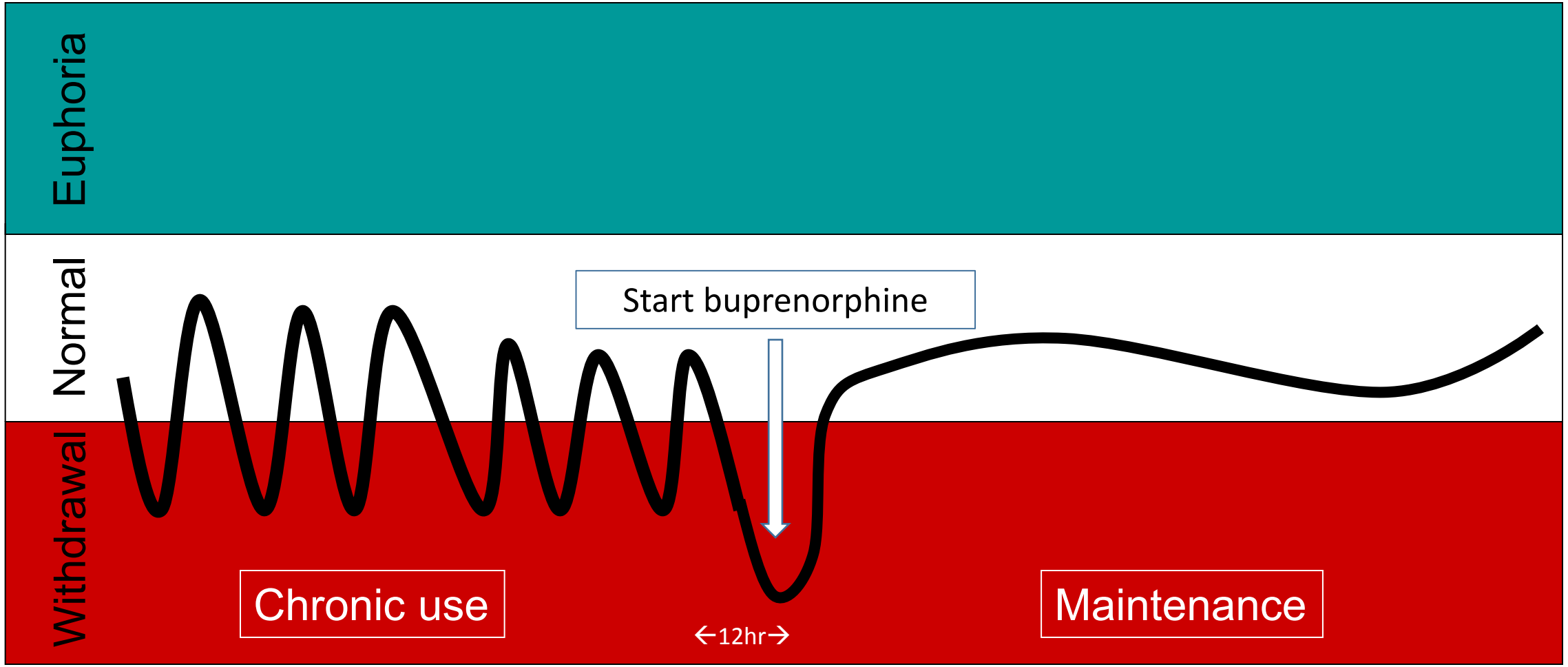
Naltrexone

Krupitsky E, et al. Lancet, 2011

Outcomes	NTX	placebo
Trial completion	53%	38%
Abstinence at 24 weeks	90%	35%
Change in craving score	-10.1	0.7

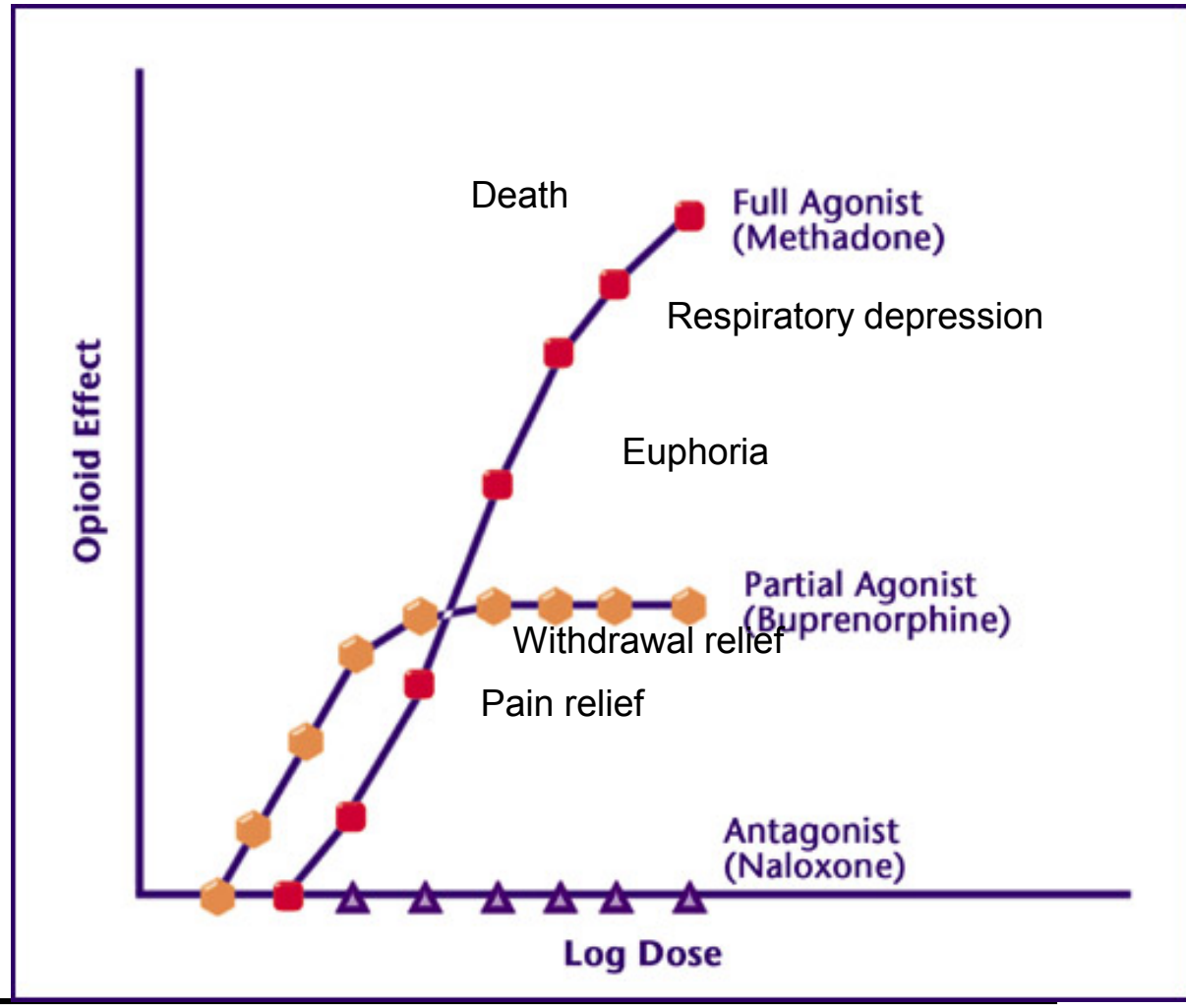
- Pure opioid antagonist
- Injectable naltrexone (Vivitrol®)
  - Monthly IM injection
  - FDA approved 2010
  - Patients must be opioid free for a minimum of 7-10 days before treatment
- Oral naltrexone
  - Duration of action 24-48 hours
  - FDA approved 1984
  - 2008 Cochrane Review
    - No clear benefit in treatment retention or relapse at follow up over placebo
    - Physicians > 80% abstinence at 18 months

Maintenance Treatment for Severe Opioid Use Disorder



How does buprenorphine work?

