

ASAM

TREATMENT OF OPIOID USE DISORDER COURSE

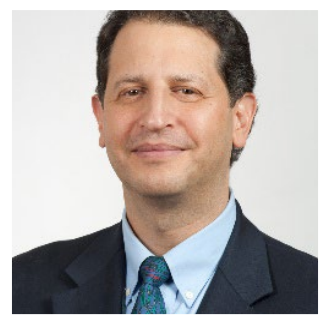
Course in Addiction Medicine

Announcements

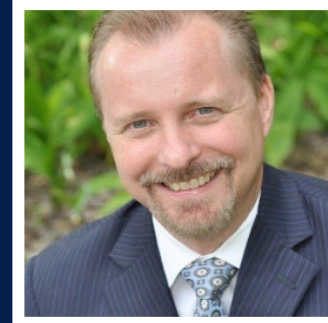
Handouts & More Questions

- Where do I find the handouts for this presentation?
 - Copies of the slides and other resources are available on the ASAM e-Learning Center under “Materials & Resources”
- How do I get specific questions answered?
 - If you have specific questions about the Patient Limit Increase or the recently-passed CARA bill, please email advocacy@ASAM.org.

Faculty



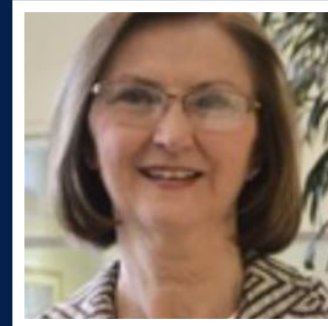
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Disclosure Information

Name, Titles

- *No Disclosures*

Learning Objectives

1. Identify the importance of screening for substance use disorders.
2. Describe the mechanism of opioid withdrawal.
3. Discuss options to treat opioid withdrawal.
4. Explain the safety and efficacy of buprenorphine to treat OUD.
5. Explain the safety of MOUD in antepartum, postpartum, and breastfeeding period.
6. Describe how to start a patient (induction) on the medication.
7. Discuss successful non-pharm ways to treat NOWs.

Treating Pregnant & Breastfeeding People With Opioid Use Disorder



Session 1: Introduction to
Treating Pregnant &
Postpartum People With OUD

In this session, we will review:



The Reward
Circuitry



The
Epidemiology of
Opioid Use
Disorder and
Pregnancy



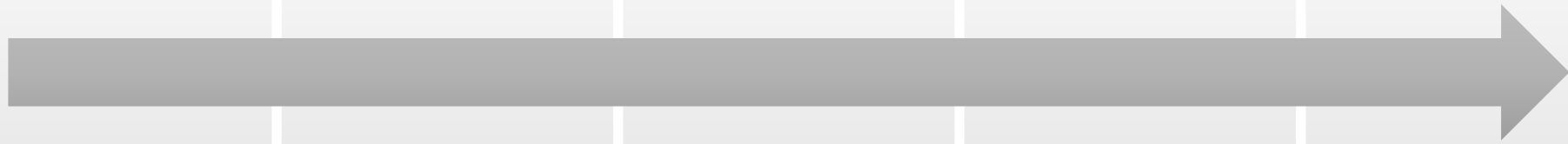
Barriers to
Treatment in
Pregnancy



Screening or
Opioid Use
Disorder



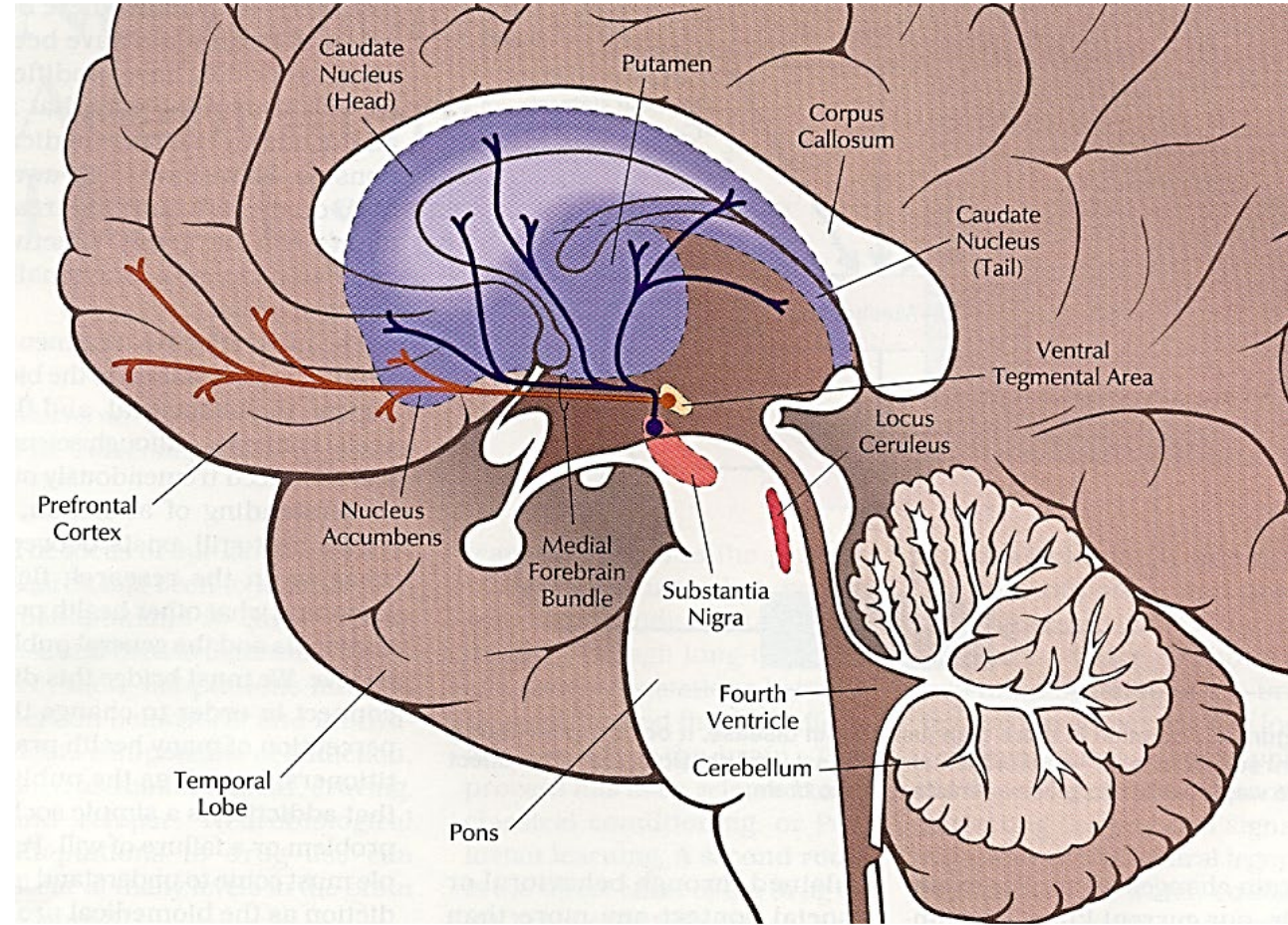
Trends in
Prescription
Opioid Use



Reward & Reinforcement is...

...in part controlled by *mu* receptors in the **Reward Pathway**.

- Ventral Tegmental Area (VTA)
- Nucleus Accumbens with projections to Prefrontal Cortex
- Dopaminergic system



Epidemiology: OUD and Pregnancy

5.4% of birthing people ages 15-44 used illicit substances

- Higher in young women with 14.6% in women 15-17 years vs. 3.2% in women 26-44 years

~21,000 birthing people aged 15 to 44 misused opioids in the past month

Between 2000 - 2009 the prevalence of opioid use among people who gave birth increased from 1.2 to 5.6 per 1,000 births annually

Pregnancy: Barriers to Treatment

Stigma

- Pregnant people with SUD feel intense shame and guilt
- Pregnant people fear disclosure to spouse/partner, family, and health care providers

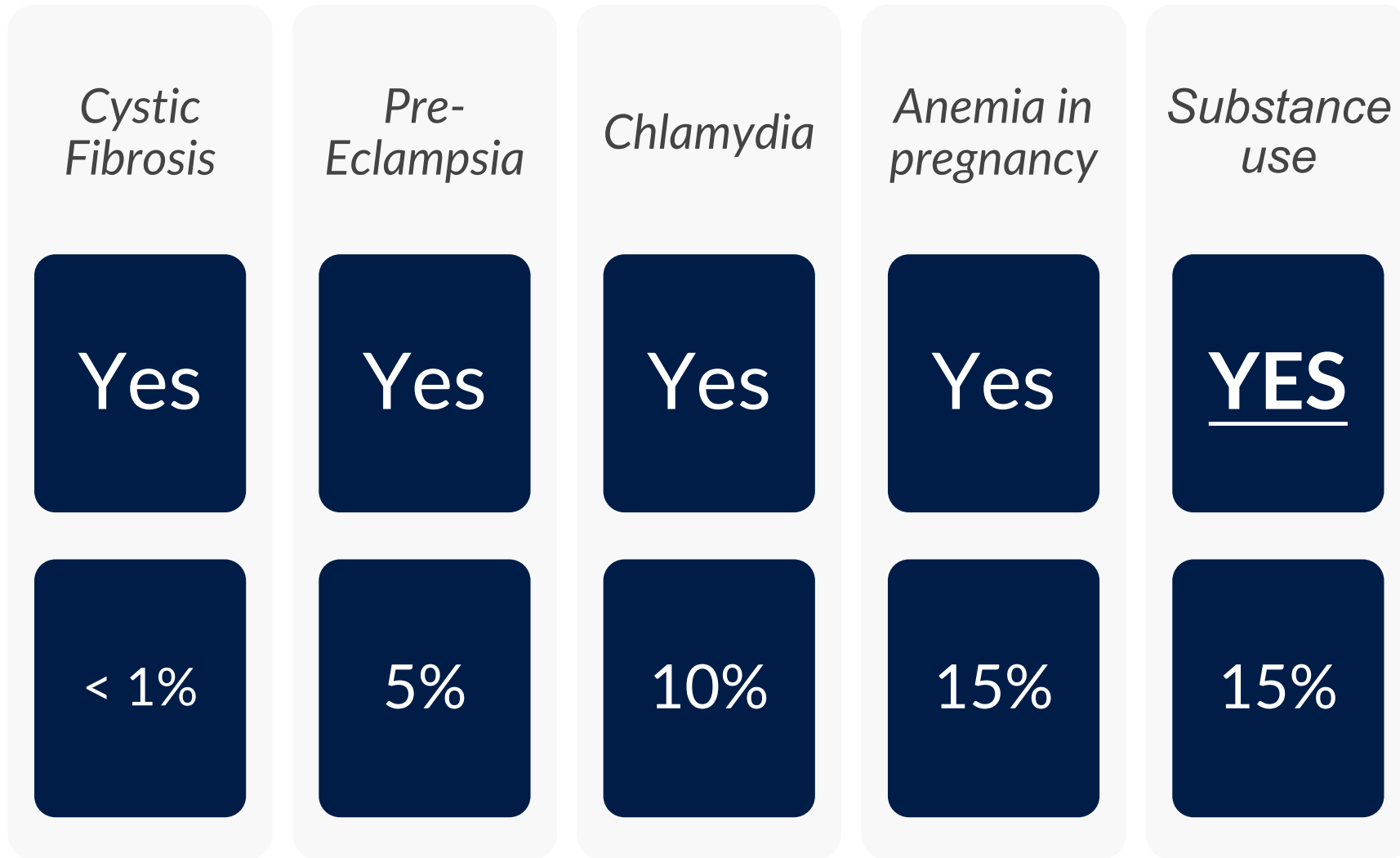
Fear of Legal Ramifications

- In some states substance use in pregnancy can be prosecuted as child abuse under civil child-welfare statutes and can be grounds for civil commitment

Healthcare System

- Most inpatient treatment facilities are unequipped to care for pregnant people
- Few obstetric practices specialize in SUD treatment
- Many addiction medicine practices are uncomfortable continuing treatment for a newly pregnant patient

Are You Screening for SUD?



