

# Understanding Buprenorphine Formulations

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# Disclosures

There are no relevant financial relationships with ACCME-defined commercial interests for anyone who was in control of the content of this activity.



# Overview

- ▶ Buprenorphine formulations
- ▶ Choosing the most appropriate formulation
- ▶ Questions and discussion

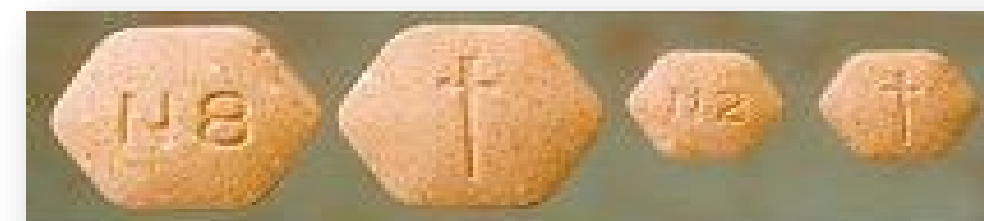


# Buprenorphine



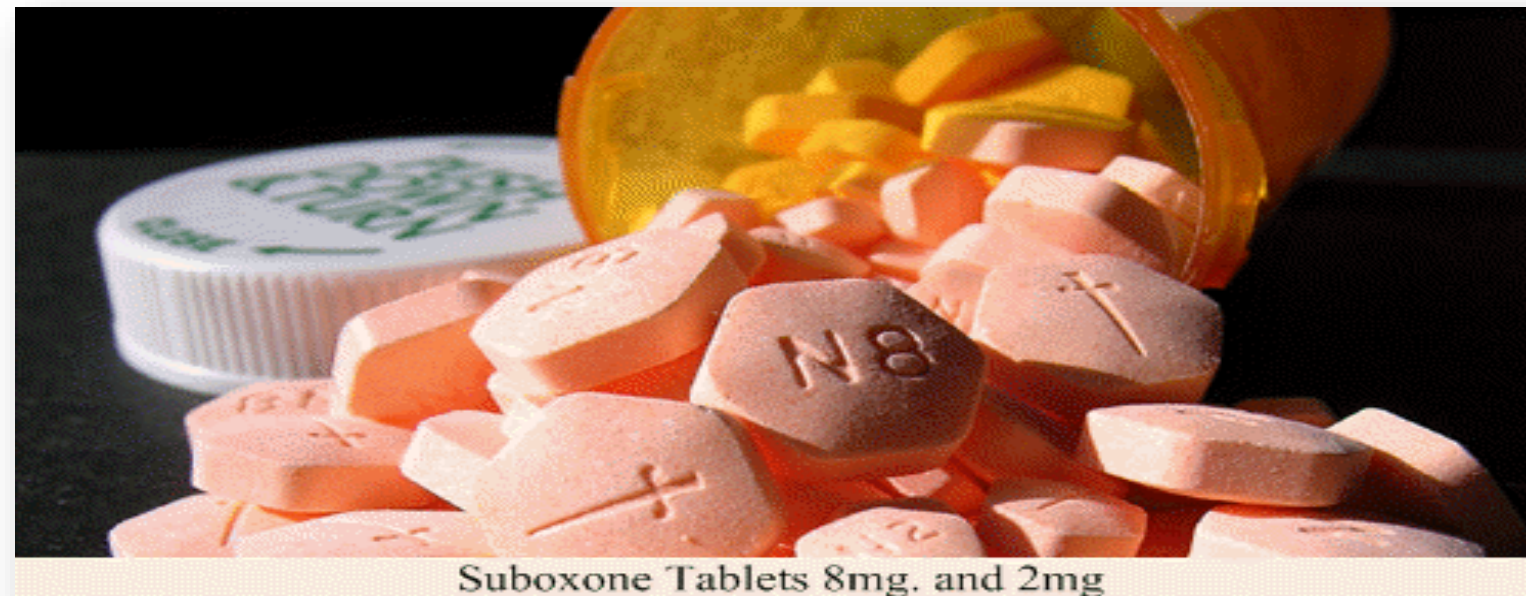
# Transmucosal Buprenorphine Formulations

- ▶ 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)



