

# Opioid Substitution in Primary Care Practice

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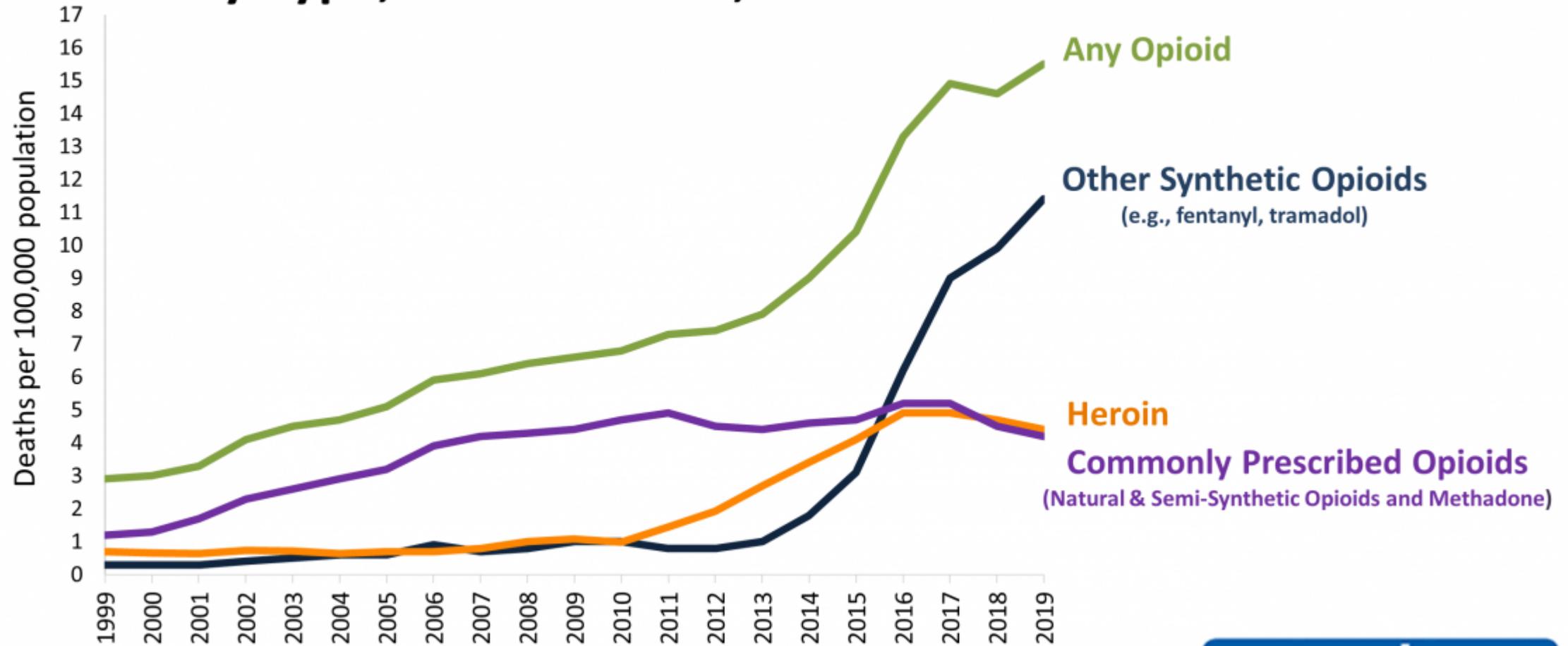
# Opioid deaths by year

30% increase

40% increase in monthly opioid overdose death rate in May  
2020



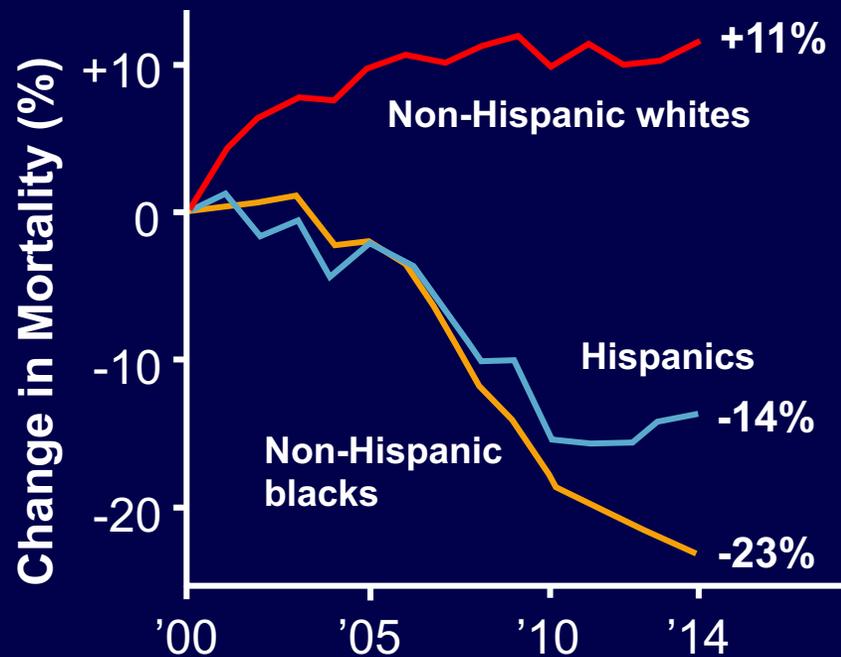
# Overdose Death Rates Involving Opioids, by Type, United States, 1999-2019



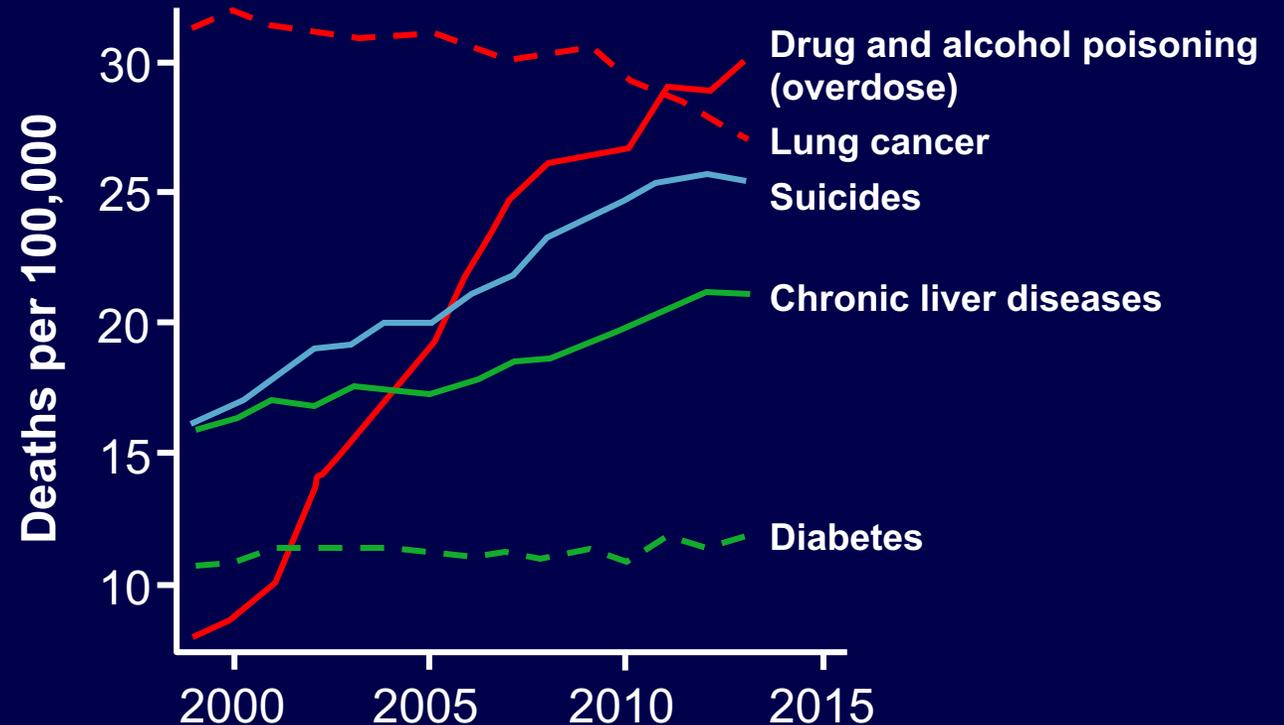
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2020. <https://wonder.cdc.gov/>.