In 2016, **15%** of birthing people had used illicit substances in the past year.

SBIRT

Screening

Referral

Brief
Intervention

If the answer is yes to any of the above, then the screen is positive, and an assessment should be done.

In the last 1 year have you...

- Smoked tobacco or vaped?
- Had more than four drinks of alcohol in one day or more than 10 in one week?
- Used a prescription for something other than prescribed?
- Used an illegal or illicit drug?
- Used marijuana*?

* For states that have legalized recreational or medical cannabis.

The 5Ps

Parents

Did any of your parents have a problem with alcohol or other drug use?

Partner

Does your partner have a problem with alcohol or drug use?

Peers

Do your peers have a problem with alcohol or drug use?

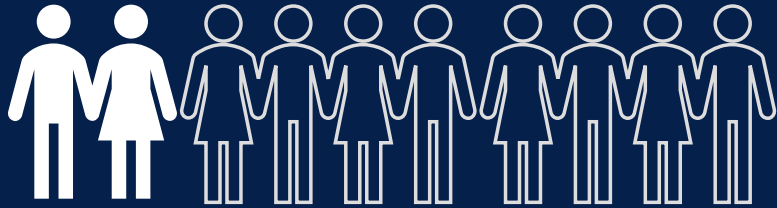
Past

In the past, have you had difficulties in your life due to alcohol or other drugs, including prescription medications?

Pregnancy

In the month before you knew you were pregnant, how many cigarettes did you smoke? How much alcohol did you drink? How much marijuana did you smoke?

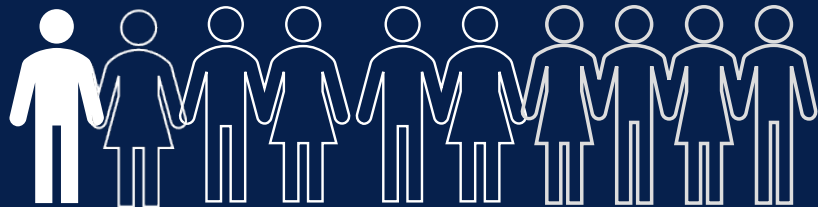
Demographics: Chronic Pain



15-20% population has severe chronic pain at some point

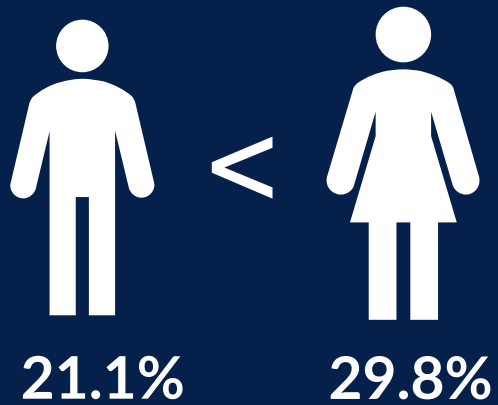


15-20% of people with chronic pain have underlying addictive process



Up to 8-12% of patients given opioids for chronic pain develop a use disorder

Birthing People & Prescription Opioids



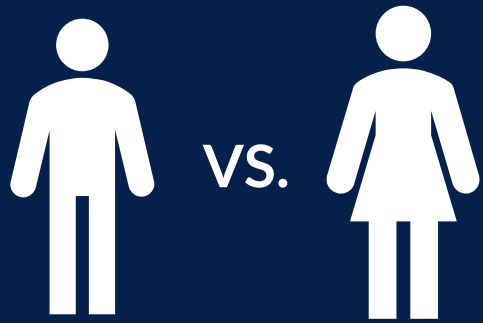
Birthing people were more likely to report use of any prescription opioid ($p < 0.001$)¹

Birthing people more likely to be given opioids for pain and higher doses²



Birthing people given these medications were likely to be child-bearing age

Birthing People & Prescription Opioids



- 1999 – 2010: Prescription opioid overdose deaths among birthing people increased from 1,287 to 6,631 (400%).
- 2000 – 2009: the use of opioids during pregnancy from 1.19 to 5.63 per 1,000 hospital births.
- 2009-2015: Prescription opioid overdose increased 471% in birthing people vs. 218% in men. 850% increase in synthetic opioid-related deaths in birthing people.
- 2013-2019: Overdose deaths involving synthetic opioids/fentanyl were nearly 12x higher in 2019 than in 2013. More than 36,000 people died from overdoses involving synthetic opioids in 2019.
- 2020-2021: The latest provisional drug overdose counts through May 2020 suggest an acceleration of overdose during the COVID-19 pandemic.

Racial Disparities & Prescription Opioids

- 2007-2016, the pregnancy-related mortality ratios 2-3 times higher for black and American Indian/Alaska Native (AI/AN) birthing people than for white, Hispanic, and Asian/Pacific Islander ones.
- Among birthing people with a college degree or higher, the pregnancy-related mortality ratio over 5 times higher for black birthing people compared to white, Asian/Pacific Islander, and Hispanic ones.
- College-educated black birthing people are more likely to experience a pregnancy-related death than white, Asian/Pacific Islander, and Hispanic ones without a high school diploma.
- Social determinants of health have a strong impact on racial and ethnic birthing parent health disparities.

Pregnancy & Postpartum: Opioid Agonist Maintenance

MOUD Remains the Standard of Care

Opioid agonist pharmacotherapy (either *methadone* or *buprenorphine*) is endorsed by the American College of Obstetricians and Gynecologists (ACOG) as the optimal treatment for OUD during pregnancy.

Methadone and buprenorphine are safe and effective treatment options in pregnancy and postpartum.

Pregnancy: Benefits Opioid Agonist Therapy

Benefits to the Birthing Person

70% reduction in overdose related deaths.

Decrease in risk of HIV, HBV, HCV.

Increased engagement in prenatal care and recovery treatment.

Benefits to the Fetus

Reduces fluctuations in maternal opioid levels; reducing fetal stress.

Decrease in intrauterine fetal demise.

Decrease in intrauterine growth restriction.

Decrease in preterm delivery.

Options for Opioid Dependence During Pregnancy

Methadone

Buprenorphine

Medically Supervised Withdrawal is NOT Safe

Bell et al (2016): 301 patients underwent medically supervised withdrawal during pregnancy

Birthing people tolerate the cardiovascular effects of withdrawal, but the result of treating a chronic disease with a temporary short fix contributes to: (1) return to use, (2) maternal and fetal complications and (3) potential overdose.

TABLE 1

Demographics, gestational age at the time of detoxification, neonatal intensive care unit admission, and pregnancy outcome of the opiate detox study population

Demographics	Group 1	Group 2	Group 3	Group 4	Total
Number	108	23	77	93	301
Mean maternal age, y	26.9 ± 3.7	26.4 ± 3.5	26.6 ± 3.6	27.2 ± 3.9	26.8 ± 3.7
Maternal age range, y	18–43	17–38	18–39	17–39	17–43
Maternal age <30 y	82 (76%)	18 (78%)	55 (71%)	67 (72%)	222 (74%)
Multiparity	94 (87%)	14 (61%)	54 (70%)	73 (78%)	235 (78%)
White	85 (79%) ^a	22 (96%)	74 (96%)	84 (90%) ^a	265 (88%)
African-American	22 (20%)	1 (4%)	3 (4%)	8 (9%)	34 (11%)
Gestational age at detoxification and NICU admission					
Detoxification first trimester, 5–13 wks gestation	10 (9%)	4 (17%)	12 (15%)	2 (2%)	28 (9%)
Detoxification second trimester, 14–27 wks gestation	65 (60%)	10 (43%)	36 (47%)	37 (40%)	148 (49%)
Detoxification third trimester, ≥28 wks gestation	33 (31%)	9 (39%)	29 (38%)	54 (58%)	125 (42%)
Preterm deliveries prior to 37 wks gestation	21 (19%)	3 (13%)	13 (17%)	16 (17%)	53 (17.6%)
Neonatal intensive care unit admission	32 (30%)	5 (22%)	60 (78%)	22 (24%)	119 (40%)
Pregnancy outcome					
Rate of NAS	20 (18.5%)	4 (17.4%)	54 (70.1%)	16 (17.2%)	94 (31%)
Rate of relapse ^b	25 (23.1%)	4 (17.4%)	57 (74.0%)	21 (22.5%)	107 (36%)

Group 1 consisted of acute detoxification (incarcerated patient). Group 2 consisted of inpatient detoxification with intense behavioral health follow-up. Group 3 consisted of inpatient detoxification without intense behavioral health follow-up. Group 4 consisted of slow outpatient buprenorphine detoxification.

NAS, neonatal abstinence syndrome; NICU, neonatal intensive care unit.

^a One Hispanic in group 1 and one Asian in group 4; ^b Relapse rate is defined as a positive drug screen on admission, an admission by the patient at the time of delivery that she had relapsed, or a positive neonatal meconium test (and includes all of the patients who had neonates treated for neonatal abstinence syndrome).

Bell et al. *Opiate detox during pregnancy*. *Am J Obstet Gynecol* 2016.

- **No adverse fetal outcomes** (2 IUFDs of those acutely withdrawn during first trimester)
- **NOWS/NAS rates: 31%** (17-70)
- **Return to Use rates: 36%** (17-74)
- No control group on MOUD (Mother Study – NOWS/NAS rates: 47%)

Medically Supervised Withdrawal Management

Low treatment
retention rates



< 50% abstinent at 6
months

High return to
use rate post-
treatment



< 15% abstinent at 12
months

Increased rates of
overdose due to
decreased
tolerance

*Withdrawal management is not treatment, it is just
the start of treatment.*

Treating Pregnant & Breastfeeding People With Opioid Use Disorder



Session 2: Medications For Opioid Use Disorder (MOUD) In Pregnancy

In this session, we will review:



Legislative Topics



Opioid Pharmacology



Medications for
Opioid Use Disorder
(MOUD) in Pregnancy



*The Role of Non-
Pharmacological
Treatment*



Legislative Topics



2000

Drug Addiction Treatment Act (DATA 2000)



2016

Comprehensive Addiction and Recovery Act (CARA)



2016

Final Rule on 275 Patient Limit



2019

SUPPORT for Patients and Communities Act (HR6)

Drug Addiction Treatment Act of 2000 (DATA 2000)

- Allows physicians to prescribe an FDA approved opioid for the treatment of opioid use disorder.
- Physicians must meet certain qualifications:
 - At least 8 hours of education
 - Patient limits: 30, 100
 - Application must be submitted online at the SAMHSA website
 - Receive “X-number” after application approval

Final Rule on 275 Patient Limit

- Announced in August 2016
- Allows qualified providers to increase patient limit to 275
 - Requires “qualified practice setting”
 - Requires new waiver application
 - Must reaffirm eligibility every 3 years (90 days before end of waiver year)

CARA & SUPPORT Acts

- CARA expanded prescribing to NPs and PAs
- SUPPORT Act expanded prescribing to CRNAs, CNMs, and CNSs
- Requires 24 hours of education

DATA 2000 – Practice Guidelines

The Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder

- SAMHSA Statement Regarding X-Waiver: On January 14, 2021, HHS announced forthcoming Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder.
- The new policy exempts eligible, DEA-registered practitioners from federal certification requirements related to training, counseling, and other ancillary services that are part of the process for obtaining a waiver to treat up to 30 patients with buprenorphine – a step toward helping Americans with opioid use disorder access evidence-based addiction care
- ASAM notes that an elimination of the X-waiver should be combined with needed education about the identification and treatment of substance use disorder in patients seen in daily practice. Proper education increases clinicians' willingness to administering life-saving, addiction care. ASAM commends HHS for recognizing that substance use disorder education is not yet uniformly integrated into medical education and that colleges of medicine and training programs are strongly encouraged to develop or to continue implementing comprehensive training in substance use disorder diagnosis and management as a component of their core, required curriculum.