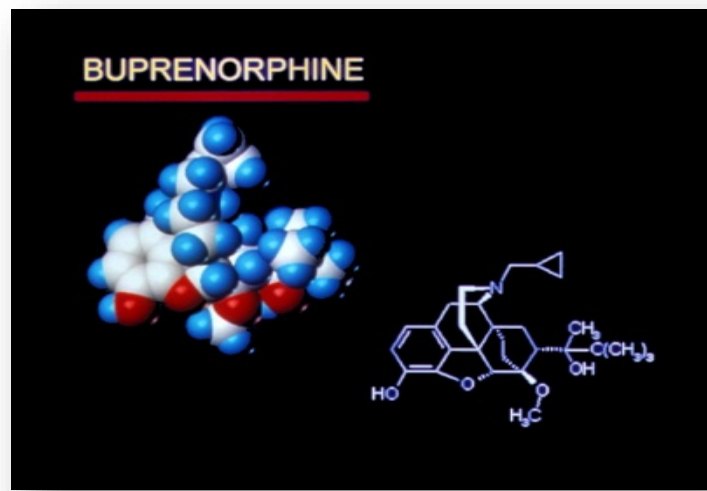
# Buprenorphine for Opioid Use Disorder

- ▶ 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

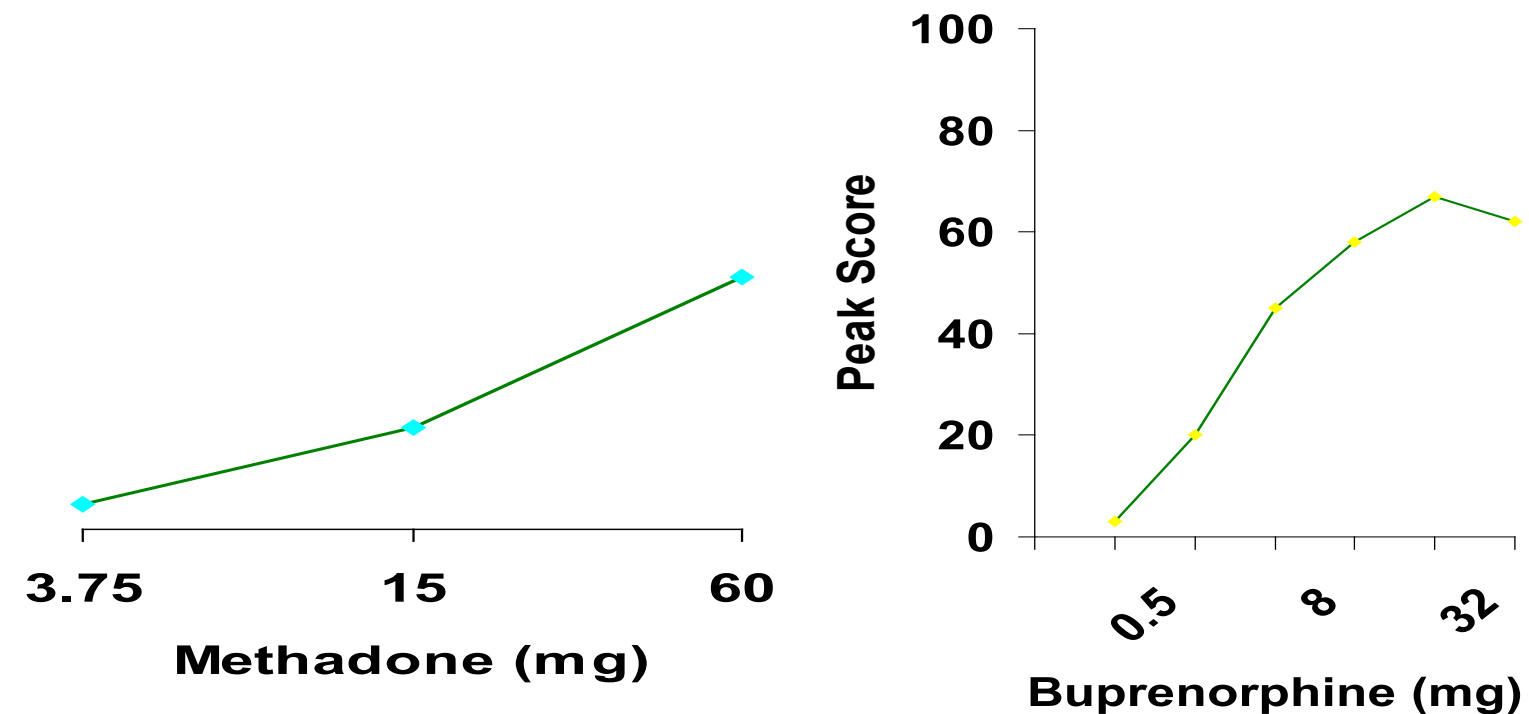




# Buprenorphine: Pharmacological Characteristics

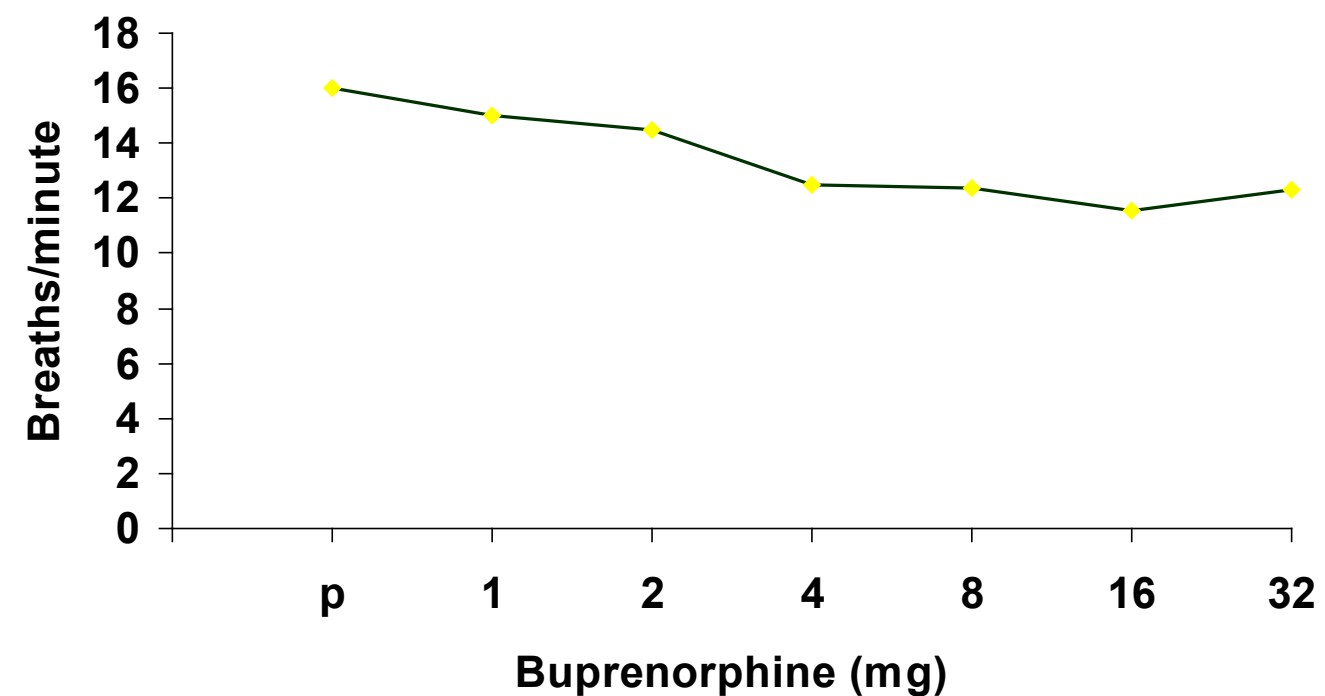
## Partial Agonist (ceiling effect)