- High affinity, but low activity at the mu opioid receptor
  - Low activity is enough activity to TREAT WITHDRAWAL and REDUCE CRAVINGS
  - Low activity results in a CEILING EFFECT
    - Euphoria is unusual
    - Overdose occurs only with other drugs of abuse
    - Opioid dependent patients FEEL NORMAL
  - High affinity means it is a BLOCKER, more active opioids can not stimulate the receptor in presence of buprenorphine



How do buprenorphine + naloxone work?

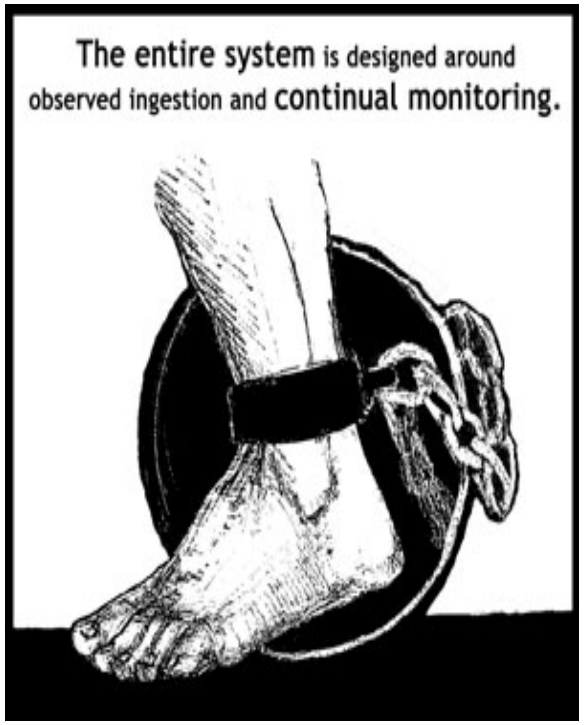
- Buprenorphine has good sublingual and IV bioavailabilty but poor GI bioavailability
- Naloxone (Narcan) has good IV bioavailabilty, but poor GI and sublingual bioavailability
- The combination results in decreased abuse and diversion for IV use

Methadone Maintenance Treatment

Highly Structured

- Daily nursing assessment
- Weekly individual and/or group counseling
- Random supervised toxicology screens
- Medical director oversight
- Methadone dosing
  - Observed daily ⇒ “Take homes”

- Separate system not involving primary care
- Limited access
  - 5 states: 0 clinics
  - 4 states: < 3 clinics
- Inconvenient and highly punitive
- Mixes stable and unstable patients
- Lack of privacy
- No ability to “graduate”
- Stigma



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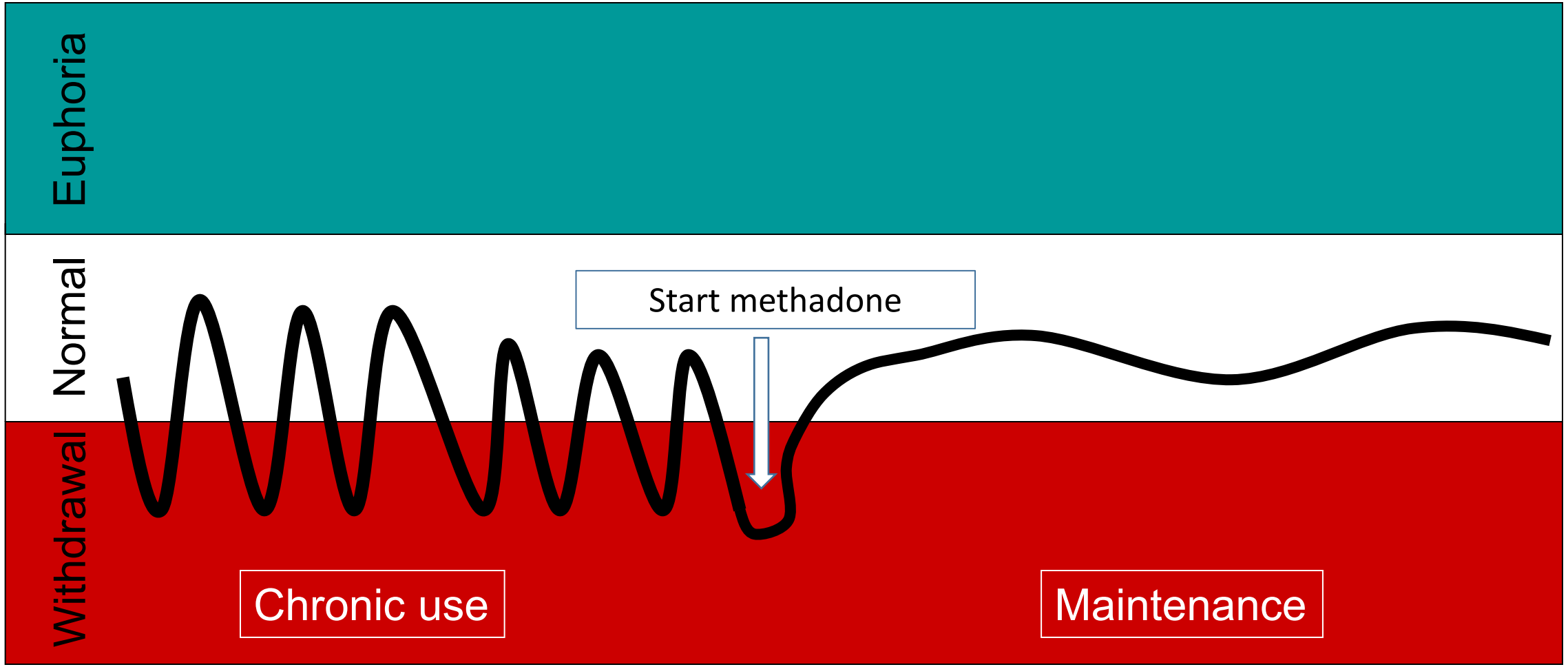


