Understanding Buprenorphine Formulations

Monday, March 22nd, 2021

Cheryl J. Ho, MD

Valley Homeless Healthcare Program

Pacific Southwest ATTC (HHS Region 9)

Project ECHO®

University of California Los Angeles
Integrated Substance Abuse Programs

Disclosures

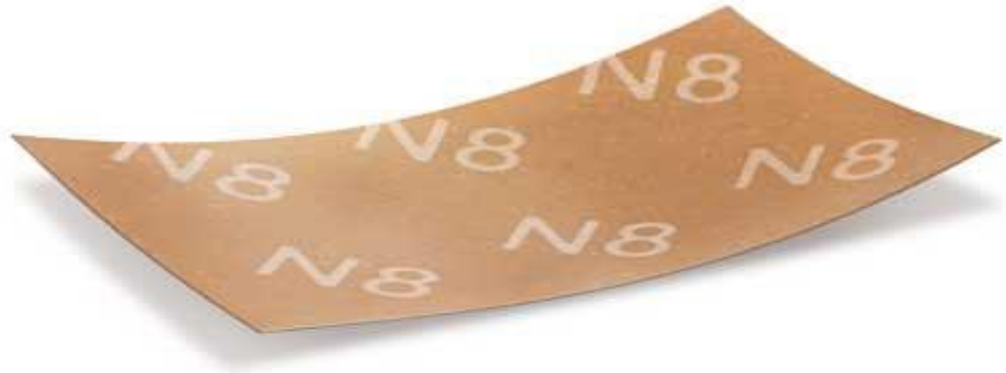
There are no relevant financial relationships with ACCME-defined commercial interests for anyone who was in control of the content of this activity.

Project ECHO®
University of California Los Angeles
Integrated Substance Abuse Programs

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)

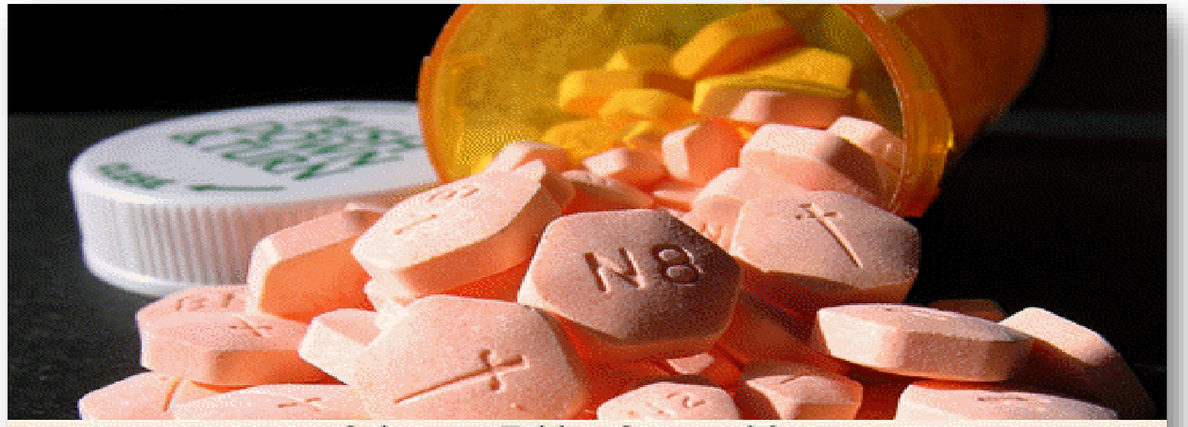
Transdermal Buprenorphine Formulations

- Butrans (5, 7.5, 10, 15, 20 mcg/hr)

