- Daniel A. Nauts, MD, FASAM
- Trainer/consultant Montana Primary Care Association
- No disclosures

BUPRENORPHINE SHORT COURSE FOR NOI WAIVED PROVIDERS WITH FOCUS ON HOSPITAL-BASED MEDICINE

BUPRENORPHINE BOOTCAMP

- FOR EMERGENCY MEDICINE PROVIDERS
- AN ANDY KING AND NICK RADEMACHER PRODUCTION
- PERMISSION GRANTED FROM DRS. KING AND RADEMACHER FOR USE IN MONTANA, SLIDES ADDED AND SOME REVISIONS PER DAN NAUTS

PREREQUISITES

- Shatterproof/ACEP Stigma Video, shatterproof.org
- CA-Bridge Protocols

COURSE CONTENT

A Little Epidemiology

Neurobiology of SUD

Pharmacology of Medications for Opioid Use Disorder (MOUD)

Evidence Supporting MOUD

Making the Diagnosis

How to "Bup" in the ED/or Hospital

How to Home Induct

- Concepts of Maintenance Therapy
- Special Populations
- Management of Acute Pain
- Misc Topics

INTRODUCTION

- April 28, 2021 educational requirement no longer necessary to obtain X-waiver for those prescribing to fewer than 30 patients at one time (YOU!)
- APPs must be working under a physician with a DEA license
  - Physician does not need X waiver
- No longer required to be able to offer counseling or other ancillary services
- Everyone must submit an application through the SAMSHA website designated as a "Notice of Intent" or NOI

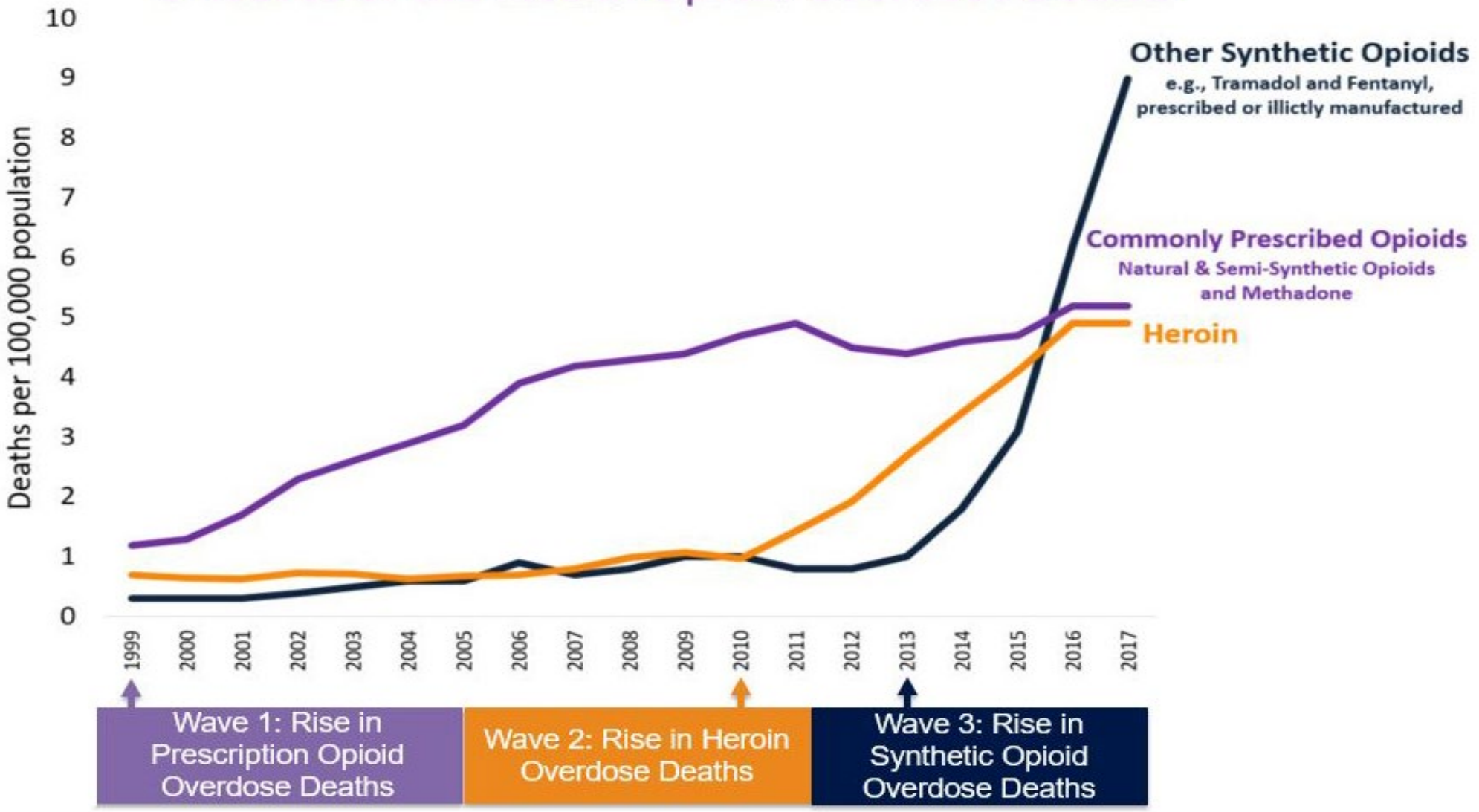
HHS Federal Register, 2021

Addiction Terminology Do's and Don'ts

Grayken Center for Addiction
Boston Medical Center

Non-stigmatizing Language	*Stigmatizing Language*
Person with a substance use disorder	Substance abuser or drug abuser Alcoholic Addict User Abuser Drunk Junkie
Babies born with an opioid dependency	Addicted babies/born addicted
Substance use disorder or addiction Use, misuse Risky, unhealthy, or heavy use	Drug habit Abuse Problem
Person in recovery Abstinent Not drinking or taking drugs	Clean
Treatment or medication for addiction Medication for opioid use disorder/alcohol use disorder Positive, negative (toxicology screen results)	Substitution or replacement therapy Medication-assisted treatment Clean, dirty

3 Waves of the Rise in Opioid Overdose Deaths



SOURCE: National Vital Statistics System Mortality File.

SCOPE OF THE PROBLEM

- For year ending August 2020 overdose deaths rose 26.8%
  - More than 88,000 total—most in 12 month span EVER (by end of 2020, over 93,000) Updated data from April 2020 to April 2021 over 100,000 deaths! Also, an increase in methamphetamine related deaths in the same time frame—"the COVID Effect"
  - Typically age 25-54
- Those with untreated OUD have 20-fold higher mortality rate
  - Overdose, infectious disease, trauma, suicide
  - Those presenting to ED post overdose with 5-10% 1-year mortality rate. If homeless increases to 50%

1. HHS Federal Register, 2021
2. Mancher, 2019
3. Weiner, 2020

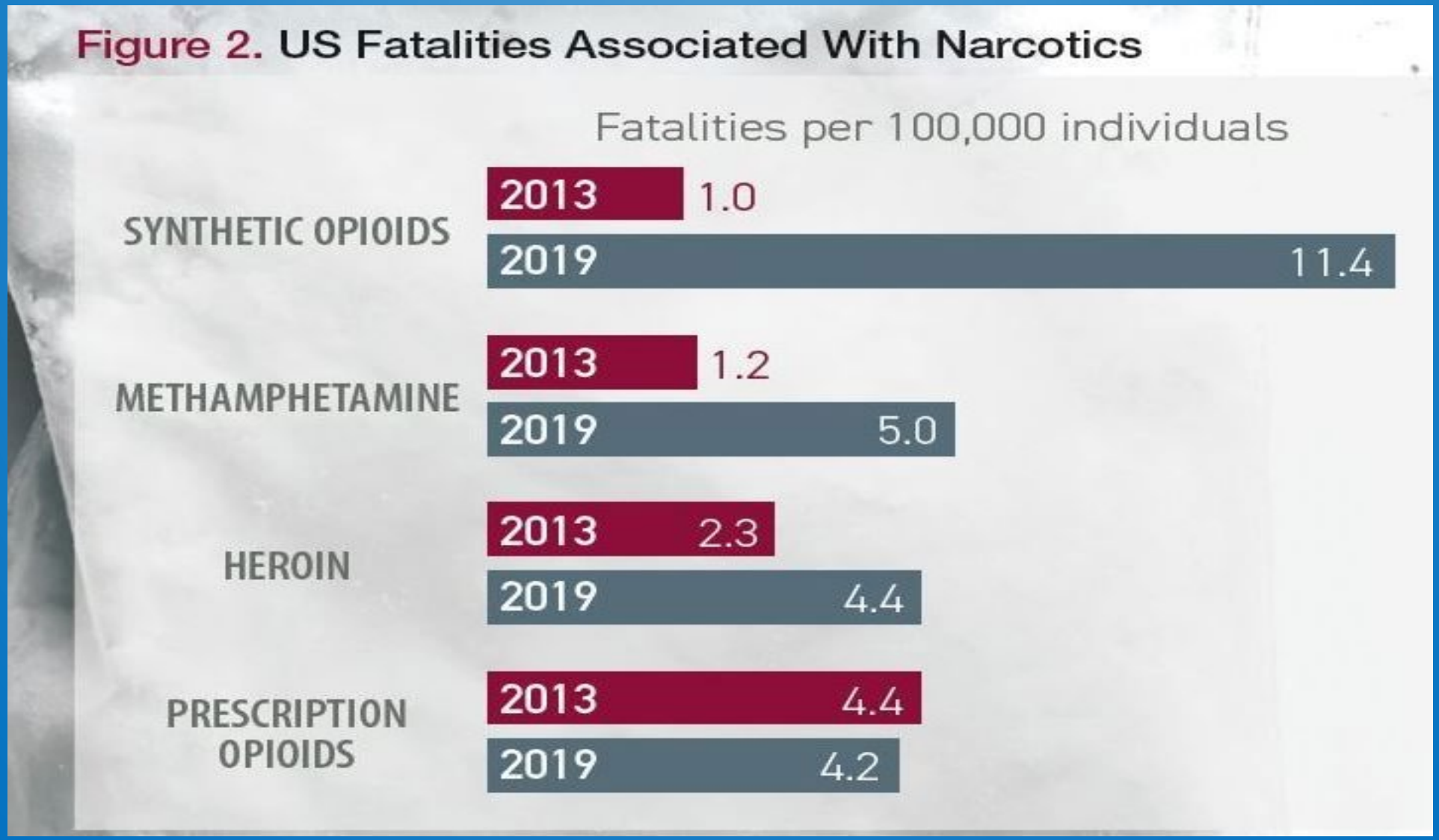
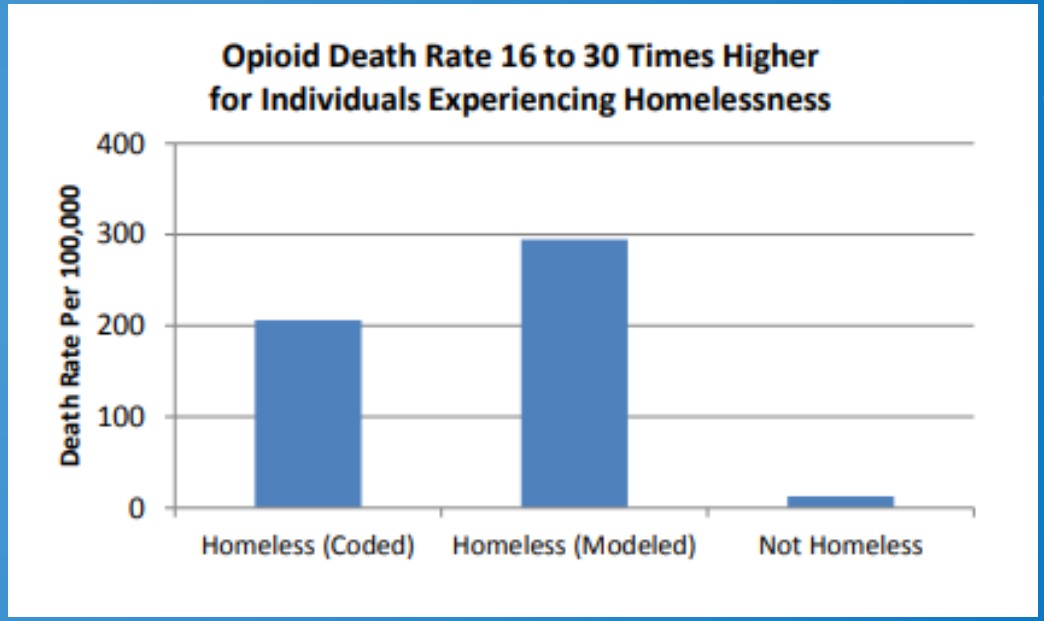
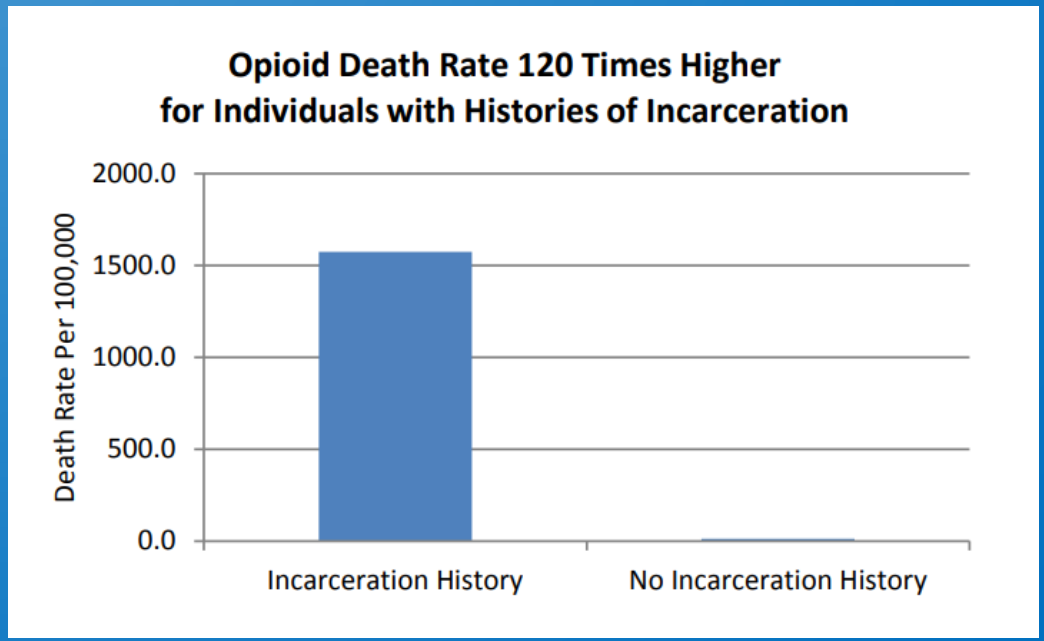


Figure 2. US Fatalities Associated With Narcotics
Fatalities per 100,000 individuals
SYNTHETIC OPIOIDS
2013 1.0
2019 11.4
METHAMPHETAMINE
2013 1.2
2019 5.0
HEROIN
2013 2.3
2019 4.4
PRESCRIPTION OPIOIDS
2013 4.4
2019 4.2

Overdose *Does* Discriminate

- Those at greatest risk of death often most marginalized
- People experiencing incarceration, homelessness, serious mental illness have markedly higher rates of overdose death
- Treatment models not designed with these populations in mind





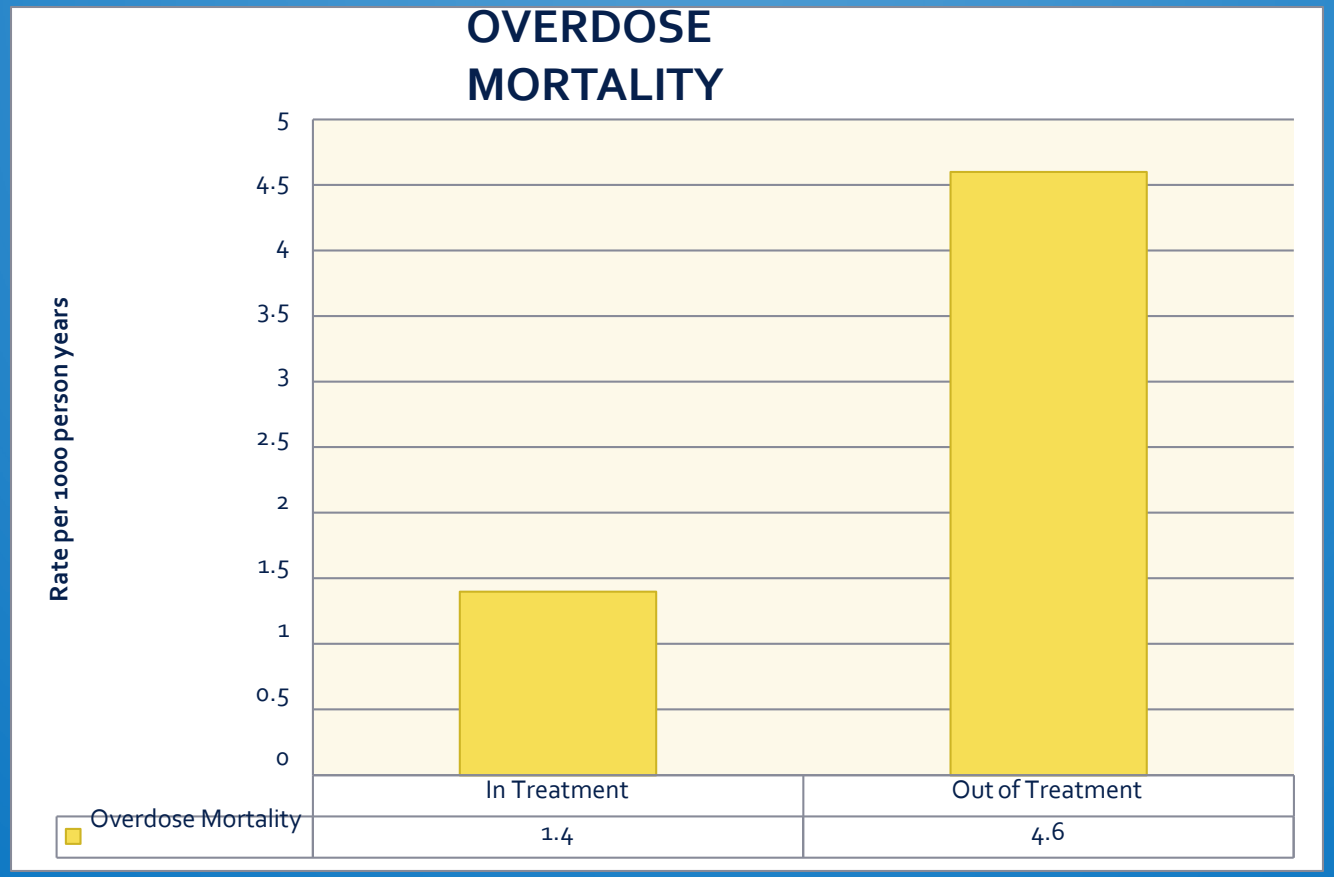
MA DPH. https://www.mass.gov/files/documents/2017/08/31/legislative-report-chapter-55-aug-2017.pdf

MOUD AND OPIOID MORTALITY 17568 OD SURVIVORS TO MOUD

- **Decrease in opioid related mortality**
  - ***59% methadone***
  - ***38% buprenorphine***
  - ***Both meds associated with a decrease in all cause mortality***

- ***No association found between Naltrexone and mortality!***
- **Marc Larochelle, Annals of Internal Med, Aug 2018**

Deaths Increase When Treatment Stopped/Unavailable



N=15 831 people treated with buprenorphine over 1.1-4.5 years (Sordo BMJ. 2017 Apr 26;357:j1550.)

Sordo et al. *BMJ* 2017;357:j1550

AMERICAN SOCIETY OF ADDICTION MEDICINE (ASAM) DEFINITION OF ADDICTION, SEPT 15, 2019

- Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with substance use disorders use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

- Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

WHICH DSM-5 CRITERIA DOES THE PATIENT MEET?

The DSM-5 defines a substance use disorder as the presence of at least 2 of 11 criteria

Criterion	Category
1. Taking more or for longer than intended	Impaired Control
2. Unsuccessful efforts to stop or cut down use	
3. Spending a great deal of time obtaining, using, or recovering from use	
4. Craving for substance	
5. Failure to fulfill major obligations due to use	Social Impairment
6. Continued use despite relationship problems caused or exacerbated by use	
7. Important activities given up or reduced because of substance use	
8. Recurrent use in hazardous situations	Risky Use
9. Continued use despite physical or psychological problems	
10. Tolerance to effects of the substance*	Physiologic Adaptation
11. Withdrawal symptoms when not using or using less.*	

* Persons who are prescribed medications are not necessarily to be considered to have a substance use disorder

Mild = 2-3 criteria, Moderate = 4-5 criteria, Severe = 6 or more criteria

MCS46

DSM-5 OUD Checklist (Part 1 of 2)

Diagnostic Criteria*	Meet Criteria? (Yes/No)	Notes/Supporting Information
Opioids are often taken in larger amounts or over a longer period of time than intended		
There is a persistent desire or unsuccessful effort to cut down or control opioid use		
A lot of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects		
Craving or a strong desire to use opioids		
Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home		
Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids		

***Opioid Use Disorder requires at least 2 criteria be met within a 12-month period.**

MCS47

DSM-5 OUD Checklist (Part 2 of 2)

Diagnostic Criteria*	Meet Criteria? (Yes/No)	Notes/Supporting Information
Important social, occupational, or recreational activities are given up or reduced because of opioid use		
Recurrent opioid use in situations in which it is physically hazardous		
Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids		
Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect (b)Markedly diminished effect with continued use of the same amount of an opioid		
Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome (b) the same – or a closely related – substance is taken to relieve or avoid withdrawal symptoms		

***Opioid Use Disorder requires at least 2 criteria be met within a 12-month period.**

DSM5 INTERVIEW

- 1. Have you found that when you started using, you ended up using more than you intended to?
- 2. Have you wanted to stop or cut down on using opioids?
- 3. Have you spent a lot of time getting or using opioids?
- 4. Have you had a strong desire or craving to use opioids?
- 5. Have you missed work or school or often arrived late because you were intoxicated, high or recovering from the night before?
- 6. Has your use of opioids caused problems with other people such as with family members, friends, or people at work?
- 7. Have you had to give up or spend less time working, enjoying hobbies, or being with others because of your opioid use?