Opioid Detox Outcomes

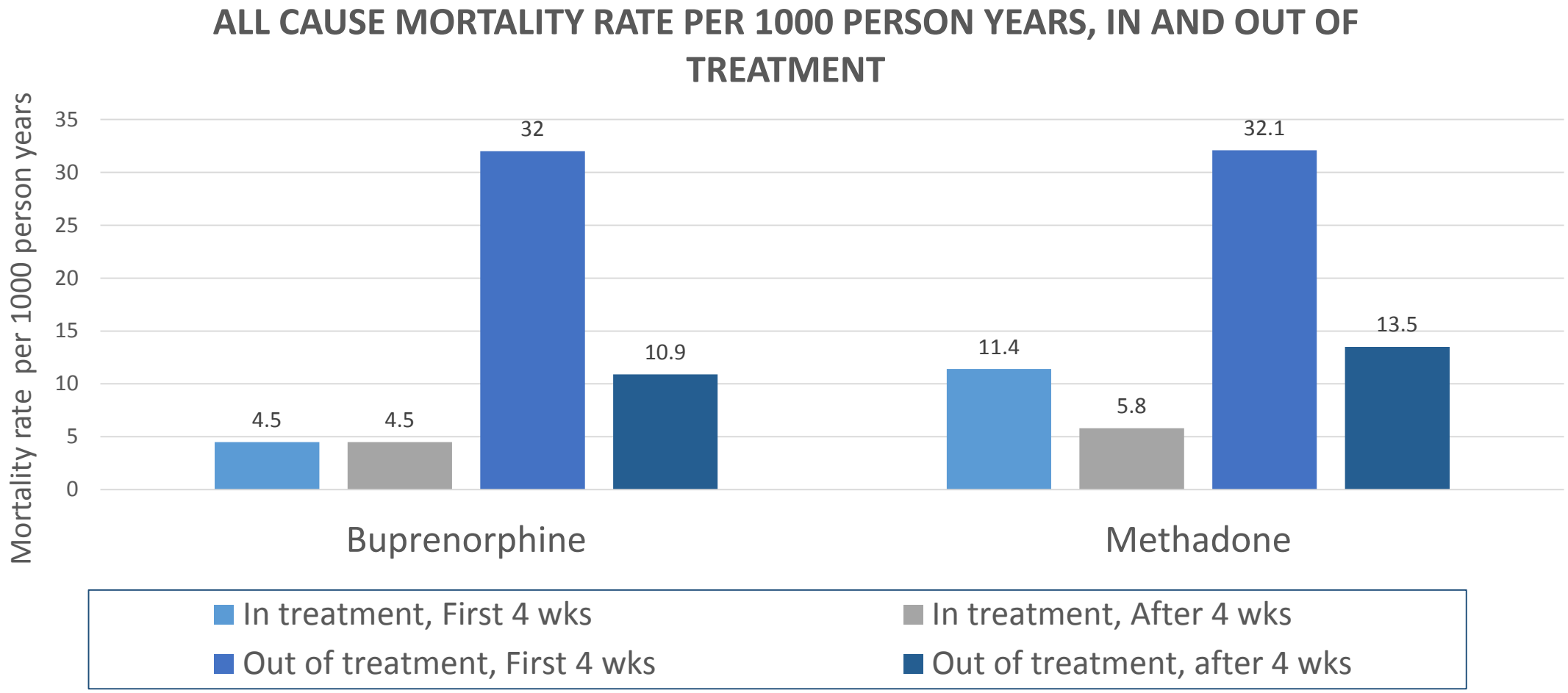
- Low rate of retention in treatment
- High rates of relapse post treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months
  - Increased rates of overdose due to decreased tolerance

So, how long should maintenance treatment last?

Long enough

O'Connor PG JAMA 2005
Mattick RP, Hall WD. Lancet 1996
Stimmel B et al. JAMA 1977

Medication saves lives. People die when medication stops.



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Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, Ferri M, Pastor-Barriuso R. Mortality risk during and after opioid substitution treatment: Systematic review and meta-analysis of cohort studies. BMJ 2017 Apr 26;357:j1550.

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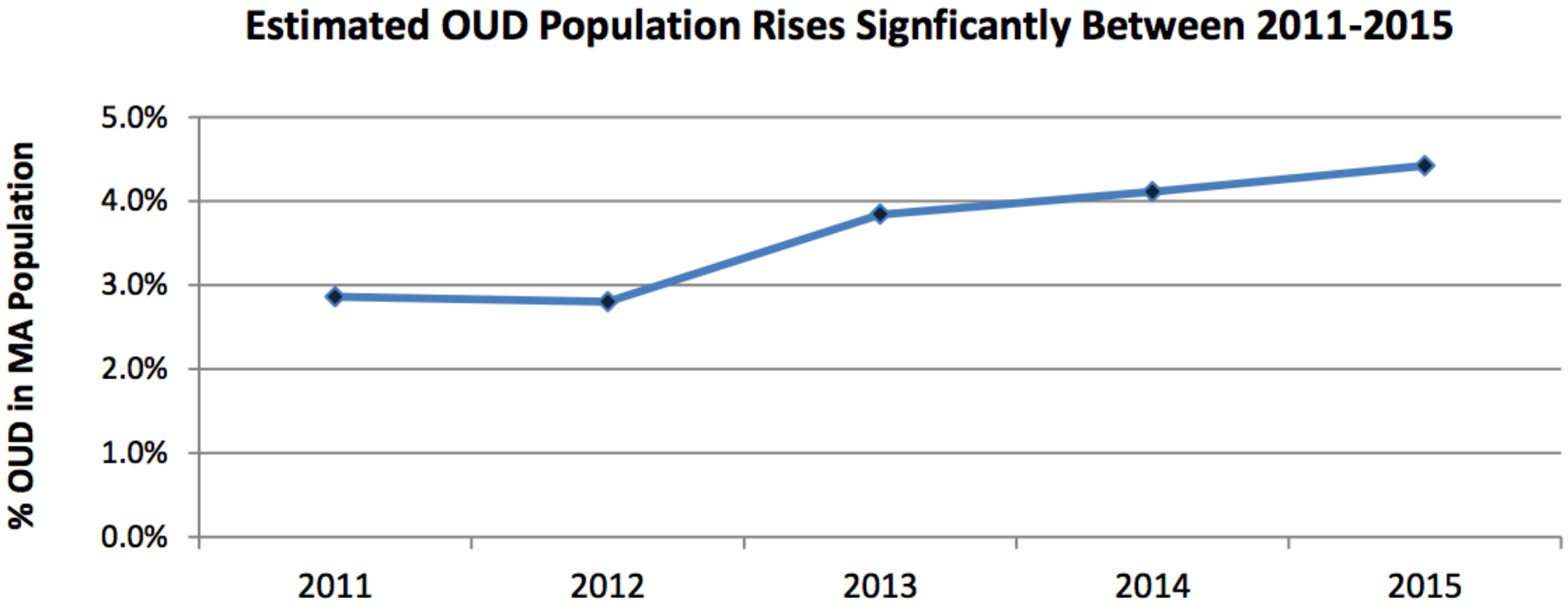
4.4% (~300K) of Massachusetts adults have opioid use disorder in 2015

- Using capture-recapture methods of 7-linked datasets with 45+% known



National survey estimate of OUD prevalence is **0.6%** = 2.1 million / 326 million adults in 2016