- ▶ -less euphoria
- ▶ -safer in overdose

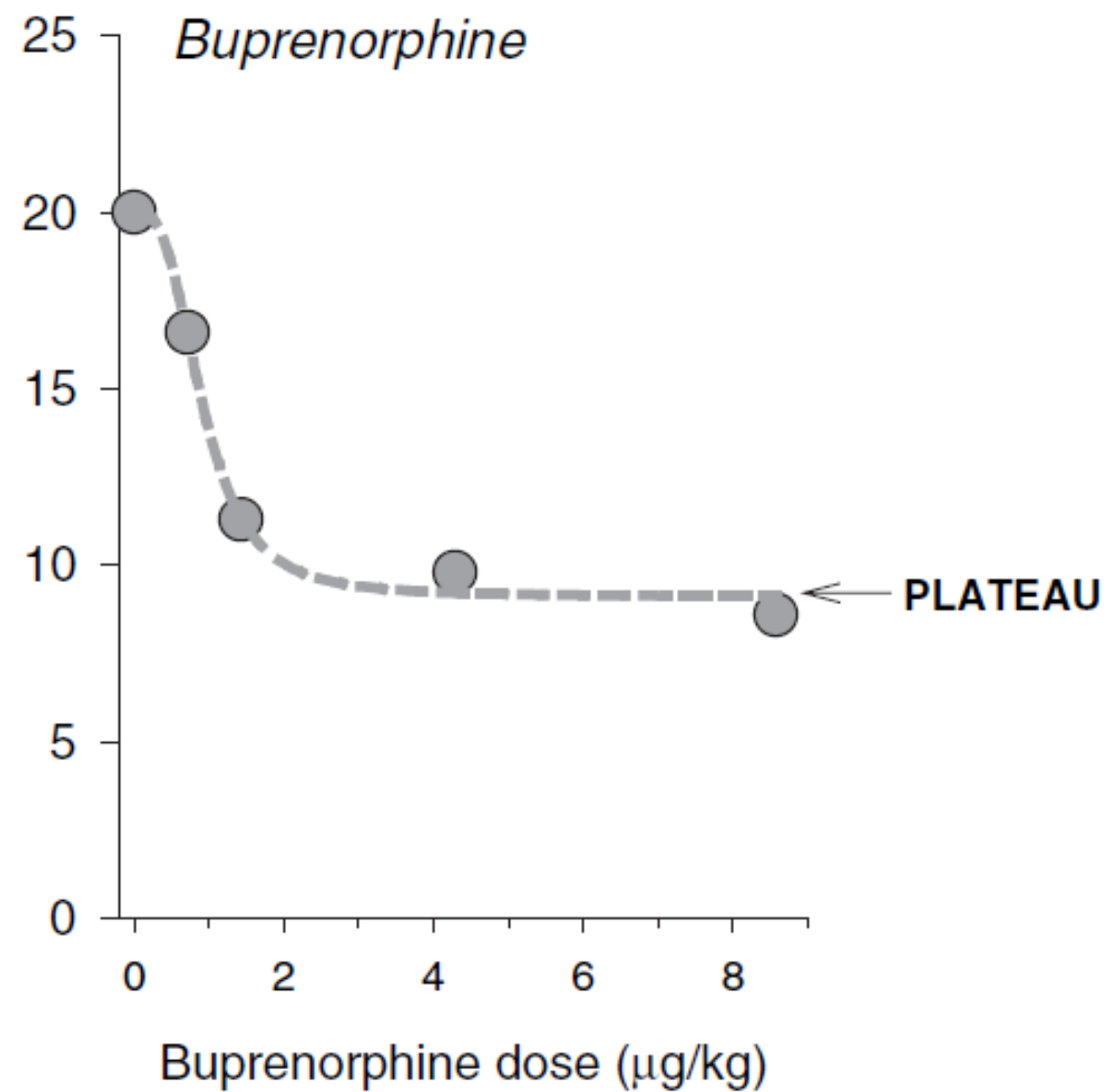