DSM5 INTERVIEW

- 8. Have you ever gotten high before doing something that requires coordination or concentration like driving, boating, hunting, climbing a ladder, or operating heavy machinery?
- 9. Have you continued to use even though you knew that the opioid caused overdoses, infections, and emotional problems such as depression, anxiety, agitation, and irritability?
- 10. Have you found you need to use much more drug to get the same effect that you did when you first started using it?
- 11. When you reduced or stopped using, did you have withdrawal symptoms or felt “dope sick” when you cut down or stopped using?
- Mild=2-3, moderate=4-5, severe=6 or more. 1 point for each yes.

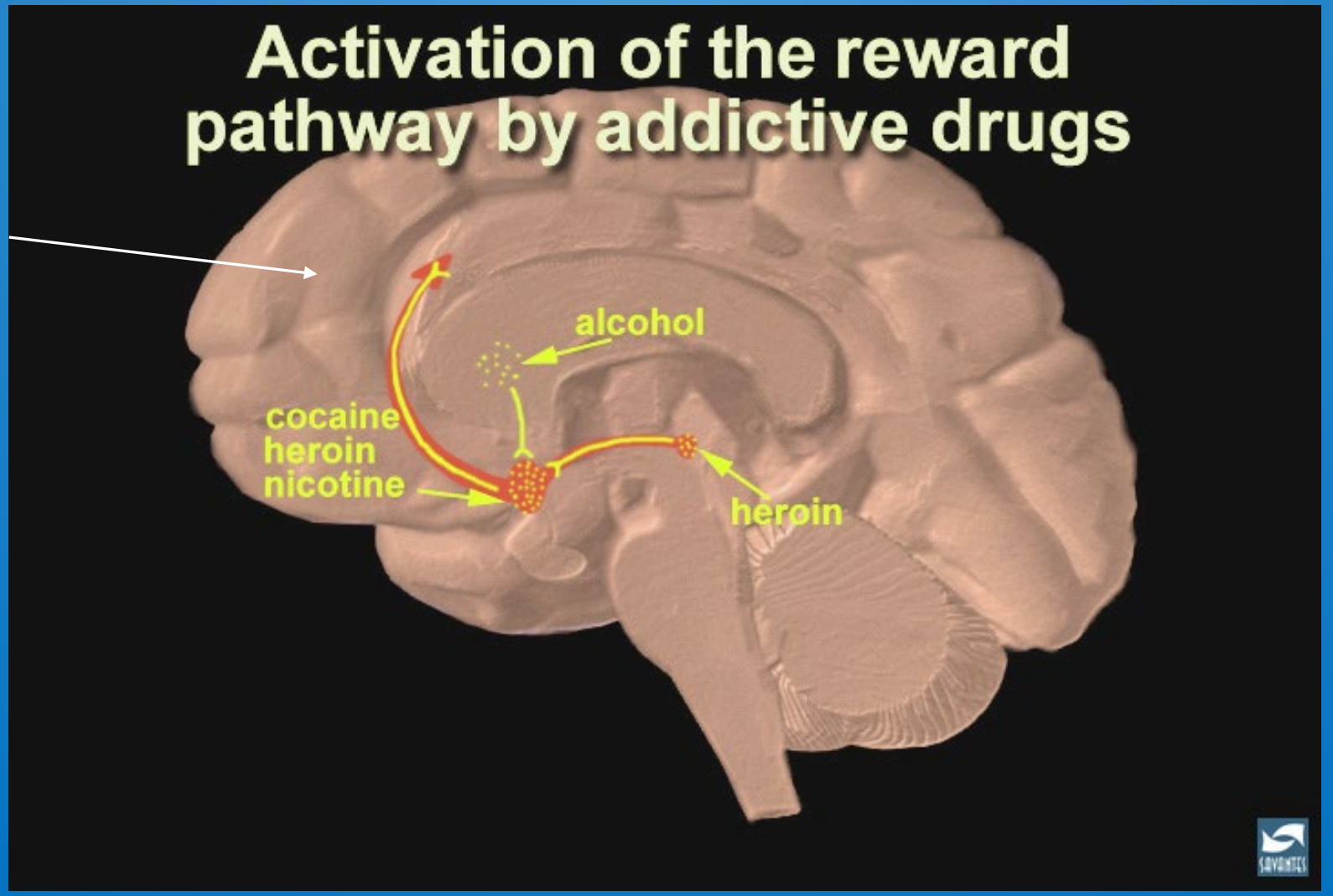
NEUROBIOLOGY OF ADDICTION

- Polymorphisms of drug receptors appear to be associated with phenotypic expression of vulnerability once opioids consumed
- Adverse Childhood Events (ACEs)
- Events surrounding first exposure are often outside the patient's control
  - Family
  - Local environment/potential recovery environment
  - Iatrogenic (the prescription opioid epidemic—Purdue Pharma and others with influence of CMS and JCAHO
- Concomitant Psychiatric Disease
  - A minority of patients with SUD have severe psychiatric illness as well, but anxiety, mood disorders, and trauma disorders common as well as personality disorders

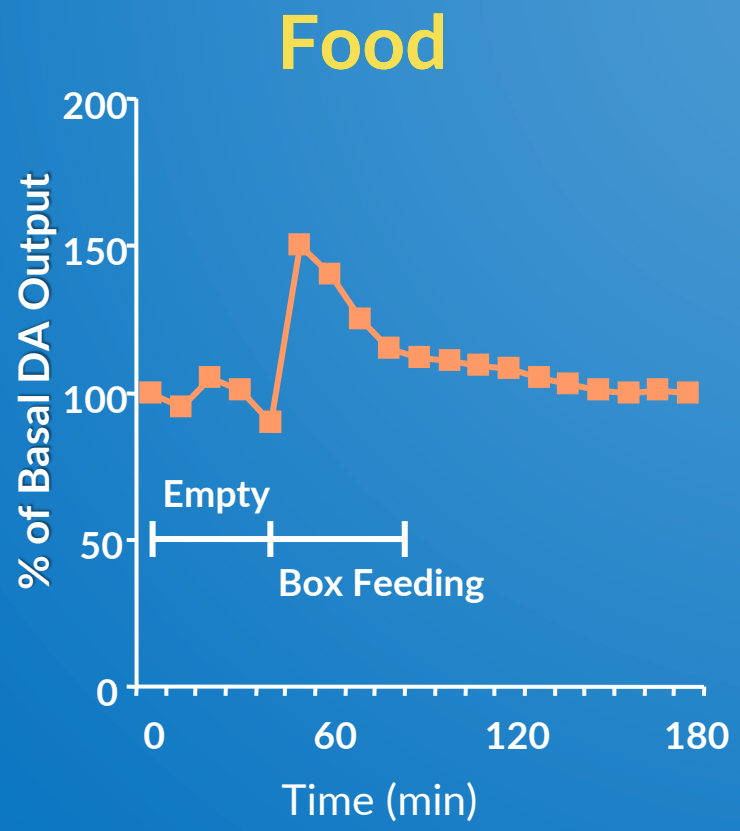
Saxon, 2005

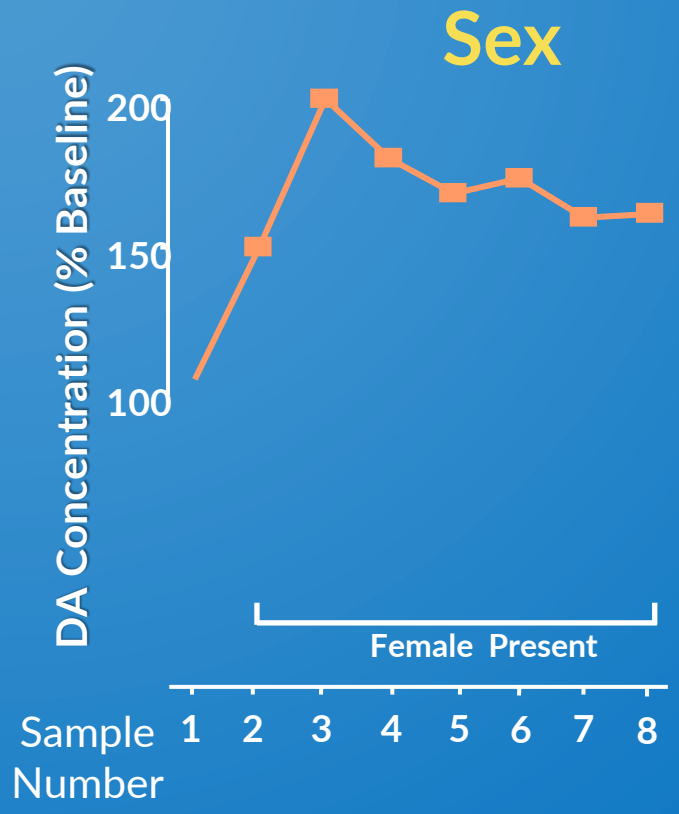
ALL ADDICTIVE DRUGS ACT DIRECTLY OR INDIRECTLY VIA DOPAMINERGIC PATHWAYS…

Dopamine



NATURAL REWARDS AND DOPAMINE LEVELS



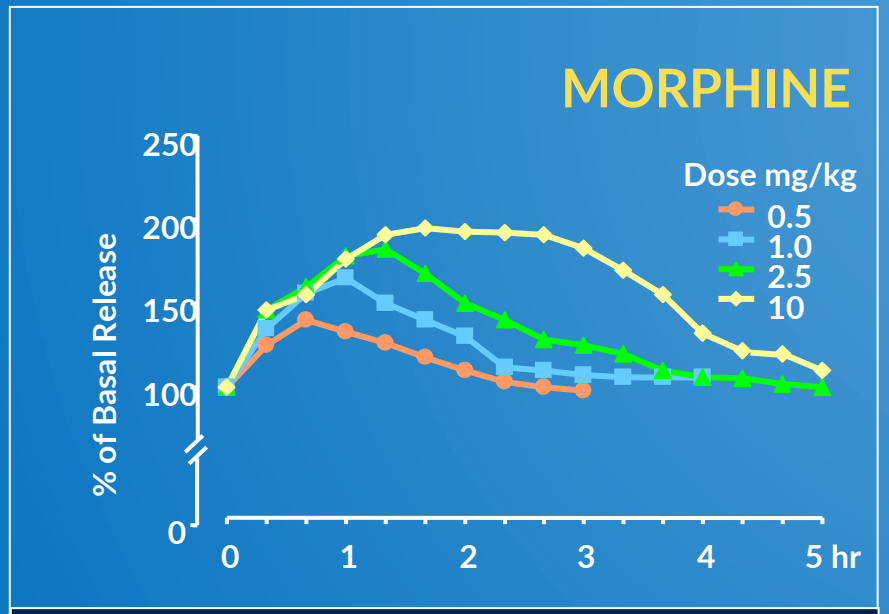


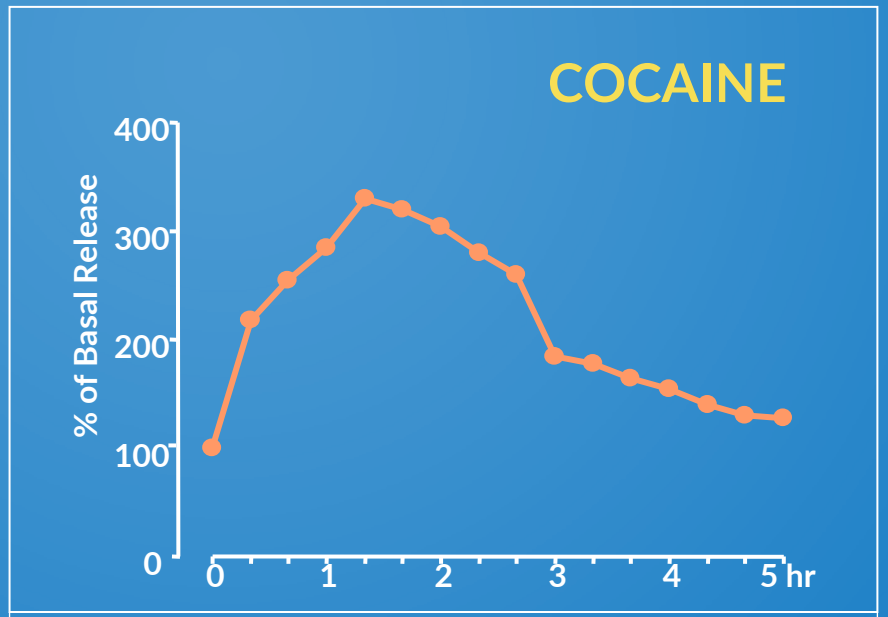
Slide courtesy of Petros Levounis, MD

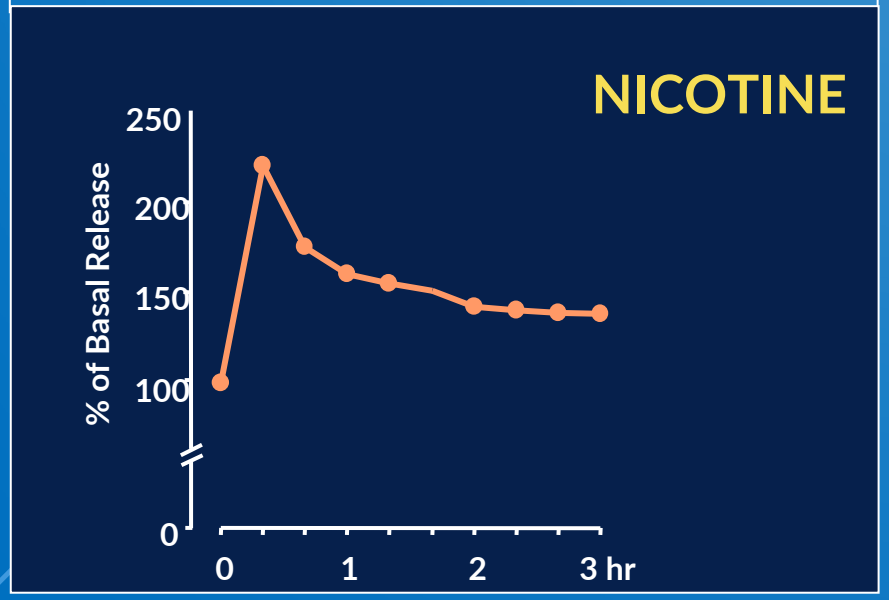
Adapted from: Di Chiara et al, *Neuroscience*, 1999

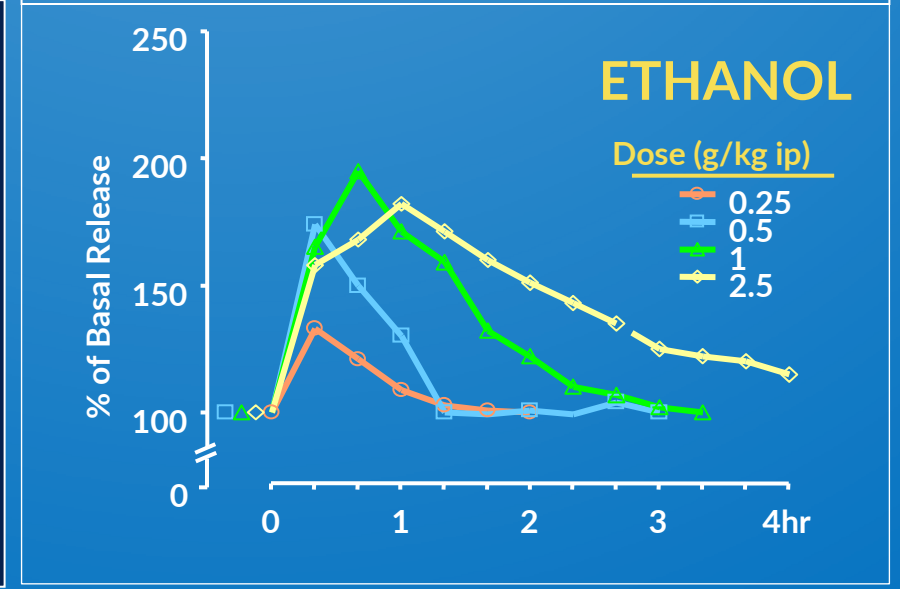
Adapted from: Fiorino and Phillips, *J Neuroscience*, 1997

EFFECTS OF DRUGS ON DOPAMINE LEVELS





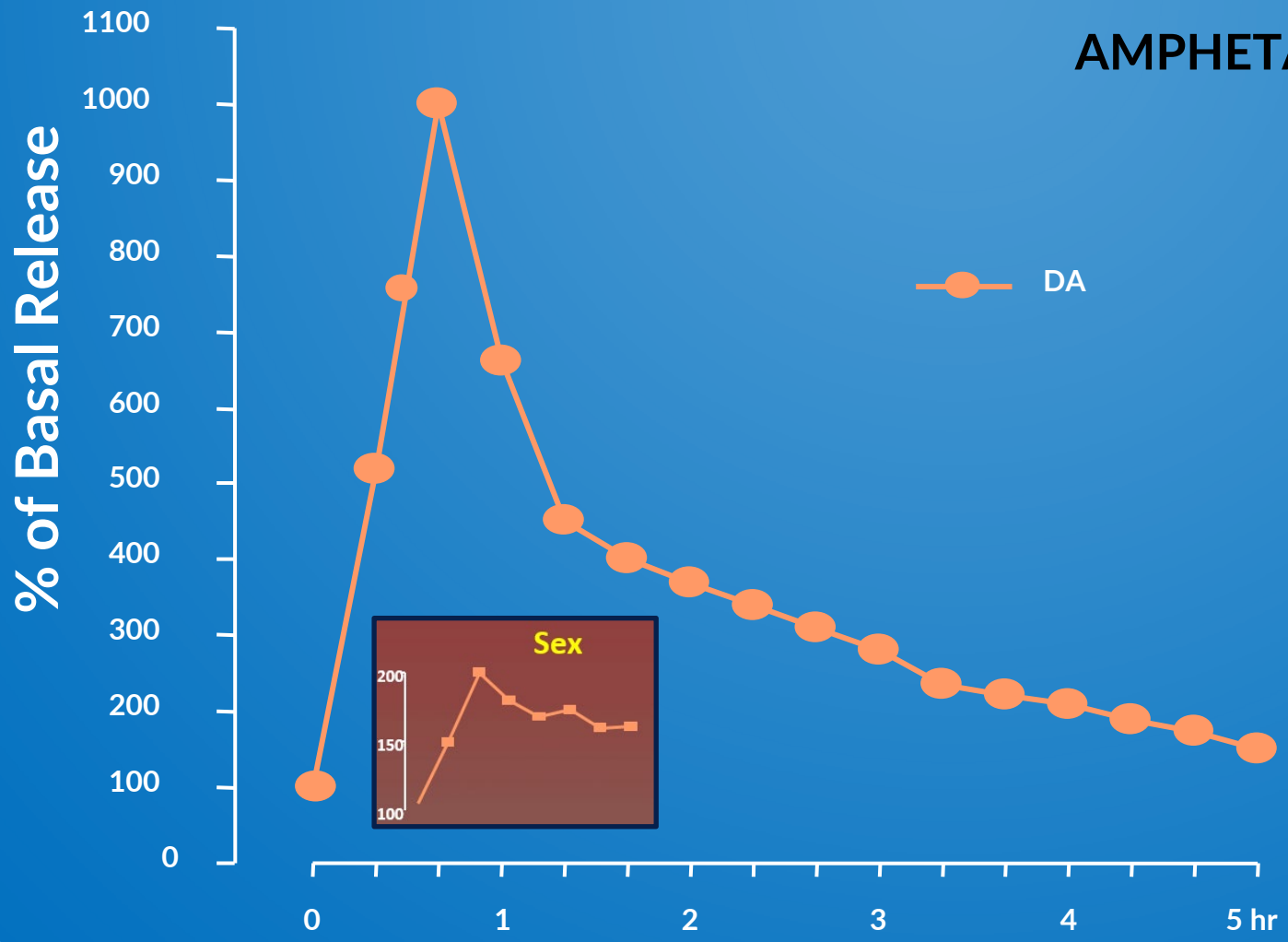




Slide courtesy of Petros Levounis, MD

Adapted from: Di Chiara and Imperato, *Proceedings of the National Academy of Sciences USA*, 1988; courtesy of Nora D Volkow, MD

