

# Understanding Buprenorphine Formulations and Clinical Guidelines for Use

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**UCLA**

The use of affirming language inspires hope and advances recovery.

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**LANGUAGE MATTERS.**

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**Words have power.**

**PEOPLE FIRST.**

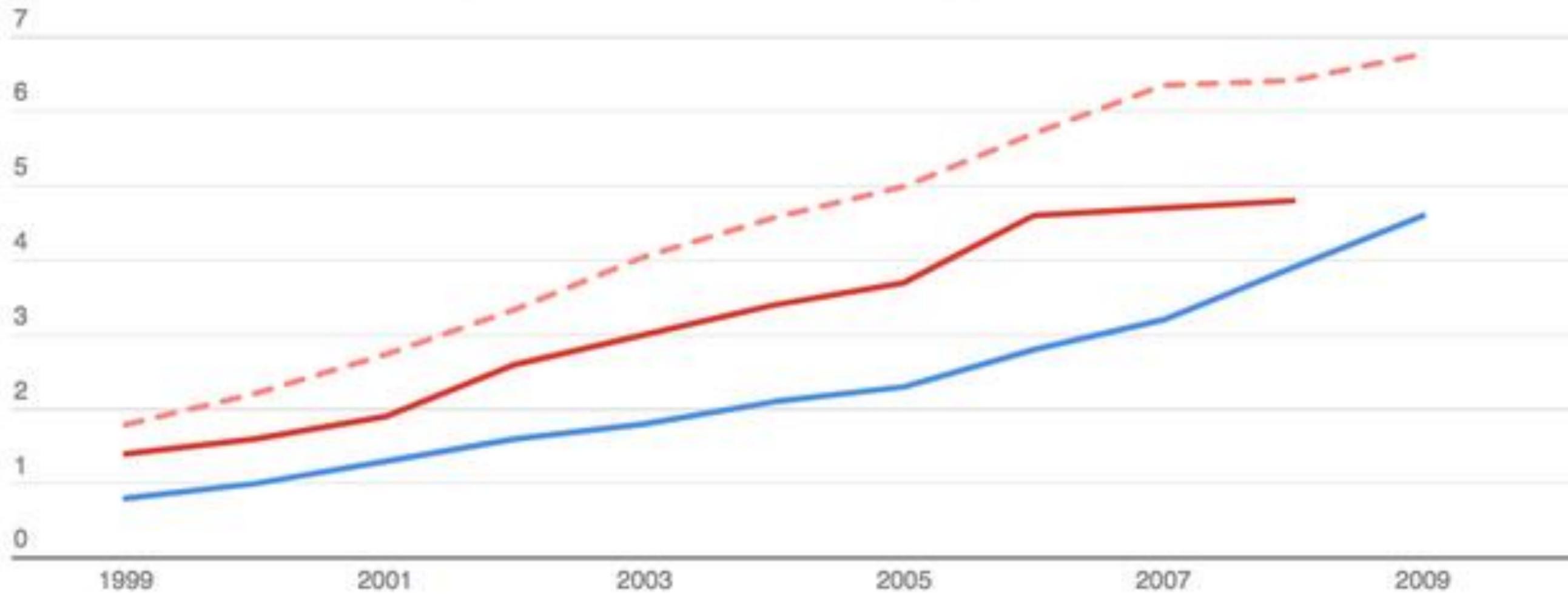
The ATTC Network uses affirming language to promote the promises of recovery by advancing evidence-based and culturally informed practices.

# Overview

- Current U.S. opioid epidemic
  - Trends in opioid use, overdose deaths
- Introduction to treatment approaches
- Consumer perspective
- Buprenorphine formulations
- Choosing the most appropriate formulation
- Questions and discussion

## Opioids on the rise

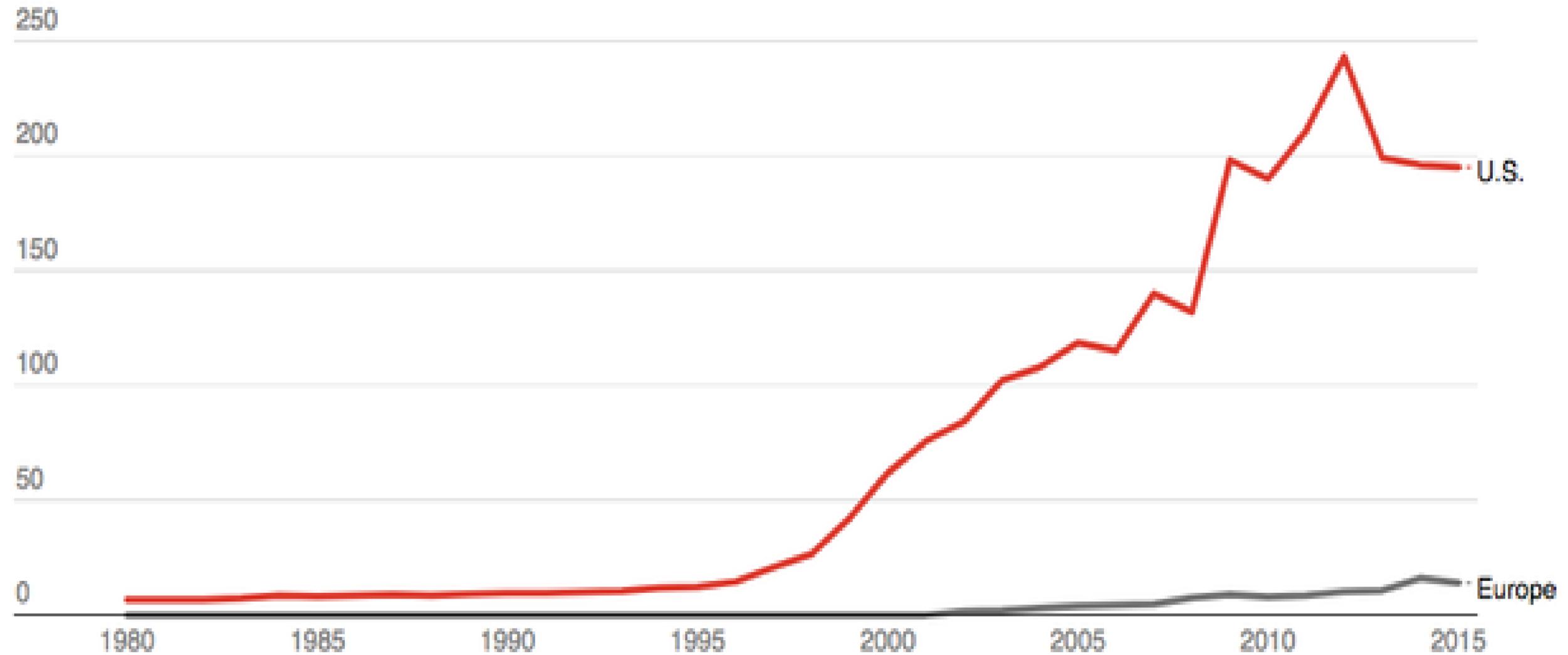
■ Opioid overdose death per 100,000 ■ Opioid treatment admissions per 10,000 ■ Opioid sales kg/10,000



Source: [Centers for Disease Control](#)