# Contributors to US Mortality

Overall Mortality Among US Adults Aged 25-54 Yrs



Overall Mortality Among US Non-Hispanic White Adults Aged 45-54 Yrs



- 1999-2014:** mortality rates increased by 34 per 100,000 for middle-aged whites, 134 per 100,000 for middle-aged whites with high school degree or lower

# The Opioid Epidemic – Medical Complications

- **Many people who misuse prescription opioids progress to injection of other opioids (eg, heroin), which has resulted in increases in HIV and HCV**
  - Heroin use increased by 60% from 2002 to 2013
- **Injected opioids have increased bacterial infections (eg, endocarditis, osteomyelitis, and skin/soft tissue infections) (2000 to 2013)**
  - Hospitalizations related to PWID increased from 7.0% to 12.1%
  - Injection-related endocarditis hospitalizations increased from 27.1% to 42.0% in those 15-34 yrs
  - Hospitalizations in whites increased from 40.2% to 68.9%



# HIV and Substance Use

- Substance use is associated with:
  - increased **sexual risk** behaviors,
  - increased **HIV risk** and poorer health outcomes,
  - contributing to destabilizing conditions, (e.g. **homelessness** and **mental illness**).
- ▣ **HIV, injection drug use (IDU), and opioid addiction** are intertwined.
- ▣ Since the beginning of the epidemic, one-third of all AIDS cases have been directly or indirectly related to IDU.
- ▣ For people with HIV, **untreated opioid addiction is associated with poor HIV treatment outcomes** and a host of other medical, psychosocial, and legal consequences.

From: Bruce, IAS-USA 5/18/18

# What are Opioids?

- ▣ Opioids are natural, fully semisynthetic/entirely manmade drugs.
- ▣ Opioids diminish the perception of and reaction to pain.
- ▣ They also produce feelings of euphoria.
- ▣ Heroin and some prescription medications (such as morphine, fentanyl, oxycodone, codeine, methadone and buprenorphine) are opioids.
- ▣ According to one SPNS study grantee, prescription opioid abuse may be proportional to the number of opioid prescriptions written to HIV-positive patients.

# What do Opioids do ?

- ▣ Opioids may be taken by mouth, through the skin (patch), or by a needle into the fat, muscle, or vein.
- ▣ They **attach to special opioid receptors in the brain** where they help to relieve pain.
- ▣ Some opioids cause **euphoria** (“high”) and sleepiness or, if taken in large amounts, **unconsciousness that may progress to death** (overdose).
- ▣ Other side effects may include itching, headache, nausea, constipation, confusion, slow pulse, and slow breathing.
- ▣ Some opioids last a few hours and some more than a day.

# What do Opioids do? (cont.)

**Any person** who uses opioids regularly may become **physically dependent** on them.

This means that you need more drug over time to get the same effect (**tolerance**) and that you have **withdrawal** symptoms if you stop using the drug.

# Why do people take drugs?

**To feel  
good**

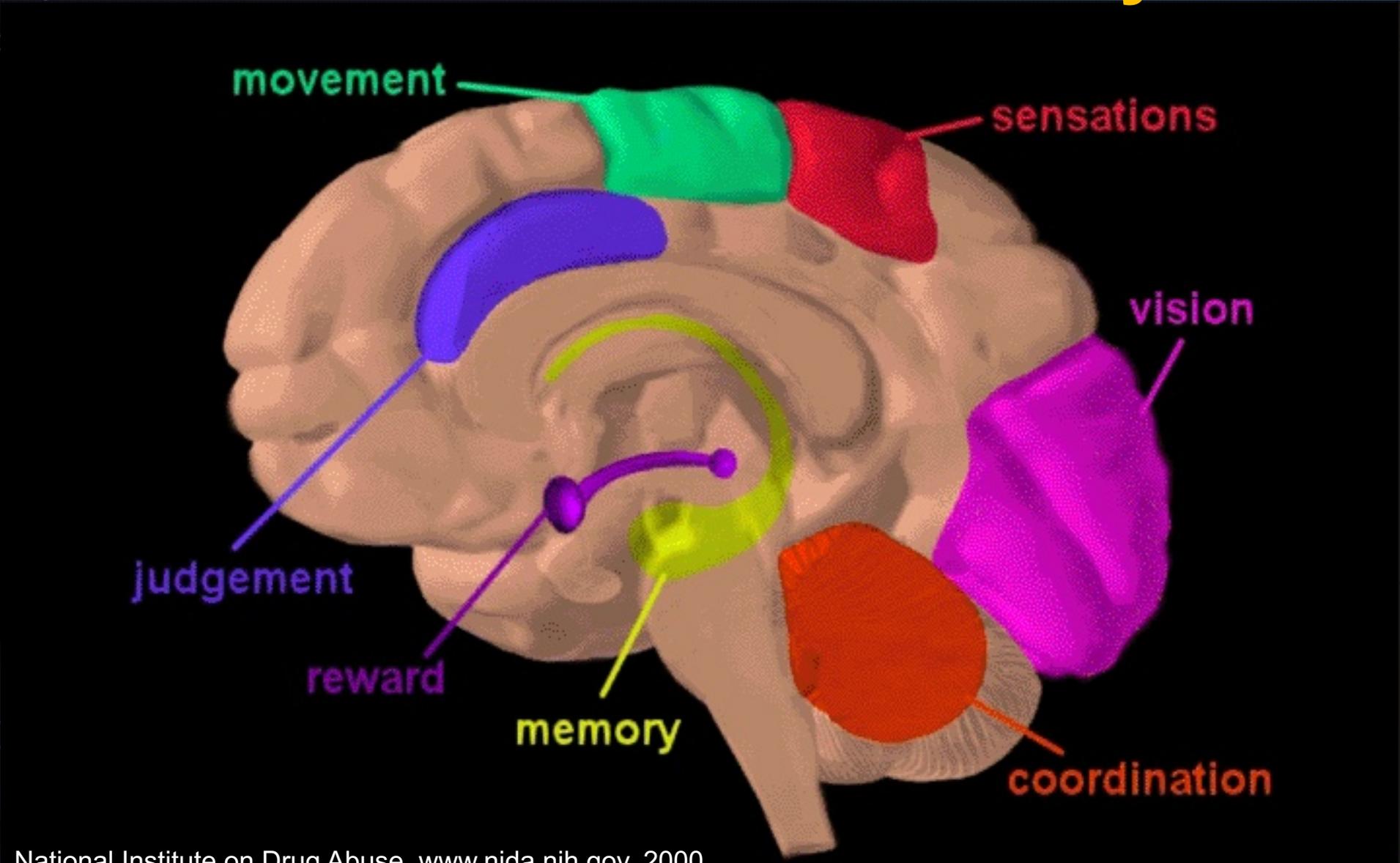
To have novel:  
feelings  
sensations  
experiences  
**AND**  
to share them