EFFECTS OF AMPHETAMINES ON DOPAMINE LEVELS

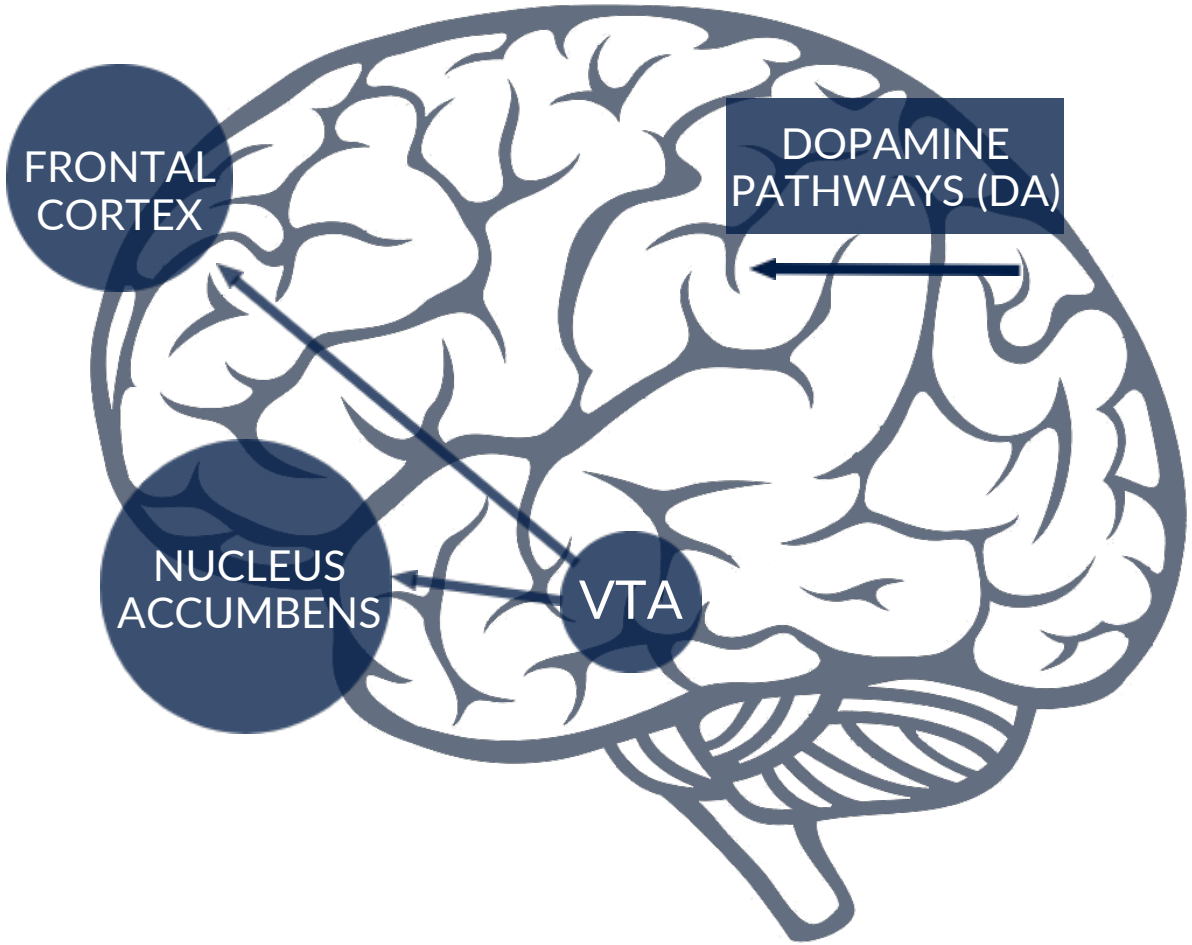


Slide courtesy of Petros Levounis, MD

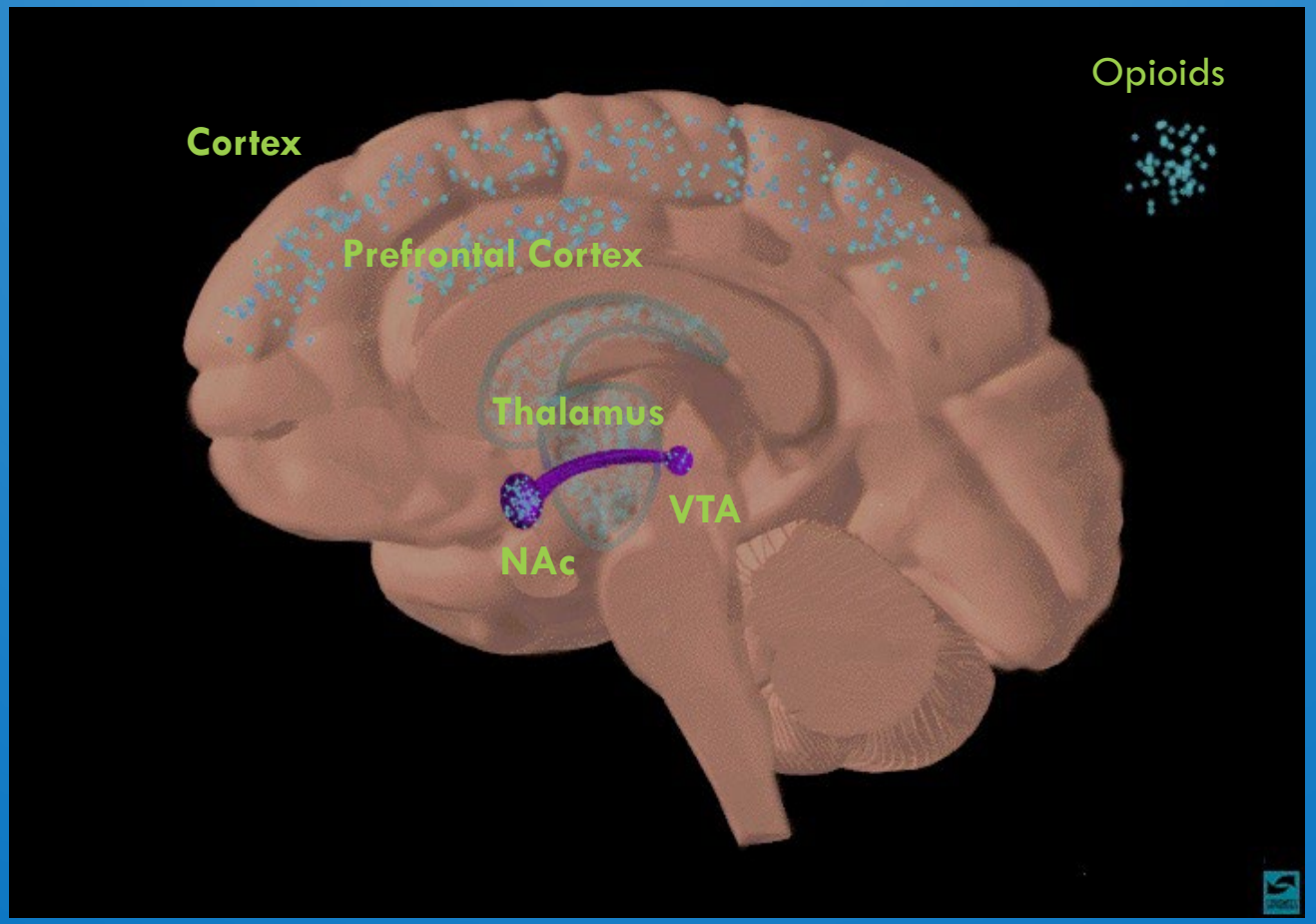
Adapted from: Di Chiara and Imperato, *Proceedings of the National Academy of Sciences USA*, 1988; courtesy of Nora D Volkow, MD.

Reward Pathways

Mesolimbic Dopaminergic Circuitry (Limbic System)

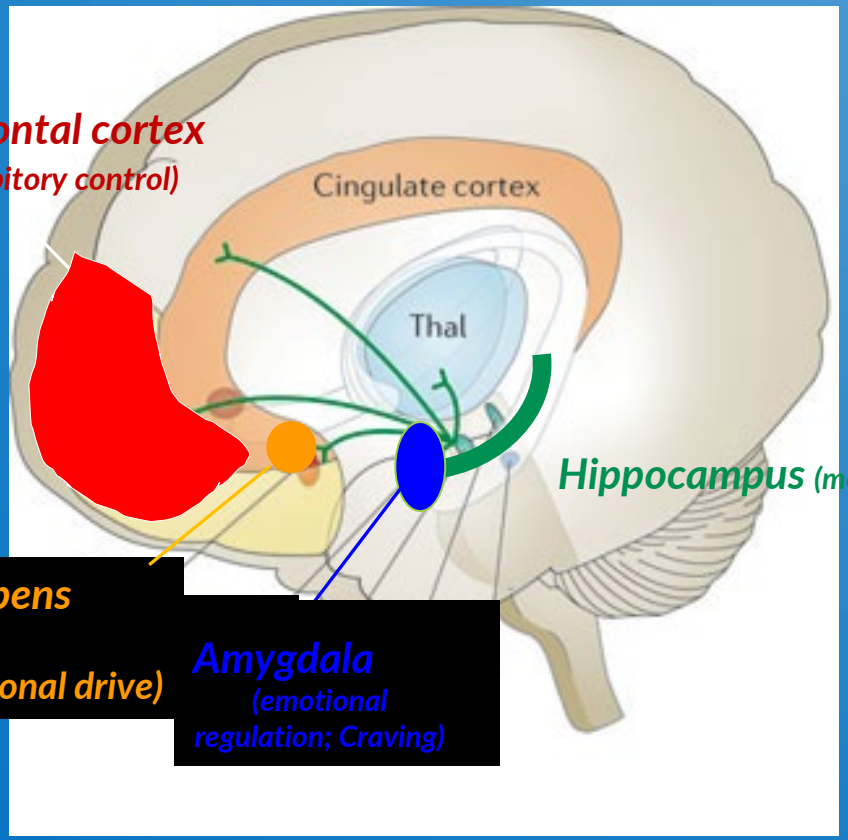


OPIOID BINDING



NIDA, 2017

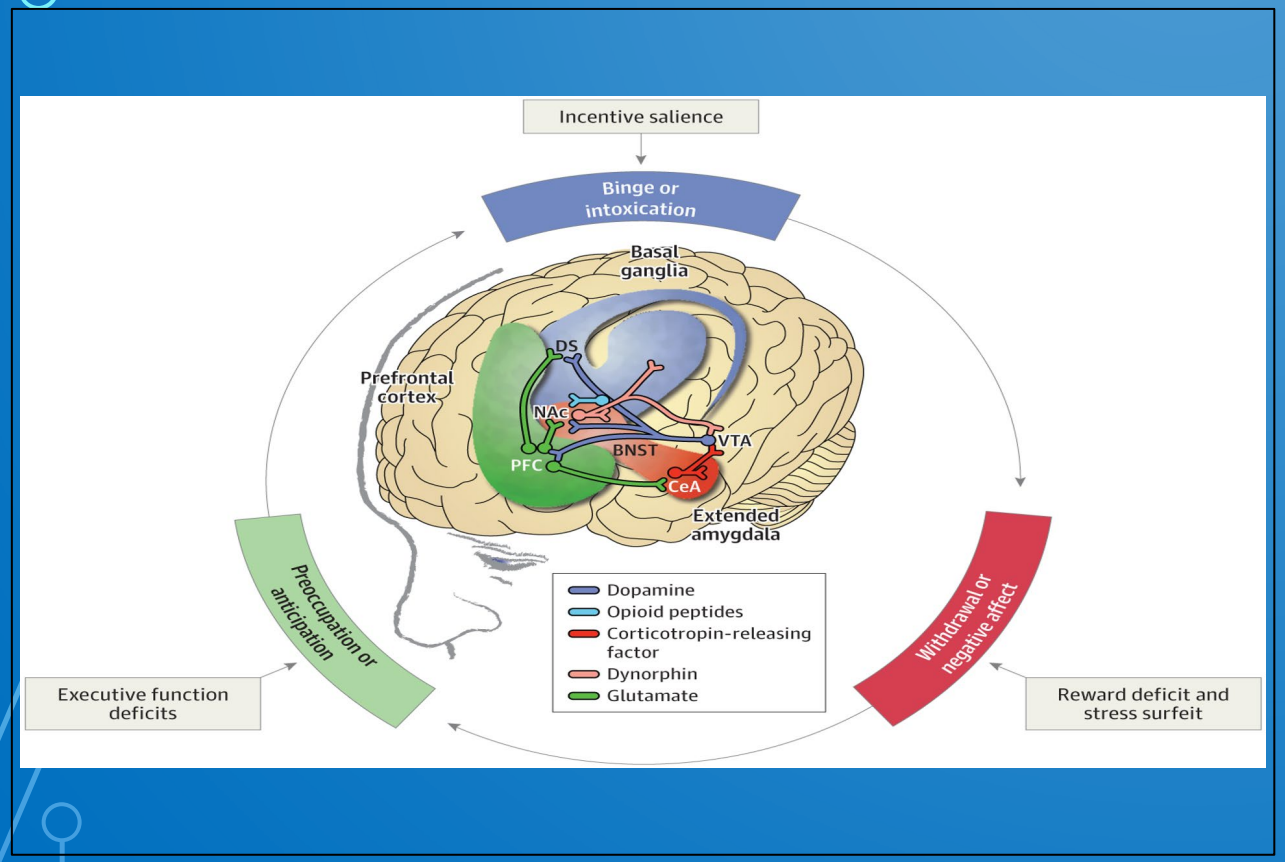
The Neurobiological Challenge of Addiction



- Inhibitory control
- Increase reward drive
- Craving
- Drug memories

Source: Yasmin Hurd, PhD

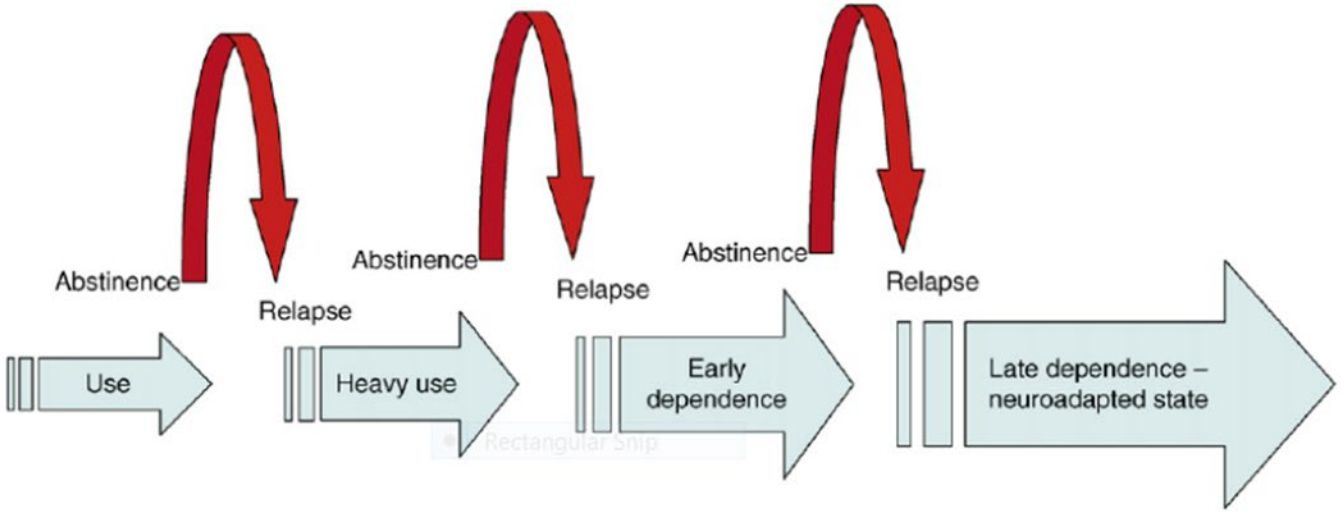
Three Stages of the Addiction Cycle and Associated Neural Circuits

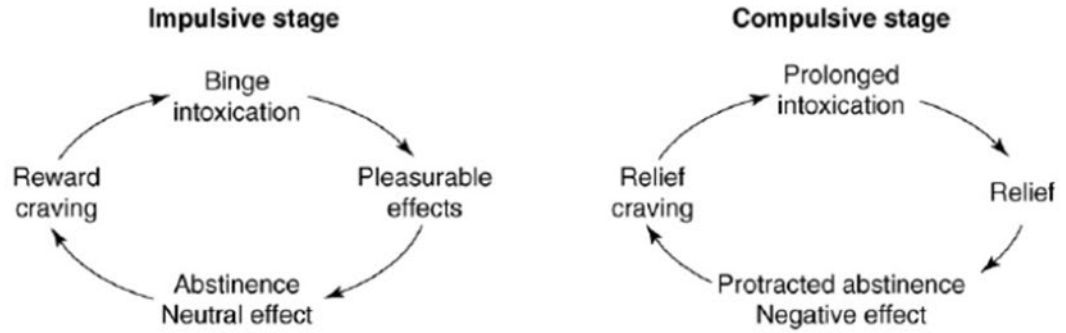


- **Stage 1:** Binge or Intoxication
- **Stage 2:** Negative Affect or Withdrawal
- **Stage 3:** Preoccupation or Anticipation (Craving)

Volkow, N. D., Jones, E. B., Einstein, E. B., & Wargo, E. M. (2019). Prevention and treatment of opioid misuse and addiction: A review

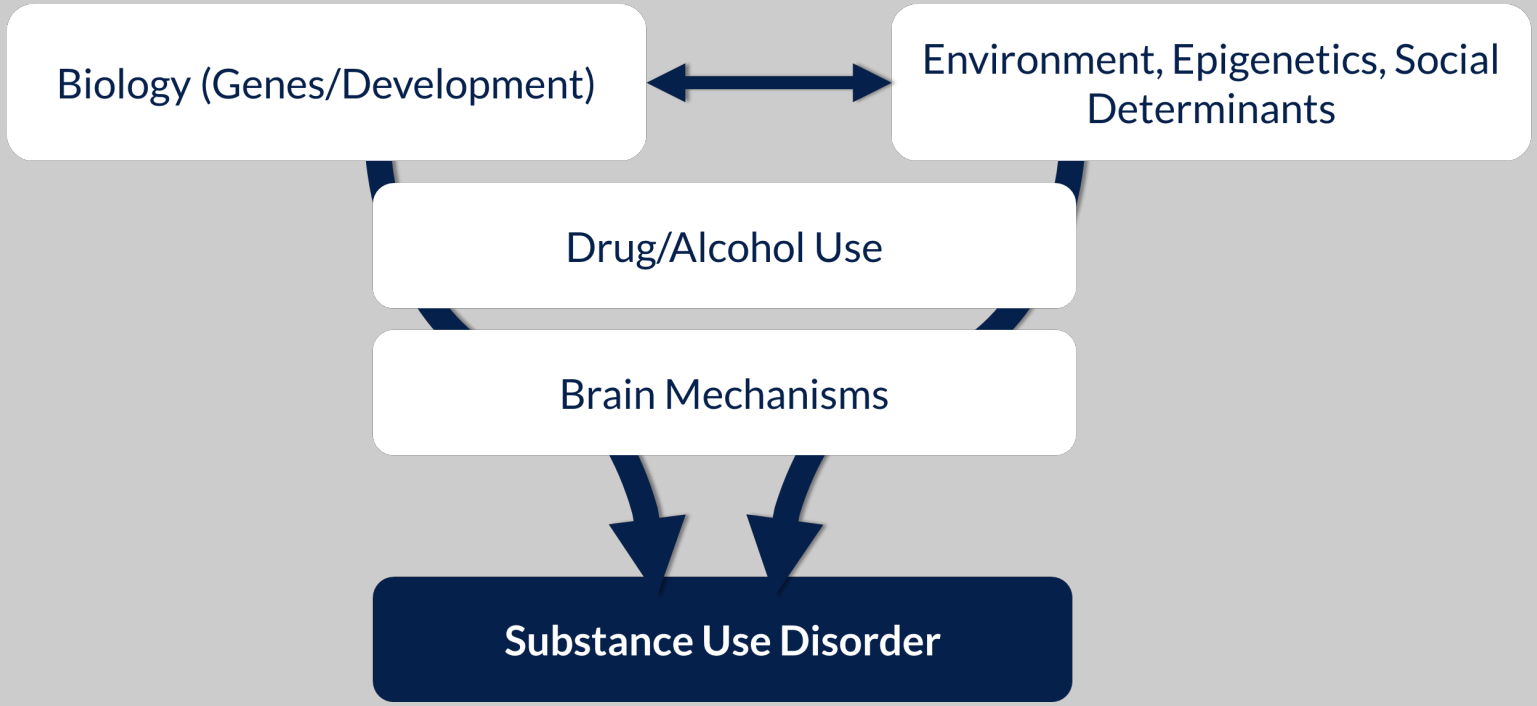
Transition from Positive to Negatively Reinforced Drug Use





Positive Reinforcement → **Negative Reinforcement**

From: Koob GF, Alcohol Clin Exp Res, 2003, 27:232-243.



Development Of Substance Use Disorders Involves Multiple Factors

Opiates and Opioids

Opiates:

Natural compounds present in opium poppies: e.g., morphine, codeine, thebaine

VS.