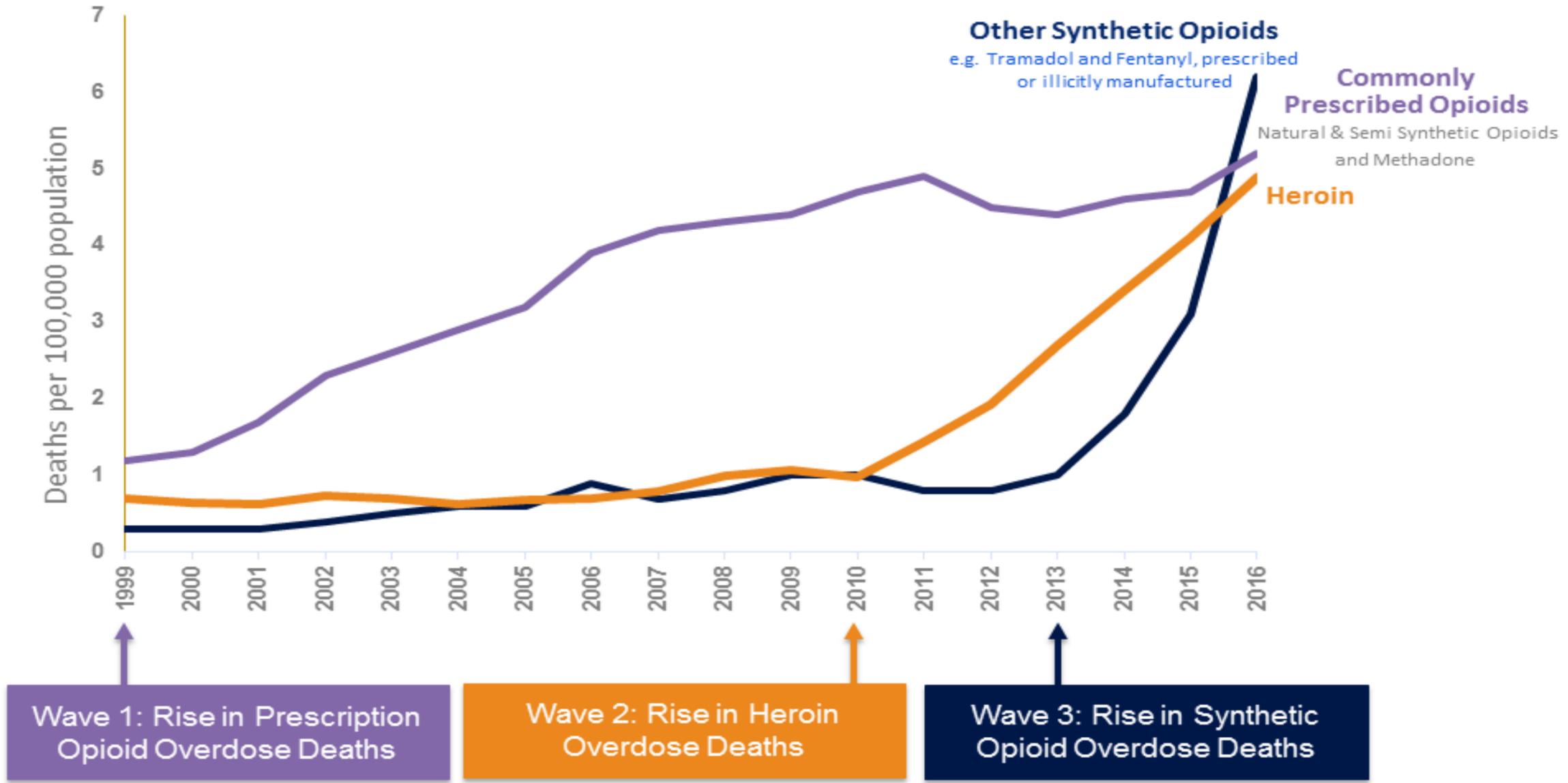
# Oxycodone consumption, mg/capita

Despite a decline in recent years, U.S. per capita opioid consumption remains much higher than oxycodone consumption in Europe.



Source: [The International Narcotics Control Board](#)

### 3 Waves of the Rise in Opioid Overdose Deaths



SOURCE: National Vital Statistics System Mortality File.

CDC: <https://www.cdc.gov/drugoverdose/epidemic/index.html>

<sup>1</sup><https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>

# Nonmedical Opioid Use and Overdose: Epidemiology

- 4 in 5 new heroin users started out misusing prescription painkillers. As a consequence, the rate of heroin overdose deaths nearly quadrupled from 2000 to 2013.
- In 2017, the number of opioid-related overdose deaths was 6 times higher than in 1999.
- 2017 overdose rates CDC: 70,237 drug overdose deaths in U.S., over 2/3 linked to opioids
  - 45% increase in fentanyl (& analog)-related deaths since 2016

# Opioid Use Disorder Treatment Approaches

- **Withdrawal management:**
  - Opioid-based (methadone, buprenorphine)
  - Non-opioid based (clonidine, supportive meds)
- **Maintenance tx/relapse prevention:**
  - Agonist maintenance (methadone)
  - Partial agonist maintenance (buprenorphine)
  - Antagonist maintenance (naltrexone)
- **Psychosocial treatment**
  - Behavioral approaches/skills



# Opioid Withdrawal Management (i.e. “detox”)

## Medications used to alleviate withdrawal symptoms:

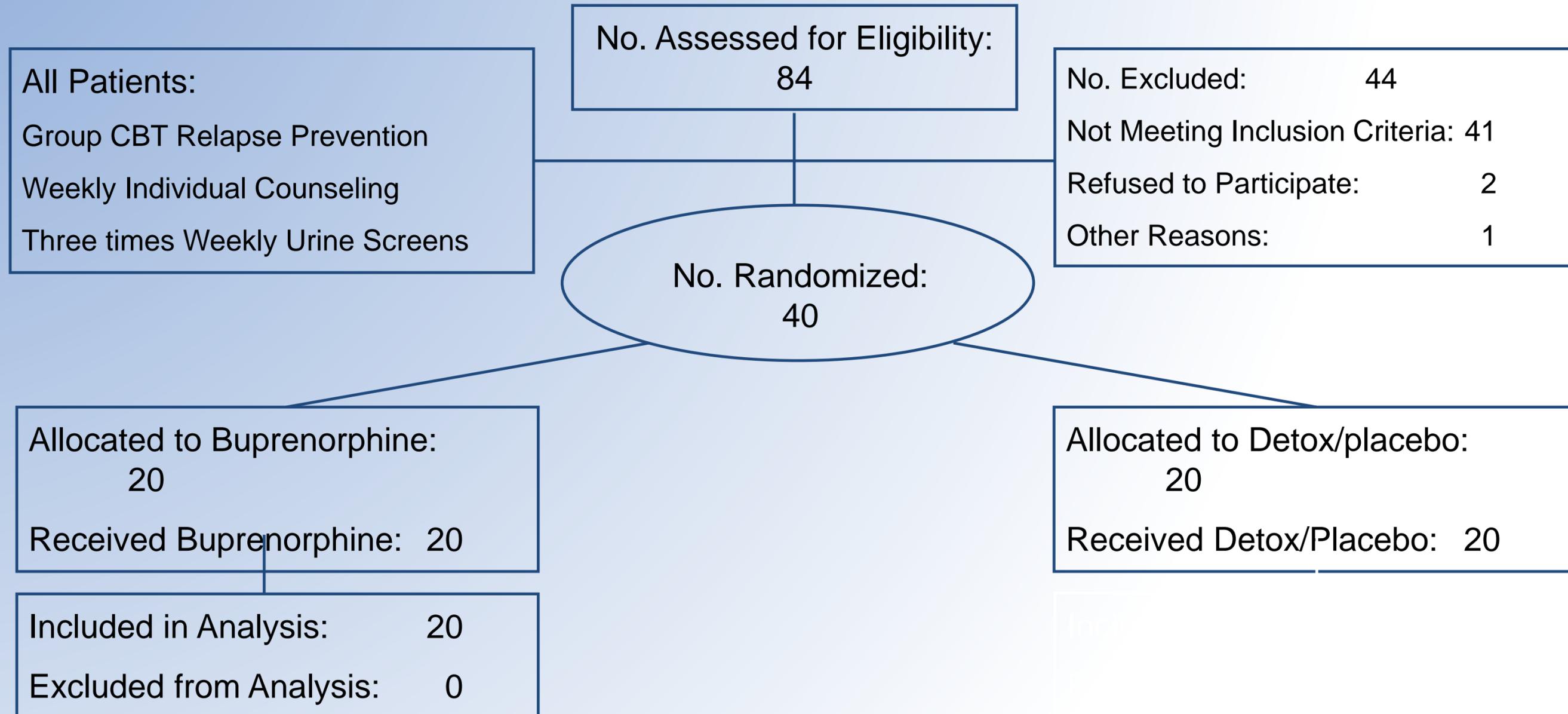
- Opioid agonists (methadone, buprenorphine)
- Clonidine, lofexidine (alpha-2 agonists)
- Other supportive meds
  - anti-diarrheals, anti-emetics, ibuprofen, muscle relaxants, BDZs