Source: https://butrans.com/

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

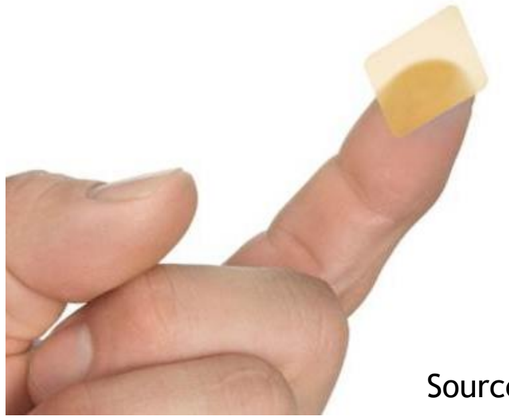


Suboxone Tablets 8mg. and 2mg

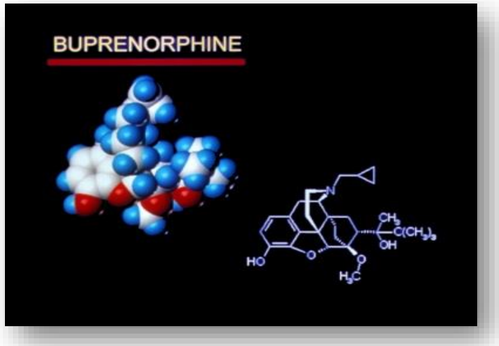
Buprenorphine for Pain

- Transdermal (Butrans) and Buccal (Belbuca) formulations
  - Butrans (5, 7.5, 10, 15, 20 mcg/hr)
  - Belbuca (75, 150, 300, 450, 600, 750, 900 mcg)

- Any provider with DEA License can prescribe



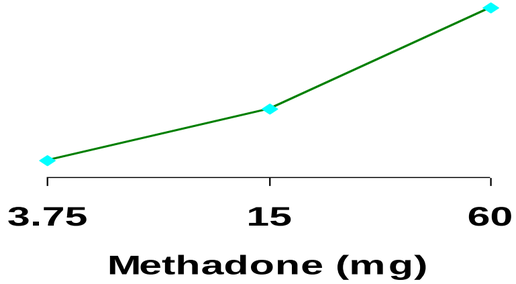
Source: https://butrans.com/

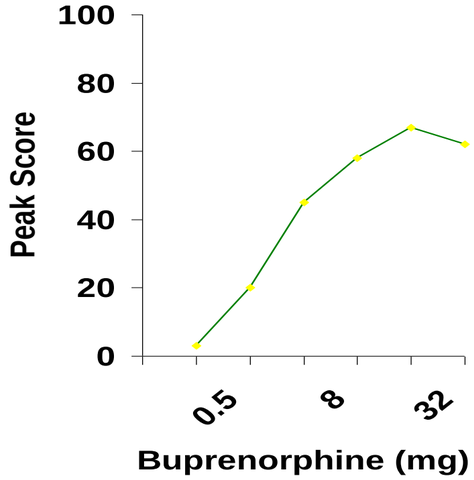


Buprenorphine: Pharmacological Characteristics

Partial Agonist (ceiling effect)