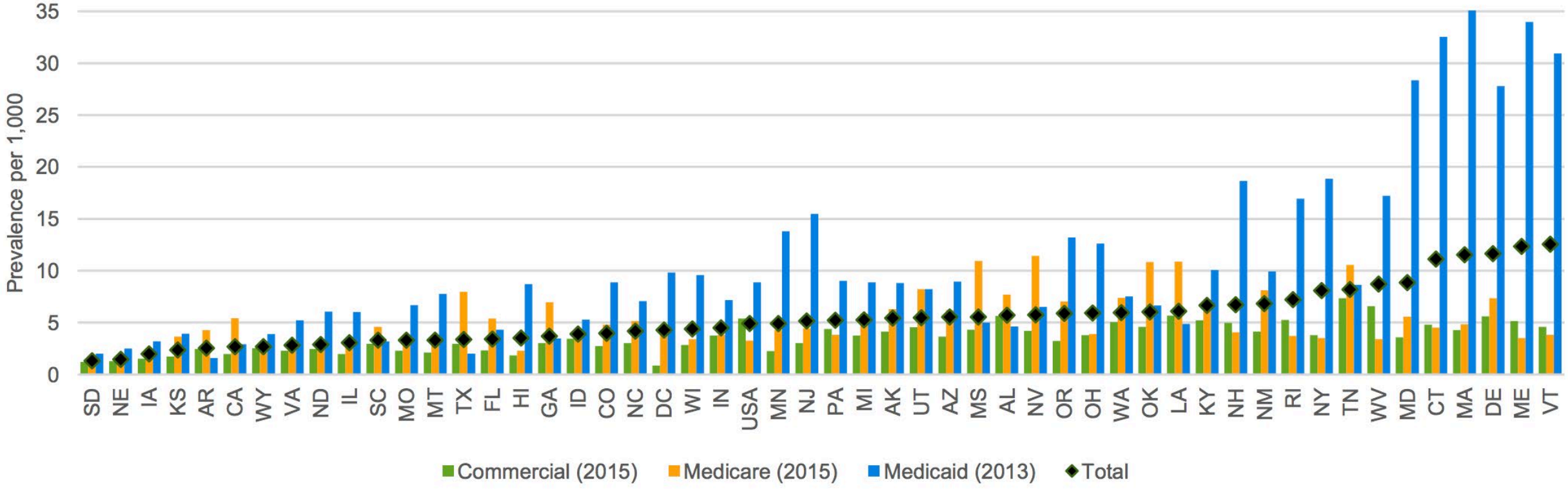
- newsletter.samhsa.gov/2017/10/12/samhsa-new-data-mental-health-substance-use-including-opioids/

www.mass.gov/files/documents/2017/08/31/data-brief-chapter-55-aug-2017.pdf

Major variation across states and payers

- Diagnosed prevalence of opioid use disorder by state and payer, 2015 (or most recent year)

FIGURE 6: DIAGNOSED PREVALENCE OF OPIOID USE DISORDER BY STATE AND PAYER, 2015 (OR MOST RECENT YEAR[14])



www.milliman.com/uploadedFiles/insight/2018/Opioid_Use_Disorder_Prevalence.pdf

Touchpoint:
A health care, public health, or criminal justice encounter were we can:

- identify individuals at high-risk for opioid overdose death
- deliver overdose risk reduction services, and/or
- link and engage in treatment

Examples: **Post-overdose, while incarcerated, when hospitalized, residential treatment, if civilly committed**

- *We are missing opportunities to engage people*
- *When people are treated with MOUD, their mortality is cut in half or more*
- *When people discontinue treatment, they die*

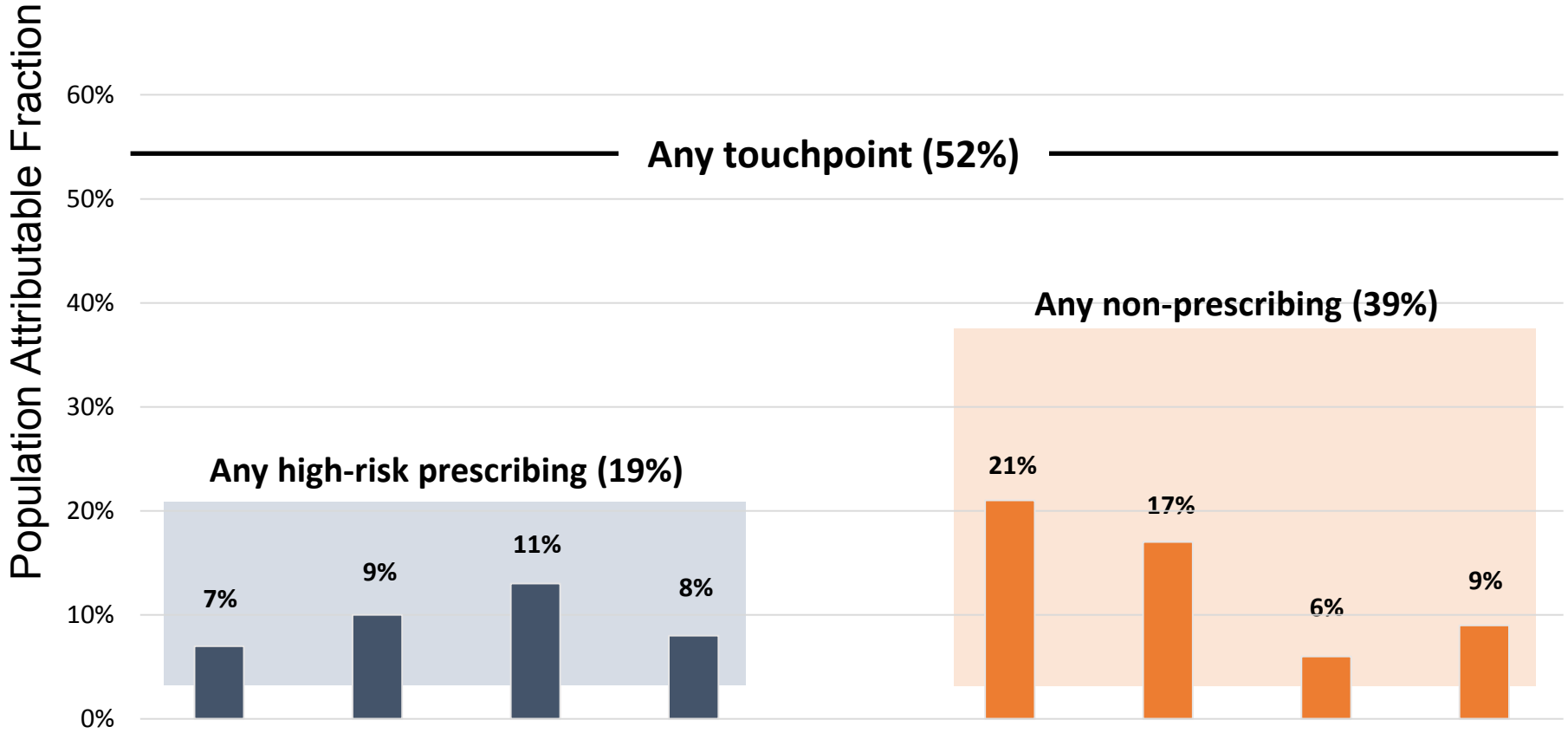
  -> We need to make the treatment work for the patient

  …..not make the patient work for the treatment

Looking back…

Population attributable fraction for touchpoints prior to opioid overdose death

(Massachusetts, 2014, n=1,315 opioid-related deaths)



Source: Larochelle et al, SGIM 2018, Data from Chapter 55 Data Set

Making the treatment work for the patient
- Initiating medication at venues for high risk patients

Buprenorphine RCT for **medical inpatients with OUD**

- Linked to outpatient care:
  - 72% vs. 12%
- Remained on bup at 6 months
  - 17% vs. 3.0%
- Median days of illicit opioid use in last 30 days at 6 months:
  - 4.0 vs. 13.9 days