**To feel  
better**

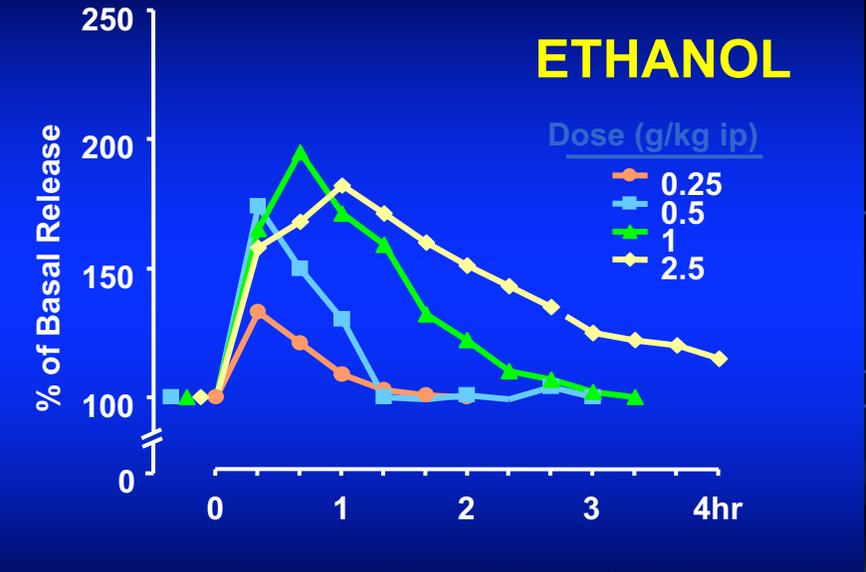
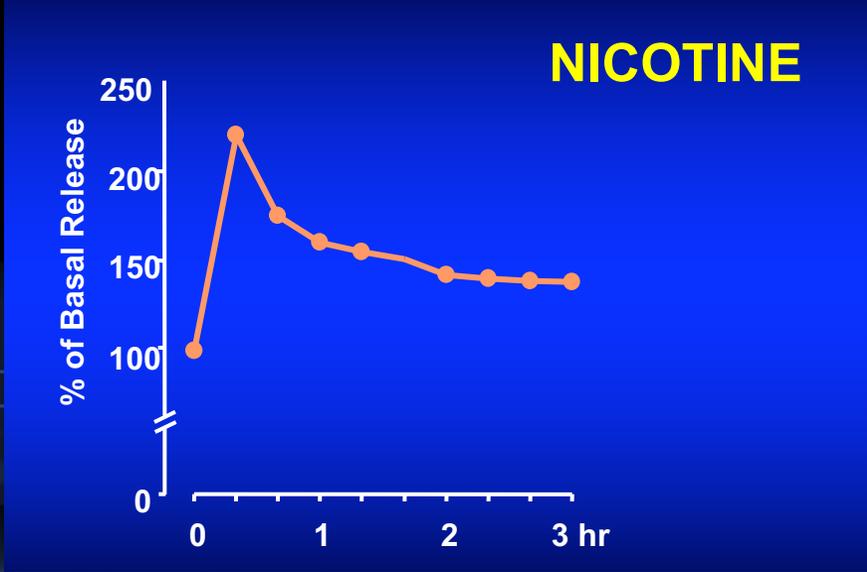
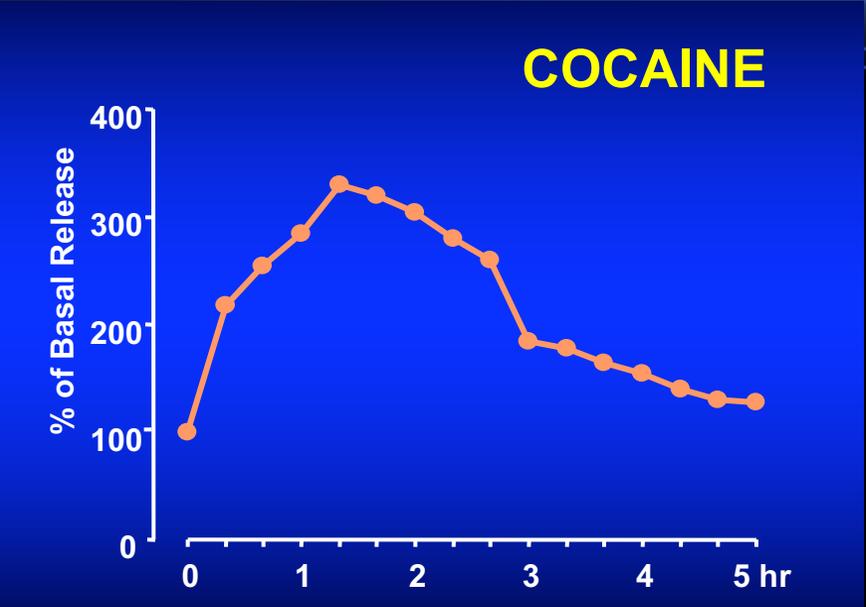
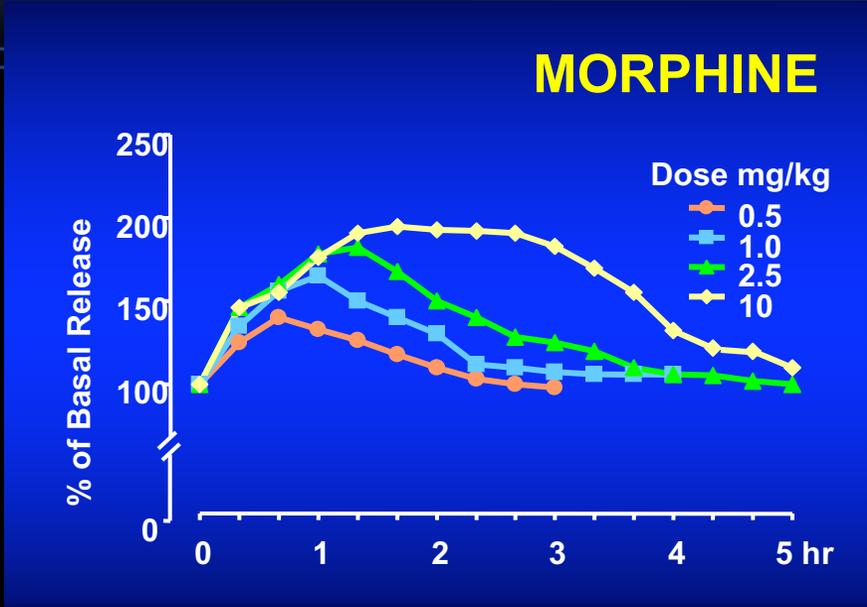
To lessen:  
anxiety  
worries  
fears  
depression  
hopelessness