# Why Not Detoxification?

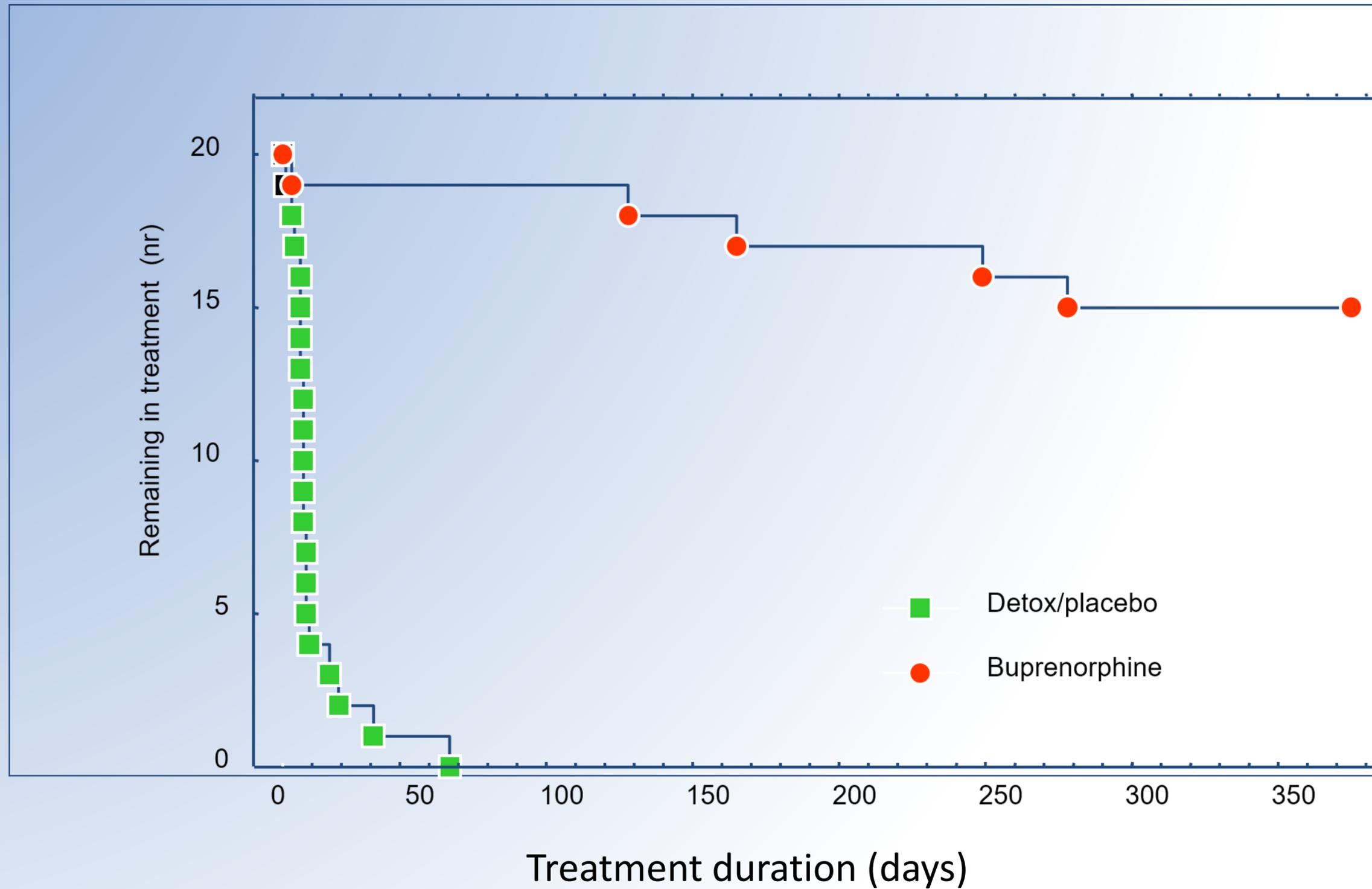
POST-DETOXIFICATION RELAPSE RATES  
APPROACH 100% WITHIN THE FIRST 90 DAYS  
FOLLOWING COMPLETION OF DETOXIFICATION.



# BUPRENORPHINE MAINTENANCE VS. TAPER



# MAINTENANCE VS. TAPER: RETENTION



## MAINTENANCE VS. TAPER: MORTALITY

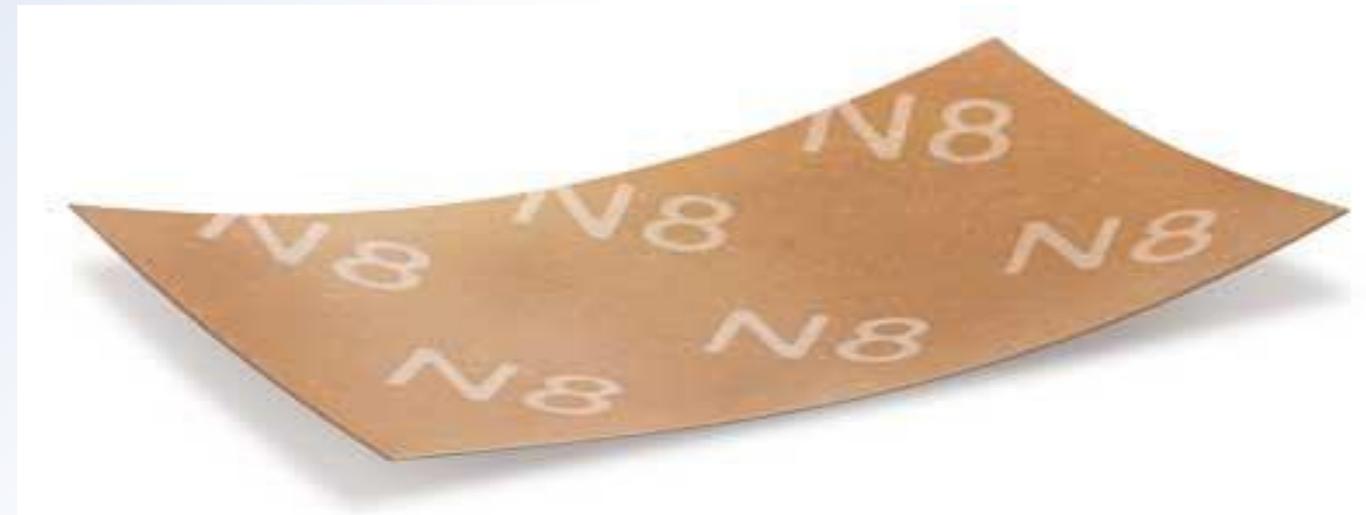
	<b>Detox/Placebo</b>	<b>Buprenorphine</b>	<b>Cox regression</b>
<b>Dead</b>	<b>4/20 (20%)</b>	<b>0/20 (0%)</b>	<b><math>\chi^2=5.9</math>; <math>p=0.015</math></b>