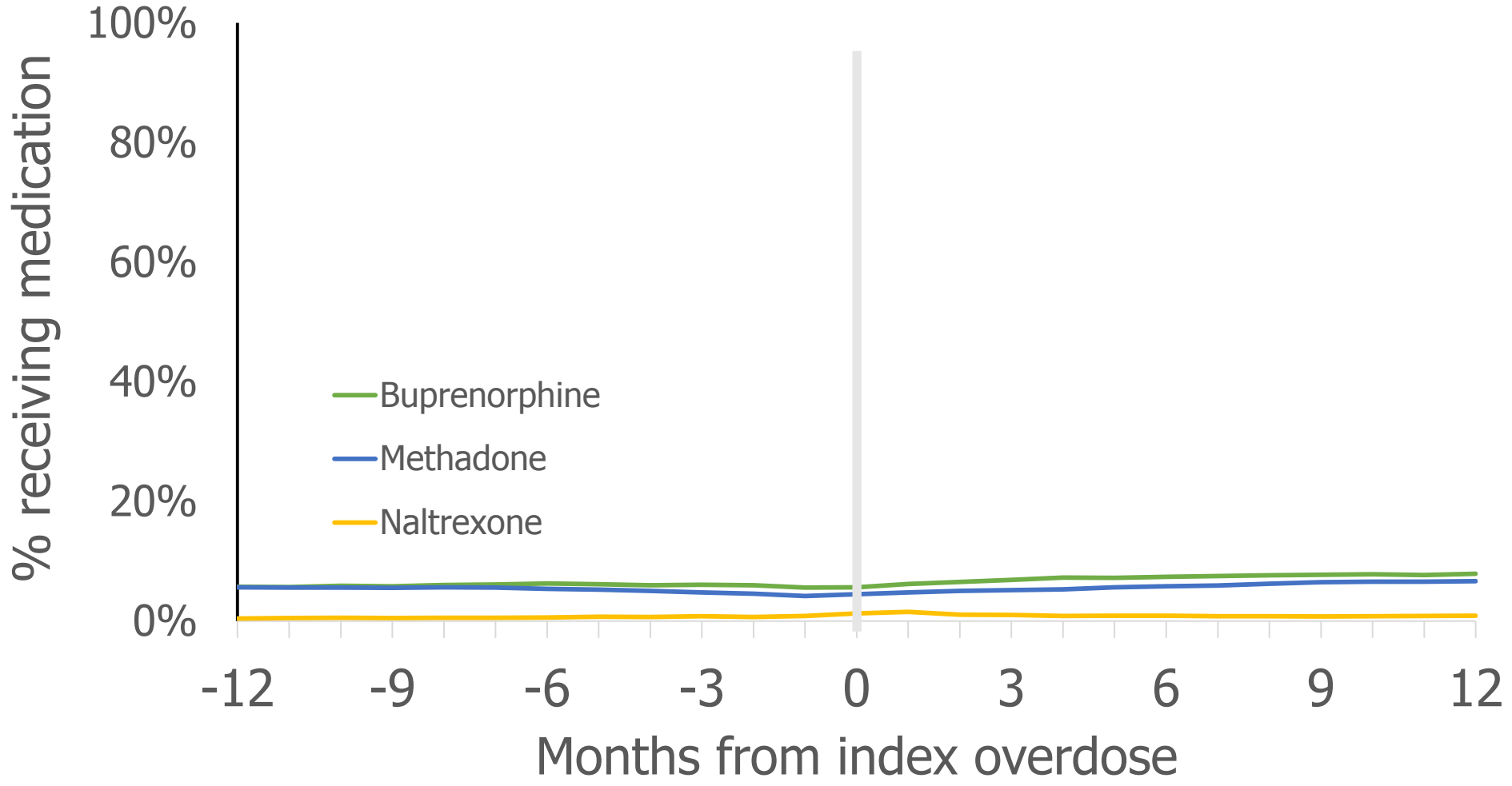
Buprenorphine RCT for **emergency patients with OUD**

- Linked to outpatient care:
  - 78% vs. 37%
- Reduction in use day per week
  - 4.5 vs. 3.1
- Admitted to inpatient treatment
  - 11% vs. 37%

Liebschutz et al. JAMA Intern Med. 2014;174(8):1369-1376
D'Onofrio et al. JAMA 2015;313(16):1636-1644. doi:10.1001/jama.2015.3474

After overdose, few survivors receive medications for OUD

Cohort of 17,755 overdose survivors in MA, 2012-2014



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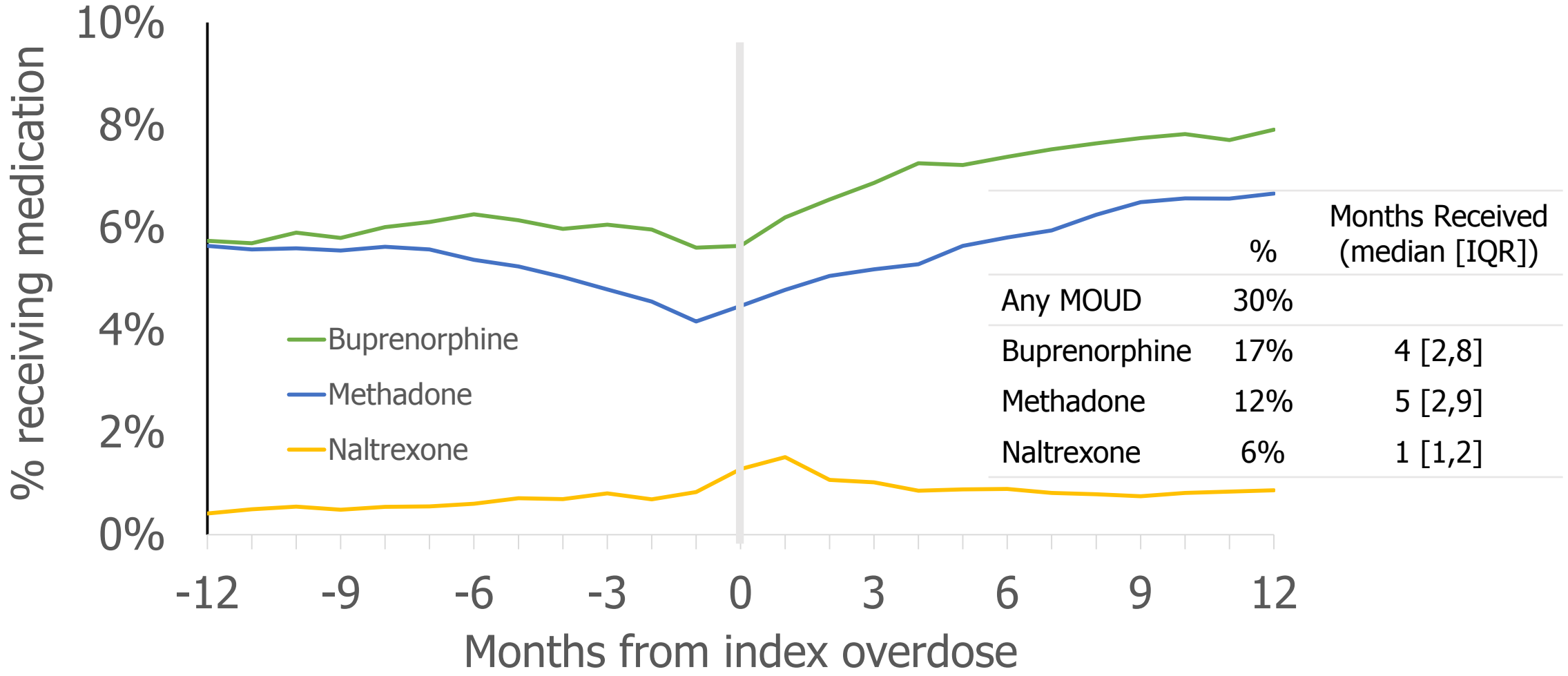