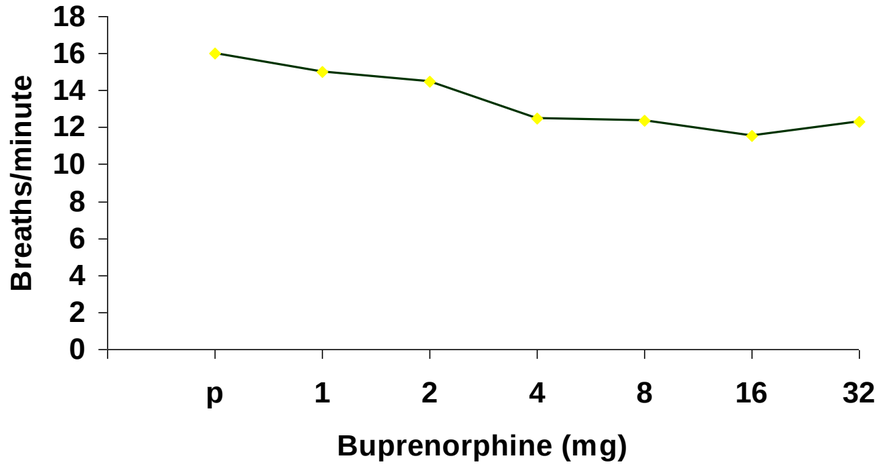
- -less euphoria
- -safer in overdose





Strong Receptor Binding

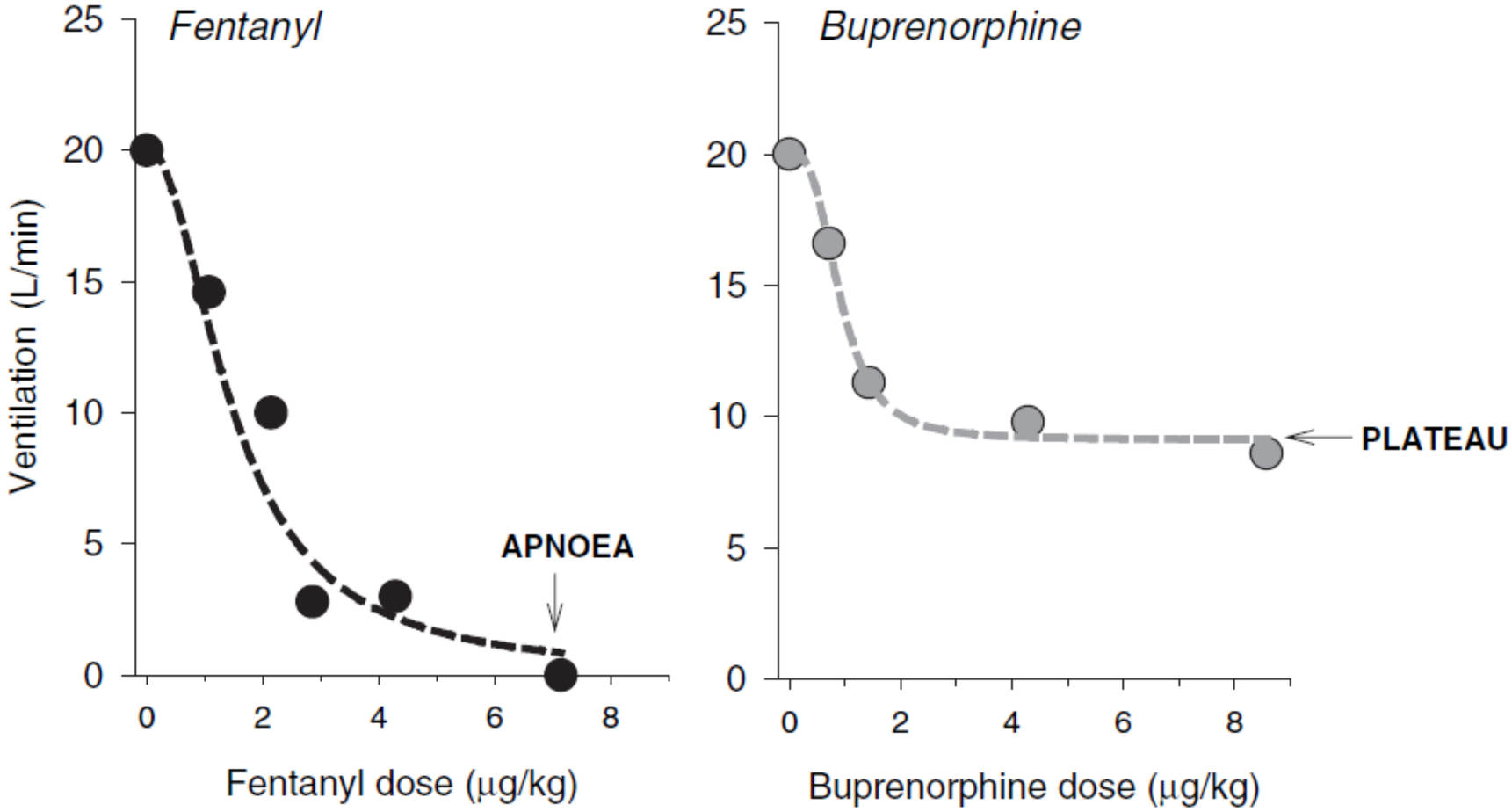
- -long duration of action
- -1st dose given during withdrawal