Patient Limits

Beginning 1st Year

- 30 patients per practitioner during first year of the waiver.
- May start at 100 patients when meeting certain requirements.

After 2nd Year

- Can increase to 275 patients – a new waiver must be obtained.

After 1st Year

- Can increase to 100 patients – a new waiver must be obtained.

Census. Patient remains on your census until the last prescription has run out.

Hospitalized Patients. w/ primary admitting diagnosis other than OUD, buprenorphine can be ordered by non-waivered physician.

Medication Requirements

FDA Approval

- Drug must be approved by FDA for use in treating opioid use disorders (OUD).

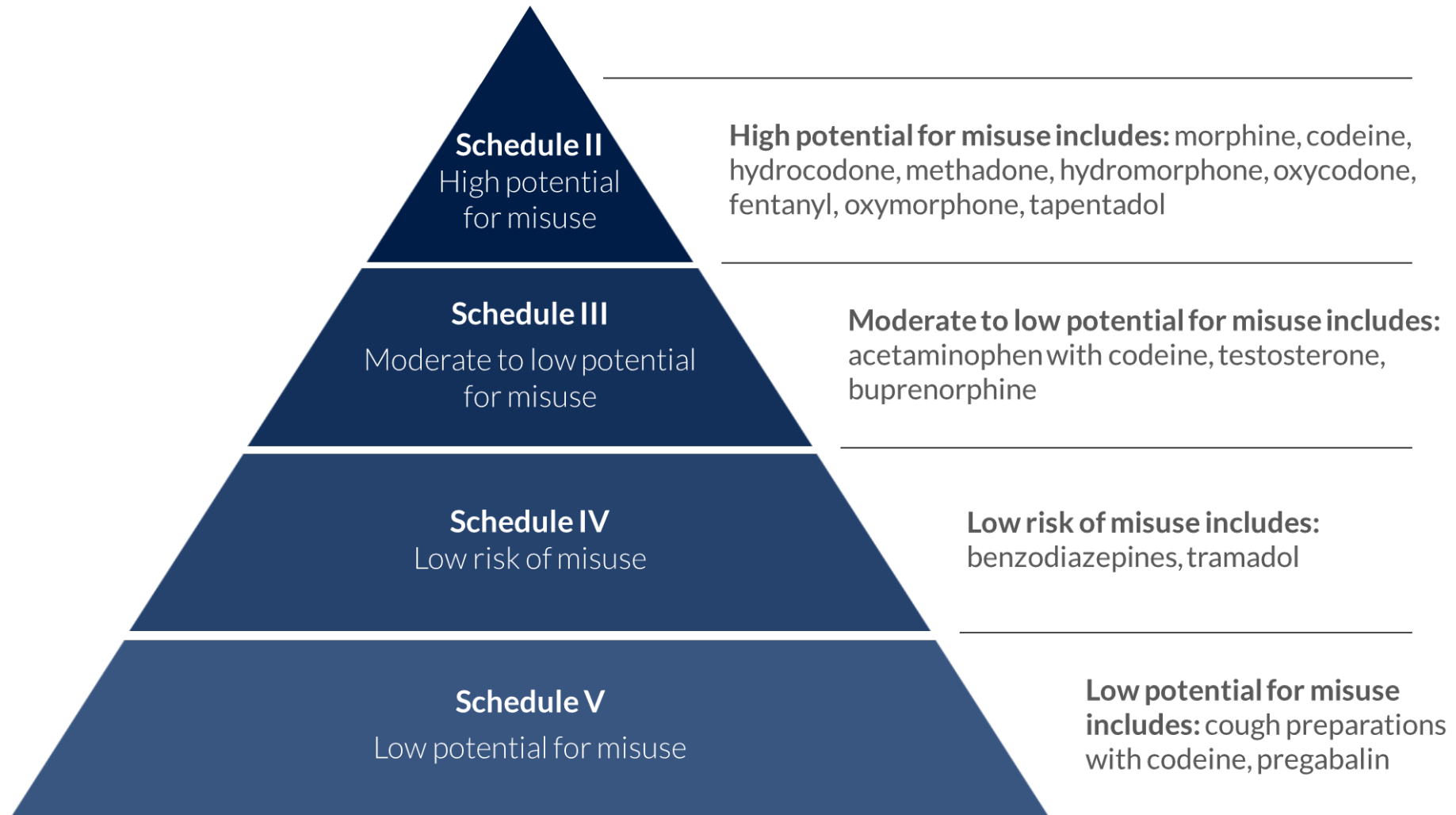
DEA Schedules

- Medication must be DEA schedule III, IV, or V (methadone is schedule II).

Buprenorphine Schedule

- Schedule III
- Certain (not all) formulations are approved for the treatment of OUD.

DEA Controlled Substance Classification



Requirements for Opioid Treatment Programs (OTP)

By Prescription:

The practitioner can prescribe approved medication in the same manner as in an office-based practice with the same patient limits (30, 100, 275).

VS

By Order to Dispense:

The practitioner can order approved medication to be dispensed in OTP setting in a manner similar to methadone with no specific limits on number of patients.

DEA Compliance

DEA continues routine practitioner inspections to assess:

- Compliance with the 30/100/275 patient limit.
- Record keeping.
- Security measures related to on-site drug storage if buprenorphine is dispensed or administered from the office.



Audience Response

Is someone who has their DEA waiver more likely to have DEA agents come to their practice?

- A. Yes, and it's a good reason not to get your waiver.
- B. Yes, and there are simple things you can do to make it less likely.
- C. Yes, because they are trying to get doctors to prescribe under a waiver.
- D. No.

Opioid Pharmacology

Opiates and Opioids

Opiates:

Natural compounds present in opium:
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

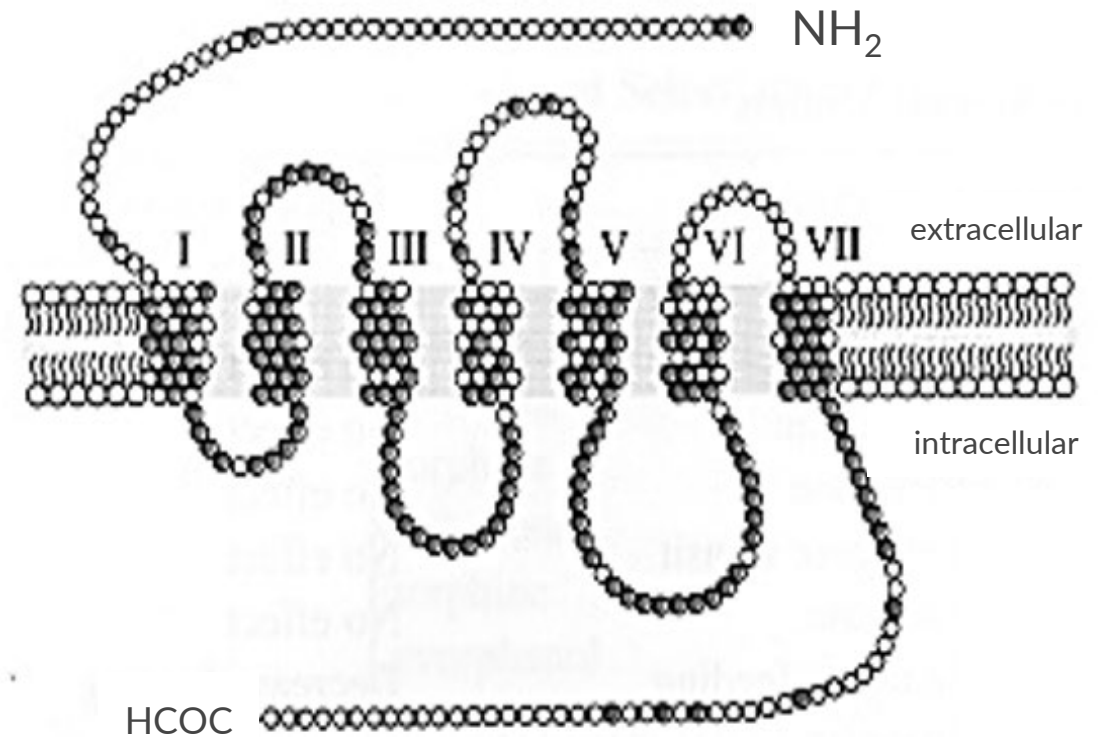
Endogenous Opioids and Their Receptors

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

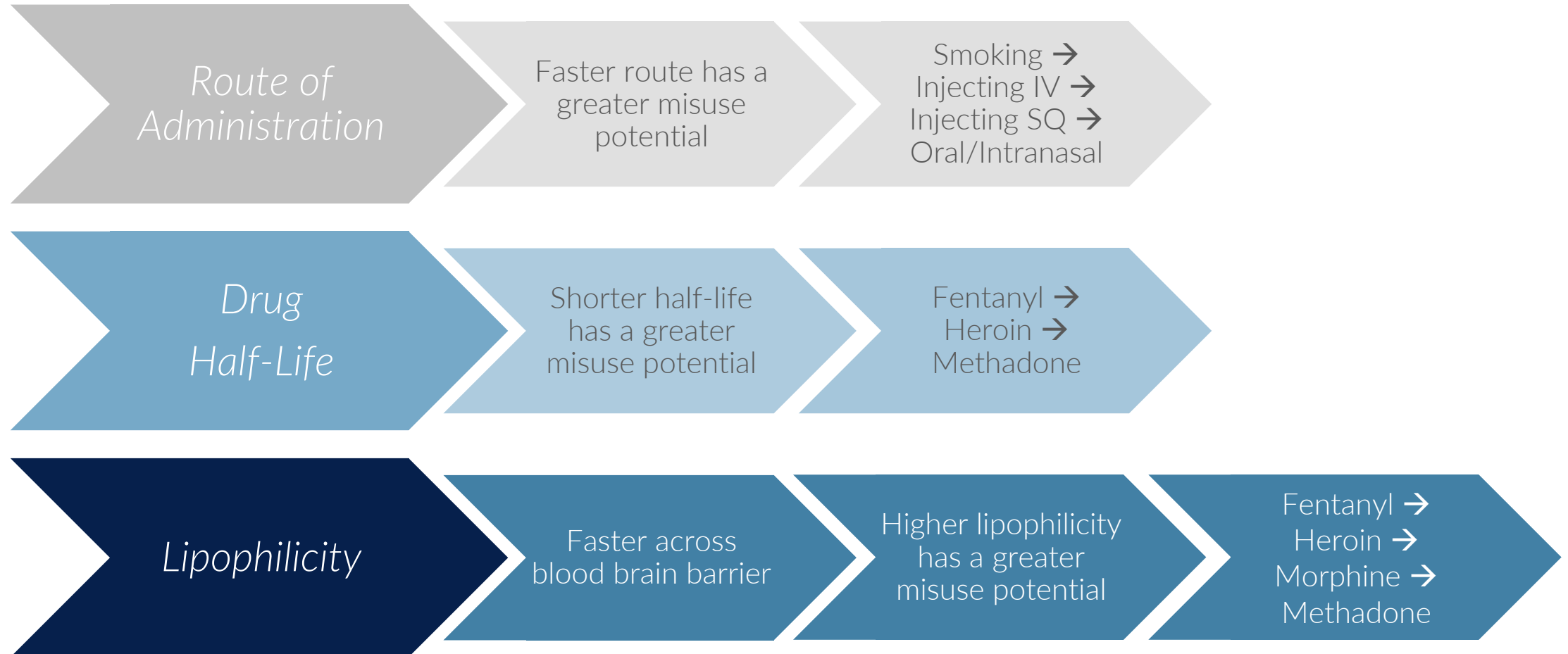
ENDOGENOUS LIGAND	OPIOID RECEPTOR TYPES
Beta Endorphins	Mu
Enkephalins	Delta
Dynorphins	Kappa
Nociceptin/OrphaninF/Q	ORL-1