	%	Months Received (median [IQR])
Any MOUD	30%	
Buprenorphine	17%	4 [2,8]
Methadone	12%	5 [2,9]
Naltrexone	6%	1 [1,2]

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Overdose survivors who receive medications have better survival

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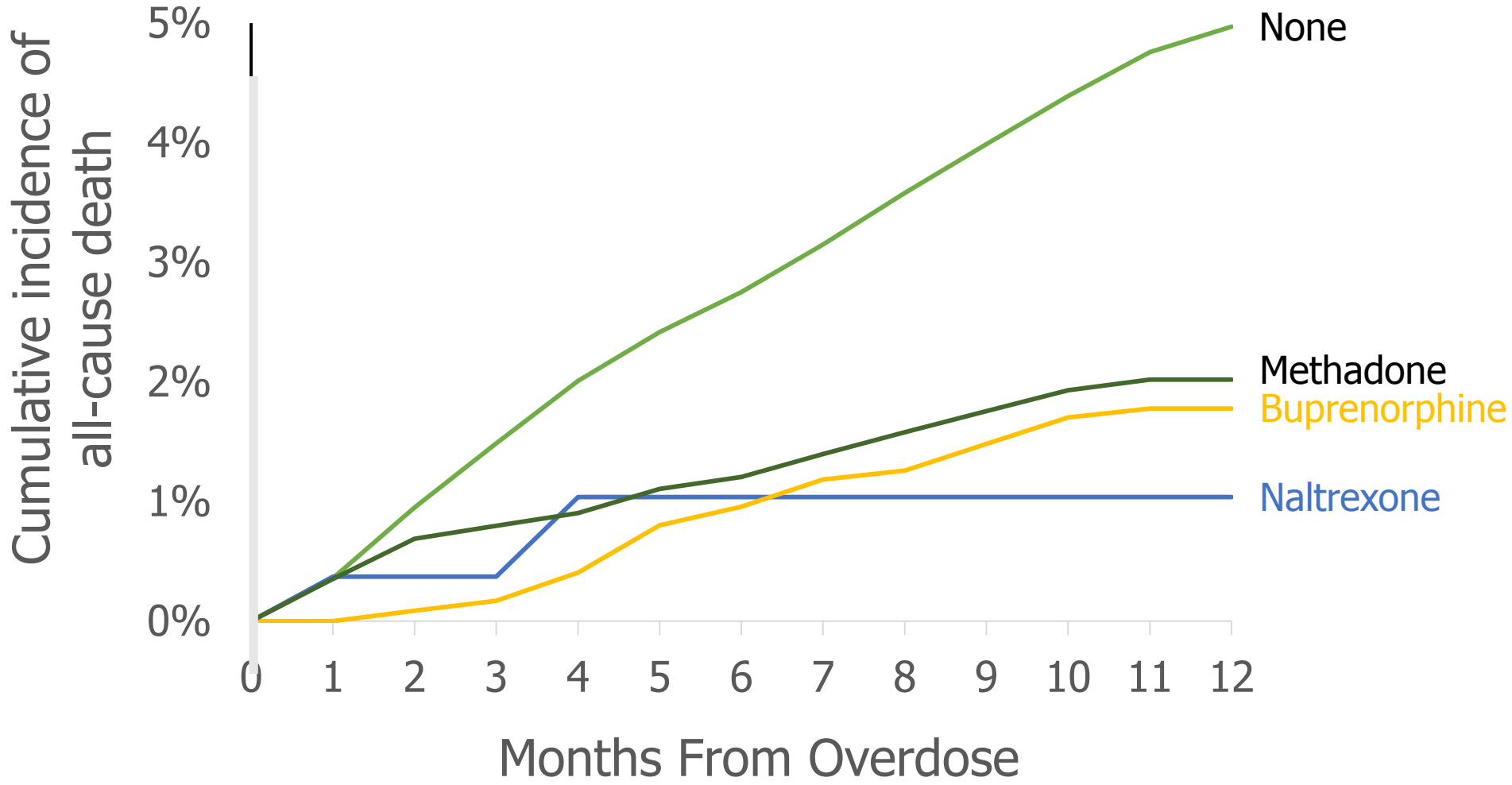

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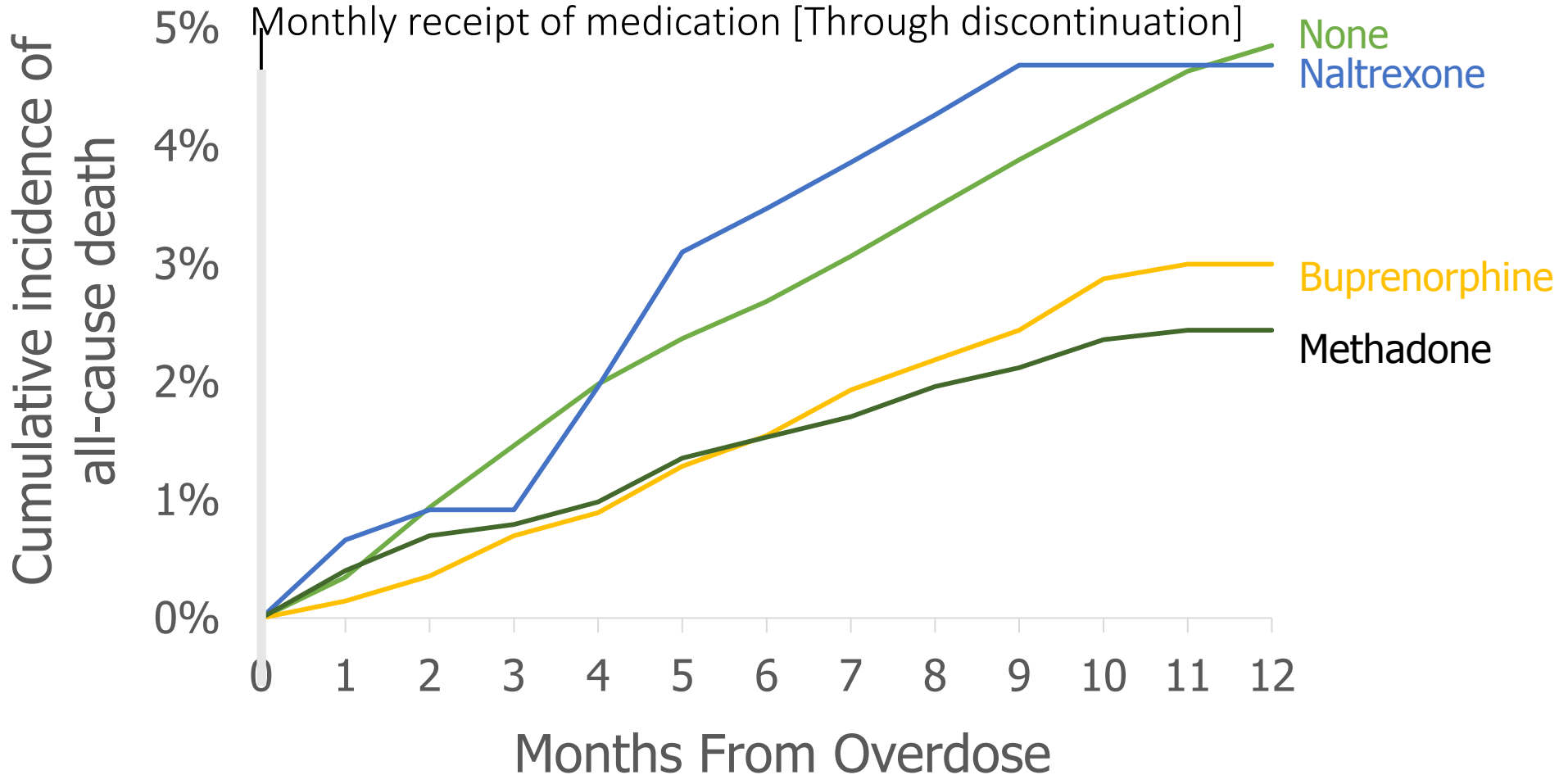