**Kakko J et al. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomized, placebo-controlled trial. Lancet 361(9358):662-8, 2003.**

# **Consumer Perspective**

## **Jyles**

# Buprenorphine



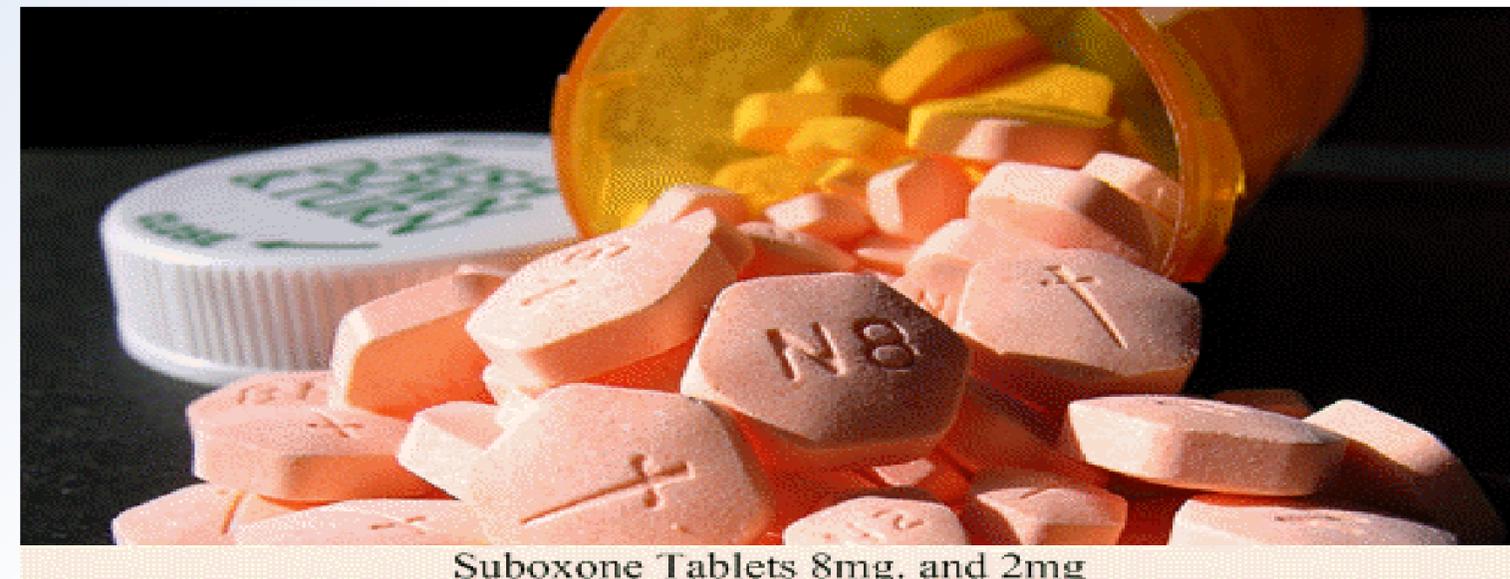
# Transmucosal Buprenorphine Formulations

- Sublingual dose: 2mg-24mg/day
- Subutex (buprenorphine) (2mg, 8mg)
- Suboxone (4:1 bup:naloxone)
  - 2mg/0.5 mg , 8mg/2mg
  - (now also in 4mg/12mg)
- Zubsolv (4:1 bup:naloxone)
  - (1.4/0.36mg- 11.4/2.9mg)
- Bunavail (6:1 buccal film bup:naloxone)
  - (2.1/0.3mg, 4.2/0.7mg, 6.3/1mg)
- Belbuca (75-900mcg buccal film for pain)

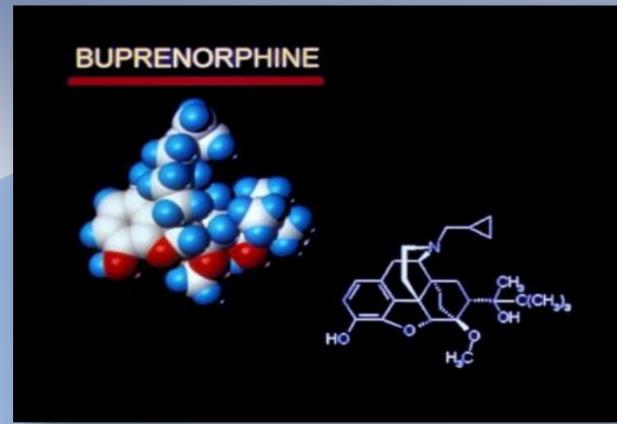


# Buprenorphine for Opioid Use Disorder

- FDA approved 2002, age 16+
- Mandatory certification from DEA (100 pt. limit)
- Mechanism: partial mu agonist
- Office-based, expands availability
- Analgesic properties
- Ceiling effect
- Lower abuse potential
- Safer in overdose



Suboxone Tablets 8mg. and 2mg



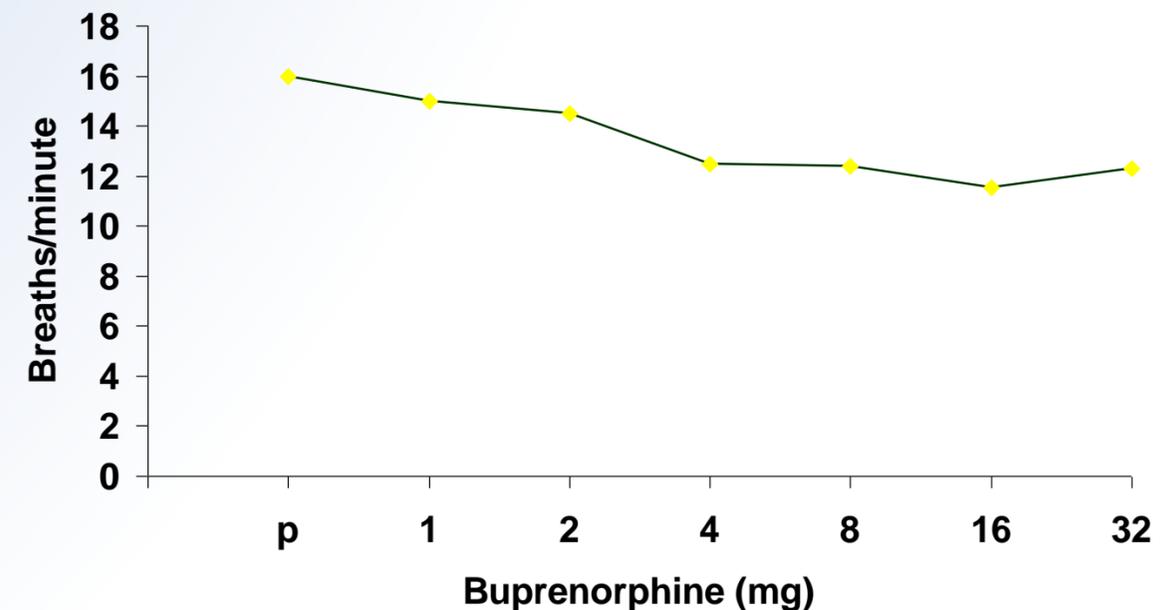
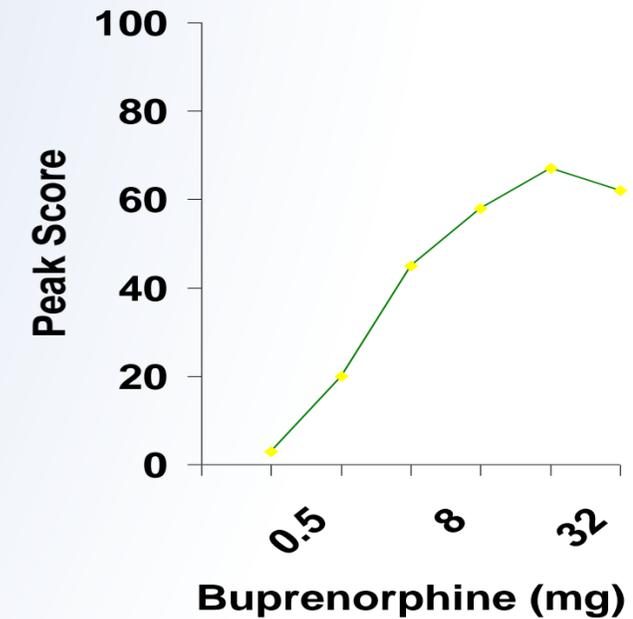
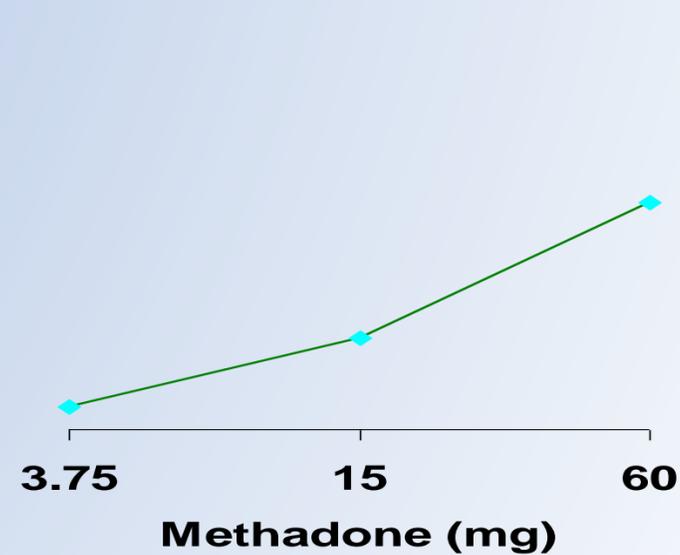
# Buprenorphine: Pharmacological Characteristics