Mu-Opioid Receptor

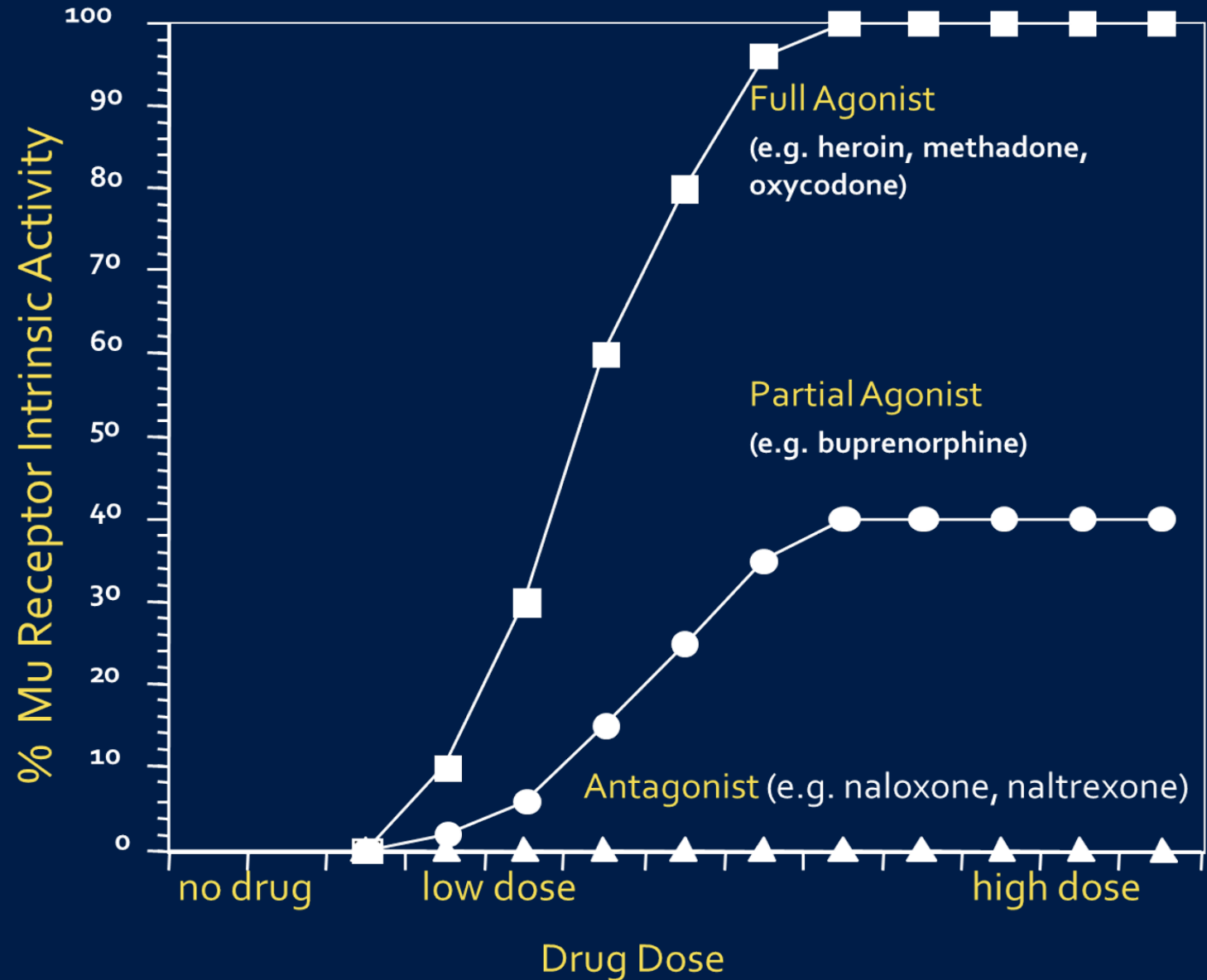
- *G-protein coupled receptor*
- *Subtypes and > 100 polymorphisms to the mu-opioid receptor gene*
- *High affinity for beta-endorphin and enkephalins*
- *High affinity for morphine*
- *Low affinity for dynorphins*
- *Acute changes in neuronal excitability via "disinhibition" of presynaptic release of GABA*



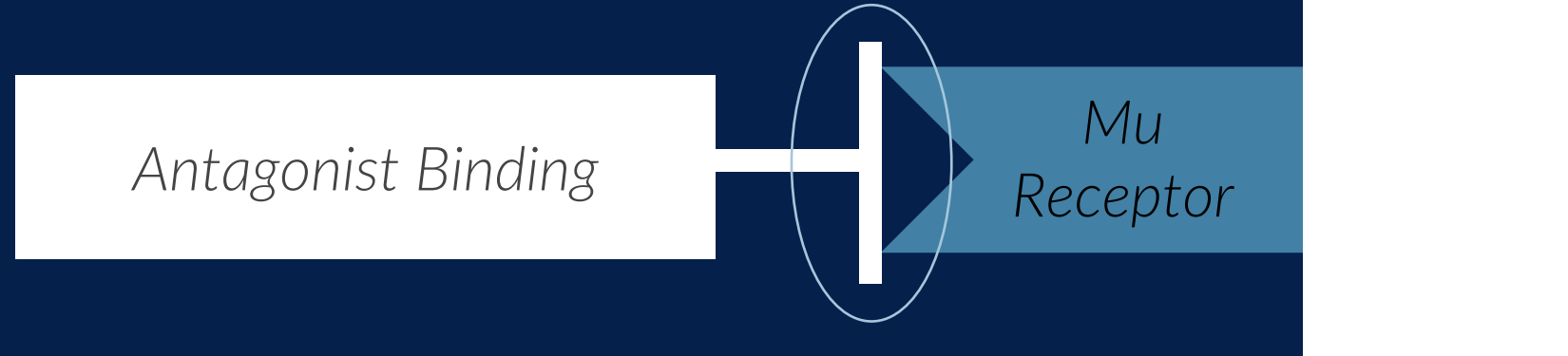
Opioid Characteristics that Increase Euphoria



Opioid Agonists and Antagonists



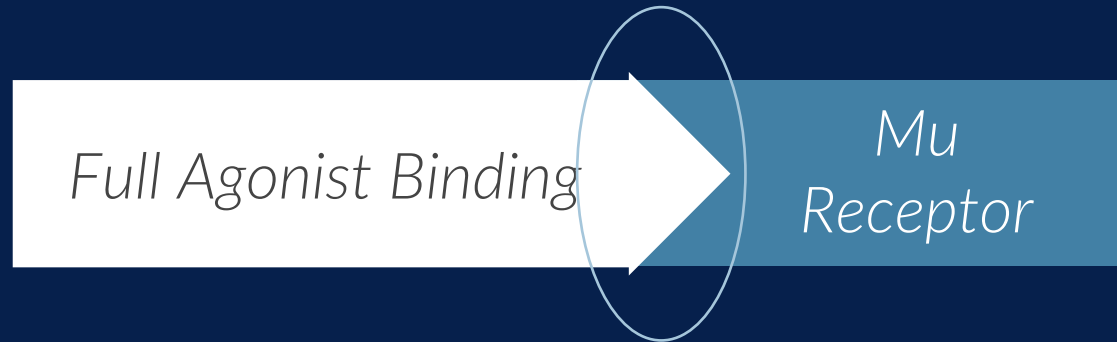
Opioid Antagonist



An antagonist

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

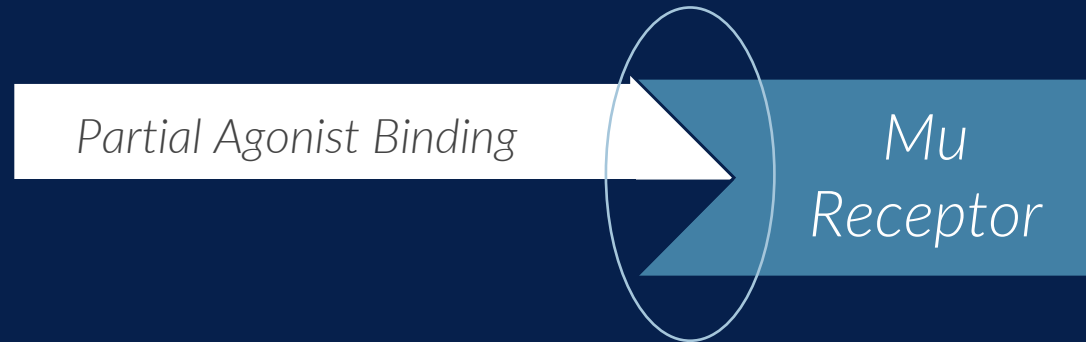
Full Opioid Agonist



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 Agonist



A partial agonist

- 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.

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).

Receptor Dissociation

Dissociation



- **Dissociation** is the speed (slow or fast) of disengagement of the drug from the receptor.
- **Buprenorphine's dissociation** is slow.
- **Buprenorphine stays on the receptor** for a long time and blocks full agonist from binding.

Acute Opioid Withdrawal

Symptoms / Signs

Mild

Anxiety, drug craving

Yawning, sweating, runny nose, tearing eyes, restlessness, insomnia

Dilated pupils, gooseflesh, muscle twitching, muscle & joint aches

Nausea, extreme restlessness, elevated BP, heart rate > 100, fever

Severe

Vomiting, diarrhea, abdominal cramps, curled-up body position

Clinical Opiate Withdrawal Scale (COWS):

pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh

- 5-12 *mild*
- 13-24 *moderate*
- 25-36 *moderately severe*
- >36 *severe*

Determinants of Withdrawal Risk

- Exposure to steady state level of medication:
 - Neuro-adaptation to opioids
- Higher intensity withdrawal from:
 - Higher steady state levels
 - Longer term exposure
 - Faster rate of medication clearance
 - Short vs. long half-life agents

Spontaneous Acute Opioid Withdrawal

- **Develops spontaneously in a person with physical dependence.**
 - Someone who suddenly stops, or markedly decreases the opioid.
- **Half-life opioids:**
 - Severity is usually less with longer half-life opioids.
 - Duration depends on half-life of opioids person uses.