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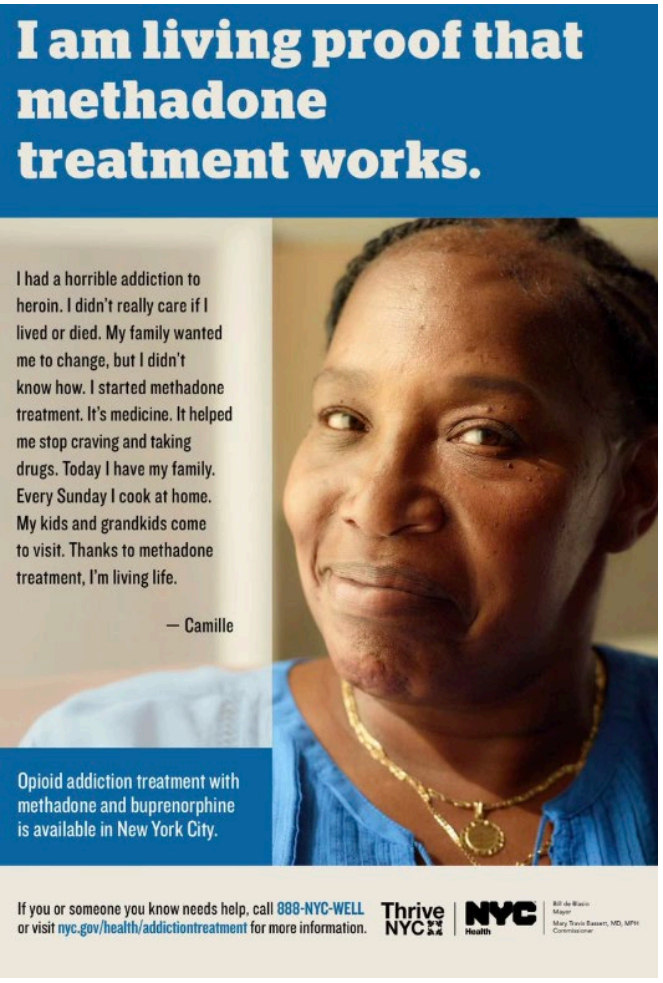
Cost Savings of Treatment

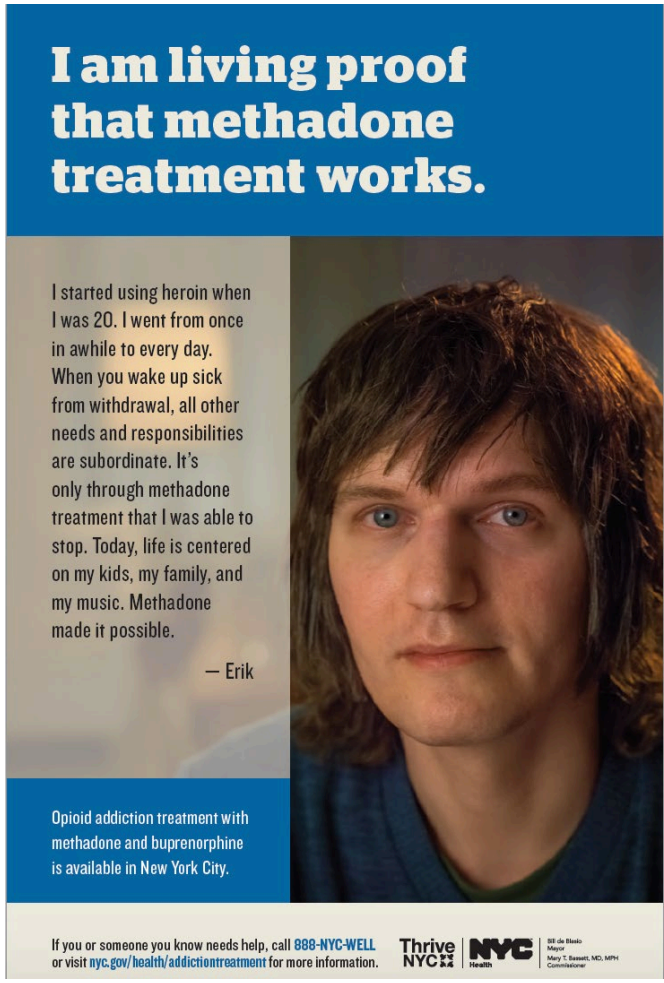
- **Methadone** maintenance patients health care costs 50%-62% lower than those not on MMT
- Adherence to **buprenorphine** has higher pharmacy, but lower outpatient, inpatient, ED, and total healthcare costs ($28K vs. $49K)

McCarty et al. Drug Alcohol Depend. 2010 Oct 1;111(3):235-40.
Tkacz J et al. JSAT 2014. 46 (2014) 456–462.
Lynch FL et al. Addict Sci Clin Pract. 2014; 9(1): 16.

MOUD Access Innovations



- Opt out, instead of opt in
  - Convert "detox" into induction sites
  - Hospital/ED patients, especially post-OD
  - MOUD in jails/prisons
  - MOUD through pharmacies
- More evidence-based MOUD choices
  - 24-hour oral morphine
  - Injectable opioid agonist treatment – heroin and hydromorphone



Realistic Expectations!