Project ECHO®

University of California Los Angeles
Integrated Substance Abuse Programs

Fentanyl vs. Buprenorphine

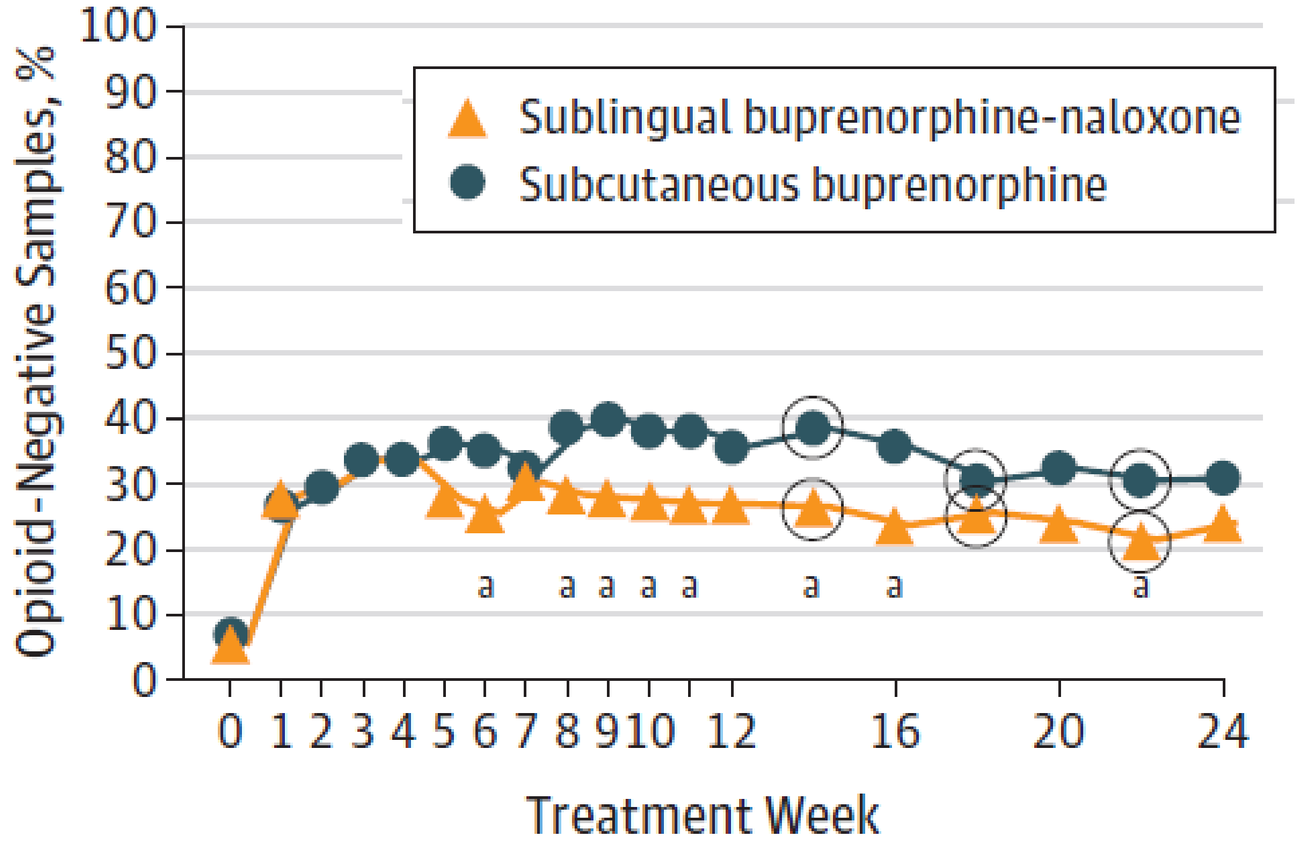


Dahan et al., 2006

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



[a] $P \leq .05$ per time point (using analysis of variance) between groups;

Lofwall et al., 2018

Serum concentrations after XR-bupe injection

Table 6. Comparison of Buprenorphine Mean Pharmacokinetic Parameters Between SUBUTEX and SUBLOCADE

Pharmacokinetic parameters	SUBUTEX daily stabilization		SUBLOCADE		
Mean	12 mg (steady-state)	24 mg (steady-state)	300 mg# (1st injection)	100 mg* (steady-state)	300 mg* (steady-state)
$C_{avg,ss}$ (ng/mL)	1.71	2.91	2.19	3.21	6.54
$C_{max,ss}$ (ng/mL)	5.35	8.27	5.37	4.88	10.12
$C_{min,ss}$ (ng/mL)	0.81	1.54	1.25	2.48	5.01

#Exposure after 1 injection of 300 mg SUBLOCADE following 24 mg SUBUTEX stabilization

*Steady-state exposure after 4 injections of 100 mg or 300 mg SUBLOCADE, following 2 injections of 300 mg SUBLOCADE

Serum concentration peaks on Day 1

Source: FDA Insert for XR-Bupe

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209819s000lbl.pdf

Slide taken with permission from David Tian, MD UCSF ADMF Case Conference March 19, 2021