<i>Opioid</i>	<i>Onset</i>	<i>Peak</i>	<i>Duration</i>
<i>Heroin</i>	4-6 hours	~ 3 days	4-7 days
<i>Methadone</i>	1-2 days	~ 7 days	12-14 days

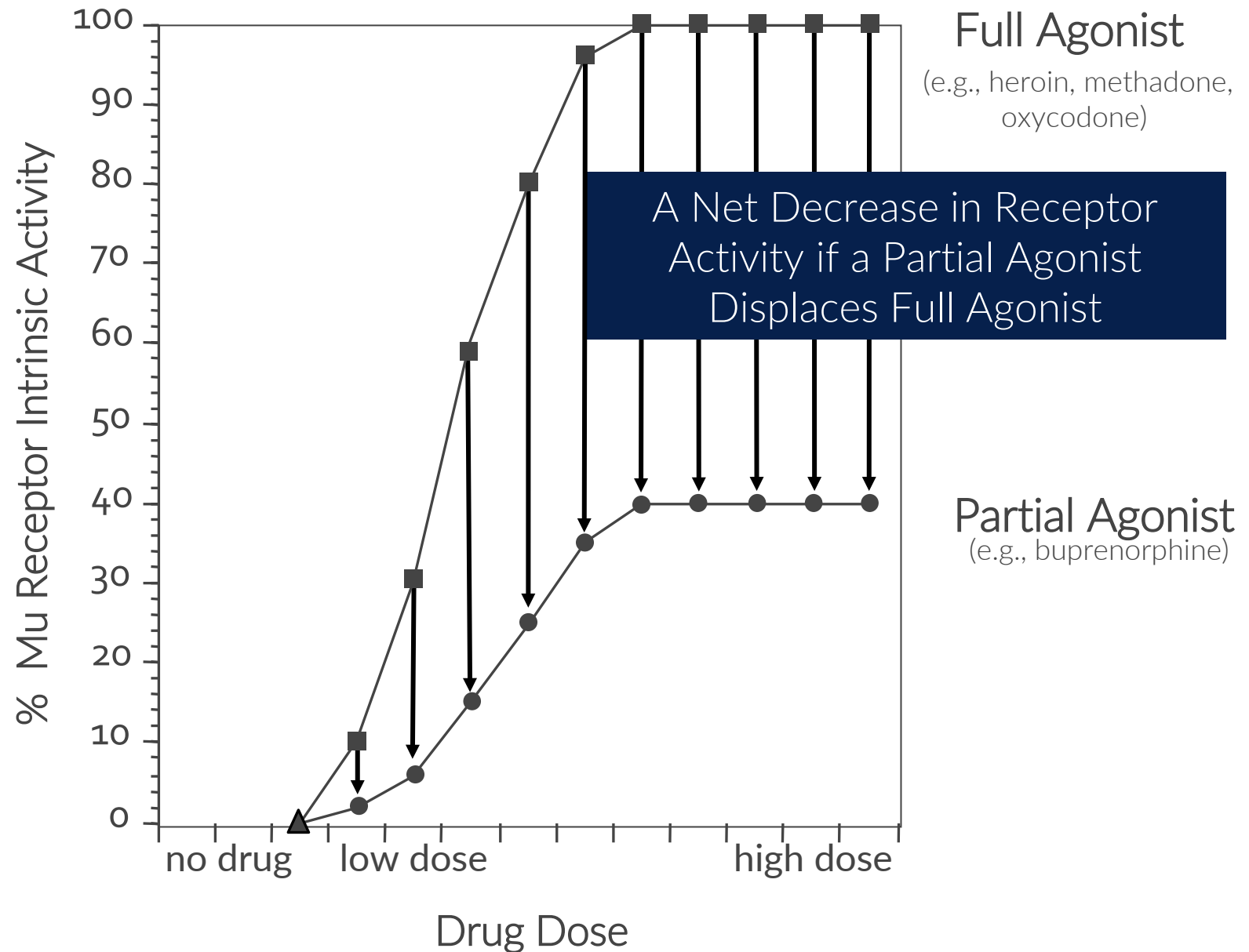
Precipitated Acute Opioid Withdrawal

- **Precipitated in a physically dependent person, by administration of an:**
 - opioid antagonist drug (e.g., naloxone, naltrexone), or
 - opioid partial agonist drug (e.g., buprenorphine)
- **Qualitatively similar to a spontaneous withdrawal but it has a faster onset.**
- **Duration depends upon half-life of drug.**

<i>Opioid antagonist drug/ Opioid Partial Agonist Drug</i>	<i>Onset</i>	<i>Peak</i>	<i>Duration</i>
<i>Naloxone</i>	Minutes	Minutes	~ 20 minutes
<i>Naltrexone</i>	Minutes	Minutes	1-2 days
<i>Buprenorphine</i>	Minutes	Minutes	1-2 days

Precipitated Acute Withdrawal

Buprenorphine will precipitate withdrawal when it displaces full agonist off the Mu receptors.



Audience Response

Which of the following is a characteristic of a partial agonist?

- A. It activates the mu receptor with a ceiling effect.
- B. It is relatively more reinforcing/rewarding.
- C. It is a riskier opioid type (i.e., sedation and respiratory depression).
- D. Methadone is an example of a partial agonist.

Medications for Opioid Use Disorder in Pregnancy

Pregnancy: MOUD Remains the Standard of Care

Methadone and buprenorphine

- ◆ Both category C
- ◆ Safe and effective treatment options for pregnancy

The decision of which therapy to start is complex and *should be individualized for each person*

- ◆ Based on available options, patient preference, patients' previous treatment experiences, disease severity, social supports, and intensity of treatment needed

Pregnancy: MOUD Remains the Standard of Care

Goals

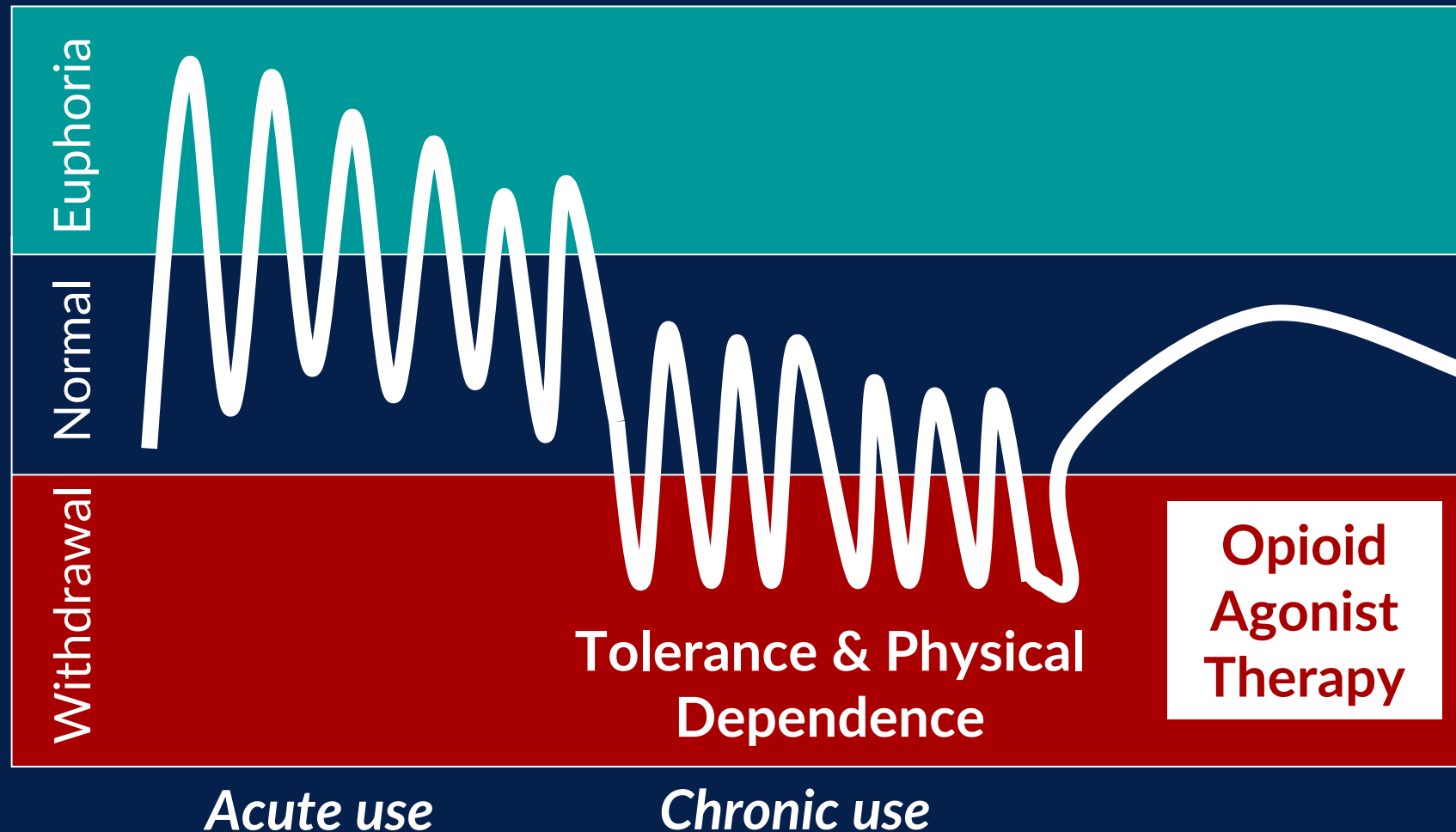
- ◆ Alleviate signs/symptoms of physical withdrawal
- ◆ Opioid receptor blockade
- ◆ Diminish and alleviate drug craving
- ◆ Normalize and stabilize perturbed brain neurochemistry

Options

- ◆ Opioid Antagonist
 - ◆ **Naltrexone** (full opioid antagonist; not recommended to start in pregnancy; we have limited data to suggest benefits)
- ◆ Opioid Agonist
 - ◆ **Methadone** (full opioid agonist)
 - ◆ **Buprenorphine** (partial opioid agonist)

Opioid Agonist Therapy:

Methadone & Buprenorphine



Buprenorphine

- High affinity mu receptor partial agonist/kappa opioid antagonist.
- Ceiling effect = reduced risk of overdose; ceiling effect for respiratory depression; none for analgesia (Note: pregnant people likely need higher and more frequent dosing.)
- Easier withdrawal.
- More expensive.
- Office based = need an “X number” or DEA waiver; New X-Waiver Rules offer education/training for providers.

Buprenorphine Preparations



Buprenorphine
sublingual
tablet.



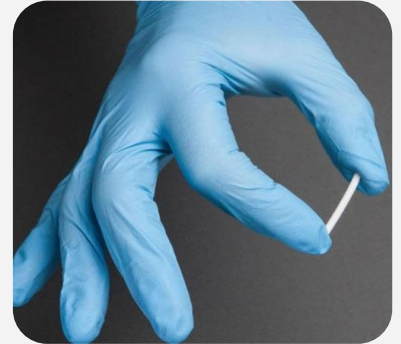
Buprenorphine
/ Naloxone
sublingual
tablet.



Buprenorphine
/ Naloxone
film.



Buprenorphine
long-acting
injection.



Buprenorphine
implant.

Buprenorphine Monoproduct Sublingual Tablet

*Buprenorphine
Only*

- Does not contain naloxone
- Usually only for birthing people or induction (7 days)
- Rare intolerance to naloxone
- Much higher risk diversion due to potential for intravenous use



Buprenorphine/Naloxone Sublingual Tablet



- Available in 2/.5 mg and 8/2 mg
- Dissolves in 8-10 minutes
- Orange flavor

Buprenorphine/Naloxone Sublingual Films



- Prior to 2019, brand only
- 2019 – Generic versions released
 - “Preferred” formulation by many insurance companies
- Individually wrapped in foil wrappers
 - Marketed to prevent pediatric exposure

Other (Less Common) Formulations



- Sublingual Rapidly dissolving tablet
 - Different dosing
- Buccal film



Long-acting Buprenorphine Subcutaneous



- Depot formulation, every 4 weeks
- Sustained release from a small deposit that dissolves slowly
- Cannot be used for induction
- Only two doses, 100 mg and 300 mg
- Low risk of diversion

Methadone Hydrochloride

- Full opioid agonist
- Oral: 80-90% bioavailability
- Liquid, tablets (for pain), parenteral
- PO onset of action: 30-60 min
- Duration of action:
 - 24-36 hours to treat OUD
 - 6-8 hours to treat pain
- Proper dosing for OUD:
 - 20-40 mg for acute withdrawal
 - Need to slowly titrate dose toward due to long half-life and risk of respiratory depression if increased too rapidly.
 - >80 mg for cravings and opioid blockade

The Role of Non-Pharmacological Treatment

Non-Pharmacological Treatment

- **Psychosocial services are often helpful.** Psychosocial services encourage utilization.
- **Additional Behavioral Therapy:** Three trials showed that additional behavioral therapy does NOT significantly improve outcomes over that achieved by buprenorphine PLUS “medical management” or “medical counseling.”
- **Patients should not be denied medication** should they refuse psychosocial services or if psychosocial services are not available.