## Partial Agonist (ceiling effect)

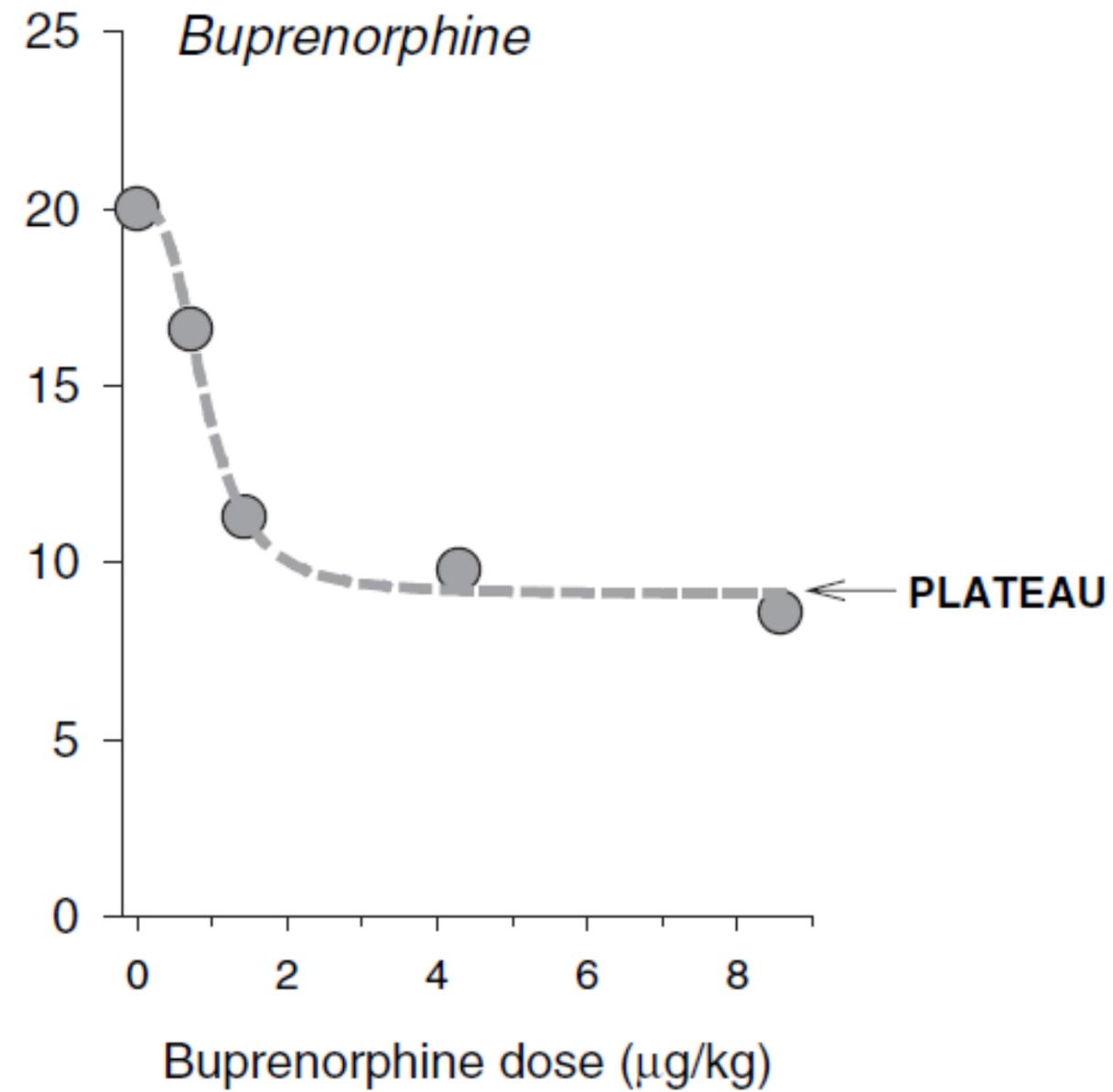
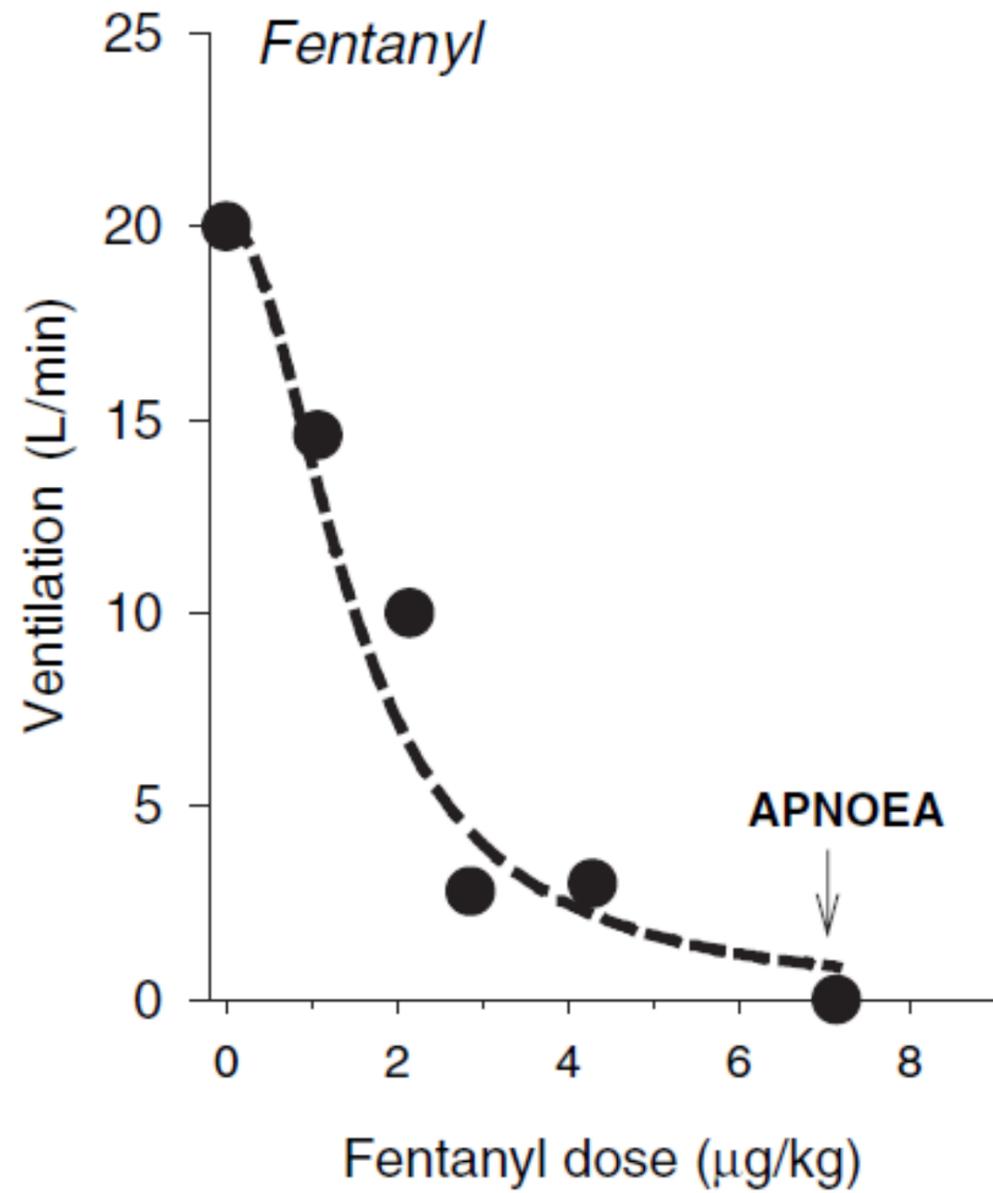
- -less euphoria
- -safer in overdose