# Pleasure-Reward Pathways

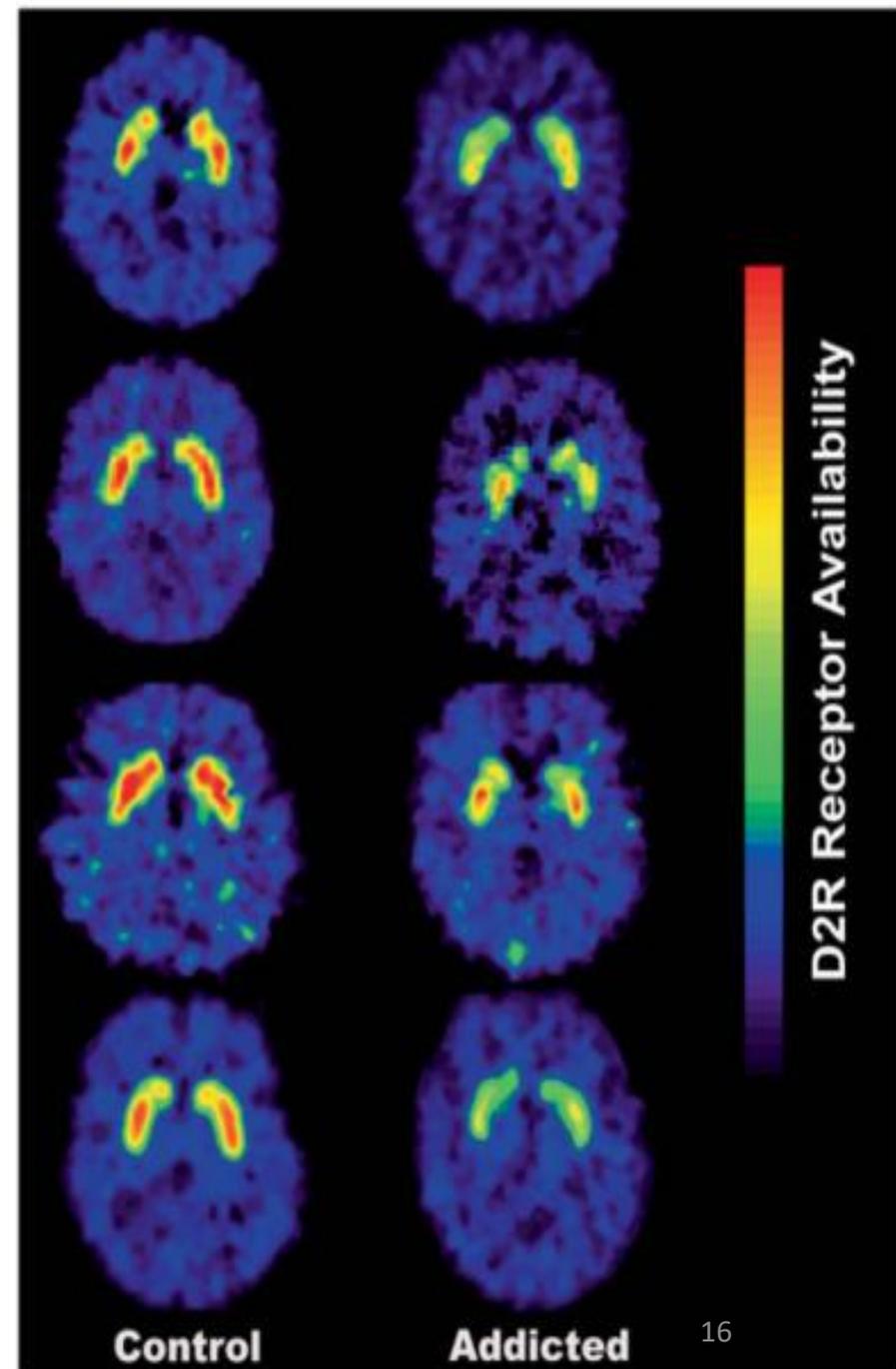


National Institute on Drug Abuse, [www.nida.nih.gov](http://www.nida.nih.gov), 2000.

# Effects of Drugs on Dopamine Levels



# Brain changes:





# Addiction

- A state in which a person engages in compulsive behavior
  - The behavior is **reinforcing** (that is, pleasurable or rewarding)
  - There is a **loss of control** in limiting the intake of the substance

# Addiction is a Brain Disease

- ▣ **Over time, nerve cells in the brain learn to crave opioids.**
- ▣ **When opioids are not present, the opioid receptors send pain signals to the rest of the brain (withdrawal).**
- ▣ **This is a physical condition, not caused by a lack of willpower or morals and not cured by good advice.**
- ▣ **Addiction is a chronic and treatable disease, like diabetes and heart disease.**



# Opioid Use Disorder

- Chronic, relapsing disease involving brain reward, motivation, and related circuitry characterized by compulsive drug seeking and use despite harmful consequences<sup>[1,2]</sup>
- Ongoing opioid use results in altered neurotransmitter (dopaminergic) and metabolic (cAMP) pathways<sup>[3]</sup>
- Abstinence-based programs have low success rates<sup>[4,5]</sup>
- Best treated with long-term pharmacological therapies targeting the mu receptor, with longer-term retention on treatment resulting in the best treatment outcomes<sup>[6]</sup>

# Language: keep it person centered

## **Standard of practice**

- Drug screen + or –
- DSM5 language: person with opiate use disorder
- Neurobiologically most correct:
  - Addiction involving xyz
- Iv drug use, intranasal use

## **Just don't**

- Dirty/ clean urine, popping +
- Addict, junkie, druggie, alcoholic, substance abuser
- “habit” “user” “pot head” “strung out” “on the needle”
- Replacement/ substitution therapy

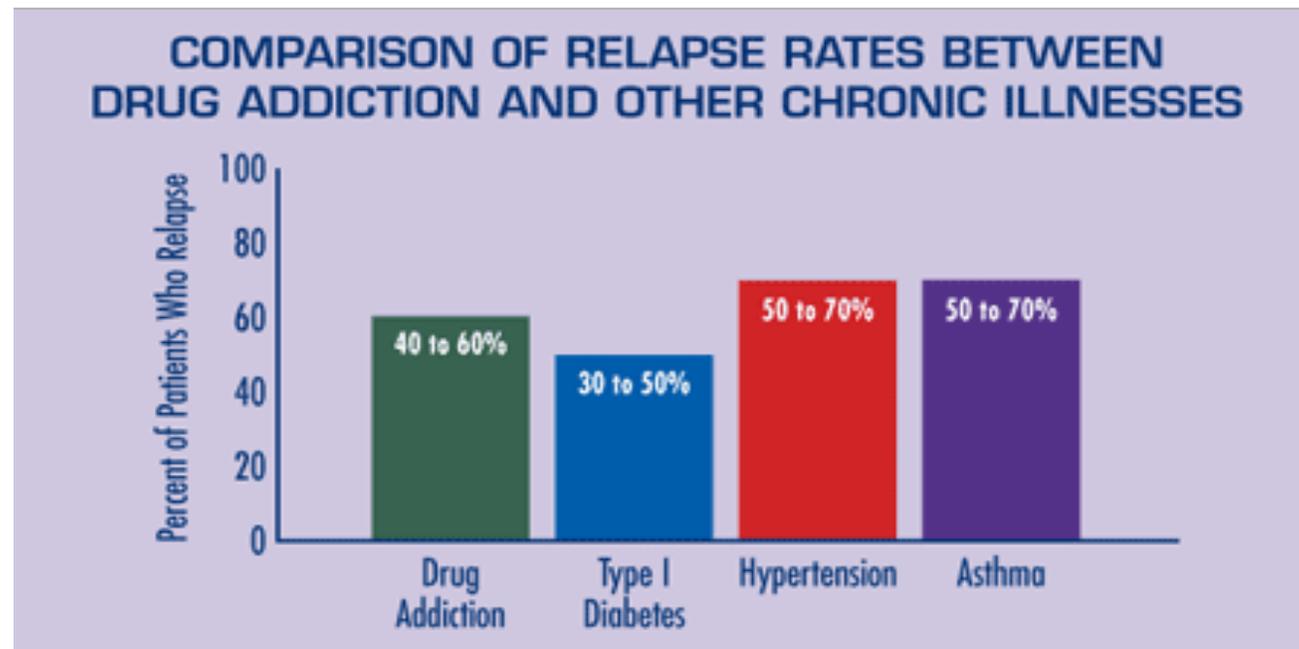
# **Medication assisted therapy /Opiate substitution**