Psychosocial Treatment Examples



- Individual counseling
- Group therapy
- Marital/family counseling
- Mutual help groups (e.g., AA, NA)
- SMART Recovery
- Women for Sobriety
- Secular Organizations for Sobriety (SOS)

Audience Response

Psychosocial treatment for persons with opioid use disorder should include:

- A. A mandate to be in therapy to access medications.
- B. Requirements to be in therapy early in treatment that decrease over time in treatment.
- C. Offering of person-centered therapy options.
- D. Having on-site counseling available including 24-hour call coverage.



Session 3: Managing Your Patient: Inductions, Dosing, Intrapartum and Postpartum Care

In this session, we will review:



Medication
Options for
Pregnant
People



Initial
Evaluations



Induction of
Medication
for Opioid
Use
Disorder



Managing
Pain:
Obstetric
and Non-
Obstetric
Pain



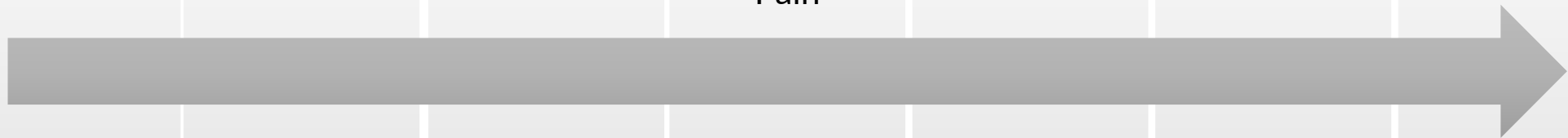
Medication
Doses



Managing
Your Patient
in Labor



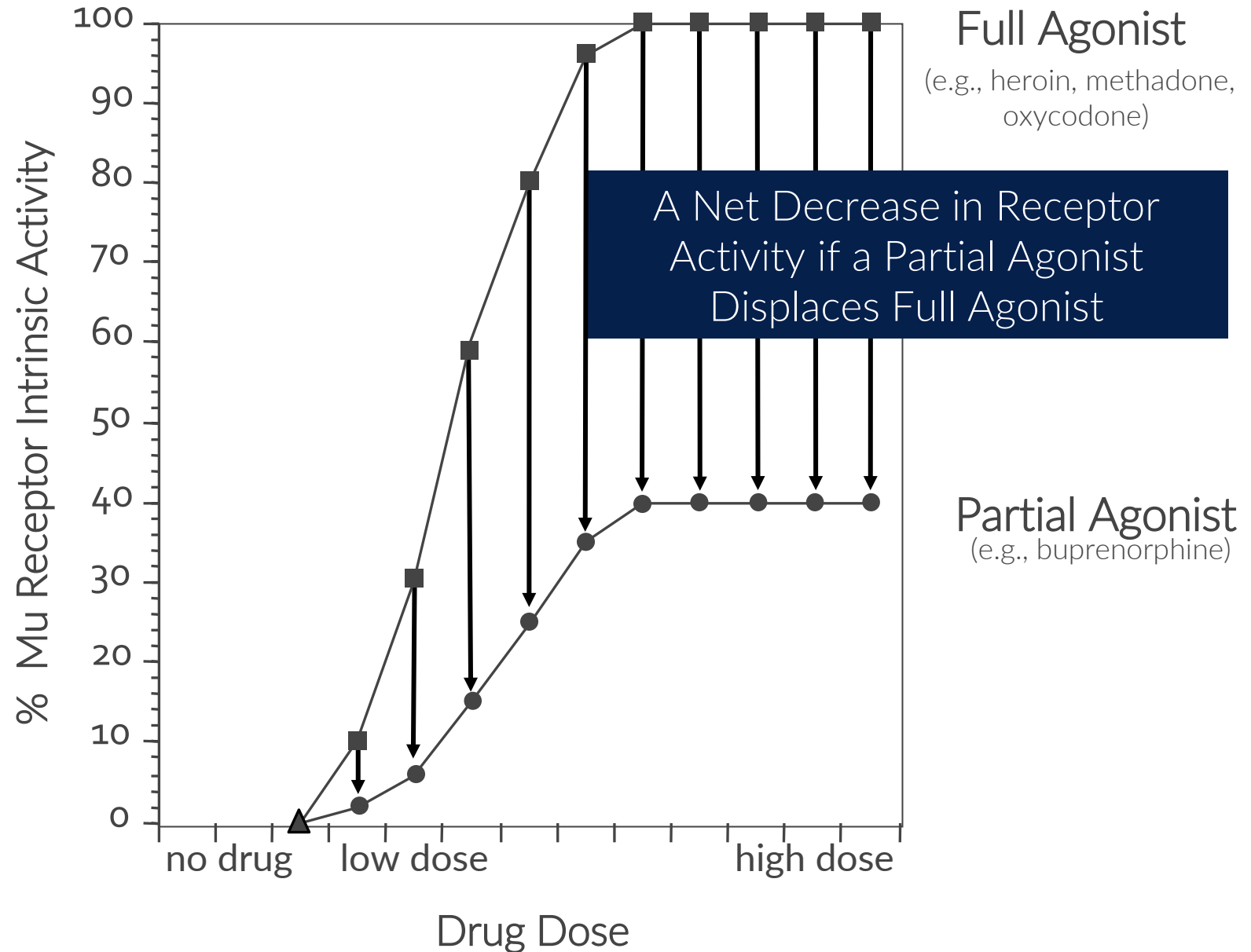
*Neonatal
Opioid
Withdrawal
Syndrome
(NOWS)*



Buprenorphine is a Partial Agonist

Buprenorphine will precipitate withdrawal when it displaces full agonist off the Mu receptors.

HIGH AFFINITY = SLOW DISSOCIATION



Which one for my patient?



Methadone



Buprenorphine

Let's examine the evidence...

MOTHER Study

Randomized trial of methadone versus buprenorphine.

Primary outcome: NOWS/NAS

- Similar prevalence of treatment for NOWS/NAS
- Less neonatal abstinence severity and treatment (Bup)
- Shorter neonatal LOS (Bup)
- Bigger HC

Table 2. Primary and Secondary Outcomes in the Methadone and Buprenorphine Groups.*

Outcome	Methadone (N=73)	Buprenorphine (N=58)	Odds Ratio (95% CI)	P Value
Primary outcomes				
Treated for NAS — no. (%)	41 (57)	27 (47)	0.7 (0.2–1.8)	0.26
NAS peak score	12.8±0.6	11.0±0.6		0.04
Total amount of morphine for NAS — mg	10.4±2.6	1.1±0.7		<0.0091†
Duration of infant's hospital stay — days	17.5±1.5	10.0±1.2		<0.0091†
Infant's head circumference — cm <i>But...</i>	33.0±0.3	33.8±0.3		0.03
Secondary neonatal outcomes				
Duration of treatment for NAS — days	9.9±1.6	4.1±1.0		<0.003125†
Weight at birth — g	2878.5±66.3	3093.7±72.6		0.03
Length at birth — cm	47.8±0.5	49.8±0.5		0.005
Preterm, <37 wk — no. (%)	14 (19)	4 (7)	0.3 (0.1–2.0)	0.07
Gestational age at delivery — wk	37.9±0.3	39.1±0.3		0.007
Apgar score				
1 min	8.0±0.2	8.1±0.2		0.87
5 min	9.0±0.1	9.0±0.1		0.69

MOTHER Study

Secondary outcomes:

- Bigger neonates (Bup)
- No difference preterm birth
- Longer gestational age (Bup)

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1 min	8.0±0.2	8.1±0.2		0.87
5 min	9.0±0.1	9.0±0.1		0.69

MOTHER Study

Secondary outcomes: maternal outcomes

- Fewer medical/ delivery complications (Bup)
- Increased % of people randomized to buprenorphine did not complete the study

Table 2. Primary and Secondary Outcomes in the Methadone and Buprenorphine Groups.*

Outcome	Methadone (N=73)	Buprenorphine (N=58)	Odds Ratio (95% CI)	P Value
Secondary maternal outcomes				
Cesarean section — no. (%)	27 (37)	17 (29)	0.6 (0.2–2.0)	0.23
Maternal weight gain — kg	8.6±1.0	8.3±0.9		0.80
Abnormal fetal presentation during delivery — no. (%)	10 (14)	3 (5)	0.3 (0.0–2.4)	0.09
Analgesia during delivery — no. (%)	60 (82)	49 (85)	1.1 (0.3–4.8)	0.85
Positive drug screen at delivery — no. (%)	11 (15)	5 (9)	0.5 (0.1–2.7)	0.27
Medical complications at delivery — no. (%)	37 (51)	18 (31)	0.5 (0.2–0.9)	0.03
Did not complete study — no. (%)	16 (18)	28 (33)	2.6 (1.3–5.6)	0.02
Amount of voucher money earned for drug-negative tests — U.S. \$	1,570.00±121.72	1,391.39±123.59		0.31
No. of prenatal obstetrical visits	8.8±0.5	8.7±0.4		0.86

Childhood Development Outcomes

Findings strongly suggest *no deleterious effects of buprenorphine relative to methadone.*

No deleterious effects for NOWS/NAS severity relative to not-treated for NOWS/NAS.

- Growth
- Cognitive development
- Language ability
- Sensory processing
- Temperament

Summary of outcomes:	FAVORS Methadone	EQUIVALENT	FAVORS Buprenorphine
Maternal			
Treatment efficacy	*better for women that failed treatment in past	X*	*can be considered reasonable first line treatment
Access to treatment			X
Requires withdrawal for initiation	X		
Treatment automatically coordinated	X		
Maternal medical complications			X
Neonatal			
Long-term outcome: data	X		
Birthweight			X
Gestational age			X
% requiring NOWS/NAS treatment		X	
Severity of NOWS/NAS symptoms			X
Duration of NOWS/NAS treatment			X

Take Home Messages

- Either is appropriate for care depending on patient preference/access to care
- Use patient-centered and trauma-informed approach to empower autonomy and patient's "choice and voice"

Take-Home Message

Take-home message regarding methadone and buprenorphine for the treatment of opioid dependence during pregnancy.

- Methadone or buprenorphine may be used during pregnancy depending on patient preference/access to care.
- Use patient-centered and trauma-informed approaches to support patient autonomy and honor their “choice and voice.”
- It is acceptable care to initiate or maintain pregnant people on buprenorphine when treatment criteria are met and for whom it is the best therapeutic option.
- Many centers are use buprenorphine routinely for patients presenting for care as treatment compliance/access are typically improved with buprenorphine.
- Buprenorphine may have some benefits over methadone for fetal and neonatal outcomes. If present, NOWS/NAS may be milder.
- Buprenorphine has beneficial fetal effects including milder clinical opiate withdrawal scores (COWS).

Use of Buprenorphine During Pregnancy: *With Naloxone*

Buprenorphine/Naloxone (Medication Containing Two Medicines/Combination Product)

- No known teratogenic effects in animals
- Controlled studies have *not* been conducted in humans
- Increasing evidence that buprenorphine/naloxone may be safe in pregnancy
- However, buprenorphine *without* naloxone is recommended during pregnancy.
 - Note: It is acceptable to continue birthing people on buprenorphine/naloxone through pregnancy. In areas with high incidence of buprenorphine diversion, routine use of buprenorphine with naloxone is acceptable.