Addiction is a chronic relapsing condition

Over time treatment works
People get better

Thank you!
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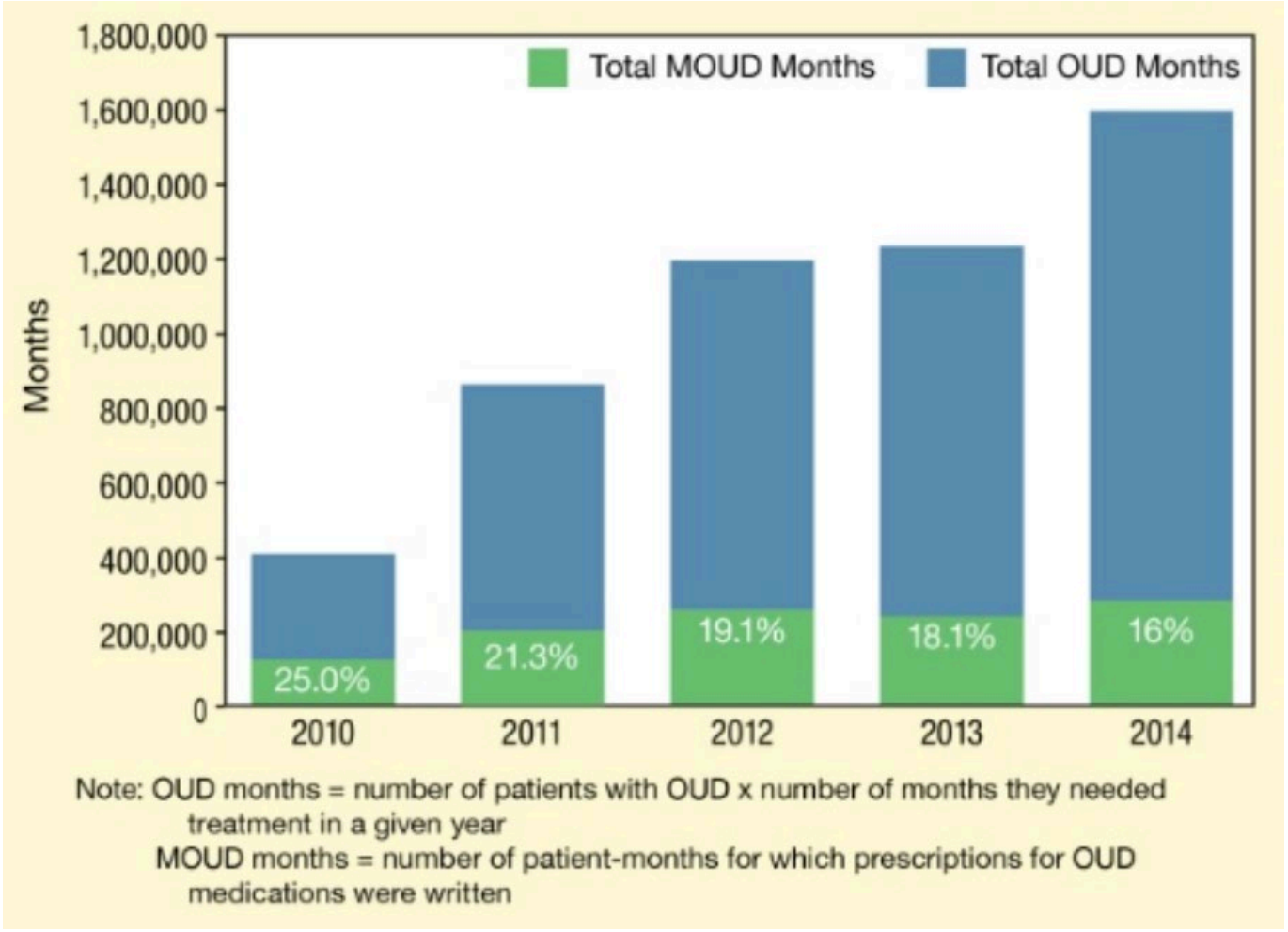
Treatment has not kept pace with incidence

2010-14 claims database of >200 million commercially insured in US

- 4-fold-increase in OUD dx
  - 0.12% → 0.48%
- BUT, proportion treated decreased
  - 25% → 16%



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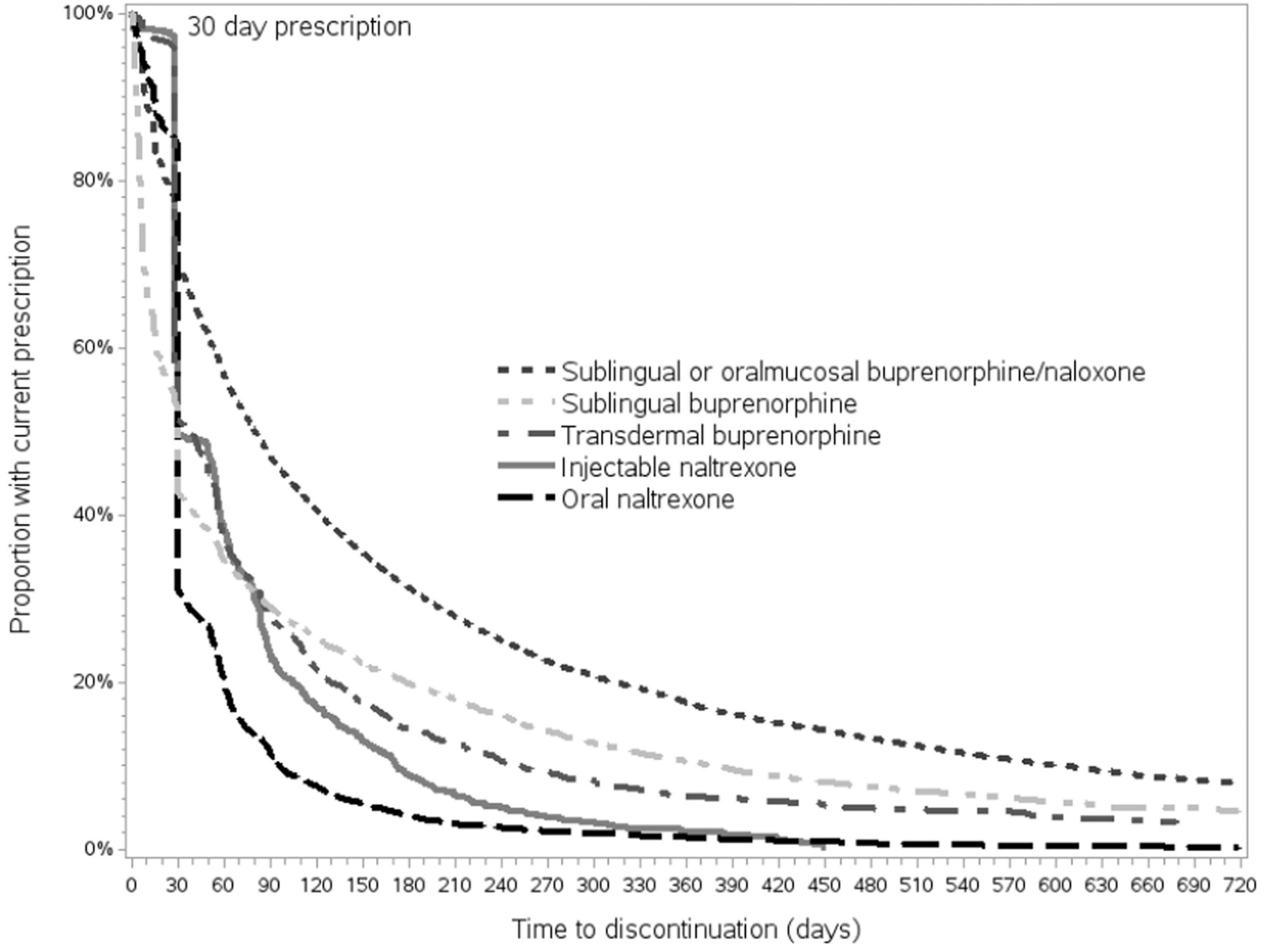
Treatment has not kept pace with incidence

- *Discontinuation is common, especially with naltrexone*



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