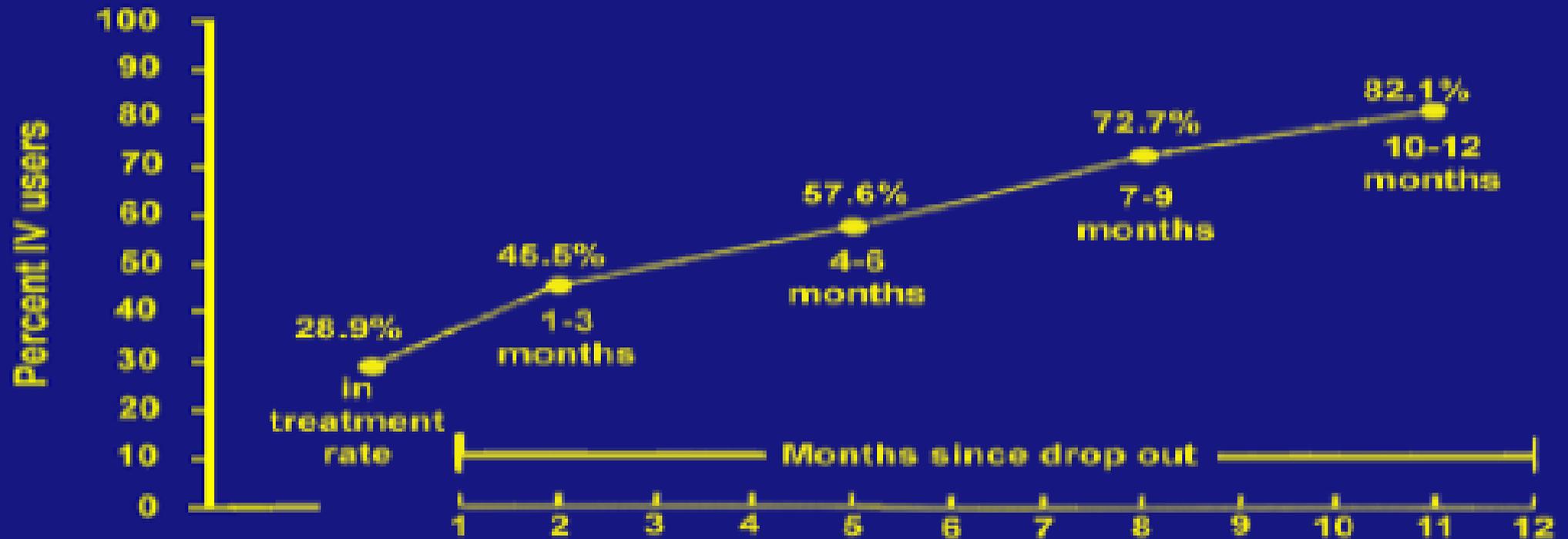
# What is medication assisted treatment?

- Opioid substitution treatment and medication assisted treatment are the same, but what is it?
- Buprenorphine and methadone can
  - reduce injection related HIV risk behavior
  - decrease psychosocial & medical morbidity
  - increase access to and retention with ARV
  - improve overall health status
  - are associated with decreased criminal activity

# More reasons for maintenance treatment:

- Relapse rate to heroin is about 70-90%
- Even with 15 years abstinence 25% relapse
- Some brain changes seem to be permanent





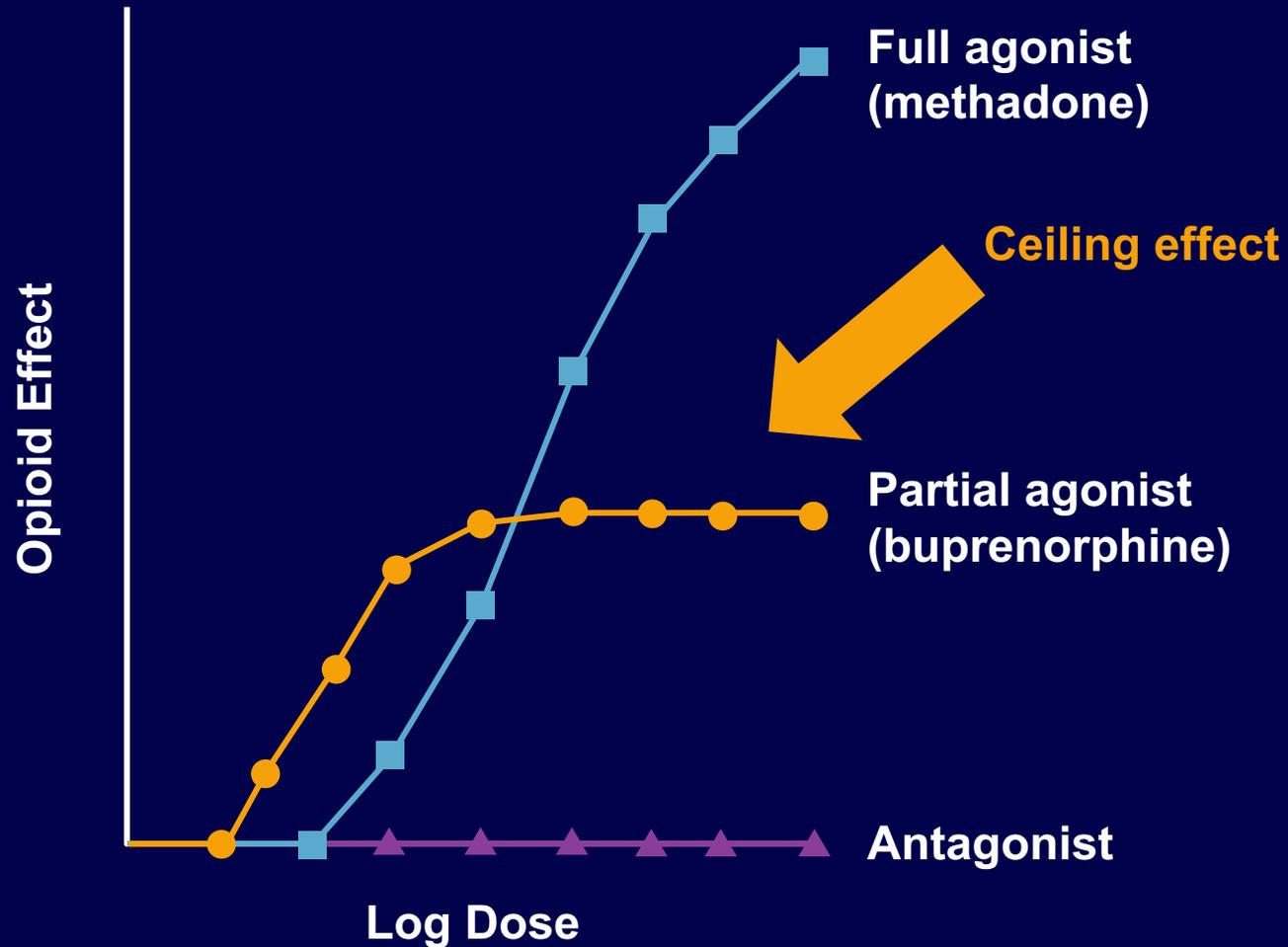
**Relapse to intravenous drug use after methadone maintenance treatment for 105 male patients who left treatment.**

From the Effectiveness of Methadone Maintenance Treatment (p. 182) by J. C. Ball and A. Ross, 1991, New York: Springer-Verlag. Copyright 1991 by Springer-Verlag New York, Inc. Reprinted with permission.

# FDA-Approved Medications

# Pharmacological Treatment Targets the Opioid Mu Receptor

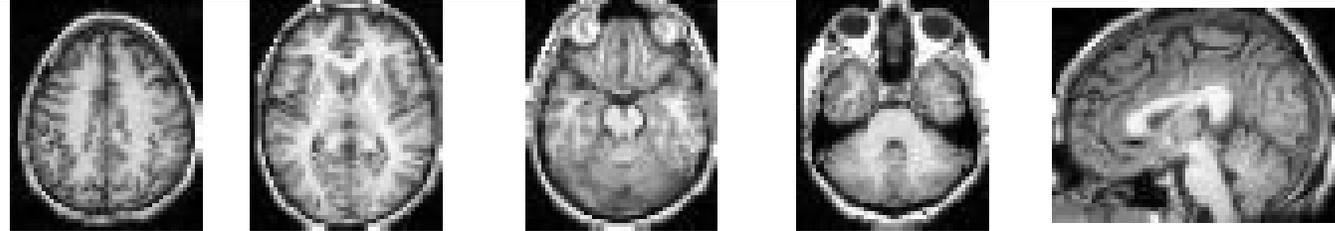
Differences in opioid effect by type of antagonism of mu receptor