Opioids:

Manufactured as:

- **Semi-synthetic opioids**: derived from an opiate, e.g., heroin, oxycodone, hydromorphone, buprenorphine
- **Synthetic opioids**: completely synthesized to function similarly to natural opiates, e.g., methadone, fentanyl

ENDOGENOUS OPIOIDS AND THEIR RECEPTORS

Endogenous Ligand	Opioid Receptor Types
Beta Endorphins	**Mu**
Enkephalins	Delta
Dynorphins	**Kappa**
Nociceptin /OrphaninF / Q	ORL-1

Most of the clinically-significant effects of prescribed and illicit opioids are attributed to activity at the **mu-opioid receptor**

BUPRENORPHINE KAPPA-OPIOID RECEPTOR ANTAGONIST

Stimulation of kappa-opioid receptor with dynorphin-like peptides

- Inhibits dopamine release in the striatum (nucleus accumbens and caudate putamen), inducing negative mood state in humans and animals

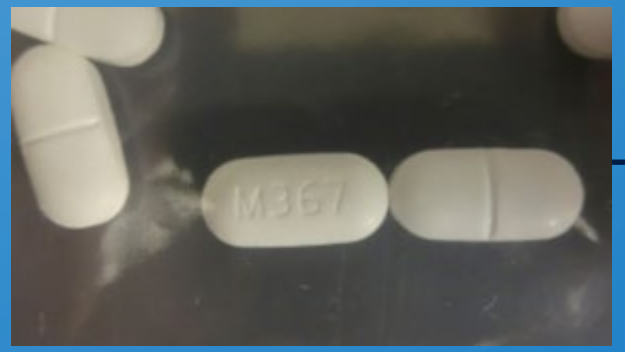
Buprenorphine is an antagonist at the kappa receptor

- Antidepressant-like effects
- Anxiolytic effects
- Prevent stress-induced negative emotional states

"Death Pill"–

Fentanyl disguised as other drugs linked to spike in US overdoses.

Fentanyl Laced Cocaine

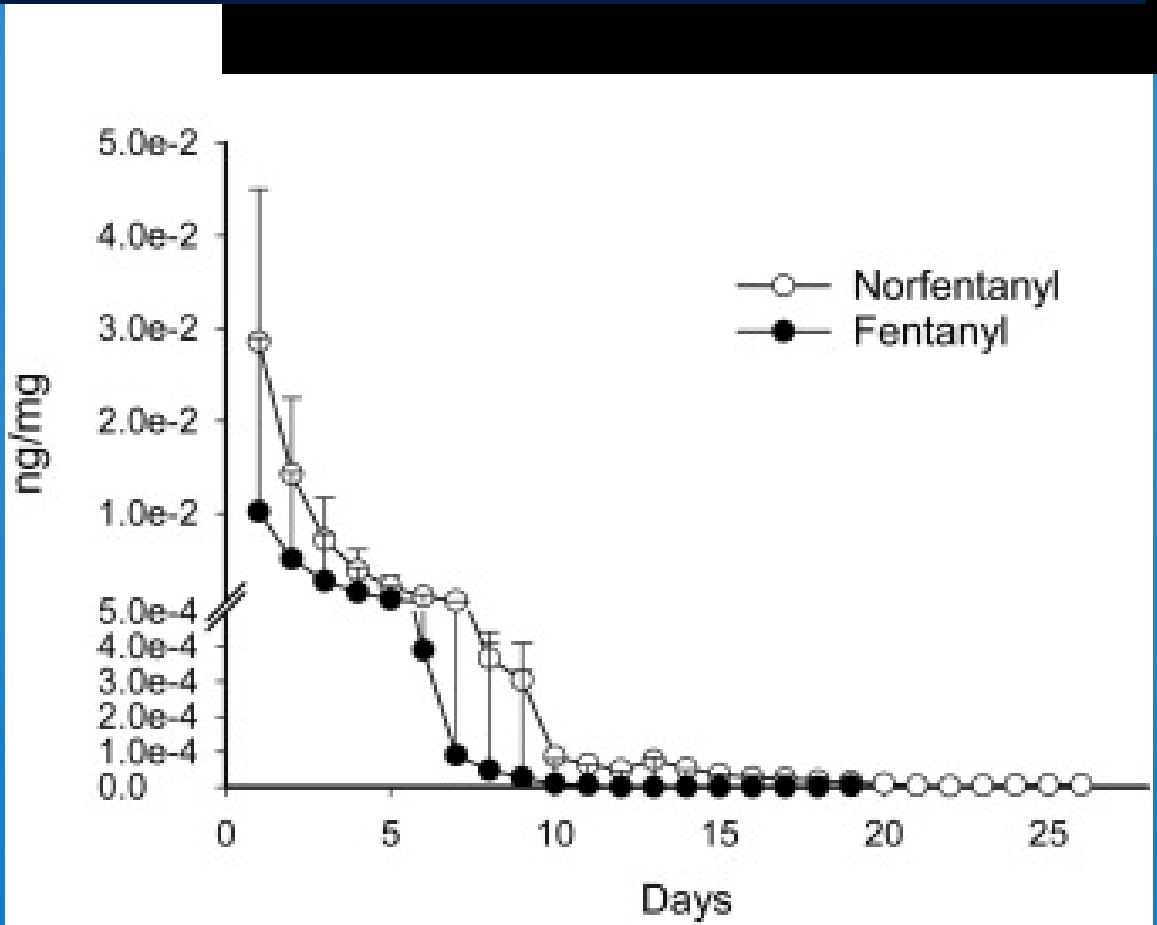


Fentanyl Laced Hydrocodone

Fentanyl Laced Xanax

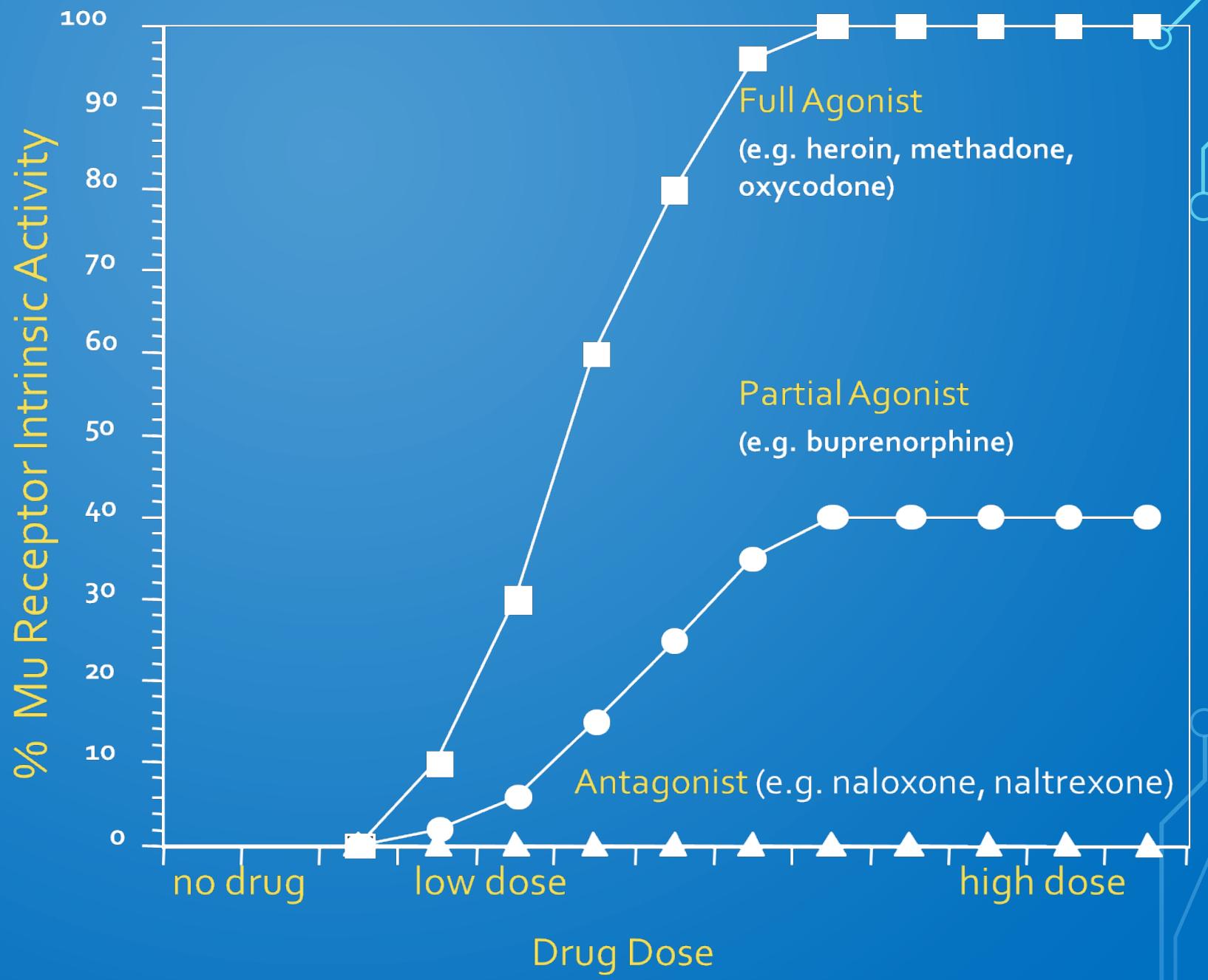
Image sources: NIDA, SF Public Health

Fentanyl and Norfentanyl Elimination



Huhn, AS, et al. Protracted renal clearance of fentanyl in person with opioid use disorder. Drug and Alcohol Dependence. 2020; 214: 1-4

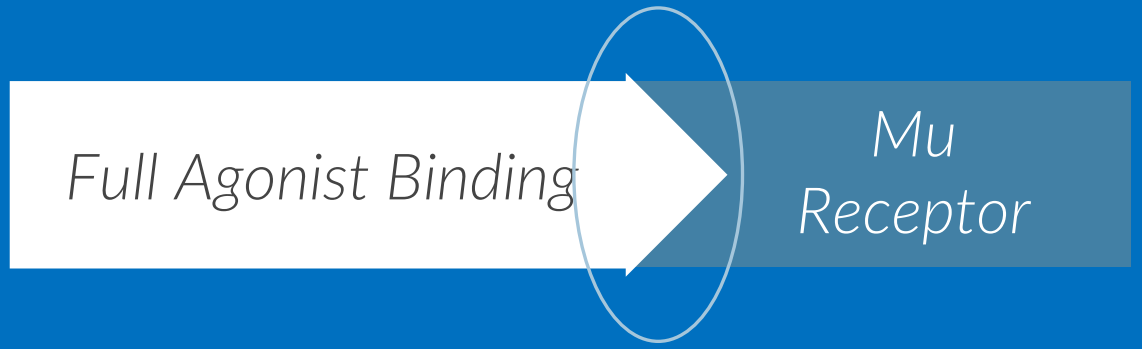
OPIOID AGONISTS AND ANTAGONISTS



Opioid Characteristics that Increase Euphoria

Route of Administration	Faster route has a greater misuse potential	Smoking → Injecting IV → Injecting SQ → Oral/Intranasal
Drug Half-Life	Shorter half-life has a greater misuse potential	Fentanyl → Heroin → Methadone
Lipophilicity	Faster across blood brain barrier	Higher lipophilicity has a greater misuse potential	Fentanyl → Heroin → Morphine → Methadone

Full Opioid Agonist



A full agonist

- activates the Mu receptor.
- is reinforcing/rewarding.
- is the riskiest opioid type (i.e., sedation and respiratory depression).
- includes fentanyl, heroin, methadone, & others.

PARTIAL OPIOID AGONISTS

Mu receptor

Partial agonist binding …

activates the Mu receptor with ceiling effect

is relatively less reinforcing/rewarding

is a less risky opioid type (i.e., sedation and respiratory depression)

includes buprenorphine

Slide created by Tom Pichot, MD

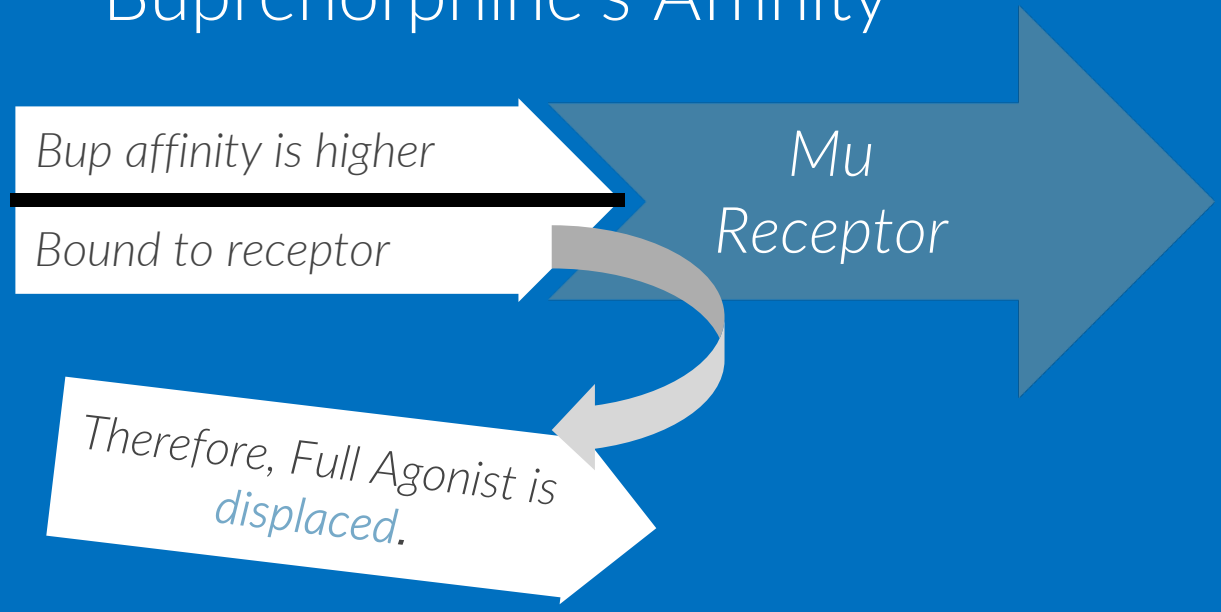
FULL OPIOID ANTAGONIST

- occupies without activating
- is not reinforcing/rewarding
- blocks or displaces opioid agonists
- includes naloxone and naltrexone

Slide created by Tom Pichot, MD

Receptor Affinity

Buprenorphine's Affinity



- ***Affinity*** is the strength with which a drug physically binds to a receptor.
- ***Buprenorphine's affinity*** is very high; it will displace full agonists.
- ***Receptor binding strength,*** high or low, is NOT the same as receptor activation (agonist or antagonist).

HIGH AFFINITY BINDING

Mu Opioid Receptor Range of Ki Value	
Buprenorphine	0.21 to 1.5
Fentanyl	0.7 to 1.9
Methadone	0.72 to 5.6
Naloxone	1 to 3 (antagonist effects)
Morphine	1.02 to 4
Codeine	65 to 135

PDSP Ki Database https://pdsp.unc.edu/databases/pdsp.php
Wang D, Sun X, Sadee W. Different effects of opioid antagonists on μ, δ-, and κ-opioid receptors with and without agonist pretreatment. *J Pharmacol Exp Ther.* 2007;321(2):544-52.

RECEPTOR DISSOCIATION

DISSOCIATION is the speed (slow or fast) of dis-engagement of drug from the receptor

Buprenorphine's dissociation is slow

Buprenorphine stays on the receptor a long time and blocks full agonist from binding

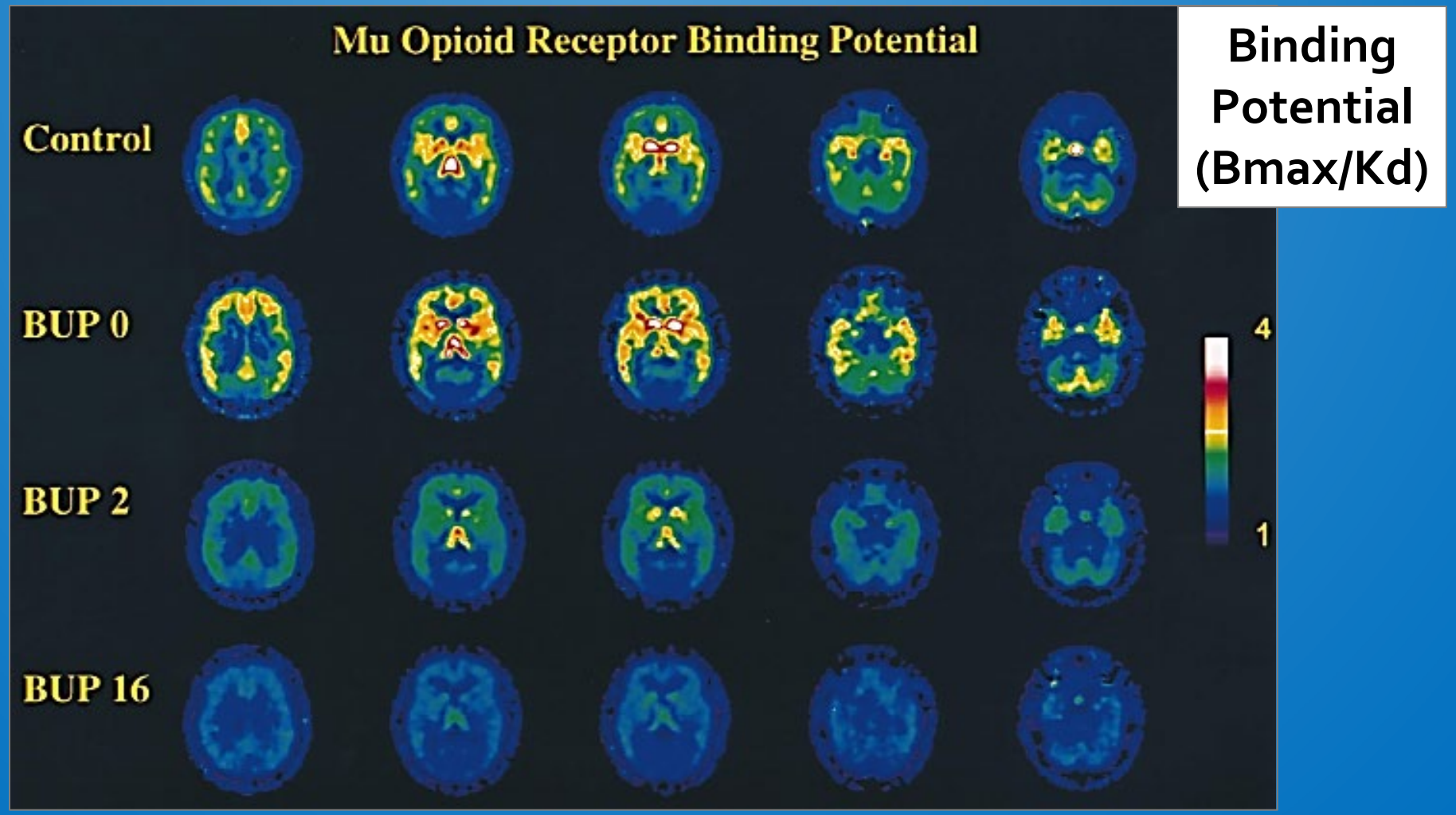
Mu Receptor

Bup dissociation is slow

Therefore, Full Agonists can't bind

Slide created by Tom Pichot, MD

OPIOID BLOCKADE



Zubieta et al. Neuropsychopharmacology 23:326–334, 2000

PHARMACOLOGY HIGHLIGHTS BUPRENORPHINE

- High affinity partial mu opioid agonist (higher than naloxone, fentanyl)
- Long half-life when used to prevent overdose and cravings
- Analgesic properties are shorter lived (4-6 hours)
- “Ceiling effect” on respiratory depression

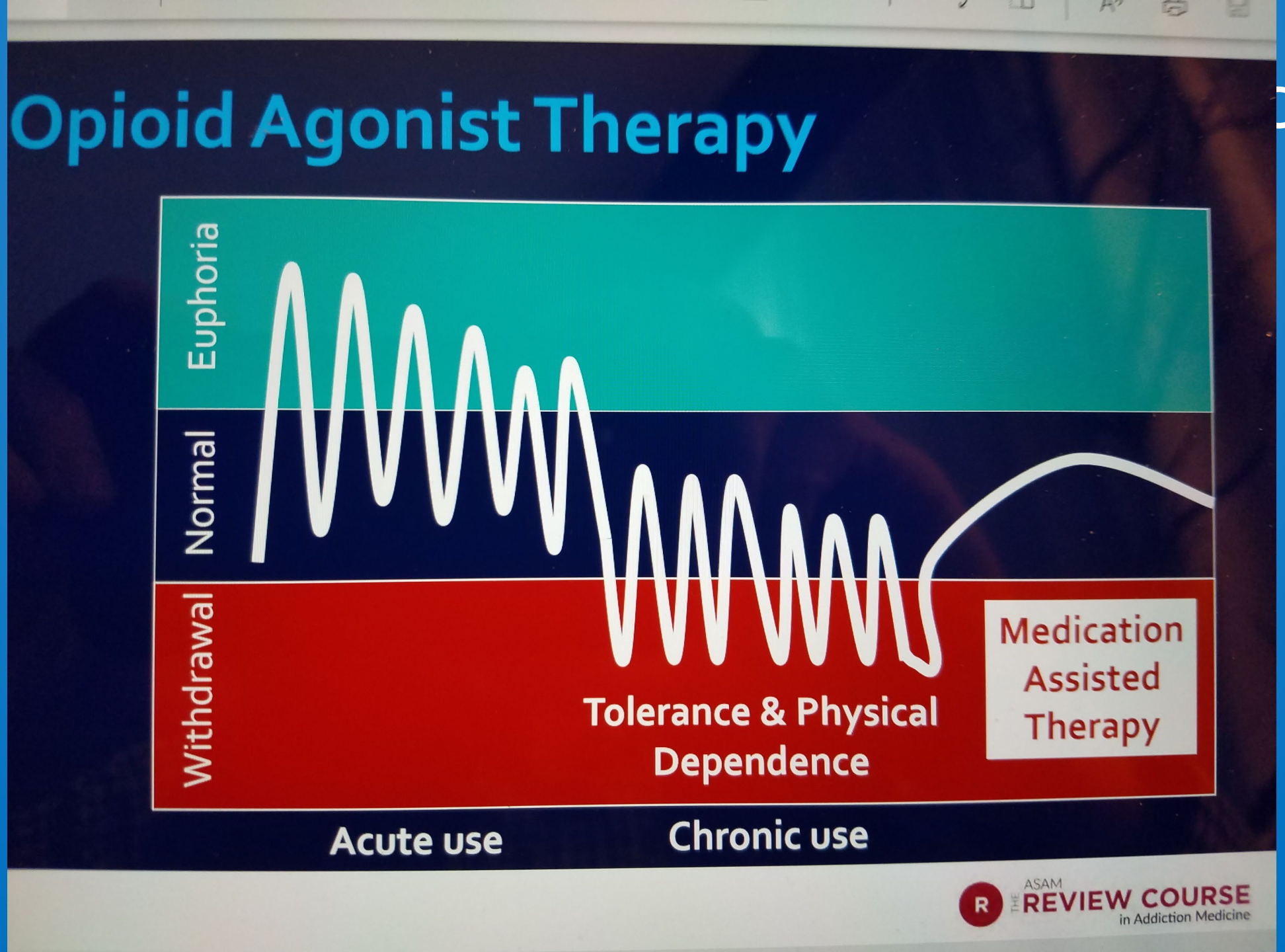
PHARMACOLOGY HIGHLIGHTS BUPRENORPHINE

- Generally given sublingually
  - Moderate (~30%) bioavailability
  - ~0%-5% when swallowed
- Can also be given IV at a much lower dose (0.3mg) due to 100% bioavailability