Use of Buprenorphine During Pregnancy: *Without Naloxone*

Buprenorphine (Monoproduct)

- Buprenorphine *without* naloxone is recommended during pregnancy.
 - Note: It is acceptable to continue pregnant people on buprenorphine/naloxone through pregnancy. In areas with a high incidence of buprenorphine diversion, routine use of buprenorphine with naloxone is acceptable.

Pregnancy: *Initial Evaluation*

Specialized Treatment Services

- Inform yourself about specialized treatment services available in the community for birthing people with OUD.
- A referral should be offered/encouraged regardless of the patient's decision to continue the pregnancy.
- Evaluate for intrauterine pregnancy, rule out ectopic or abnormal pregnancy immediately.

Educate

- Inform your patient about treatment options.
- Obtain informed consent for opioid agonist therapy prior to induction/initiation.
- Engage patient in shared decision-making to foster patient-centered approach.

Pregnancy: *Induction of Maintenance Therapy*

Goal

- Reach the dose just high enough to stop use and block cravings.

Management

- The dose should be individualized and based on patients' symptoms.

Dose Adjustments

- This is often necessary with advancing gestational age based on the physiology of pregnancy.
- Current evidence suggests benefits from split and higher dosing in facilitating steady plasma levels and medication stability given accelerated metabolic and renal clearance during pregnancy.

Patient on Buprenorphine: *The Newly Pregnant*

For persons stable on buprenorphine/naloxone who become pregnant.

- Current standard of care has been to switch to buprenorphine monotherapy at the same dose *if* it will not destabilize the patient or if it is not contraindicated by state policy or insurance coverage; however, recent clinical evidence suggests efficacy and safety of the combination therapy is equal to monotherapy and therefore continuation of the combination product is acceptable. Educate the patient about available treatment options to encourage autonomy and allow the patient to make a choice.
- Use of the combination therapy has been limited due to the unknown level of risk associated with exposure to naloxone in pregnancy and concern for misuse causing acute withdrawal and fetal distress.

Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. *Obstet Gynecol.* 2015 Feb;125(2):363-368. doi: 10.1097/AOG.0000000000000640. PMID: 25569005.



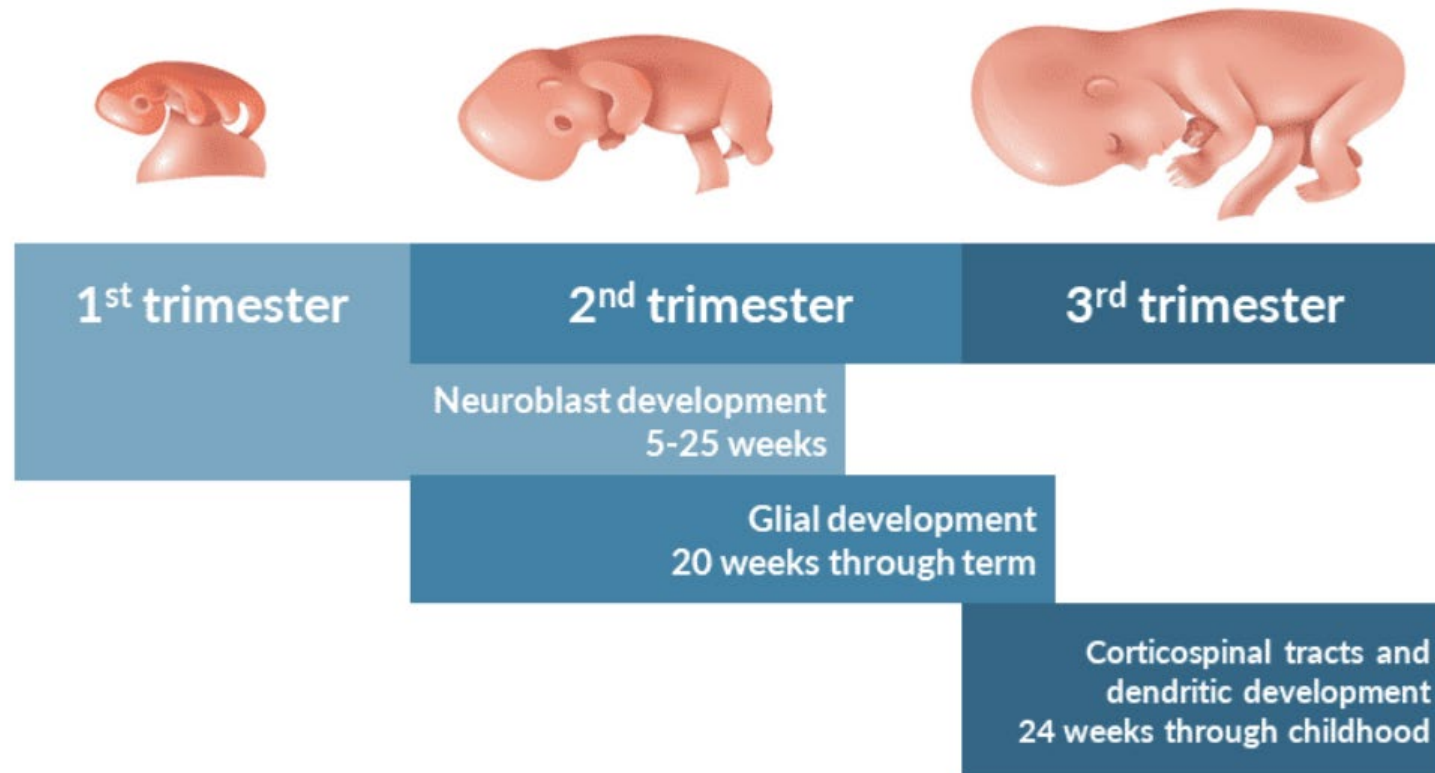
How and When to Initiate Buprenorphine

If we're so worried about withdrawal, how and when do we start buprenorphine?

- Ensure moderate withdrawal before initiating treatment; quickly work to get pregnant people comfortable with small incremental dosages and ancillary medications
 - COWS 12
- Induction from methadone to buprenorphine can be associated with higher rates of increased withdrawal, dissatisfaction with buprenorphine, and is not recommended in pregnancy unless there is a contraindication to continued methadone use such as side effects, increased QT interval or moving to area without access to methadone
 - Methadone has
 - a long half-life.
 - higher rates of precipitated withdrawal.
- Pregnant persons tolerate the cardiovascular effects of moderate withdrawal well. The provider should work closely with the patient to offer safe care, and ensure a successful start to buprenorphine usage, and ongoing treatment engagement.
- Fetal data is necessary:
 - Third trimester inductions usually done in hospital

Fetal Neurologic System Development

Theoretically, fetal withdrawal should not occur until late in gestation.



Inductions

The Other “Induction”



Office



Inpatient



Home

Office Inductions: *Sample Protocols for Treating your Patients with Opioid Dependence*

- Perform a brief phone interview to determine if patient is appropriate for office-based opioid treatment (OBOT).
- Instruct no opioids for at least **12-18 hours** (to ensure withdrawal).
- Call in a small supply of medications for the patient for the induction, usually eight 2 mg tablets of buprenorphine.
- In office: offer education on OUD/MOUD, review risks/benefits of medication, engage in shared decision-making and offer/sign consent (not all practices require signed consent).
- Record Clinical Opiate Withdrawal Scale score (COWS) and put in chart.

COWS: Clinical Opiate Withdrawal Scale

CLINICAL OPIATE WITHDRAWAL SCALE (COWS)

For Buprenorphine/naloxone induction: Enter scores at time zero, 1-2 h after first dose, and at additional times that buprenorphine/naloxone is given over the induction period.

	DATE/TIME:	DATE/TIME:	DATE/TIME:
Resting Pulse Rate: (record beats per minute) <i>Measured after patient is sitting/lying for one minute.</i> 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120			
Sweating: <i>Over past ½ hour not accounted for by room temperature or patient activity.</i> 0 no report of chills or flushing 1 one subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face			
Restlessness: <i>Observation during assessment.</i> 0 able to sit still 1 report difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds			
Pupil Size: 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only rim of the iris is visible			
Bone or Joint aches: <i>If patient was having pains previously, only the additional component attributed to opiate withdrawal is scored.</i> 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort			
Runny nose or tearing: <i>Not accounted for by cold symptoms or allergies.</i> 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks			
GI Upset: <i>Over last ½ hour</i> 0 no GI symptoms 1 stomach cramps 2 nausea or loose stools 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting			
Tremor: <i>Observation of outstretched hands</i> 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching			
Yawning: <i>Observation during assessment</i> 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute			
Anxiety or Irritability 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable, anxious 4 patient so irritable or anxious that participation in the assessment is difficult			
Gooseflesh skin 0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection			
Total Score			
Observers Initials			
Blood Pressure/Pulse			
Dose of Buprenorphine/naloxone Given			

Note: Give first dose when COWS score \geq 7

SCORE: 5-12 = Mild
 13-24 = Moderate
 25-36 = moderately severe
 More than 36 = severe withdrawal

Office Inductions: *Administering Medication*

- Administer first dose 2-4 mg, under observation.
- Keep patient in office, passively observe patient for an hour and record in medical record.
- Give more medication (4 mg) every hour if relief has not been achieved. Usually at 12-16 mg on first day of office induction.
- If patient responds appropriately, give enough prescription until follow-up visit, usually 1-3 days but may be up to one week.
- A telephone follow-up that evening or next day is encouraged.

Office Induction: *Pitfalls*

Patient is not in sufficient withdrawal:

- They may have previously exaggerated symptoms.
- They are using methadone or fentanyl.

Precipitated withdrawal:

- The patient will start to become very sick usually within 20-30 minutes.
- Try to give more buprenorphine and offer ancillary medications to overcome the effect.
- Hold off induction until later in the day or next day.
- Can hospitalize and give full agonist; however, usually best to continue.

Office Induction: Treating Precipitated Withdrawal

- **Buprenorphine:**
 - Repeat doses of 2 mg every 1-2 hours.
- **For anxiety:**
 - Clonidine 0.1 mg every 8 hours – Careful: This medication can cause hypotension, so check blood pressure every X hour (or as needed).
 - Hydroxyzine 25-50 mg every 8 hours.
- **For Nausea:**
 - Zofran
 - Phenergan
 - Hydroxyzine 50 mg



Office Induction: Treating Precipitated Withdrawal

- **For Sleep:**
 - Trazodone, which may be used long-term. A side effect of trazodone is that it can cause vivid dreams.
 - Mirtazapine HS
- **For Restlessness:**
 - Tizanidine 2mg every 8 hours
 - Clonidine 0.1mg every 8 hours
 - Note: Both medications are alpha agonists and can cause hypotension and/or bradycardia (tizanidine causes less hypotension/bradycardia due to its peripheral action compared to clonidine's central mechanism of action).

Inpatient Induction

- Third Trimester
- Co-Morbidity
- Social Reasons



MOUD in Pregnancy - Buprenorphine

Buprenorphine initiation and stabilization settings:

1. Inpatient
2. Outpatient
3. Home

How scary is it to treat withdrawal?

Pregnant people tolerate moderate withdrawal well (Meyer 2014).

No evidence-based consensus on how buprenorphine induction should be conducted, including appropriate gestational age, setting, and fetal monitoring (Young 2012).

Buprenorphine Initiation- Short-acting Opioids

Evaluation. Identify and refer urgent problems. History, laboratory, medical examination, prenatal care, mental health, psychosocial assessment, social and environmental factors. Discuss treatment options, patient-centered "choice and voice", TIC, informed consent. Safety/efficacy with either buprenorphine+naloxone and buprenorphine. Plan for outpatient if stable and < 22-24 weeks or inpatient initiation if unstable and > 24 weeks.