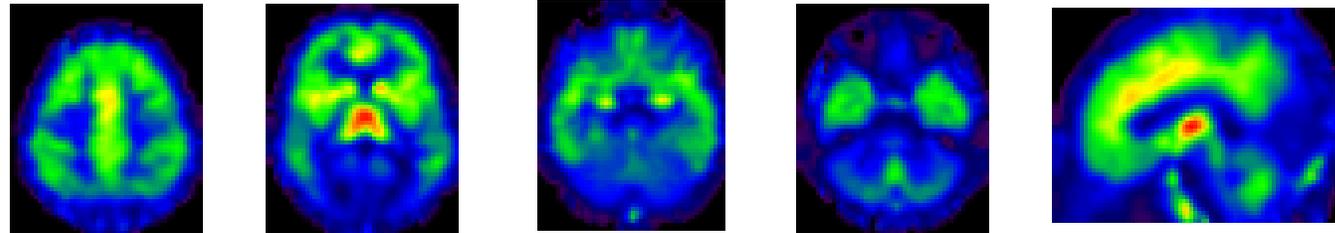
# Dose effect on mu-opioid receptor availability

Binding Potential (Bmax/Kd)

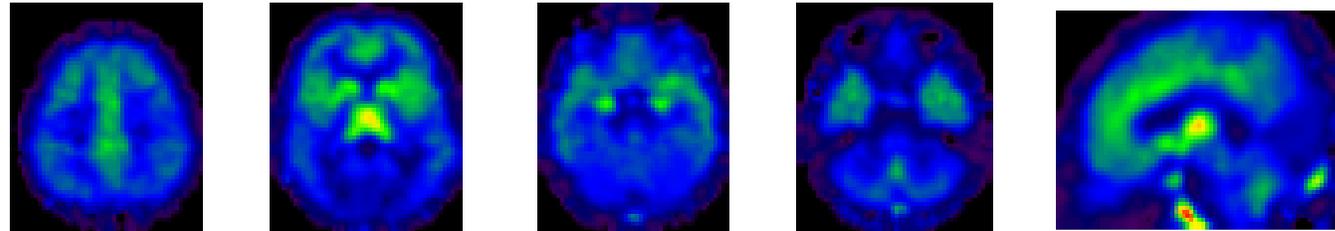
MRI



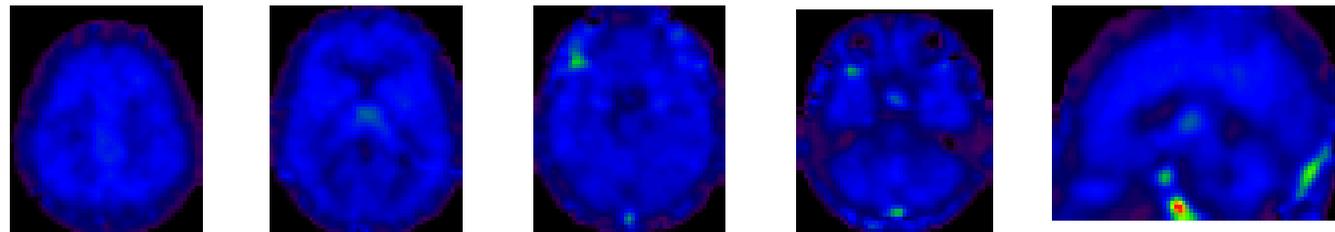
Bup 00 mg



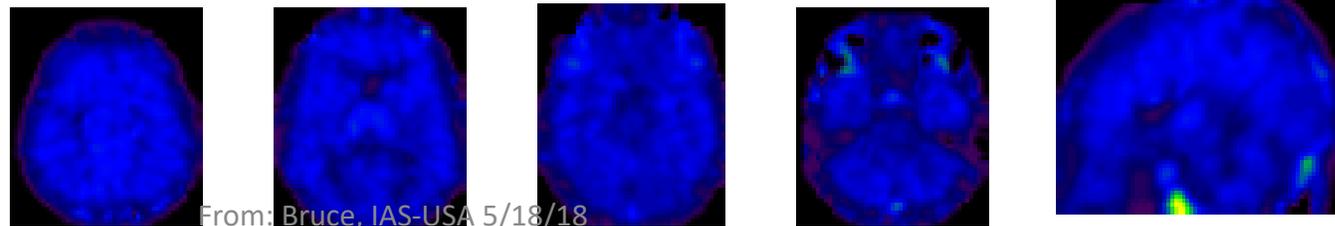
Bup 02 mg



Bup 16 mg



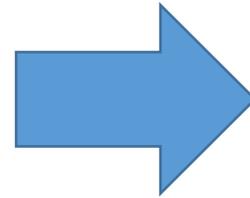
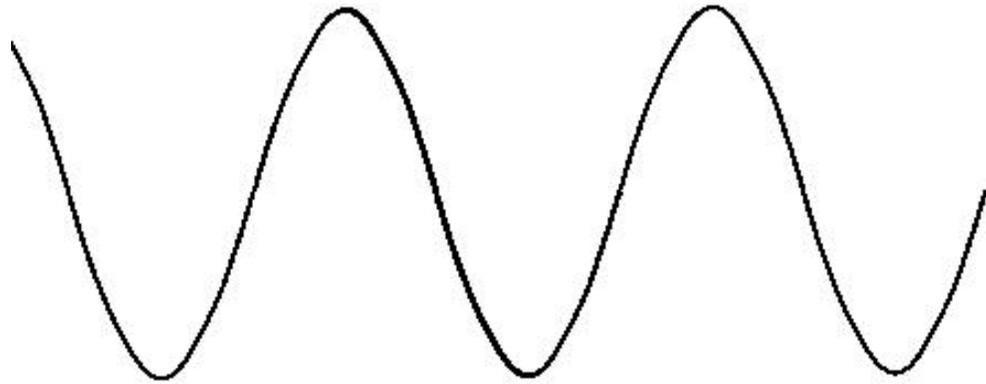
Bup 32 mg



*Slide Courtesy of Laura McNicholas, MD, PhD*

# How do those meds help treat addiction?

Cut out the highs

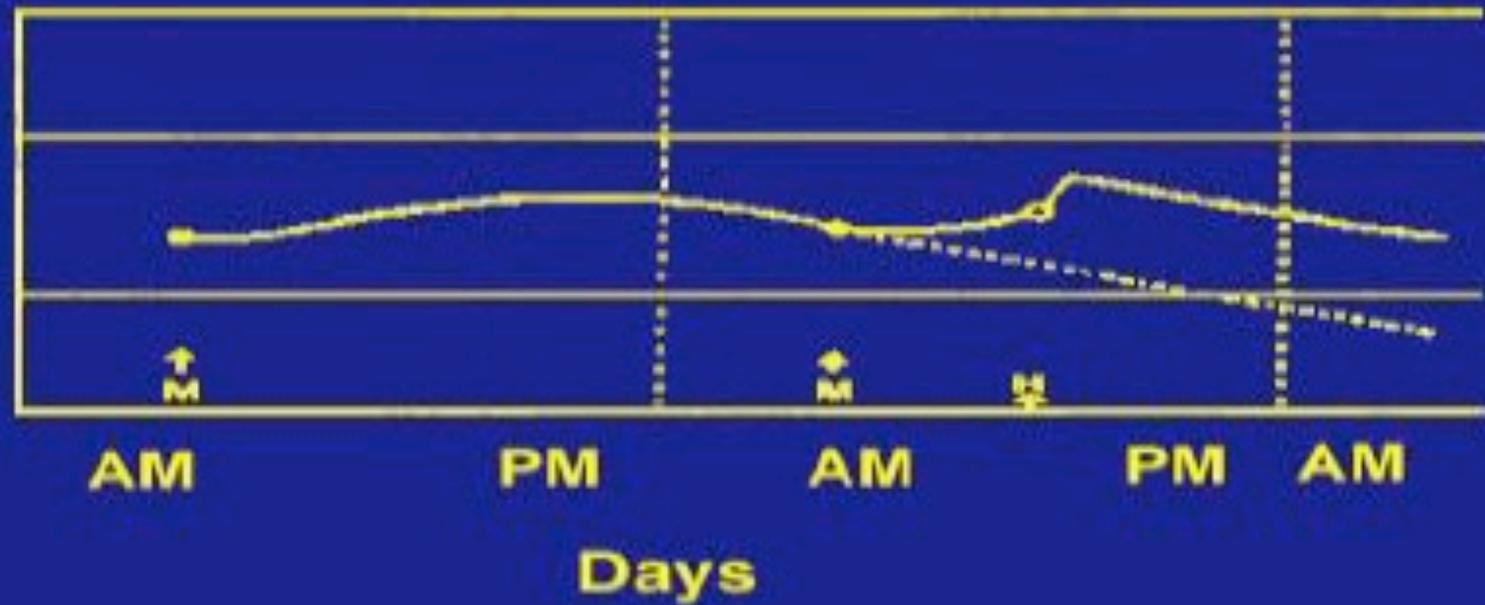


Functional state

Cut out the withdrawals

Functional state

"High"  
"Straight"  
"Sick"



**Stabilization of patient in state of normal function by blockade treatment. A single daily oral dose of methadone prevents him from feeling symptoms of abstinence ("sick") or euphoria ("high"), even if he takes a shot of heroin. Dotted line indicates course if methadone is omitted.**

From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.