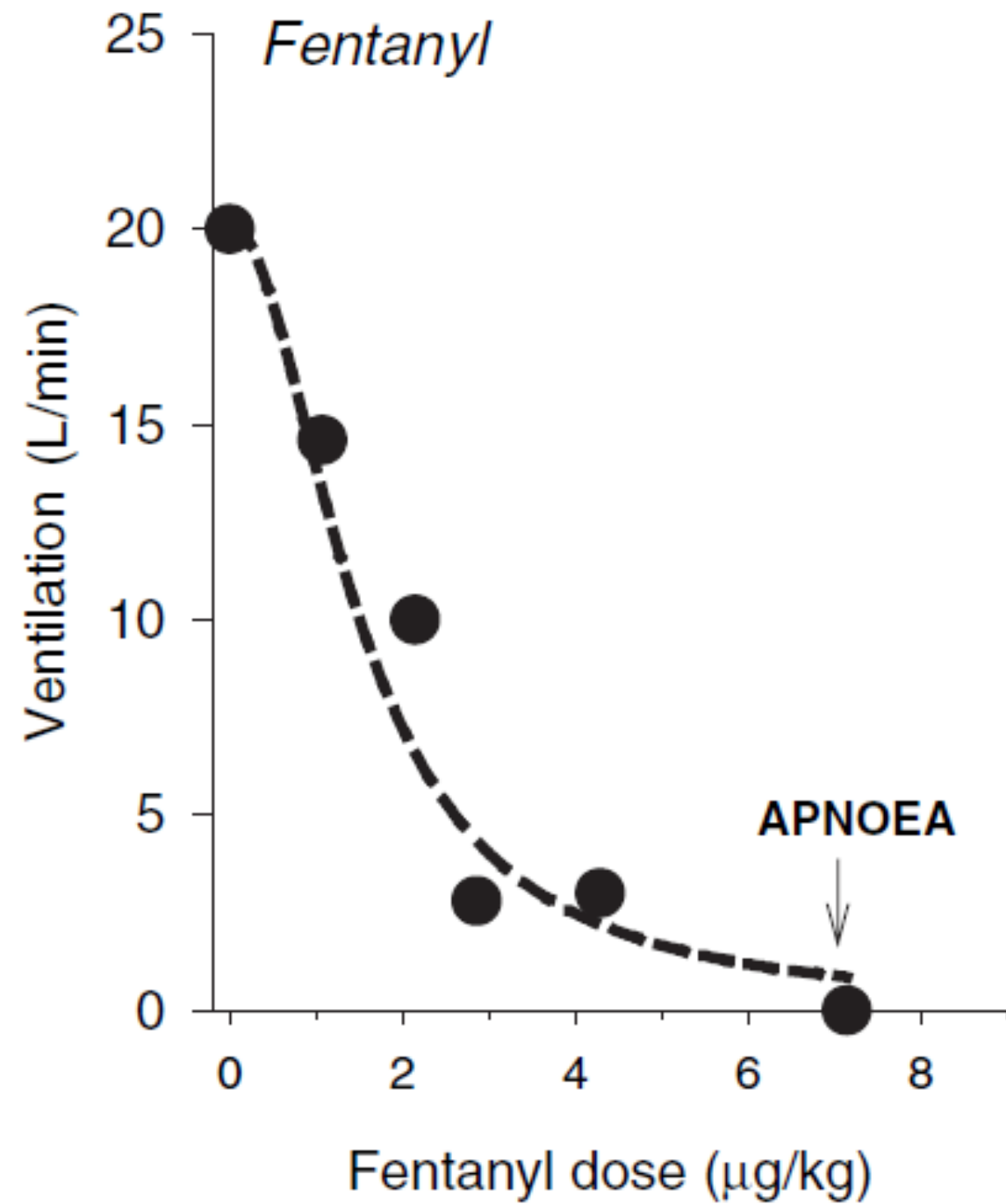