Define *fast*…

The American Journal on Addictions, 29: 345–348, 2020
© 2020 American Academy of Addiction Psychiatry
ISSN: 1055-0496 print / 1521-0391 online
DOI: 10.1111/ajad.13018

Case Series: Rapid Induction Onto Long Acting Buprenorphine Injection for High Potency Synthetic Opioid Users

John J. Mariani, MD,[1,2] Amy Mahony, LMHC,[1] Muhamm
Sean X. Luo, MD, PhD,[1,2] Nasir H. Naqvi, MD, PhD,[1,2] Fra
[1]Division on Substanc
[2]Department of Psych
State Psychiatric Institute, New
ngelos College of Physicians a

Background and Objectives: Highly potent synthetic opioids (HPSO) are increasingly responsible for opioid overdose deaths in the United States.
Methods: In an open-label, uncontrolled trial to test the feasibility of extended-release buprenorphine (BXR) injection treatment of heroin-using individuals with opioid use disorder testing positive for HPSO, participants were enrolled and began an induction with sublingual BXR ($n = 5$). During the induction, ancillary medications (clonidine, clonazepam, zolpidem, and prochlorperazine) were provided for breakthrough opioid withdrawal symptoms.
Results: Two participants received the BXR injection on the second day of the induction and three participants on the third day.
Discussion and Conclusion: All five participants were retained at least 1-month postinduction.
Scientific Significance: It may be feasible to provide BXR treatment to HPSO-positive heroin users rapidly to achieve clinical stabilization. (Am J Addict 2020;29:345–348)

https://pubmed.ncbi.nlm.nih.gov/32167629/

Slide taken with permission from David Tian, MD UCSF ADMF Case Conference March 19, 2021

Project ECHO®
University of California Los Angeles
Integrated Substance Abuse Programs

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**

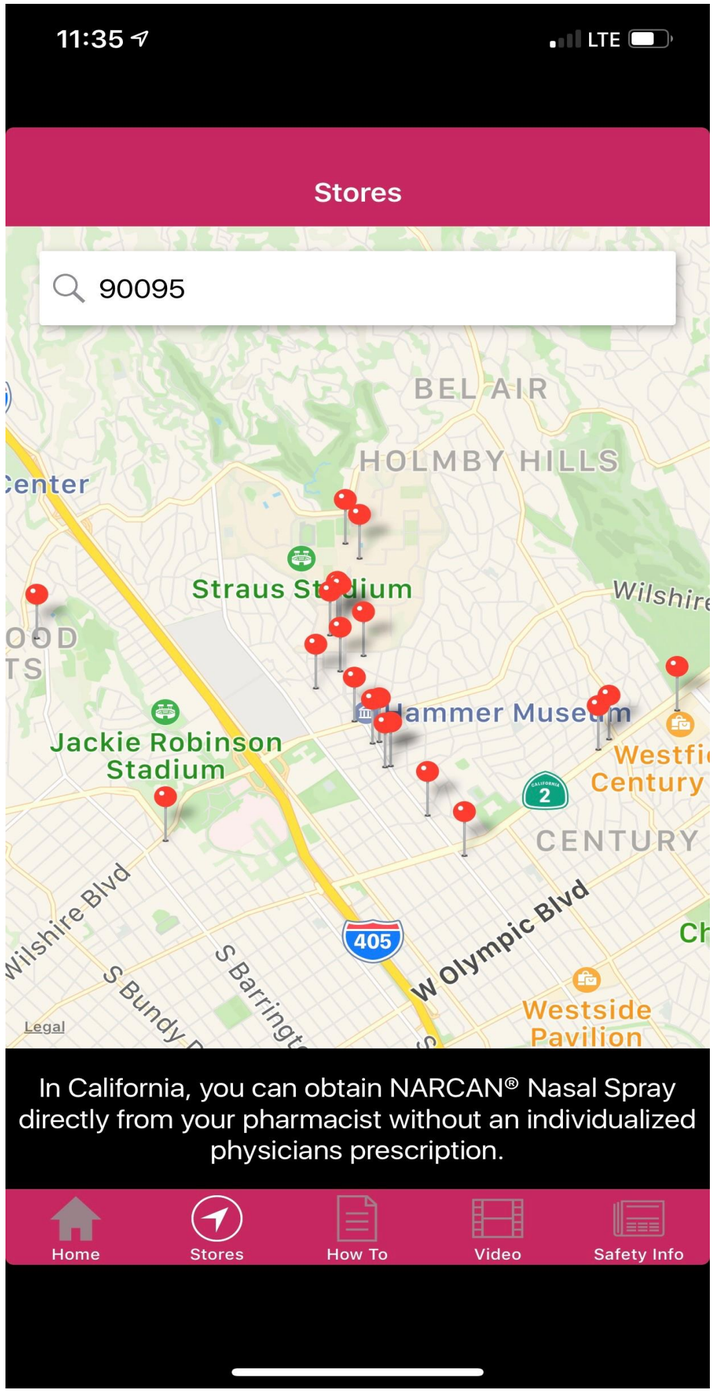
Project ECHO®
University of California Los Angeles
Integrated Substance Abuse Programs