# Percentage of People With Opioid Use Disorder Who Are Not Receiving Treatment: 2016

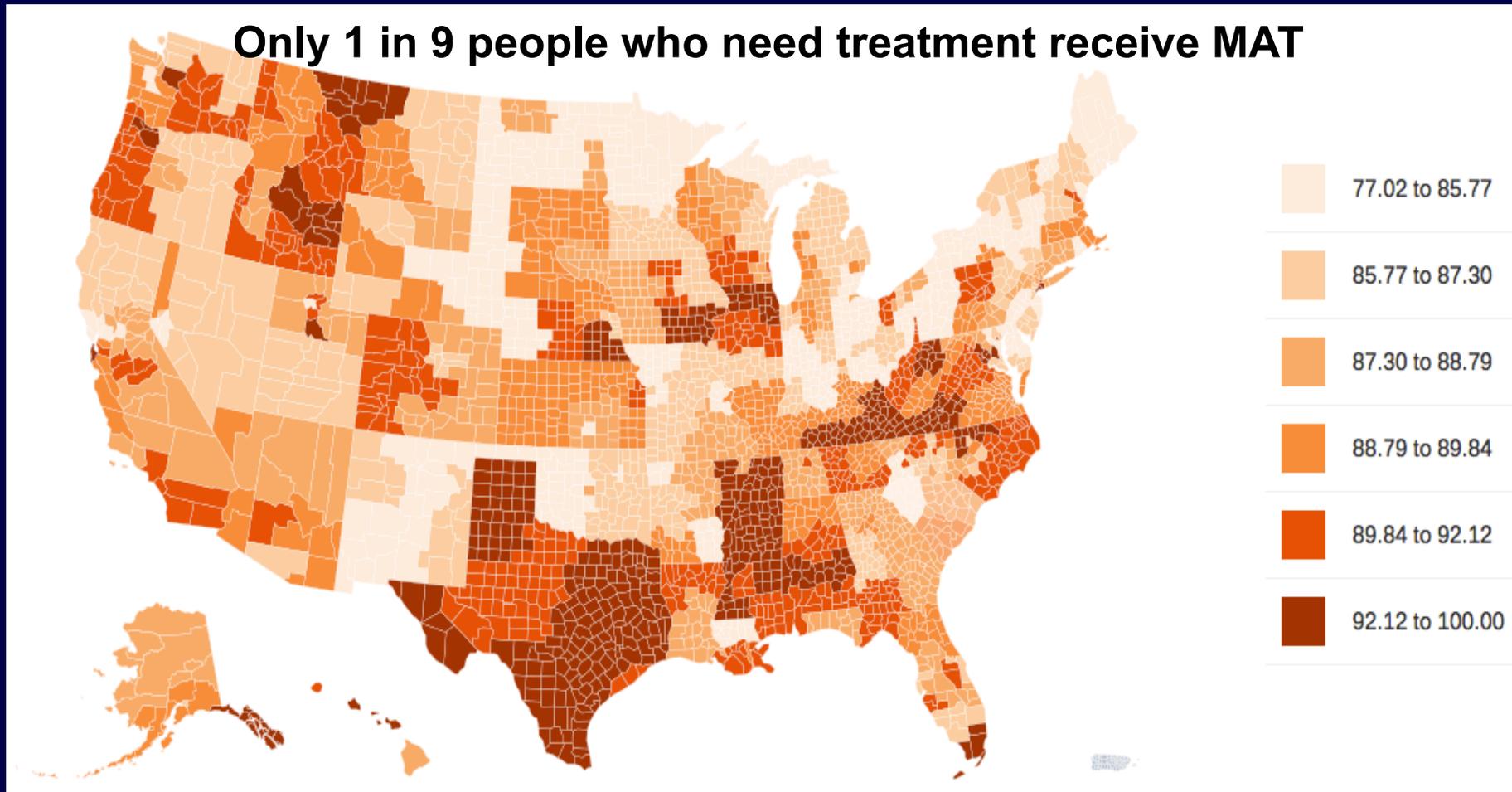


Image courtesy of amfAR. Available at:  
<http://opioid.amfar.org/indicator/pctunmetneed>.



Slide credit: [clinicaloptions.com](http://clinicaloptions.com)

# OUD Medications Overview: Methadone

- **Appropriate Patients:** Physiologically dependent and meet federal criteria for Opioid Treatment Program (OTP) admission.
- **Action:** Reduces withdrawal and craving; blunts or blocks illicit opioids' euphoric effects.
- **Patient Education:** Dose will start low. OD is a risk during the first 2 weeks (especially with benzodiazepine or alcohol use) and after stopping methadone.
- **Administration:** Oral methadone is taken daily.
- **Prescribers:** Only SAMHSA-certified OTPs can administer or prescribe methadone
- **Restrictions and requirements:** Only federally certified and accredited OTPs can dispense methadone for OUD.

*Some exceptions allow for the additional provision of methadone or buprenorphine.*

# What is Buprenorphine, and How Does It Work?

- ▣ Buprenorphine is a partial opioid agonist, so it does not fully activate opioid receptors; therefore, its effects are milder.
- ▣ Buprenorphine works by displacing other opioids from their receptors and binding to the same receptors, thereby preventing withdrawal symptoms and drug cravings while blocking the effects of other opioids.
- ▣ Buprenorphine can be offered within primary care settings by qualified physicians.

Only 5% of physicians have X waiver

43% of prescribers are PCP's

Half of those are only managing 1 patient

6% of PCP prescribers manage half of the patients (mean # 107)

Over ½ of rural counties have no waived provider.

4/21

Training no longer required for physicians treating up to 30 patients  
Must still file NOI and obtain X waiver

## **1. Do I still need to apply for the X waiver?**

Yes, these guidelines exempt eligible practitioners from certification requirements related to training and the provision of psychosocial services, which were previously necessary when dispensing or prescribing buprenorphine for the treatment of opioid use disorder (OUD) to 30 or fewer patients. **Submission and approval of a Notice of Intent (NOI) remains legally necessary in order to use buprenorphine** in the treatment of patients with OUD. To indicate the qualified training exemptions when applying on the NOI website, applicants must select a training source or the system will bump them out. To apply, mid-level practitioners (APRNs and PAs) should check SAMHSA's Providers Clinical Support System (PCSS) in "CERTIFICATION OF QUALIFYING CRITERIA," then enter "practice guidelines" in the text box for the date. **Physicians should select "Other" in "CERTIFICATION OF QUALIFYING CRITERIA," then enter "practice guidelines" in the text box for the city of the training.** The training date should be the application date.

**Further information regarding how to submit a NOI and obtain a waiver, can be found here:** <https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner>.