## Strong Receptor Binding

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



# Fentanyl vs. Buprenorphine

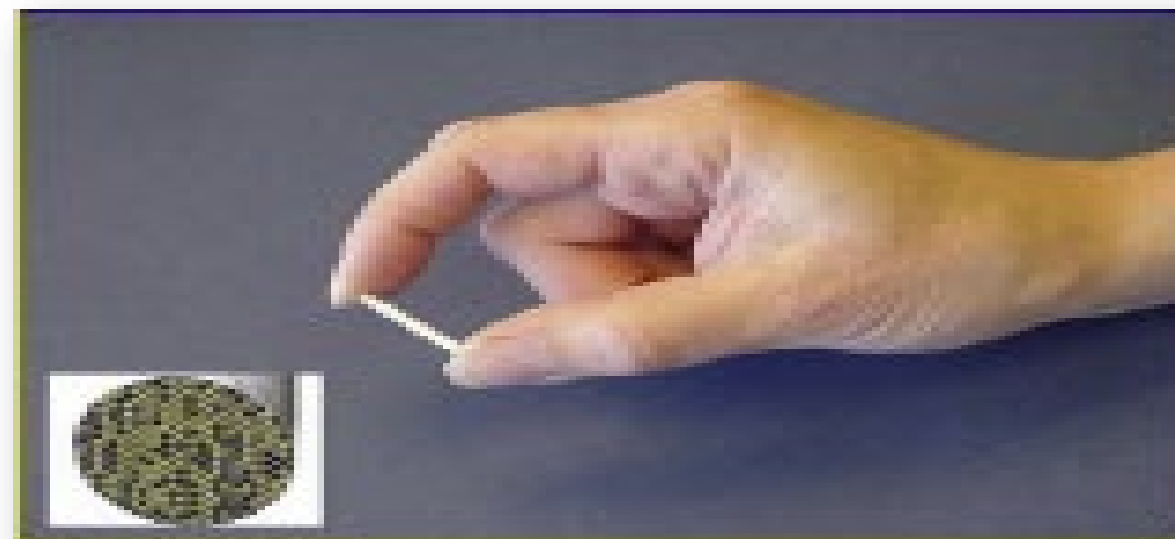


Dahan et al., 2006



# 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

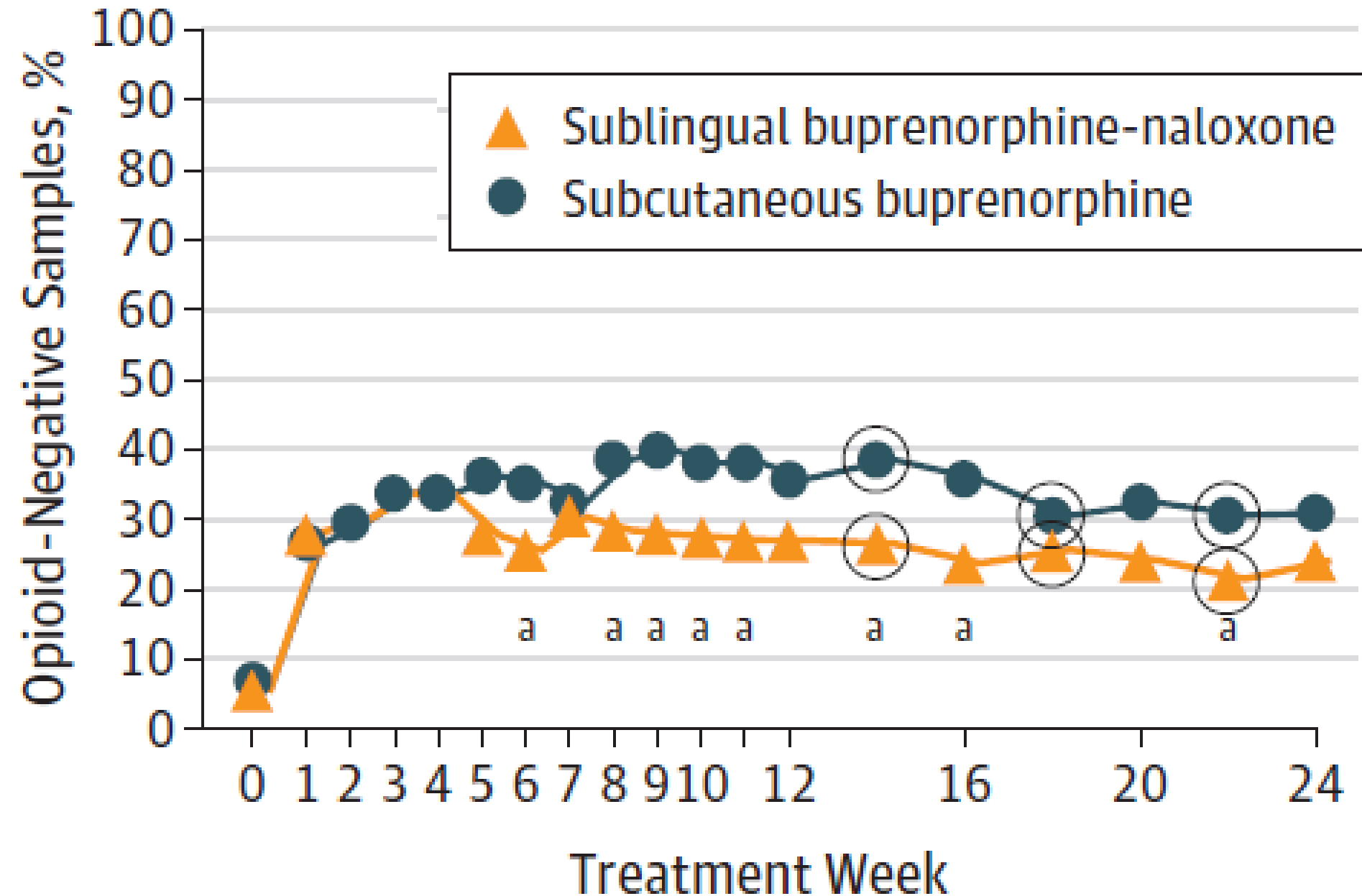


# Buprenorphine Injection: Sublocade

- ▶ 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;