Narcan Now App

Project ECHO®

University of California Los Angeles
Integrated Substance Abuse Programs

Project ECHO®
University of California Los Angeles
Integrated Substance Abuse Programs



Enter zip code in the app to find nearest pharmacy to obtain naloxone

Project ECHO®

University of California Los Angeles
Integrated Substance Abuse Programs

Where to Get Naloxone

DHCS

Services

Naloxone Distribution Project

https://www.dhcs.ca.gov/individuals/Pages/Naloxone_Distribution_Project.aspx

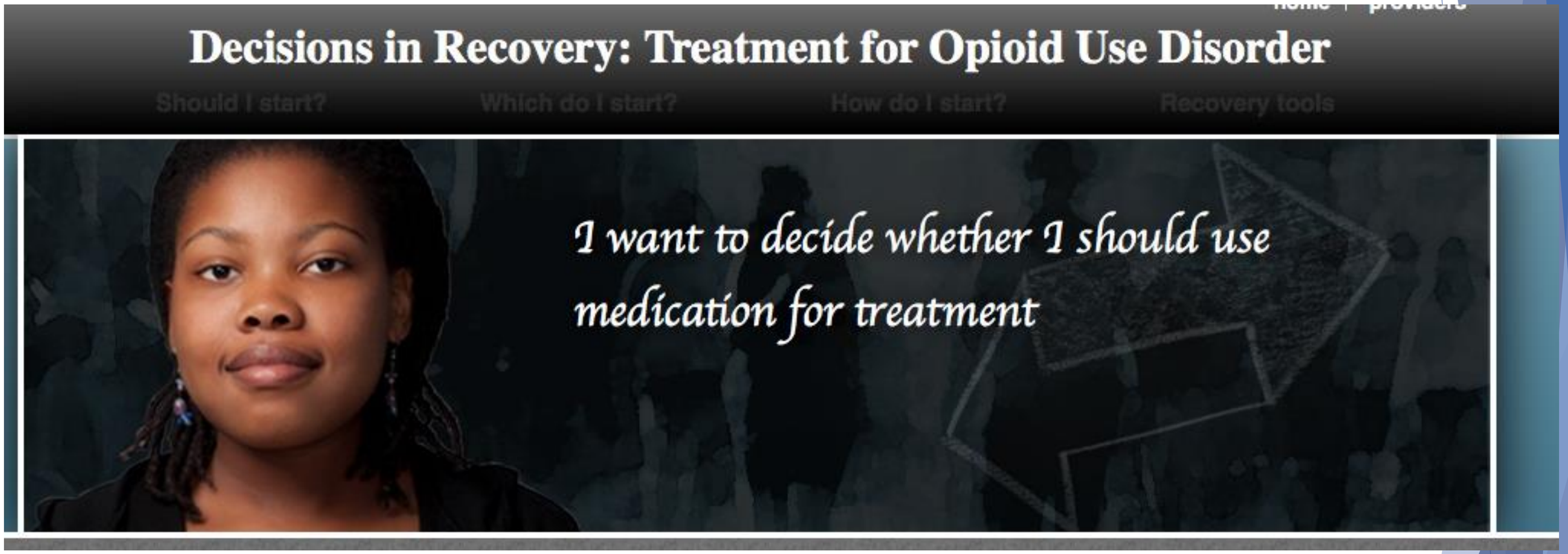
Project ECHO®

University of California Los Angeles
Integrated Substance Abuse Programs

In Southern California

Project ECHO®
University of California Los Angeles
Integrated Substance Abuse Programs

SAMHSA Decisions in Recovery Tool



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

Project ECHO®
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