# Buprenorphine Efficacy Summary

Studies (RCT) show buprenorphine (**16-24 mg**) more effective than placebo and **equally effective to moderate doses (80 mg) of methadone** on primary outcomes of:

- Retention in treatment
  - Abstinence from illicit opioid use
  - Decreased opioid craving
  - Decreased overall mortality
  - Improved occupational stability
  - Improved psychosocial outcomes
- 50% decrease in deaths from opioid use/overdose

Johnson et al. *NEJM* 2000

Sordo L et al. *BMJ* 2017

Fudala PJ et al. *NEJM* 2003

Mattick RP et al. *Cochrane Syst Rev* 2014

Kakko J et al. *Lancet* 2003

Parran TV et al. *Drug Alcohol Depend* 2010

Alford, ACP 2019

# Three Phases of Buprenorphine Treatment

1. Induction
1. Stabilization
1. Maintenance – important primary care function

# Duration of OUD Treatment

- There is no “one size fits all” approach to OUD treatment.
- **Duration of treatment should be individualized and may be lifelong.**
- Given that unintended overdose can be fatal, it is critical to base patients’ length of time in treatment on their individual needs.
- Once stabilized on OUD medication, many patients stop using illicit opioids completely.

# Integrated Treatment

- OUD medication treatment should be integrated with:
  - Mental health services
  - Medical care
  - Addiction counseling
  - Recovery support
  - Outpatient and residential treatment
  - Individualized psychosocial supports
- **Comprehensive treatments address a range of symptoms and service needs.**

Behavioral treatment (AODA, support group, Narcotics Anonymous) is desirable but not required for effective buprenorphine therapy

## The Next Stage of Buprenorphine Care for Opioid Use Disorder

Stephen A. Martin, MD, EdM; Lisa M. Chiodo, PhD; Jordon D. Bosse, MS, RN; and Amanda Wilson, MD

**Table.** Buprenorphine Care: Previous Approaches Compared With New Findings and Recommendations

Previous Approach	New Findings and Recommendations
A medical setting is needed for induction.	Home induction is also safe and effective (6).
Benzodiazepine and buprenorphine coprescription is toxic.	Buprenorphine should not be withheld from patients taking benzodiazepines (5).
Relapse indicates that the patient is unfit for buprenorphine-based treatment.	Relapse indicates the need for additional support and resources rather than cessation of buprenorphine treatment (43).
Counseling or participation in a 12-step program is mandatory.	Behavioral treatments and support are provided as desired by the patient (6).
Drug testing is a tool to discharge patients from buprenorphine treatment or compel more intensive settings.	Drug testing is a tool to better support recovery and address relapse (56).
Use of other substances is a sign of treatment failure and grounds for dismissal from buprenorphine treatment.	Buprenorphine treatment does not directly affect other substance use, and such use should be addressed in this context (43).
Buprenorphine is a short-term treatment, prescribed with tapered dosages or for weeks to months.	Buprenorphine is prescribed as long as it continues to benefit the patient (6).

# **Location of Buprenorphine Induction**

## **Previous Approach**

*A medical setting is needed for safe and effective buprenorphine induction.*

## **New Findings and Recommendations**

*Home induction is safe and effective.*

# Combining Buprenorphine With a Benzodiazepine

## Previous Approach

*Benzodiazepines and buprenorphine are a toxic combination.*

## New Findings and Recommendations

*Withholding buprenorphine because of benzodiazepine use could result in harm from untreated opioid addiction that outweighs the risks of concomitant use of these medications.*

# Relapse During Buprenorphine Treatment

## Previous Approach

*Patients who experience relapse have failed buprenorphine treatment.*

## New Findings and Recommendations

*Patients who experience relapse should be provided **additional support and resources rather than cessation of buprenorphine treatment.***

# Requirements for Counseling

## Previous Approach

*Traditional counseling is needed to benefit from buprenorphine treatment.*

## New Findings and Recommendations

*Traditional **counseling** is not necessary for successful outcomes in buprenorphine treatment.*

# Uses of Drug Testing

## Previous Approach

*Drug testing indicates which patients are unsuccessful and should be removed from buprenorphine treatment.*

## New Findings and Recommendations

*Drug testing is a **tool for supporting recovery rather than a method of punishment.***

# Use of Other Substances During Buprenorphine Treatment

## Previous Approach

*Patients who use other substances are not appropriate candidates for buprenorphine treatment.*

## New Findings and Recommendations

*Buprenorphine does not have a direct effect on other substance use, and **this use should generally not influence care for OUD.***

# Duration of Buprenorphine Treatment

## Previous Approach

*Buprenorphine treatment can readily be discontinued.*

## New Findings and Recommendations

*Patients should receive buprenorphine as long as it provides benefit.*

From: The Next Stage of Buprenorphine Care for Opioid Use Disorder

Ann Intern Med. 2018; 169(9):628-635. doi:10.7326/M18-1652

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Initial U.S. recommendations for buprenorphine treatment were unintentionally restrictive. These restrictions have been associated with a shortfall of prescribers and barriers to care for patients. Recent evidence-based recommendations more readily support initial and ongoing individualized care. Practices and policymakers should update their approaches on the basis of this evidence.

# Buprenorphine: special issues

- Urine drug testing
  - Random vs convenience
  - Witnessed vs unwitnessed
  - Test for buprenorphine
- Suspected diversion
  - Helps users self treat and reduce opioid use when out of care
  - Increase in non-prescribed buprenorphine associated with decreased overdose risk
- Telemedicine
  - In person visits no longer required (even initial visit; phone visits ok)
  - Canadian study – compared to in person care, similar retention, lower relapse rate
- Treating acute pain (especially postop) in a buprenorphine patient
- Split dosing for a drug with a half life of 20-44 hours
- Cost (buprenorphine tab < generic buprenorphine/naloxone < Suboxone film)

# Naltrexone

- ▣ Naltrexone is an opioid antagonist and another MAT option.
- ▣ Older forms of naltrexone used less commonly because of poor adherence.
- ▣ New extended-release injectable form, however, recently released from FDA.
- ▣ Offers new promise for adherence and can be offered in primary care settings.
- ▣ SAMHSA released new advisory:  
<http://store.samhsa.gov/shin/content//SMA12-4682/SMA12-4682.pdf>

# Naloxone

- For everybody!

# Resource

- [TIP 63 SAMHSA](#)
- Free!!!
- Pdf
- Assessment forms
- Consent forms

# Opioid Crisis

- **Rapidly growing numbers of Americans are dying from opioid overdose.**
- Healthcare professionals and policymakers have a responsibility to expand access to evidence-based care.
- **OUD medications are safe and effective** when used appropriately.
- **OUD medications reduce illicit opioid use**, keep people in treatment, and reduce the risk of opioid overdose death.
- Treatment with OUD medication should be considered for all patients with OUD.
- OUD should be approached as a chronic illness.
- **Chronic care management is effective.**

## Buprenorphine resources for providers

The [Providers Clinical Support System](#) offers free waiver trainings for physicians (eight hours) and advanced practice clinicians (24 hours). The organization also [pairs recently trained clinicians with more experienced mentors](#) to help them start prescribing.

<https://pcssnow.org/mentoring>

- The American Society for Addiction Medicine also offers [training in opioid use disorder treatment](#).

- <http://www.asam.org/education/live-online-cme/waiver-training>

- The Clinician Consultation Center at the University of California, San Francisco, provides [free and confidential consultations about substance use evaluation and management for clinicians](#) through the Substance Use Warmline at 855-300-3595. Consultations from experienced clinicians are available Monday through Friday between 9 a.m. and 8 p.m. ET, and voicemail is available 24/7.

- <http://nccc.ucsf.edu/clinical-resources/substance-use-resources>

- The New York University School of Medicine developed a [cartoon to guide patients through home-based buprenorphine induction](#).

- <http://bayareaaetc.org/wp-content/uploads/2016/06/bup-nx-home-induction-handout.pdf>

- The [Substance Abuse and Mental Health Services Administration \(SAMSHA\)](#) offers educational resources.

- <http://www.samhsa.gov/medication-assisted-treatment/training-resources/buprenorphine-physician-training>