## Strong Receptor Binding

- -long duration of action
- -1<sup>st</sup> dose given during withdrawal



# Fentanyl vs. Buprenorphine



# Buprenorphine Implant: Probuphine

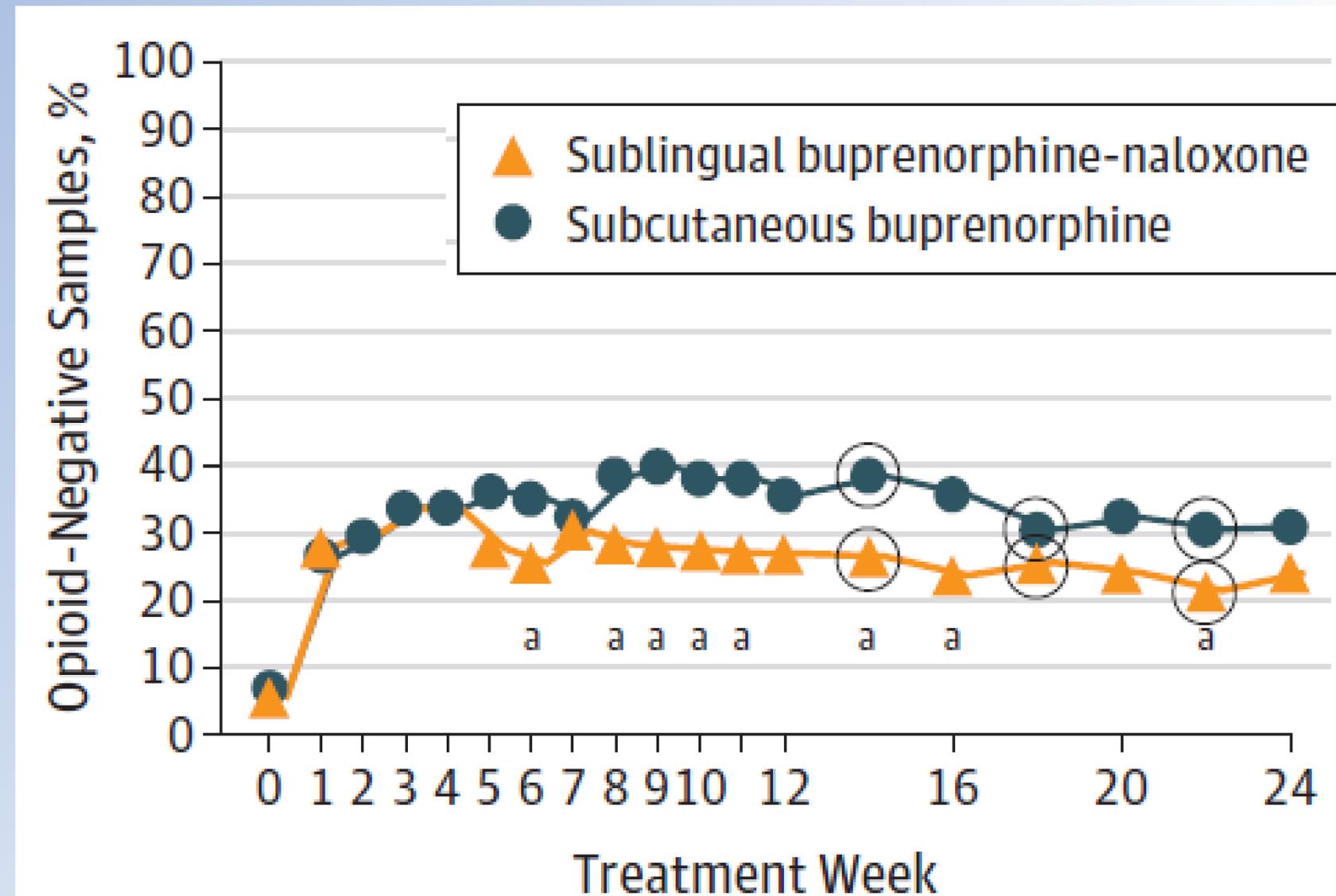
- Probuphine™ is an implantable formulation of buprenorphine HCL (80 mg) approved for the treatment of opioid use disorder in patients stabilized on 8 mg/day or less sublingual buprenorphine
- Probuphine is inserted subdermally into the inner side of the upper arm in a brief in-office procedure under local anesthetic, and provides sustained release of buprenorphine for 6 months
  - At the end of each 6-month period, Probuphine is removed in a brief, in-office procedure



# Buprenorphine Injection: Sublocade

- Sublocade is a monthly injectable formulation of buprenorphine approved in 2017 for the treatment of moderate to severe OUD in individuals who have initiated a transmucosal buprenorphine product and have been stabilized on treatment for at least seven days.
- The approved dosing regimen is 300 mg administered subcutaneously for the first two months, followed by maintenance doses of 100 mg/month.
- It must be prescribed as part of a Risk Evaluation and Mitigation Strategy to ensure that the product is not distributed directly to patients.