PHARMACOLOGY HIGHLIGHTS BUPRENORPHINE

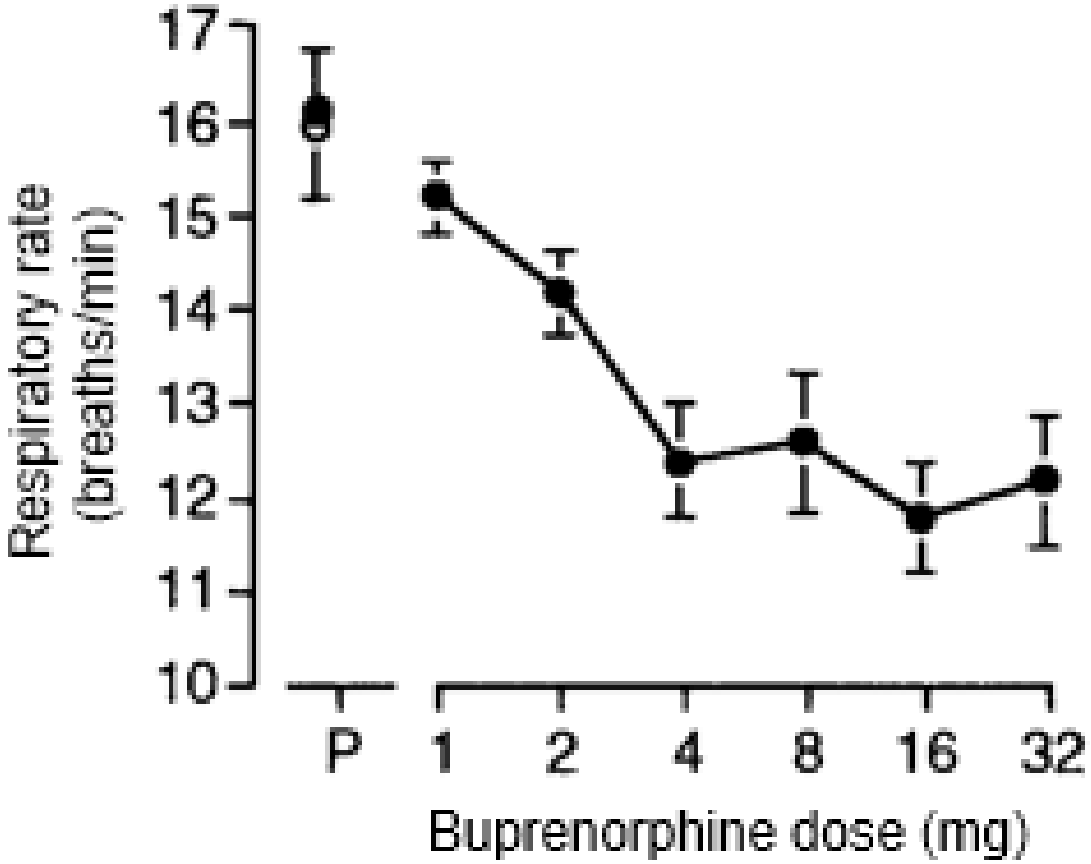
- Comes as mono (buprenorphine) and combo (bup-naloxone) products
- Naloxone is inert sublingually
- Combo products preferred to prevent diversion and misuse by injection
  - If injected, naloxone competes with buprenorphine to limit euphoria and overdose
- Use the combination products

Goldsworthy, 2008

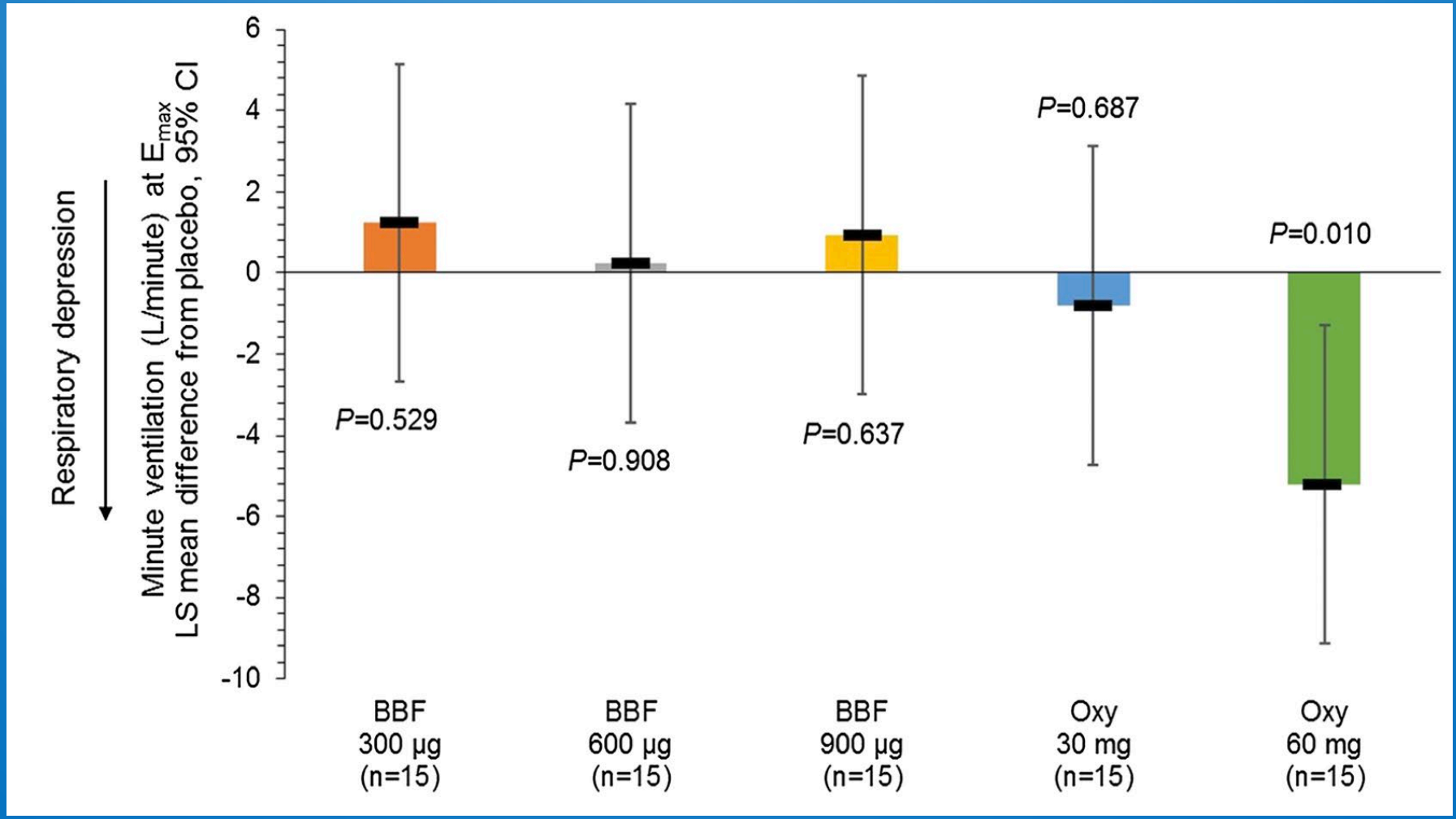

Opioid Agonist Therapy
Euphoria
Normal
Withdrawal
Tolerance & Physical Dependence
Medication Assisted Therapy
Acute use
Chronic use
ASAM
THE REVIEW COURSE
in Addiction Medicine

PHARMACOLOGY HIGHLIGHTS BUPRENORPHINE

- Walsh, 1994



PHARMACOLOGY HIGHLIGHTS BUPRENORPHINE



Webster, 2020

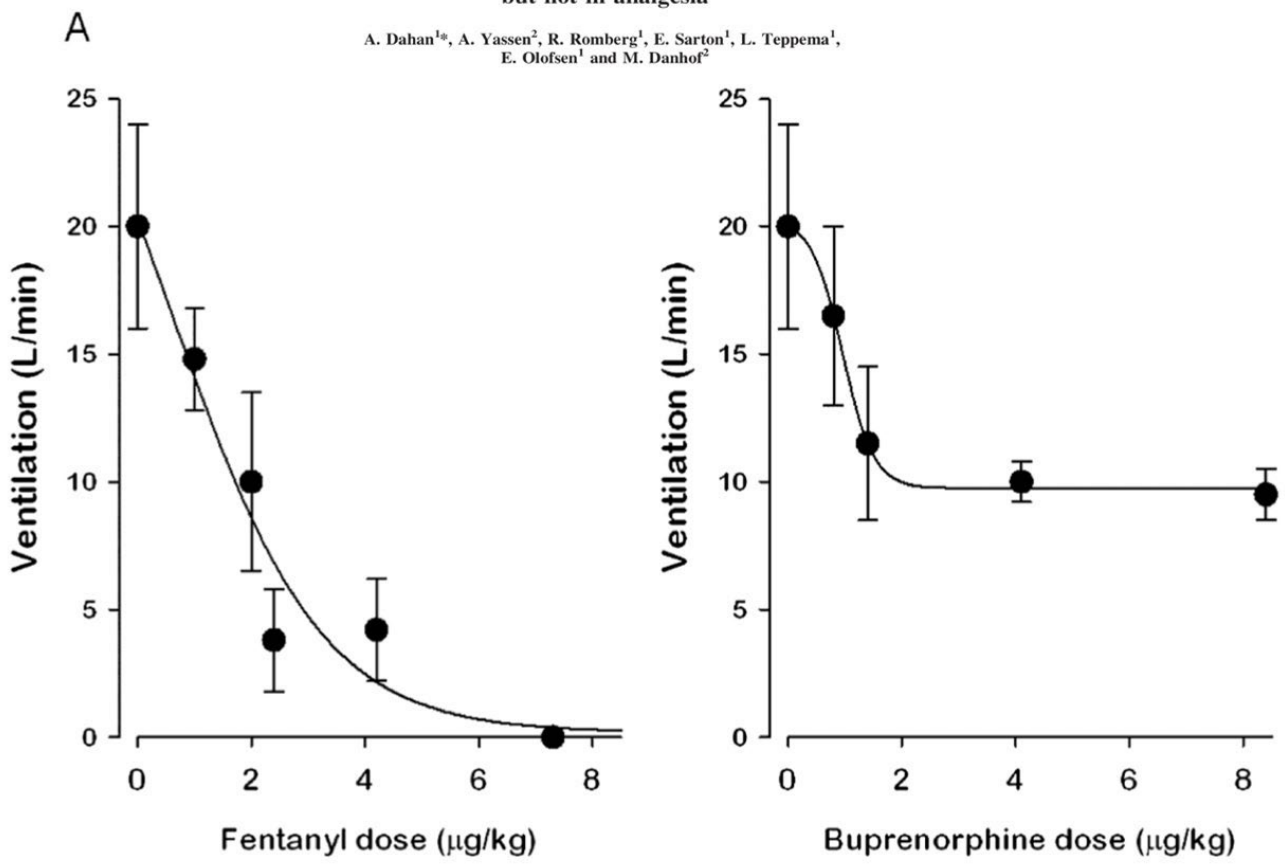
CEILING EFFECT

British Journal of Anaesthesia 96 (5): 627–32 (2006)
doi:10.1093/bja/ael051 Advance Access publication March 17, 2006

BJA

Buprenorphine induces ceiling in respiratory depression but not in analgesia

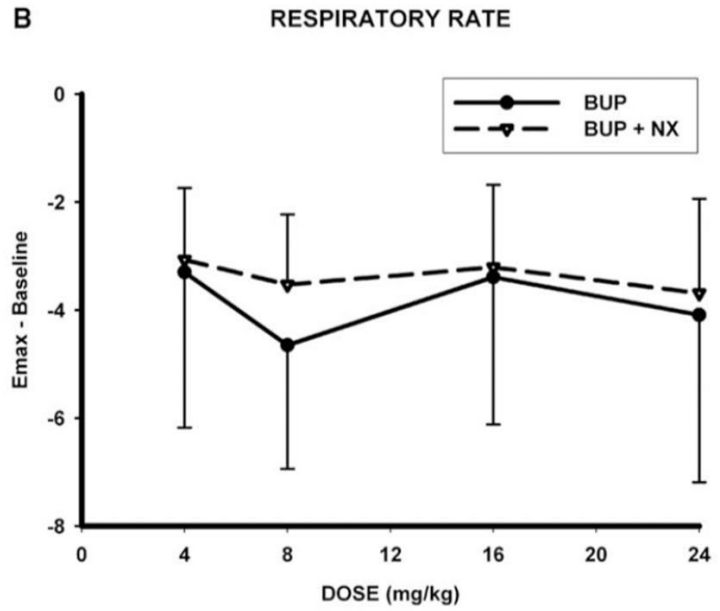
A. Dahan[1]*, A. Yassen[2], R. Romberg[1], E. Sarton[1], L. Teppema[1], E. Olofsen[1] and M. Danhof[2]



Pharmacokinetics and Pharmacodynamics of Multiple Sublingual Buprenorphine Tablets in Dose-Escalation Trials

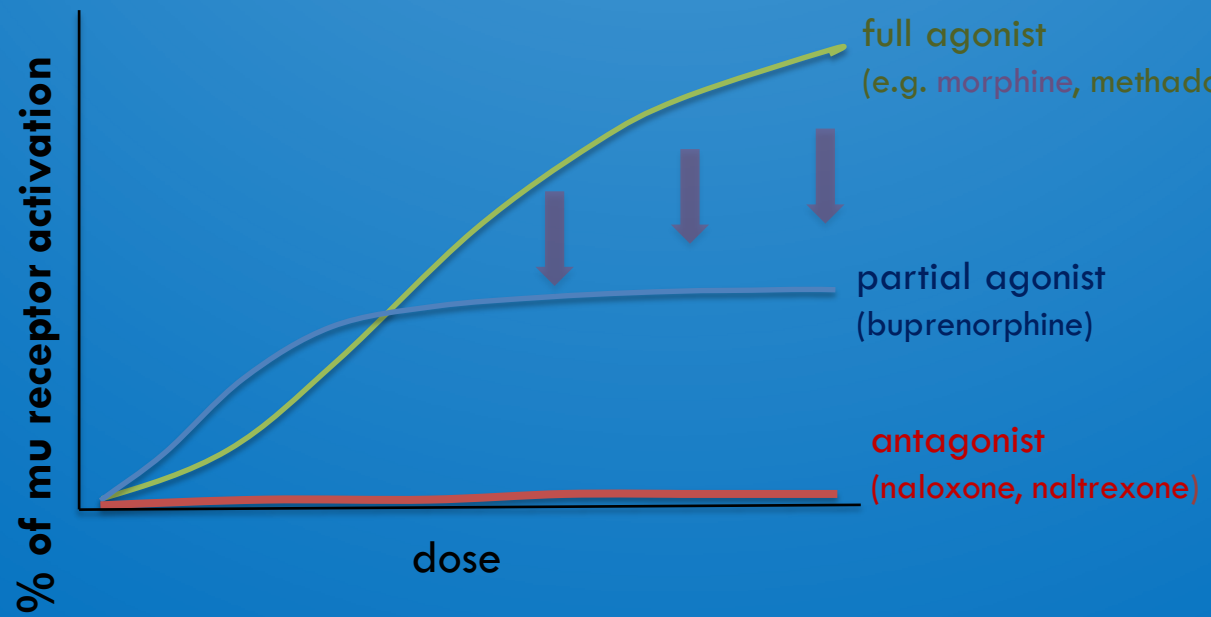
Domenic A. Ciraulo, MD, Robert J. Hitzemann, PhD, Eugene Somoza, MD, Clifford M. Knapp, PhD, John Rotrosen, MD, Ofra Sarid-Segal, MD, Ann Marie Ciraulo, RN, David J. Greenblatt, MD, and C. Nora Chiang, PhD

38 subjects



PRECIPITATED WITHDRAWAL

- Because of its high affinity for mu opioid receptors, buprenorphine can displace other agonists (such as heroin, fentanyl, methadone) that are already present
- The sudden drop from full-agonist to partial-agonist stimulation of opioid receptors can cause sudden and severe withdrawal symptoms, a condition known as ***precipitated withdrawal***



SAMHSA, 2018
Orman & Keating, 2009

PHARMACOLOGY HIGHLIGHTS BUPRENORPHINE

- 2% of IV opioid users report buprenorphine use "to get high"
- Of those using diverted buprenorphine, 72-80% report use for symptom management, e.g., withdrawal, and suppression of craving
- May be public health signal that treatment needs not being met
  - need for improved access/expansion of treatment
- Part of addiction long-term care is urine drug testing for bup with metabolites

Goldsworthy, 2008

Cicero, 2018
Daniulaityte, 2019
Genberg, 2013
Robbins, 2021

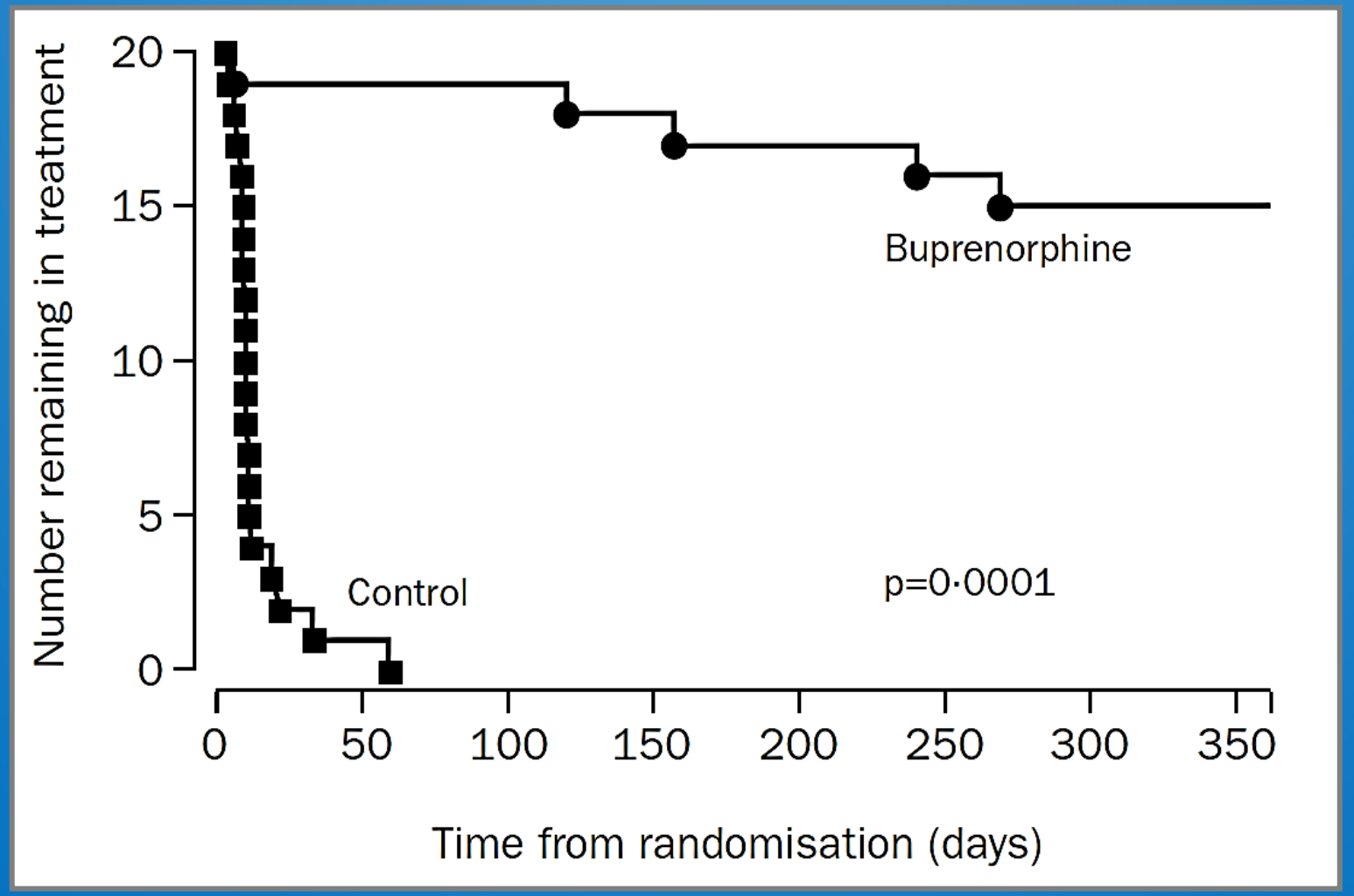
MEDICATIONS ARE THE MOST EFFECTIVE TREATMENT FOR OUD

- Opioid use disorder does not respond to the same treatments as alcohol use disorder.
- Abstinence based therapies generally DO NOT WORK: ~80 – 90+% annual relapse rate. Incarceration with forced abstinence, also does not work. Both increase the risk of lethal overdose post-discharge. Only 28% of residential programs provide MOUD.
- Twelve Step programs alone, without medications have a LOW rate of patient retention and sobriety at one year, when treating OUD (possibly <10%).*
- Retention rates in MOUD programs vary broadly, dependent upon multiple factors, with 1 year sobriety of ~10 to 80%, but average ~40-50%.