Lofwall et al., 2018



# 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)





# 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](https://www.PrescribeToPrevent.org)



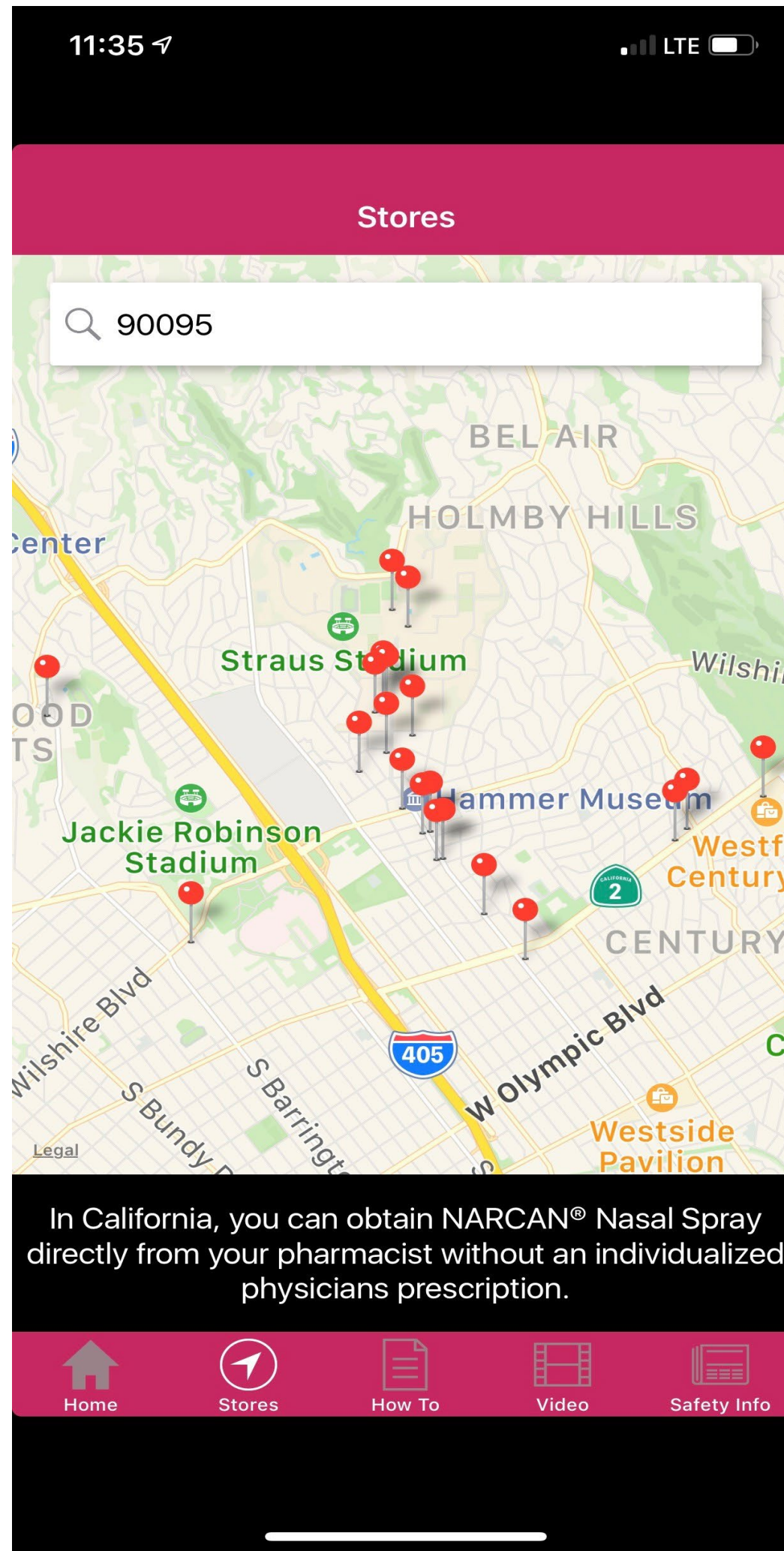


# Narcan Now App









# 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/>



University of California Los Angeles  
Integrated Substance Abuse Programs



# 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