# SL-BUP compared to XR-BUP



<sup>a</sup>  $P \leq .05$  per time point (using analysis of variance) between groups;



# Naloxone

## Short-acting opioid antagonist

- High affinity for mu opioid receptor
- Displaces opioids from receptor
- Rapidly reverses effects of opioid overdose (minutes)
- Effects last 20-90 mins
- FDA approved for IV, SC, IM, intranasal use
- Opioid overdose-related deaths can be prevented when naloxone is administered in a timely manner.
- **PrescribeToPrevent.org**

# Overdose Risk Factors

- History of prior overdose
  - Release after emergency care for overdose
- Opioid use disorder
- Prescribed more than 50 mg of oral morphine equivalents daily
- Recent release from incarcerated or residential setting
- Combining opioids with other central nervous system depressants (e.g. alcohol, benzos)
- Medical conditions (e.g. pulmonary diseases)

# Narcan Now App



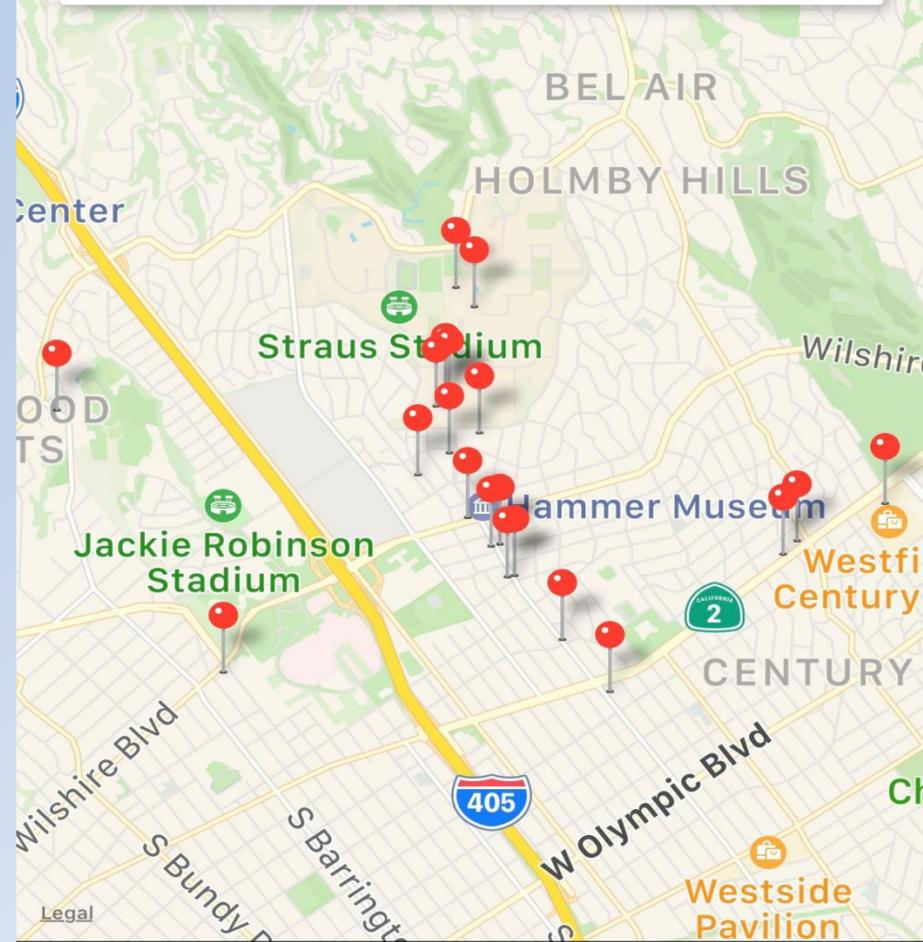


11:35

LTE

## Stores

90095



In California, you can obtain NARCAN® Nasal Spray directly from your pharmacist without an individualized physicians prescription.



Home



Stores



How To



Video



Safety Info

# SAMHSA Decisions in Recovery Tool

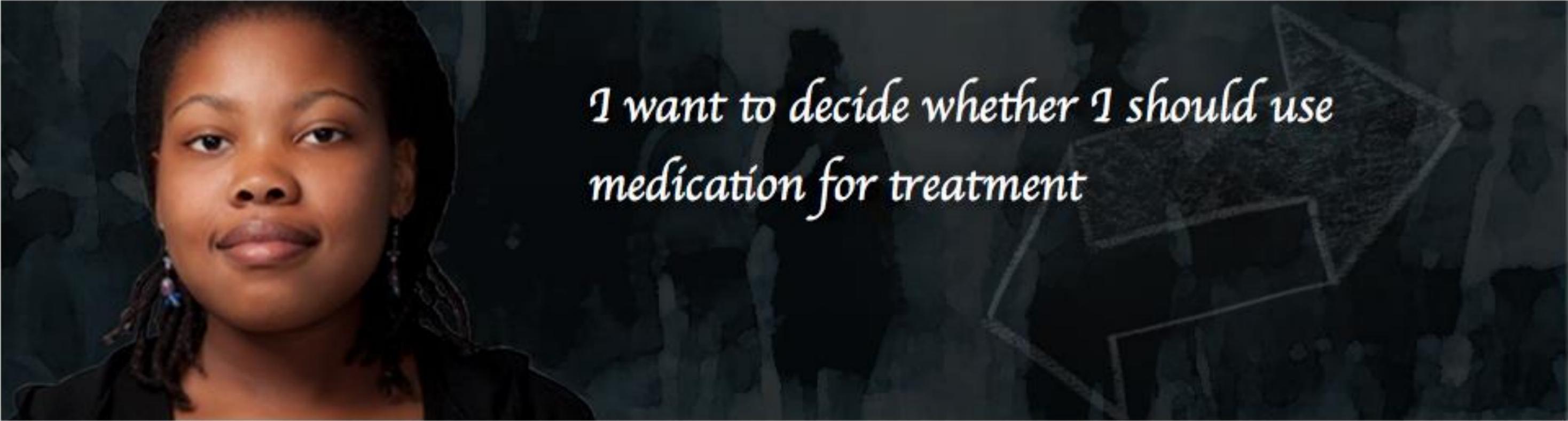
## Decisions in Recovery: Treatment for Opioid Use Disorder

Should I start?

Which do I start?

How do I start?

Recovery tools



*I want to decide whether I should use medication for treatment*

<https://mat-decisions-in-recovery.samhsa.gov/>

# Factors to Consider in Shared Decisions on Choosing Formulations – Sublingual/Buccal

- The most common dosage form in use
  - All patients must be stabilized on sublingual or buccal preparations prior to switch to injectable or implant
  - Can be administered at home or in the office (e.g., during office-based induction)
- For patients with limited or no insurance, the least expensive option
  - For patients with insurance it may be the only option
- Advantages are cost and flexibility
  - A wide range of doses can be prescribed for a few days or for 30 days with refills
- Disadvantages are the risk of diversion, the potential for drug holidays
  - Wrapper counts at each visit; Urine buprenorphine screening

# Factors to Consider in Shared Decisions on Choosing Formulations - Injection

- Less commonly used because it is more recent (approved in 2017) and more logistically challenging
  - Only available from registered pharmacies, must be refrigerated, and can only be administered in the clinic setting
- In California, available at no charge to patients with Medi-Cal
- Covers a wide range of buprenorphine doses (8 to 24 mg daily)
- Advantages over films
  - No need for take medication daily (no lost prescriptions or missed doses); No diversion risk; Lasts for one month
- Disadvantages
  - Injection can be painful and leaves a lump that slowly dissolves over time