Kakko, 2003

*Poor data collection from most of these programs.

BUPRENORPHINE: MAINTENANCE VS TAPER



Kakko J et al. *Lancet* 2003

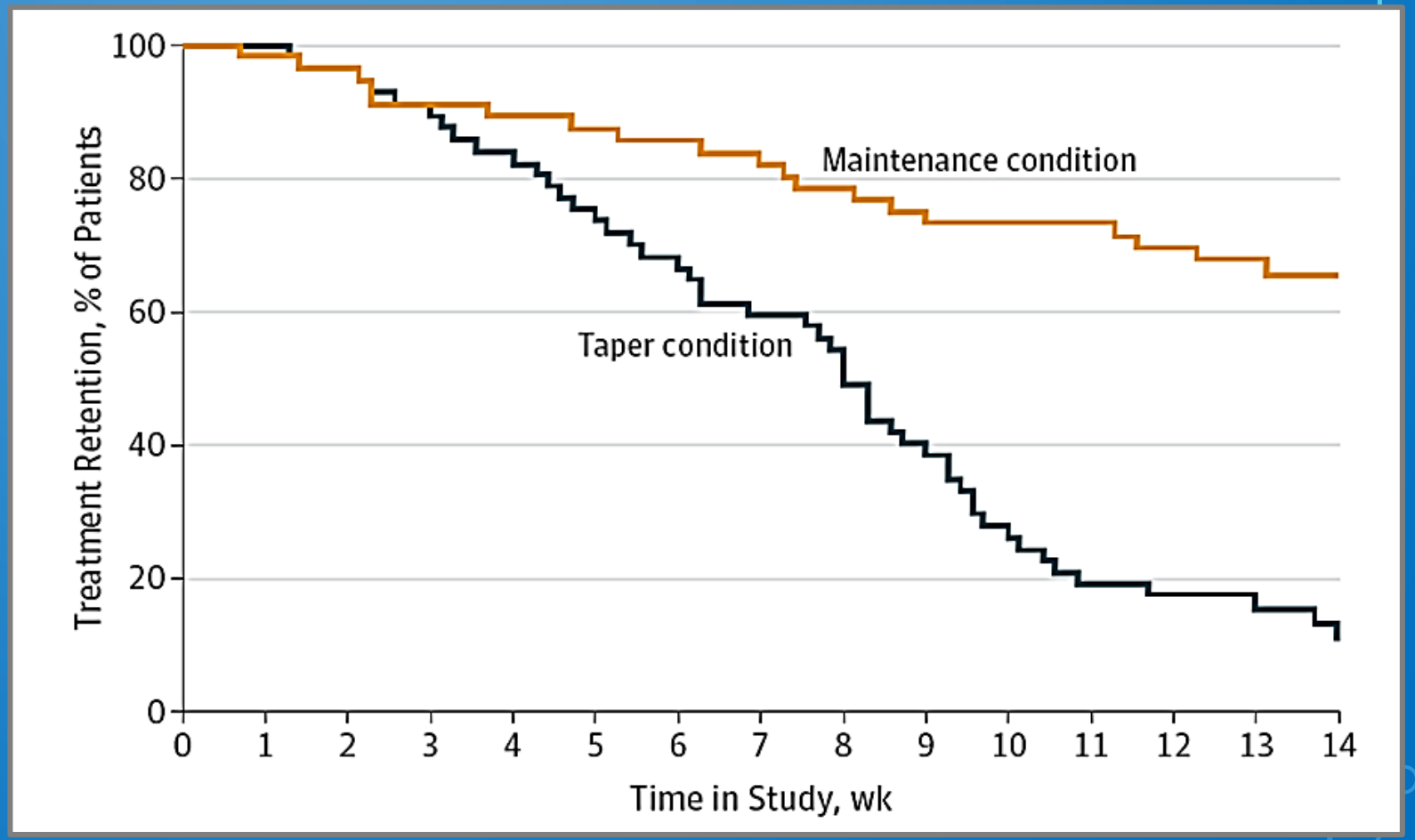
BUPRENORPHINE MAINTENANCE VS TAPER PRESCRIPTION OUD

Completion 14 wk trial:

- Taper: 11%
- Maintenance: 66%

Mean % urine negative:

- Taper: 35%
- Maintenance: 53%



Fiellin DA et al. JAMA Intern Med. 2014.

BUPRENORPHINE IN THE ED

- 75% of patients initiated in ED and given RX still on buprenorphine at 30 & 60 days
  - No precipitated withdrawal[1]
- 30% follow up in one week
  - 1 case of withdrawal[2]
- 78% were engaged in addiction care at 30 days
  - Reduction of illicit drug use from 5.4 days per week to 2.3 days[3]

Lane, 2020
LeSaint, 2020
D'Onofrio, 2015

BUPRENORPHINE IN THE ED

- EDs can act as a very important entry point for MOUD, 1/80 patients seen has an opioid use disorder, “it’s where the patients are”
- One of multiple entry points
  - Jails
  - PCPs

High Threshold vs Low Threshold Care

- PWUD face numerous barriers to engage in services:
  - Registration threshold (accessing care and staff)
  - Competence threshold (ability to communicate needs)
  - Efficiency threshold ("What about those who need 1000 cups of coffee before they start to speak about their needs?")
  - TRUST
- Low-threshold care aims to reduce barriers ('thresholds') through less stringent eligibility criteria to broaden potential reach

Edland-Gryt M. Int J Drug Policy. 2013 May;24(3):257-64.; Mofizul Islam M. Int J Drug Policy. 2013 May;24(3):220-2.

Creating a System of Low Threshold Care

- SUD Initiative Mission: *To improve the quality, clinical outcomes and value of addiction treatment for all patients with SUD. To accomplish this mission, patients must have access to **evidence based treatment** that is **readily available** and standardized across the system.*
- **Core Principles**:

1. Chronic Care Model
2. Patient Centered Approach
3. Evidence Based Treatment
4. Treatment Available on Demand without Barriers
5. Quality Standards Across Settings

New System of Care



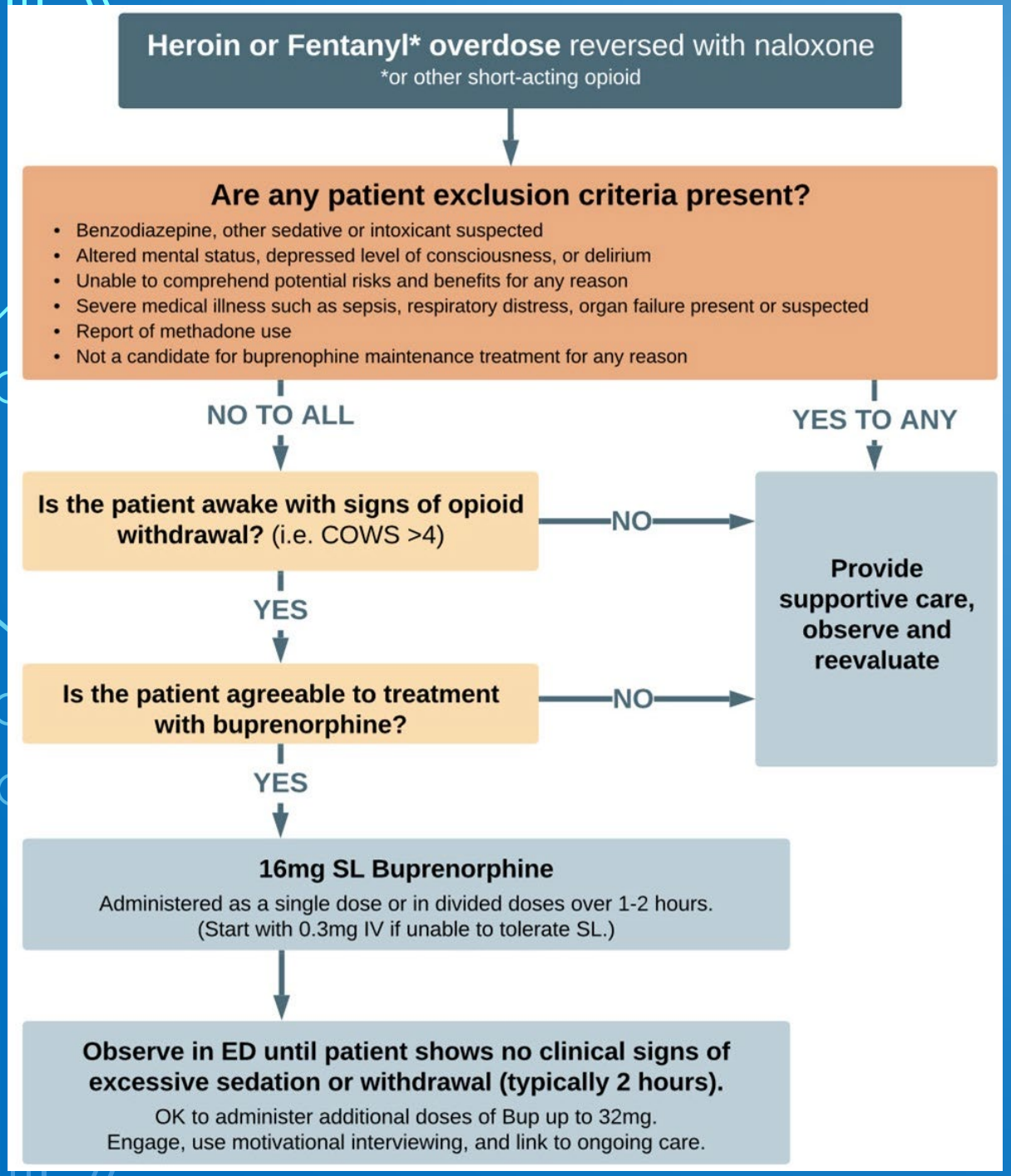

- Inpatient Consult Team
- Integrated treatment in primary care
- Recovery coaches
- HOPE Clinic
- ED initiated treatment
- Mentoring & support to specialty clinics (oncology, burns & trauma, ID, OB)
- ***Bridge clinic***

2020 | Today's Paper

The Philadelphia Inquirer

Unlimited

New Jersey first state to authorize paramedics to provide addiction-treatment drug to overdose victims



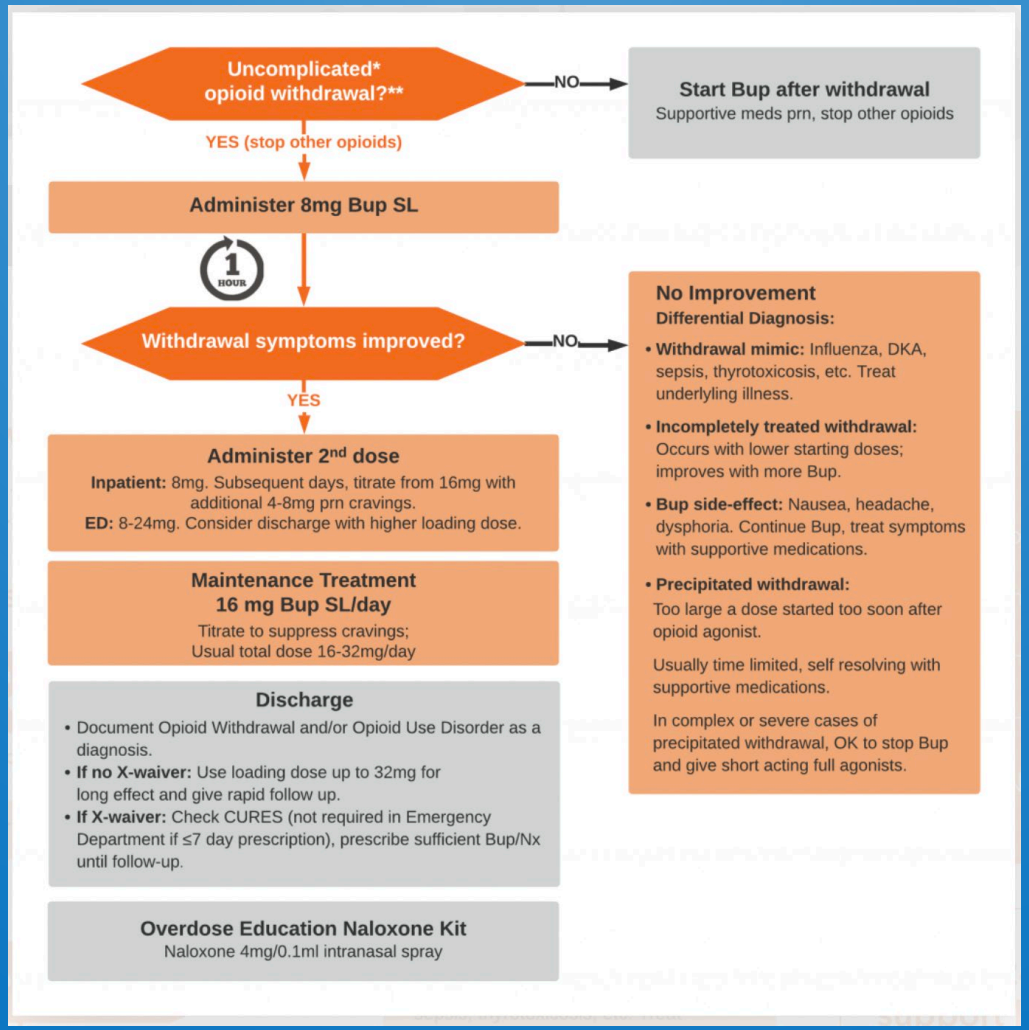
BUP INDUCTION AFTER OVERDOSE

Why is This Unique?

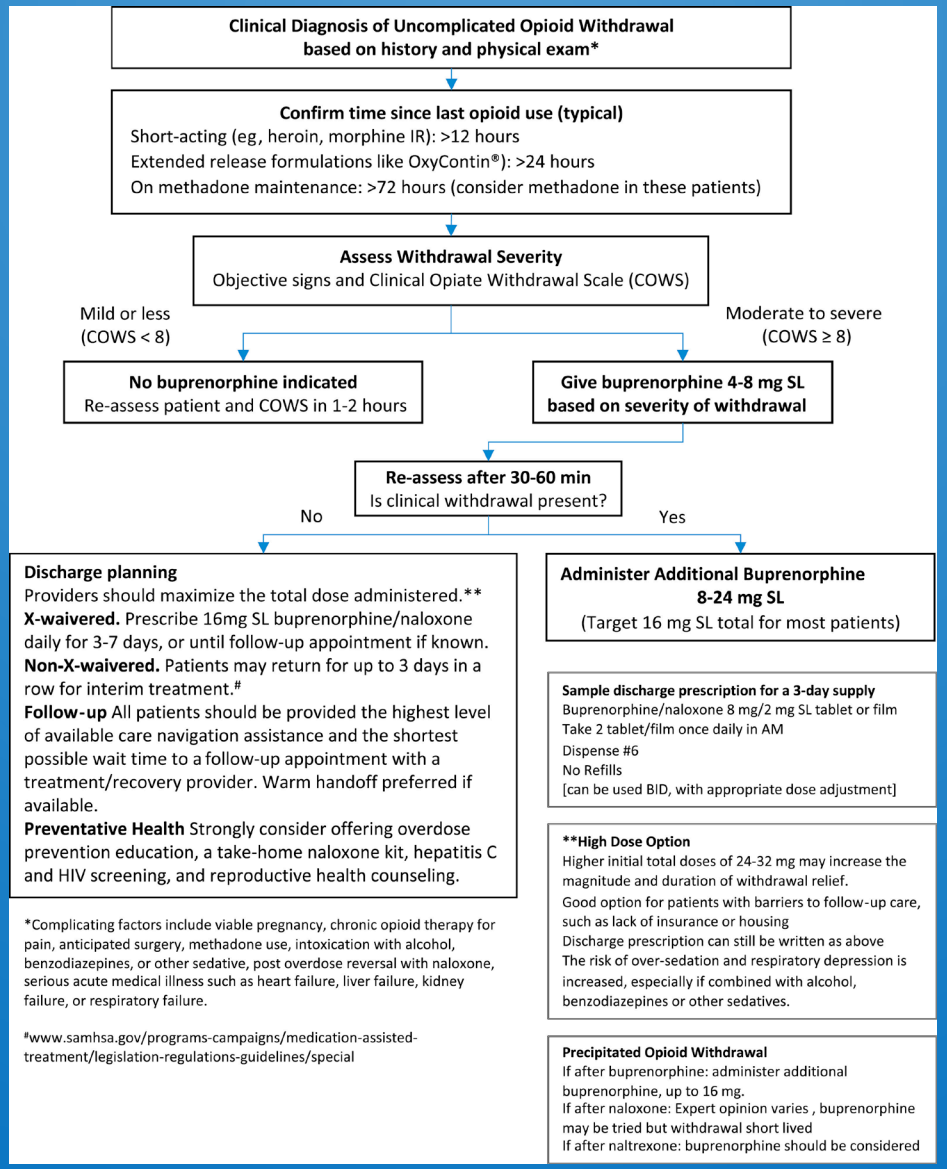
- On demand, urgent access, individualized
- Warm welcomes, warm hand offs
- Engagement is primary goal
- Same day pharmacotherapy
- Emphasis on education and support, regardless of stage, reduction of harmful consequences and motivational enhancement
- Follow up outreach for no shows, transitions
- ***No one is discharged for active illness***

How Do Patients Get to Bridge?