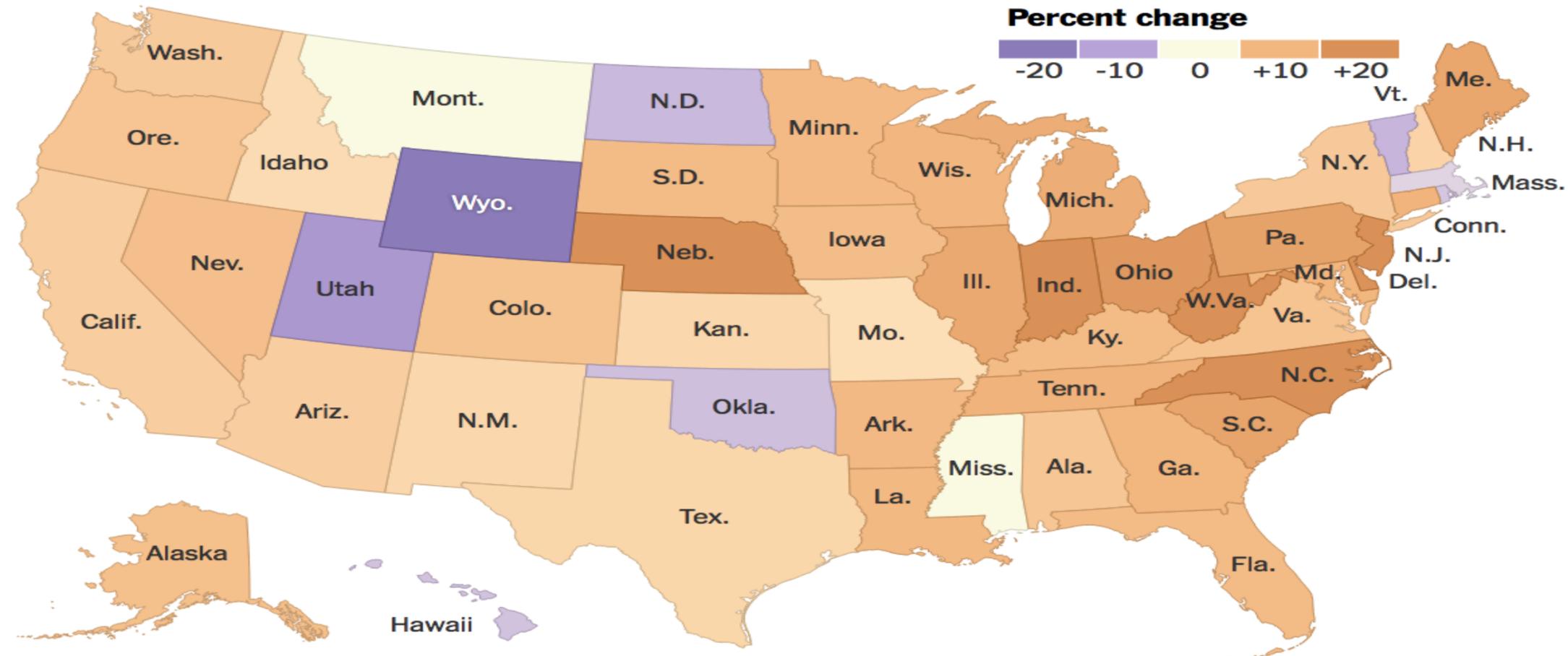
# Factors to Consider in Shared Decisions on Choosing Formulations - Implant

- Less commonly used
  - Requires additional training (above X-waiver training) to prescribe and insert
  - Insertion is a surgical procedure done under sterile procedures and may be done in a separate location
- Advantages
  - The longest-acting dosage form – 6 months
- Disadvantages
  - Only approved for patients stabilized on buprenorphine doses of 8 mg or less
  - After one insertion in each arm, transition to oral is recommended
  - Procedure to implant is straightforward, but there are risks

# Glimmers of Hope?

## Change in Overdose Deaths Last Year

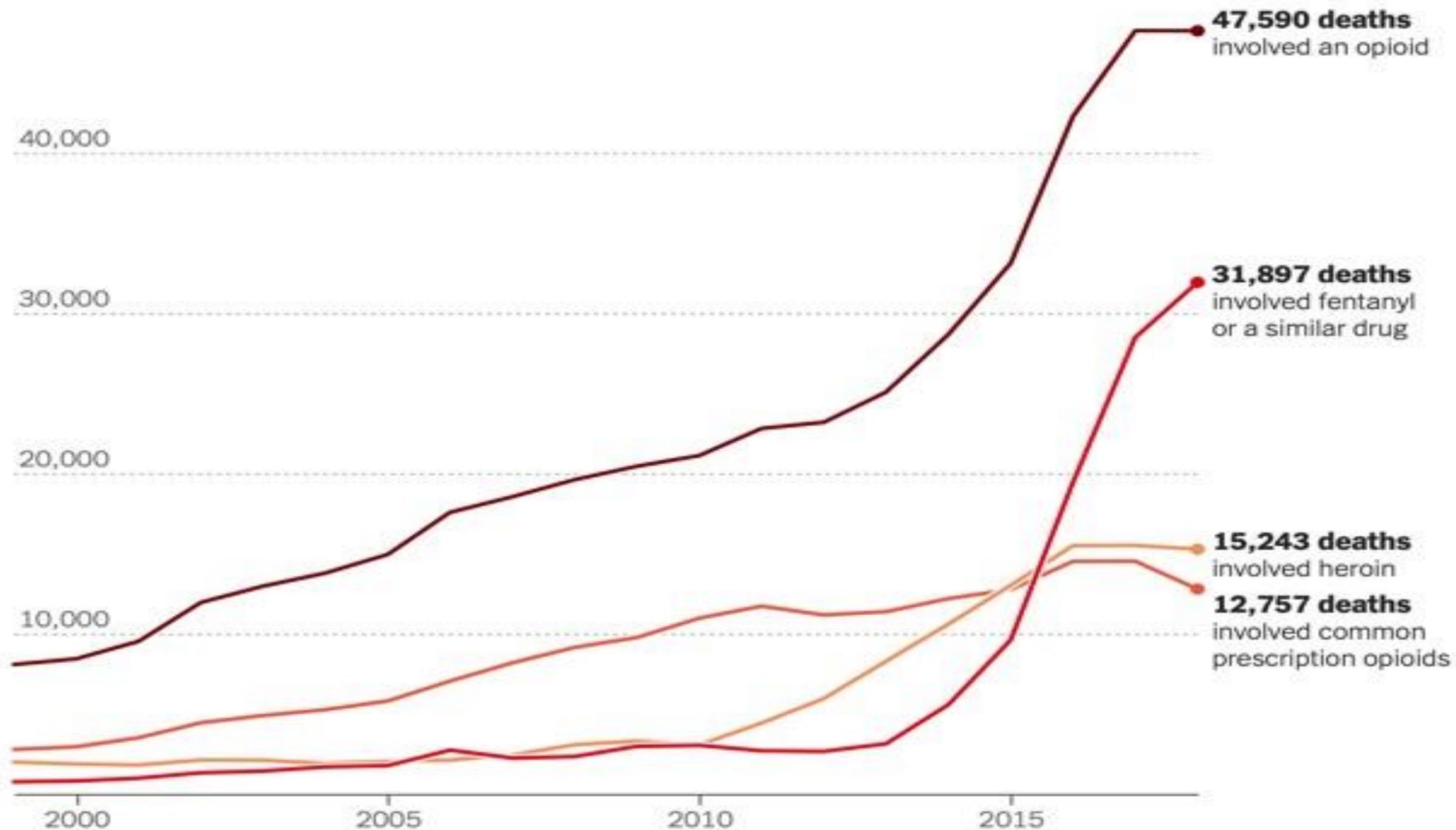
Reductions in New England give some cause for hope, while the situation in the Midwest and Mid-Atlantic remains bleak.



Note: These numbers are adjusted to account for some death investigations that are not completed. They may change slightly before they become final. Estimates for less populous states are highly variable.

Source: Centers for Disease Control and Prevention

# 2018: Reduction in US Overdose Deaths



Categories are not mutually exclusive. Deaths often involve multiple drugs. A small portion of the increase in deaths attributable to a specific drug may be due to improved cause-of-death reporting.

# Questions and Discussion

# Thank you!

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# PSATTC Post-Event Feedback

## [ATTC Event Feedback](#)

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