BUPRENORPHINE IN THE ED

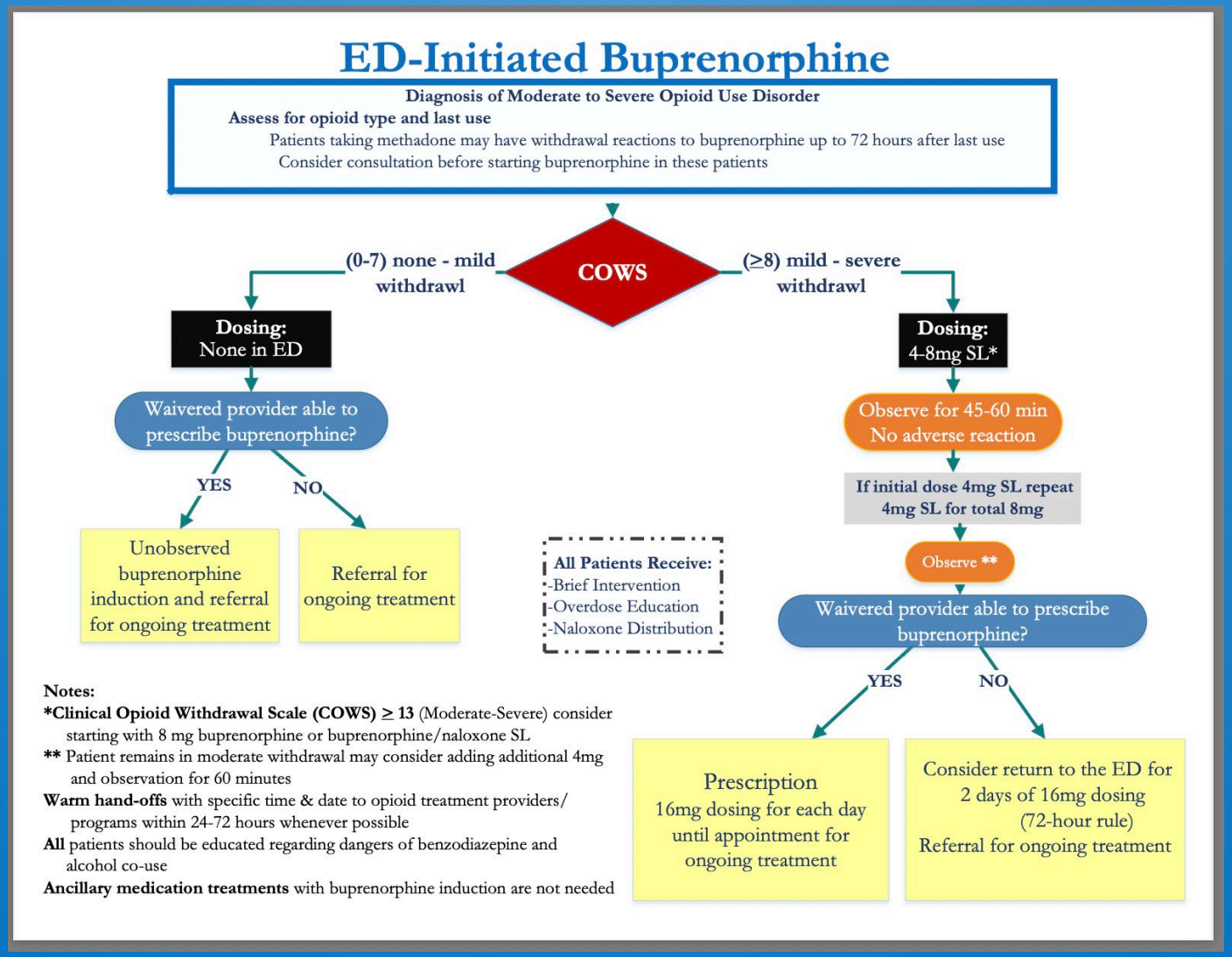


BUPRENORPHINE IN THE ED



Herring, 2019

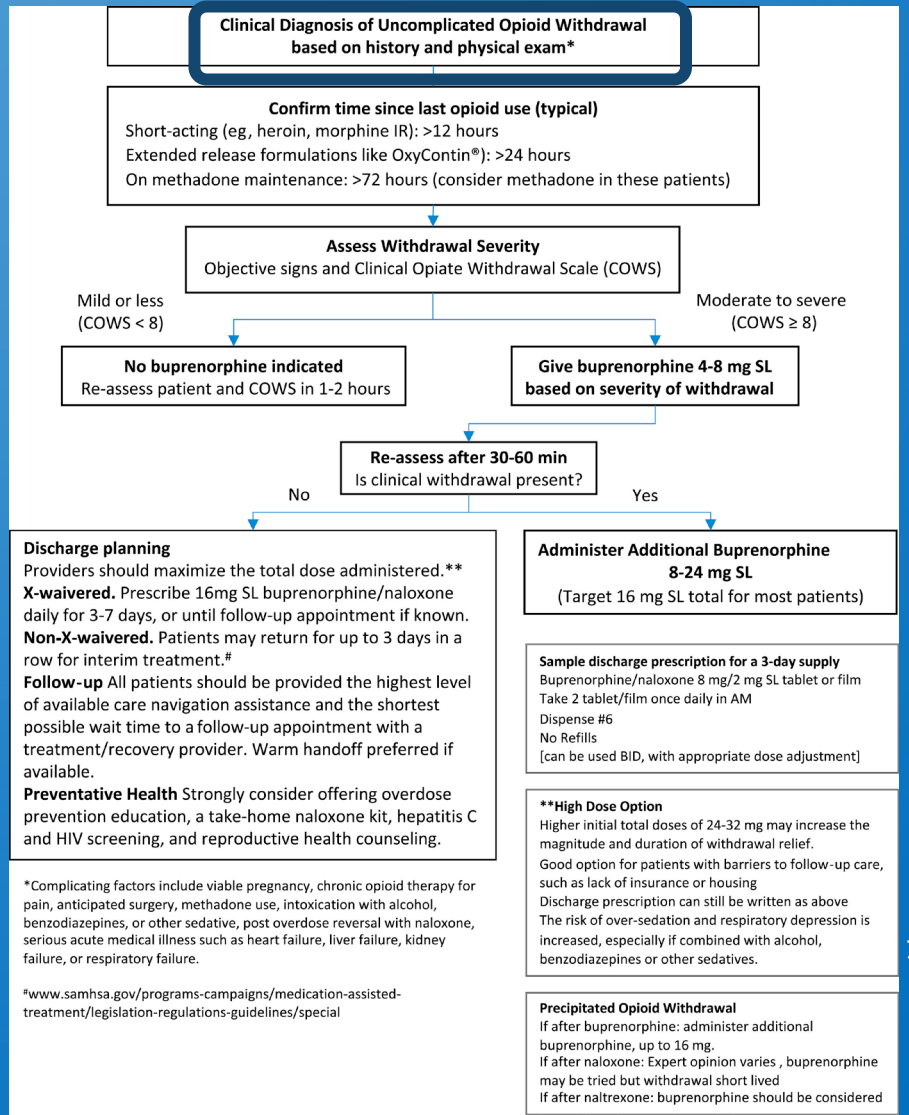
BUPRENORPHINE IN THE ED



D'Onofrio, 2015

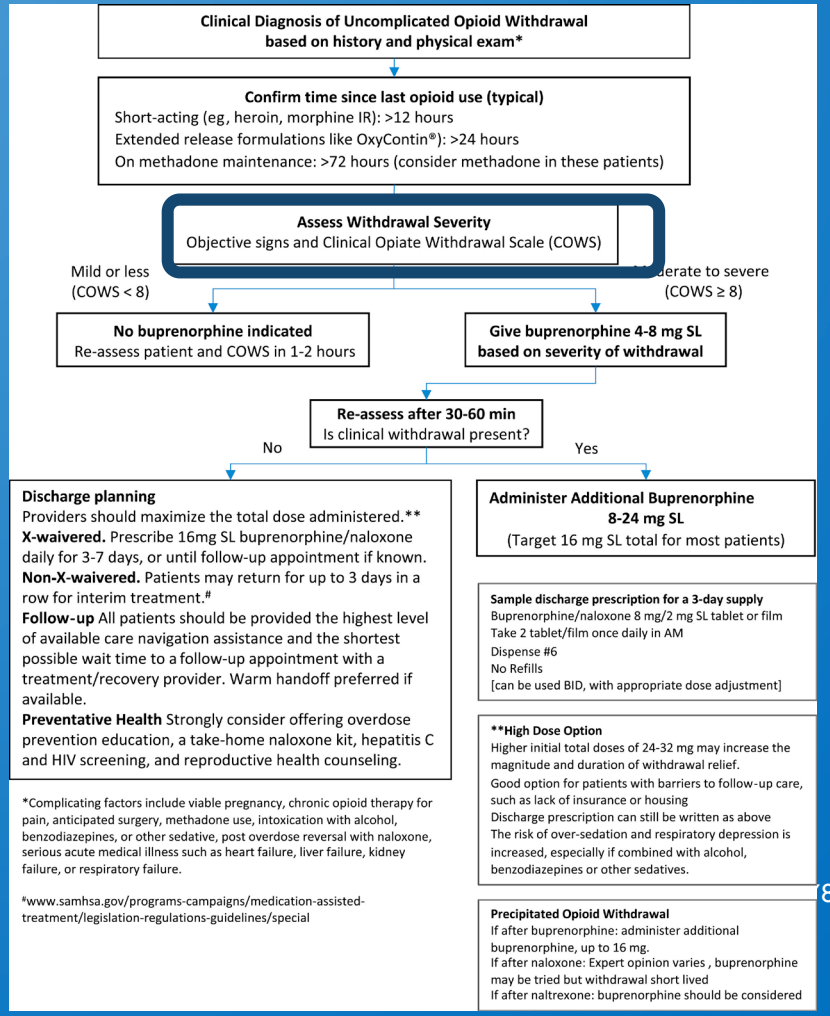
BUPRENORPHINE IN THE ED

- Step 1
  - Diagnose Opioid Use Disorder
    - Screening
    - PDMP



BUPRENORPHINE IN THE ED

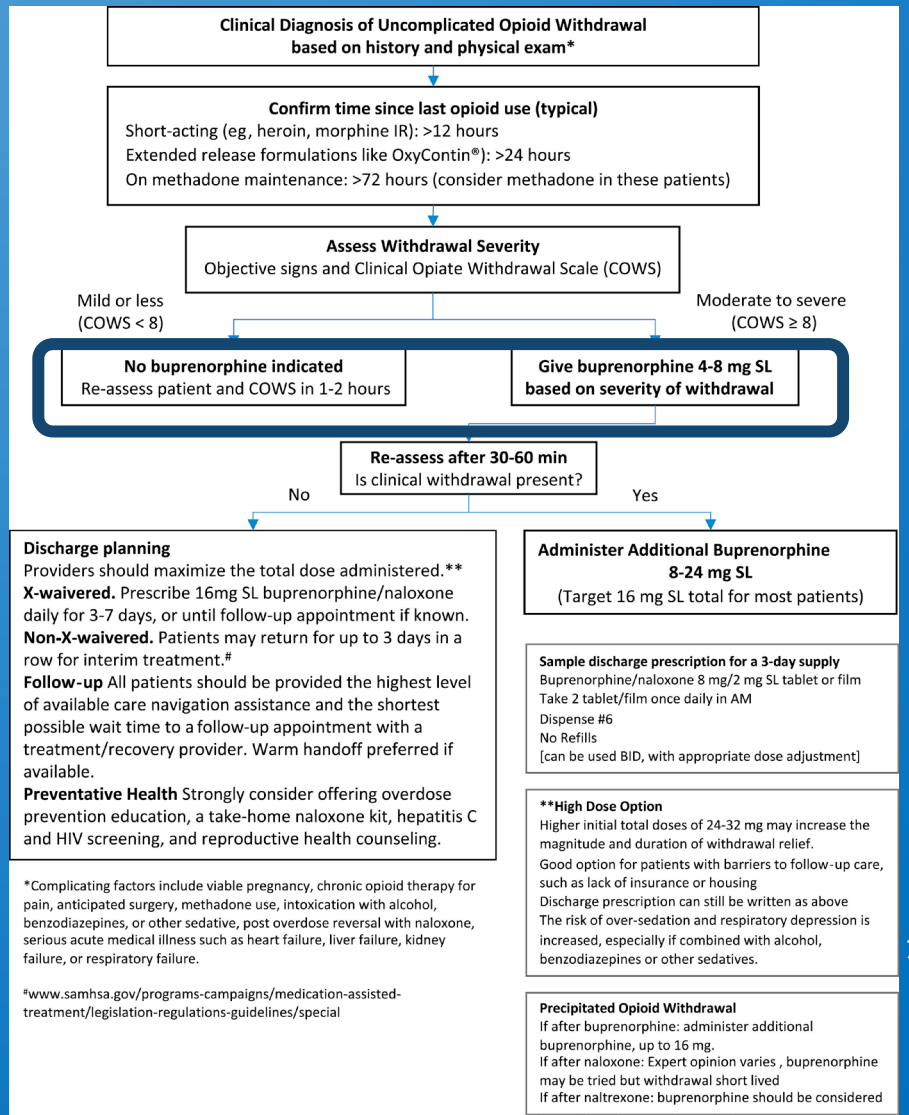
- Step 2
  - Calculate their Clinical Opioid Withdrawal Scale (COWS)
    - Pulse| Sweating| Restlessness| Pupil Size| Arthralgias| Rhinorrhea| GI upset| Tremor| Yawning| Anxiety or irritability| Gooseflesh
      - ≥8 mild-moderate withdrawal, typically ok for induction
      - ≥12 moderate suggested by some pathways



Herring, 2019
D'Onofrio, 2015
McLane, 2020

BUPRENORPHINE IN THE ED

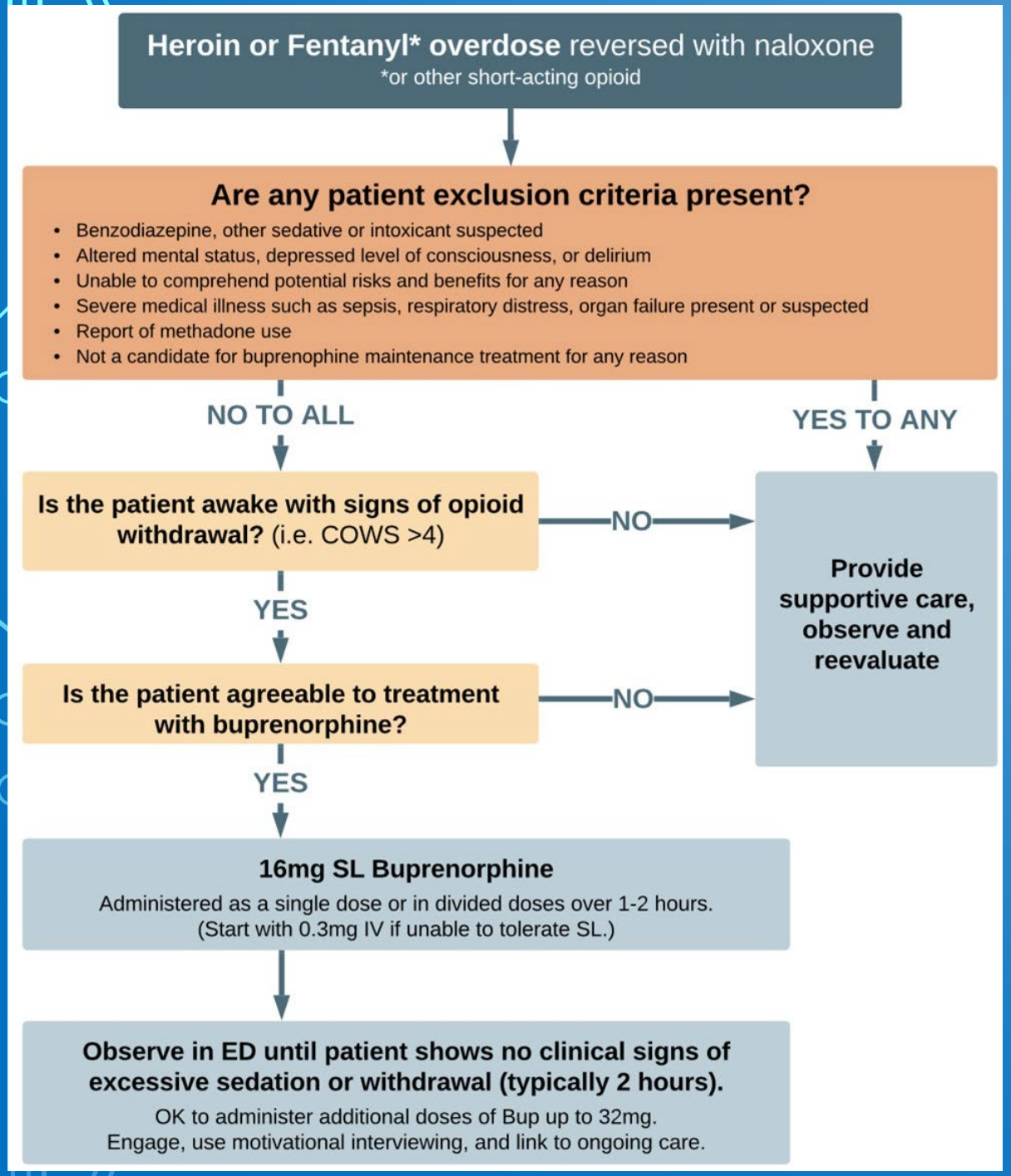
- Step 3
  - Choose your induction site
    - ED vs Home



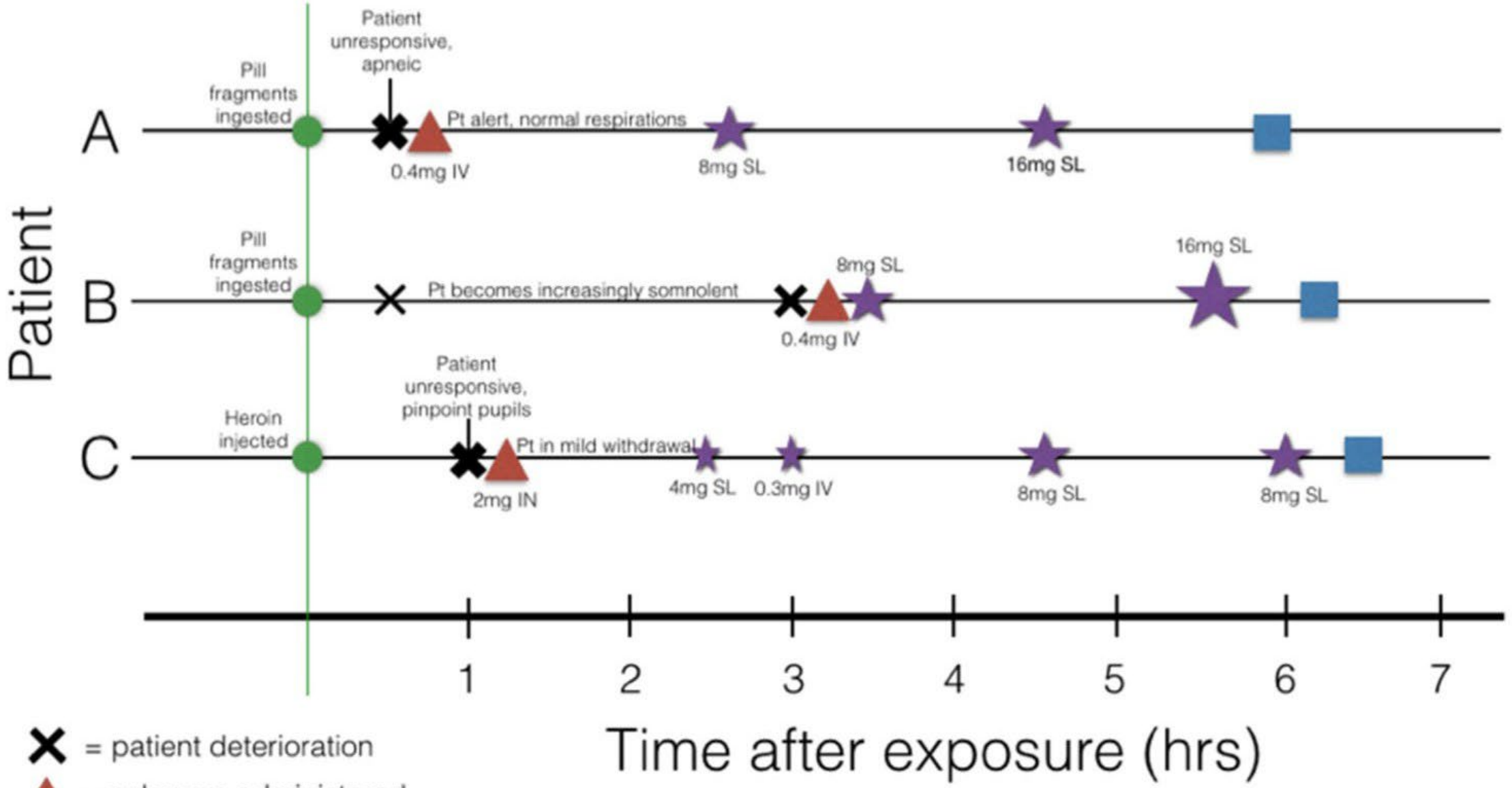
BUPRENORPHINE DOSING IN THE ED

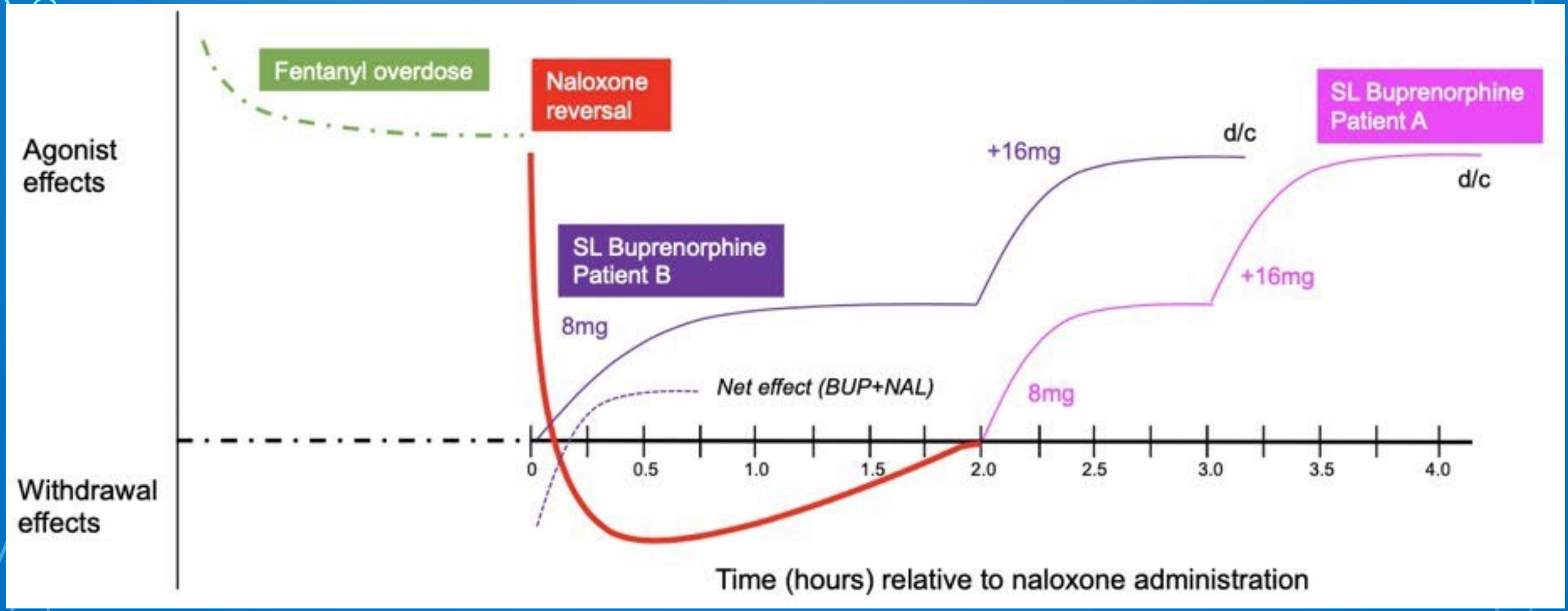
- 2, 4 or 8mg are all acceptable initial doses of buprenorphine
  - Ask your patients what they've done before
- Low initial daily dose is a prime reason for discontinuation of therapy
  - If you start with low first dose (2 or 4mg), make sure you still get to 16mg per day
- Treatment retention
  - ¼ with low dose (2-6mg)
  - 1/3 with medium dose (7-16mg)
  - ½ with high dose (>16mg)
- Higher initial doses of buprenorphine paradoxically may cause fewer incidences of precipitated withdrawal

Samples, 2018; Herring, 2019; Oakley, 2020

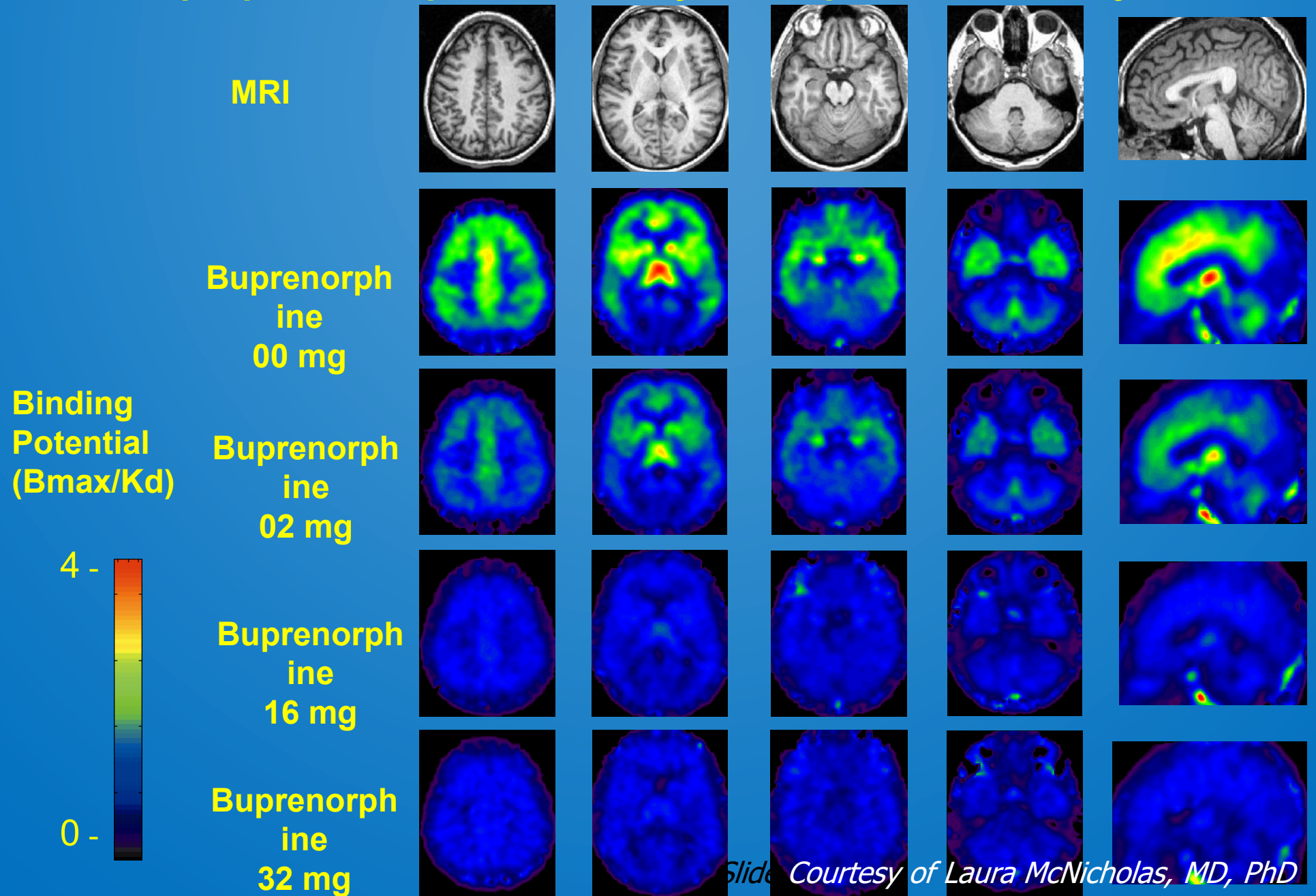


BUP INDUCTION AFTER OVERDOSE


Patient
A
B
C
Pill fragments ingested
Patient unresponsive, apneic
Pt alert, normal respirations
0.4mg IV
8mg SL
16mg SL
Pill fragments ingested
Pt becomes increasingly somnolent
8mg SL
0.4mg IV
16mg SL
Heroin injected
Patient unresponsive, pinpoint pupils
Pt in mild withdrawal
2mg IN
4mg SL
0.3mg IV
8mg SL
8mg SL
1
2
3
4
5
6
7
Time after exposure (hrs)
= patient deterioration
= naloxone administered
= buprenorphine administered
= discharge from ED in good condition


Fentanyl overdose
Naloxone reversal
SL Buprenorphine Patient A
d/c
+16mg
d/c
Agonist effects
SL Buprenorphine Patient B
8mg
+16mg
Net effect (BUP+NAL)
8mg
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
Withdrawal effects
Time (hours) relative to naloxone administration

Effects of Buprenorphine Dose on μ-Opioid Receptor Availability in a Representative Subject



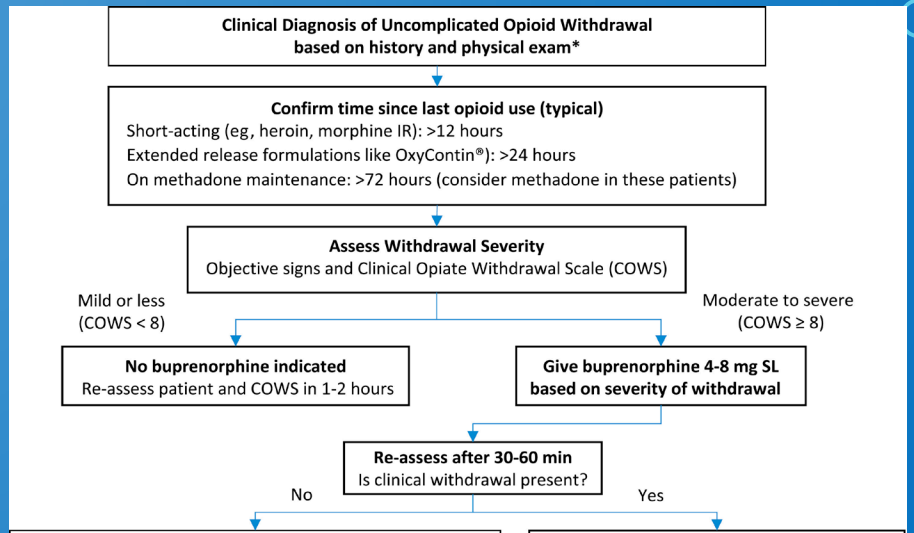
Slide Courtesy of Laura McNicholas, MD, PhD

HOME INDUCTIONS

- Primary method for office-based providers
- Typically, lower doses, starting at 2mg every hour
- First day dose is 12-16mg
- Subsequent doses 16mg daily

BUPRENORPHINE IN THE ED

- Step 4
  - Reassess in 20-40 minutes
    - If improving, provide second bup dose for total of 16mg
      - 12mg if given 4mg initially
      - 8mg if given 8mg initially

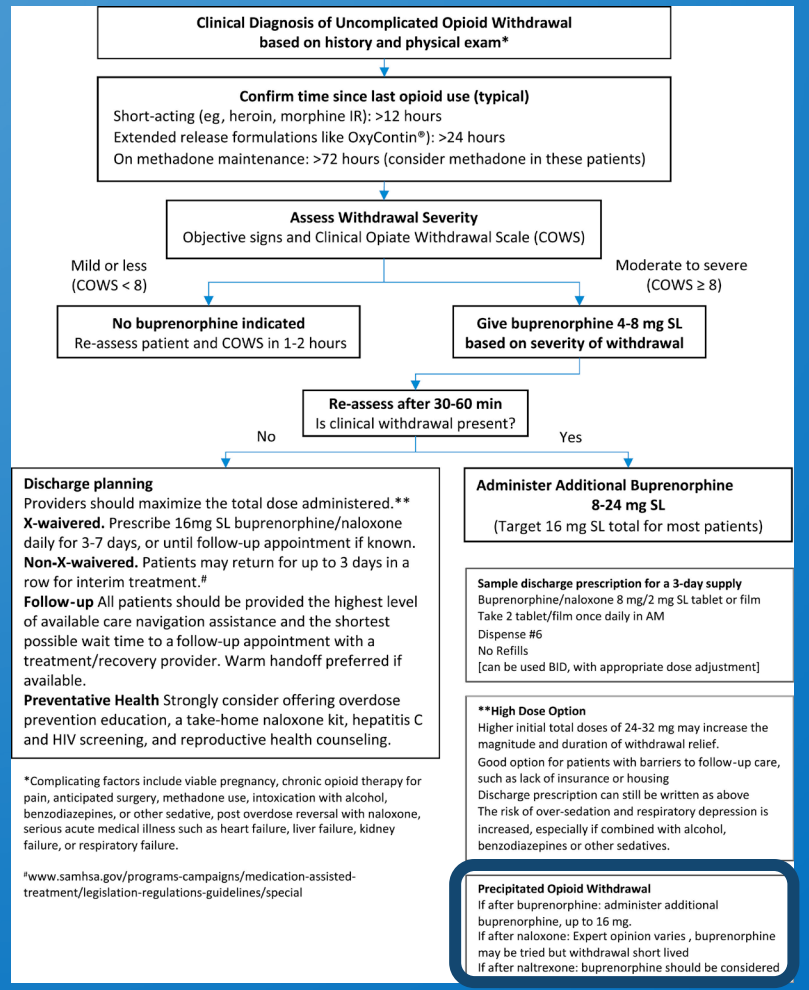


BUPRENORPHINE IN THE ED

- Step 5
  - Discharge preparation
    - Place consult to recovery coach/social work/peer support
      - May want to do this earlier if patient is hesitant or requests
    - Provide take-home naloxone kit
    - Provide specific follow up instructions (TIME AND PLACE)
    - Prescribe 8-2mg buprenorphine-naloxone every 12 hours for as long as needed to get into local clinic

BUPRENORPHINE IN THE ED

- Step 4b
  - If patient gets worse
    - May have precipitated withdrawal
      - If mild, patient may want to receive adjuncts and try home induction later
      - However, optimal treatment for precipitated withdrawal is…more bup
        - Titrate to effect
          - 8mg q 15 min
          - Nervous around 32mg



Quattlebaum, 2021

BUPRENORPHINE IN THE ED

- Naloxone precipitated withdrawal
  - Except in severe circumstances, aim to avoid this
    - 0.1 mg naloxone WHILE BVM (Bag Valve Mask) (NP airway and elevated head of bed)
    - Goal RR 10-12
  - If in NPW(Naloxone Precipitated Withdrawal) , can treat and transition with buprenorphine
    - May start with 16mg
    - Add 8mg every 15min to effect
    - When stable, can DC as you would normal induction
    - Not for methadone overdoses

TREATMENT COURSE

- Discontinuation of MOUD is associated with relapse, overdose and mortality
  - Only 23% of those tapering off buprenorphine produce opioid negative urine during first follow up
- General conclusion: Discontinuation not recommended
  - But moving from SL to subq formulations possible
  - Eventually could try a taper to IM-naltrexone
    - Prevents death with return to use
- Remember and Remind Patients this is a Chronic Disease

Zweben, 2020

SPECIAL POPULATIONS

- Polysubstance/Sedative Use
  - Up to 30% of patients on opioid maintenance treatment also receive benzodiazepine prescriptions
  - Taking benzos and Z drugs with buprenorphine elevates risk of nonfatal overdose, but not as much as the group not on buprenorphine (OR 1.64 vs 2.23)
  - Advise patients to limit sedative use
    - Bup still safer than illicit opioids
    - Bup should not be withheld

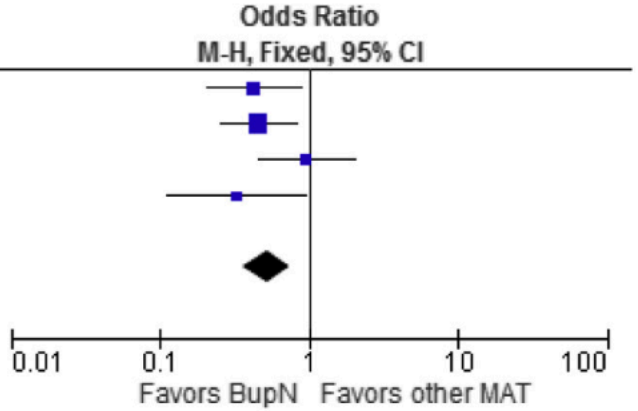
Xu, 2021

PREGNANCY

FIGURE 2
Forest plot for need for neonatal abstinence treatment

Study or Subgroup	buprenorphine/naloxone Events	Total	any MAT Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Gawronski 2014	37	58	74	92	25.7%	0.43 [0.20, 0.90]
Mullins 2019	30	85	59	108	41.7%	0.45 [0.25, 0.81]
Nechanska 2018 Norway	17	33	103	196	17.9%	0.96 [0.46, 2.01]
Wiegand 2015	8	31	16	31	14.7%	0.33 [0.11, 0.95]
Total (95% CI)		**207**		**427**	**100.0%**	**0.52 [0.36, 0.75]**
Total events	92		252			

Heterogeneity: Chi² = 3.85, df = 3 (P = 0.28); I² = 22%
Test for overall effect: Z = 3.55 (P = 0.0004)



CI, confidence interval; *MAT*, medication-assisted treatment; *M-H*, Mantel-Haenszel.

Link. Buprenorphine-naloxone use in pregnancy: a systematic review and metaanalysis. AJOG MFM 2020.

- When compared with methadone, mothers treated with buprenorphine have neonates needing fewer days of opioid agonist treatment

Link, 2020
Jones, 2010

PREGNANCY

- No difference in outcomes for mother-baby pairs receiving buprenorphine vs buprenorphine-naloxone
- No need for pregnancy test result prior to dosing
- Does help with follow up and referral to correct clinic

Link, 2020
Jones, 2010

MANAGEMENT OF ACUTE PAIN

- Patients with OUD, especially those in recovery and on opioid agonist therapy or naltrexone, deserve pain relief on par with patients without OUD
  - Novel approaches required due to pharmacology of their OAT
    - Buprenorphine: high affinity partial agonism
    - Methadone: full agonism
    - Naltrexone: high affinity full antagonism

MANAGEMENT OF ACUTE PAIN

- Buprenorphine is a high affinity partial agonist
  - ”Out-competes” most other opioids
- When possible, use non-opioid analgesia
  - Nerve blocks
  - NSAIDS
  - Acetaminophen
  - Immobilization
  - Ketamine

MANAGEMENT OF ACUTE PAIN

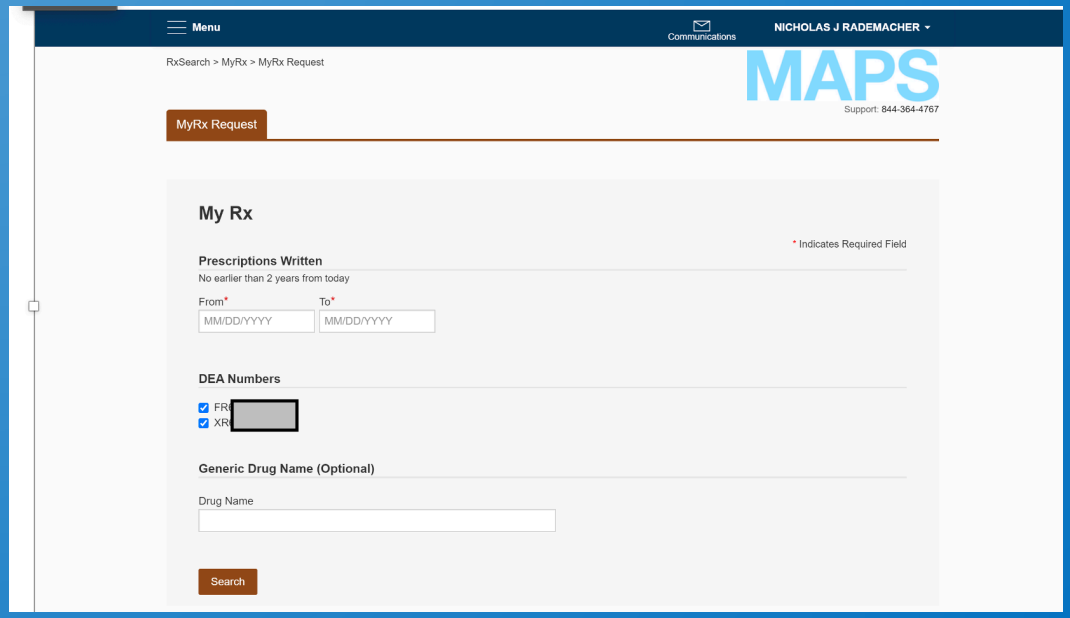
- If opioids are required
  - Select those also with high affinity
    - Fentanyl
    - Hydromorphone
  - Expect to use large doses
    - Not due to tolerance, although this contributes
    - Only a small amount of the opioid provided will outcompete buprenorphine
  - Titrate to effect

MANAGEMENT OF ACUTE PAIN

- The experience they have in the ED may influence their decision to remain engaged in opioid agonist treatment

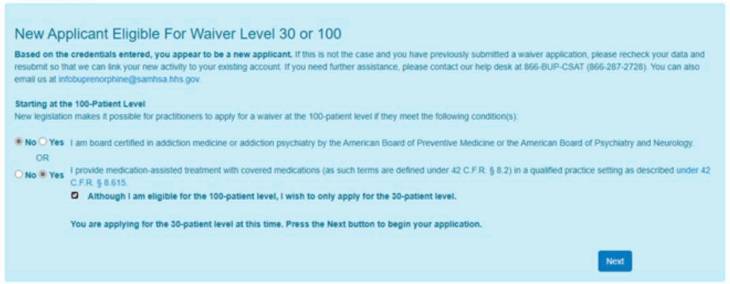
UTILIZING THE PDMP

- DEA may request a current list of patients you have buprenorphine prescriptions to
  - In MT this is easily done in the PDMP
- PDMP can also be used to help with diagnosis of OUD
  - Also shows bup Rx, past or present
  - Will not show methadone used for OUD

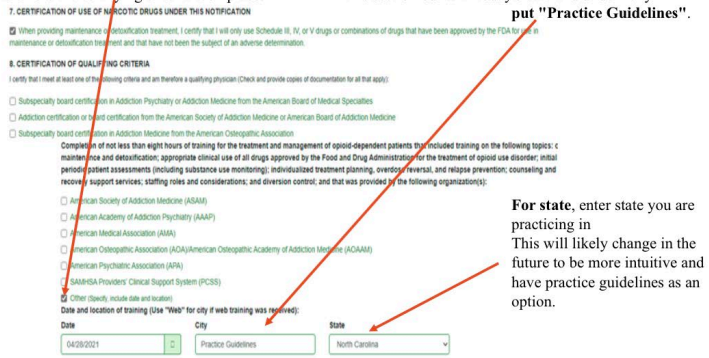


Notice of Intent Process for X-Waiver to Prescribe Buprenorphine under New Practice Guidelines

1. Go to the following link: SAMHSA DATA Waiver
2. Fill in next page with DEA number and state license number.
3. Choose to only apply for the 30-patient level. Under the notice of intent, you are only able to apply for the 30-patient level.
   See below:



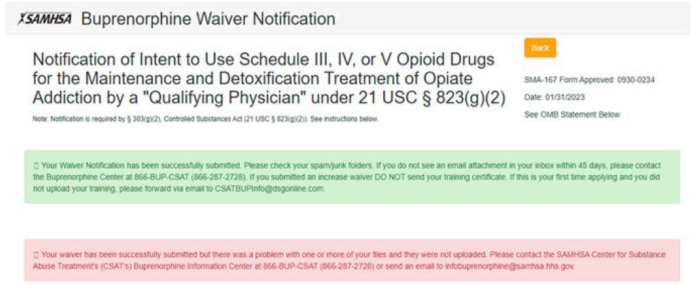
4. Under section 8, select **"other"** for the criteria for qualification. SAMHSA should be building out a different box to pop up with practice guidelines as an option. Currently that is not yet functioning and so the form asks you to fill out the date, city, and state where the certifying criteria took place. Fill this section out with today's date and under "city" **put "Practice Guidelines"**.



For state, enter state you are practicing in
This will likely change in the future to be more intuitive and have practice guidelines as an option.

5. Fill out the other areas with the appropriate information and with your preferences.

6. You may get an error that says you did not submit a form showing that training was completed.
This will change when SAMHSA updates the form in the future.



BILLING G 2213 CODE

- As of 2021 ED providers get paid just over $60 (1.9 RVUs) to “initiate medication for the treatment of opioid use disorder in the ED setting”
  - Assessment
  - Refer to ongoing care
  - Arranging access to supportive services

ASAM, 2021

REVIEW

- OUD is a highly morbid chronic medical condition
- OUD is treatable with highly effective medications
- Survival neurocircuitry has been hijacked (would you lie, cheat, and steal to stay alive?)
- The ED is one of several very important entry points for those with OUD to receive MOUD
- Reimbursement now tied with effective interventions

DON'T FORGET NALOXONE RESCUE!

But naloxone rescue without treatment engagement only delays death!

Bridge programs with warm hand-offs improve follow through

Low threshold care, diminish barriers

Long term engagement with motivational enhancement

Contingency management (meth and opioids)