Observed office initiation
Plan for 2-4 hours visit

Unobserved "home"
initiation after office visit

Inpatient initiation:
anticipated 24-72 hours

#1. Abstain from opioids 12-24 hours. COWS>10. Start buprenorphine 1-2 mg. Q2Hx2 (monitor x 1-4hrs -> home) -> 4mgQ2Hx2 -> 8mgBID/TID.
#2. Start scheduled ancillary meds TID/QID: gabapentin 300mg, hydroxyzine 25-50mg, dicyclomine 20mg, tizanidine 2mg.
Start bup 1-2 mg Q2H -> mg4Q2H -> 8mg BID.

Sober/family support to help with dispensing medications, self-care.
Upon opioid cessation, start ancillary meds TID/QID: gabapentin 300mg, hydroxyzine 25-50mg, dicyclomine 20mg, tizanidine 2mg.
Start bup 0.5mgQ6Hx2 -> 2mgQ6Hx2 -> 4mgQ6Hx2 -> 8mg BID/TID.

Admission to inpatient facility, VS, COWS. Gabapentin 300mg TID, hydroxyzine 25-50mg TID, dicyclomine 20mg TID, tizanidine 2mg TID.
Start bup 1mgQ2Hx2 -> 2mgQ2Hx2 -> 2mgQ2Hx2 -> 4mgQ2Hx2 -> 8mg BID/TID.

Warm hand-off: encourage daily phone and office Q3-7d f/u, group/peer coach/doula support, prenatal, mental health, psychosocial tx. Adjust bup in 2nd/3rd trim. Ongoing smoking cessation, overdose prevention/narcan.

Buprenorphine Initiation-Low Dose Protocol For Fentanyl / Long-acting Opiates

Evaluation. Identify and refer urgent problems. History, laboratory, medical examination, prenatal care, mental health, psychosocial assessment, social and environmental factors. Discuss treatment options, patient-centered "choice and voice", TIC, informed consent. Safety/efficacy with either buprenorphine+naloxone and buprenorphine. Plan for outpatient if stable and < 22-24 weeks or inpatient initiation if unstable and > 24 weeks.



Outpatient Initiation: Provide education on OUD, fentanyl withdrawal management.



Inpatient initiation: Provide patient-centered care/ education on OUD, withdrawal management, MOUD.



Scheduled ancillary TID/QID meds:
Gabapentin 300mg, hydroxyzine 25-50mg, dicyclomine 20mg, tizanidine 2mg.
Low dose buprenorphine:
0.5mgQ6Hx2 -> 2mgQ6Hx2 -
> 4mgQ6Hx2 -> 8mg BID/TID.
D/c ancillary meds once stable dose.



Methadone-buprenorphine crossover:
Day 1: Methadone 50mg-buprenex 0.15mg QID
Day 2: Methadone 50mg-buprenex 0.30mg QID
Day 3: Methadone 50mg-buprenex 0.60mg QID
Day 4: Methadone 40mg-buprenorphine 1mg QID
Day 5: Methadone 30mg-buprenorphine 2mg QID
Day 6: Methadone 20mg-buprenorphine 4mg QID
Day 7: Methadone 10mg-buprenorphine 8mg TID
Scheduled/prn ancillary meds.



Serial VS/COWS. Scheduled ancillary gabapentin 300mg QID, hydroxyzine 50mg QID, dicyclomine 20mg QID, tizanidine 2mg QID, mirtazapine HS. Start buprenorphine 0.15mg Q2-4Hx2 -> 0.30mg Q2-4Hx2 -> 0.60mg Q2-4Hx2 -> 1mg Q2-4Hx2 -> 2mg Q2-4H-> 4mg Q2-4Hx2 -> 8mg BID/TID, d/c ancillary meds once stable dose



Warm hand-off: encourage daily phone and office Q3-7d f/u, group/peer coach/doula support, prenatal, mental health, psychosocial tx. Adjust bup in 2nd/3rd trim. Ongoing smoking cessation, overdose prevention/narcan.



Unobserved/Home Inductions

- Alternative to observed induction
 - Evaluated prior to treatment, typically while still using opioids and not in withdrawal.
 - Receives a Rx, starts at home in privacy and ready



Home Inductions

No differences between the inductions in longitudinal outcomes.

Not studied in pregnant patients.

In 2007, a Massachusetts survey indicated 42% of physicians adopted as a regular practice.

Read more: Mintzer IL et al Ann Fam Med. 2007;5(2):146-50.
Alford DP et al. J Gen Intern Med.
Walley AY, et al. J Gen Intern Med. 2008;23(9):1393-8

Patient Selection For Home Induction

Patient familiar with the medication (e.g., already taking “street subs”)

Family members at home/Patient not home alone

Mature

Reliable (e.g., accurate phone number provided)

Unobserved/Home Inductions

- ***Advantages***

- Less time “being sick” in the waiting room
- Requires less transportation resources for patient
- Patient can withdraw in comfort of their home

- ***Disadvantages***

- Won't be able to evaluate a precipitated withdrawal
- Diversion
- Not recommended when fentanyl or another long-acting opioid is being used



Buprenorphine Treatment Benefits

- Acceptable as first line in people for whom office-based therapy is appropriate
- Outpatient, home, inpatient induction
- Moderate withdrawal symptoms well tolerated by birthing people
- Frequent small incremental doses
- Once stable, less need for medication adjustment over the course of pregnancy
- Less abuse potential
- Minimal respiratory depression
- Increase engagement in prenatal care
- Fewer medical/delivery complications
- Less incidence of infection, PPRM, PTL
- Increase in treatment retention
- Decrease in illicit opioid use/overdose
- Decrease in risk of HBV, HCV and HIV
- Improves birth outcomes (GA, BW, HC)
- Less NOWS/NAS severity, treatment, LOS
- Efficacy for chronic pain/hyperalgesia

Managing Pain



Overall Pain Management Approach

Present in labor requesting something for pain

Consider either full agonist opioid
(NO nalbuphine or butorphanol)
Or
Offer regional analgesia

(expect good response to initial placement; may need additional boluses)

Vaginal birth

Cesarean birth

Routine postpartum
orders with prn
opioid analgesics
x24 hrs

First 24 hrs: anticipate
increased needs,
consider morphine or
hydromorphone PCA;
consider PCEA; consider
TAP if your anesthesia
department does them

after 24 hrs:
increased
potency short
acting opioid
(hydromorphone
) with 50-70%
increased dose
(4-6 mg po q4-6
hrs); duration of
treatment
similar

Continue long-acting opioid agonist for treatment of opioid dependence

Common Analgesia Questions:

Birthing people maintained on methadone or buprenorphine.

Should a pregnant person stop buprenorphine before delivery to improve pain control?

Does regional analgesia work?

How should post vaginal delivery pain be managed?

How should post-op pain be managed?

Common Analgesia Questions:

Birthing people maintained on methadone or buprenorphine.

Should a pregnant person stop buprenorphine before delivery to improve pain control?

No: it will create the potential for term withdrawal and return to use, which we have tried to avoid through pregnancy.

It is reasonable to continue whatever medication for opioid dependence to avoid withdrawal.

Common Analgesia Questions:

Birthing people maintained on methadone or buprenorphine.

Does regional analgesia
work?

Yes.

Common Analgesia Questions:

Birthing people maintained on methadone or buprenorphine.

How should post vaginal delivery pain be managed?

- Like other patients:
- Non-pharm interventions
 - Scheduled NSAIDs/acetaminophen
 - Short-acting opioids for ***intractable severe pain***

Common Analgesia Questions:

Birthing people maintained on methadone or buprenorphine.

How should post-op pain be managed?

- ERAS-maximize non-pharm
- Scheduled NSAIDS/acetaminophen
- TAP blocks
- Gabapentinoids
- Low-dose ketamine

- Split dosing of maintenance medication
- IV and short-acting opioids

- Patient-controlled epidural anesthesia
- Epidural clonidine/Fentanyl

Post-Operative Analgesia for Birthing People on Buprenorphine

Sample Protocol: A Transition to Oral Scheduled Medications

- **Patient-Centered Care:**
 - Offer multidisciplinary, patient-centered care to facilitate shared-decision making and patient's preference.
 - Offer support and analgesia choices to boost equitable care, autonomy and birthing parent's "choice and voice."
- **Severe Pain Medications**
 - Continue MOUD (encourage slit dose)
 - Hydromorphone 4mg Q4H and 2-4mg Q4H prn severe pain;
 - APAP 1000mg Q6H, ketorolac 30mg Q6Hx4->IBN 600mg Q6H, Gabapentin 200mg TID

Post-Operative Analgesia for Birthing People on Buprenorphine

Sample Protocol: A Transition to Oral Scheduled Medications – CONT'D

- **Other Medications and Key Supports:**
 - Lidocaine patch
 - Abdominal binder
 - Scheduled stool softeners
 - Smoking cessation (nicotine replacement therapy)
 - Emphasized benefits of good nutrition
 - Hydration
 - Ambulation
- Aromatherapy
- Mindfulness, stress reduction, grounding/coping techniques
- Peer, doula, family support
- **Birthing Parent-Child Bonding**
 - Continue MOUD (encourage slit dose)
 - Hydromorphone 4mg Q4H and 2-4mg Q4H prn severe pain;
 - APAP 1000mg Q6H, ketorolac 30mg Q6Hx4->IBN 600mg Q6H, Gabapentin 200mg TID

MOUD and Pain Management in Intrapartum & Postpartum Period

Expected vaginal delivery:

- Continue MOUD medications and doses.
- Discuss analgesia expectations (patient, provider, and nursing team)
- Give acetaminophen 1000mg Q6H in early labor.
- Early epidural is effective and decreases need for intrapartum IV opioids, which may not be effective.

Post delivery:

- Give acetaminophen 1000mg Q6H and ibuprofen 600mg Q6H x 24 hours
- Provide scheduled stool softeners
- Educate your patient on NOWS, breastfeeding, birthing parent-baby dyad, and bonding quality time

MOUD And Pain Management In Intrapartum & Postpartum Period

Expected cesarean delivery:

- Continue MOUD medications and doses.
- Discuss analgesia and plan of care.
- Pre-medicate acetaminophen 1000mg 30-60min prior to arrival in the operating room.
- Pre-op pregabalin 150mg or gabapentin 300mg → less opioid analgesic use x first 24hrs.
- Neuraxial anesthesia
- Prolonged Epidural – 12-24 hrs post-operatively
- Transversus Abdominis Plane (TAP) regional block

Post-Cesarean Pain Management

Opioid pain management:

- Severe, intractable pain: hydromorphone PCA x 6-12 hrs: dose range 0.2-1 mg (0.6-2mg)
- Transition to PO hydromorphone 4-6mg Q4H (4mg Q3H prn)- 3-5 times normal dosing

Non-opioid pain management:

- Acetaminophen 1000mg Q6H (PO/IV), ketorolac 30mg Q6H x 4 doses -> Ibuprofen 600mg Q6H
- Gabapentin 200mg Q8H
- Lidocaine patch
- Hydroxyzine 25-50mg Q6H prn nausea/vomiting (dysphoria/anxiety D2, 5HT2A)
- Scheduled stool softeners, abdominal binder

Non-pharmacological pain management:

- Nutrition, hydration, ambulation
- Smoking cessation
- Stress reduction (mindfulness, visualization, relaxation, aromatherapy)
- Facilitate breastfeeding, birthing parent-baby dyad, “parental love/zero separation”

Benefits Of Trauma Informed MOUD For Pregnant People

- Compassionate care
- Healing kindness
- Breaking shame and guilt
- Positive affirmations
- Powerful therapeutic alliance
- Addiction recovery- lifetime journey
- De-stigmatization of addiction and MOUD
- Reaching out for help- it takes a village, longitudinal team effort

Yes, we can!

Medication Doses



How Much Buprenorphine is Enough?

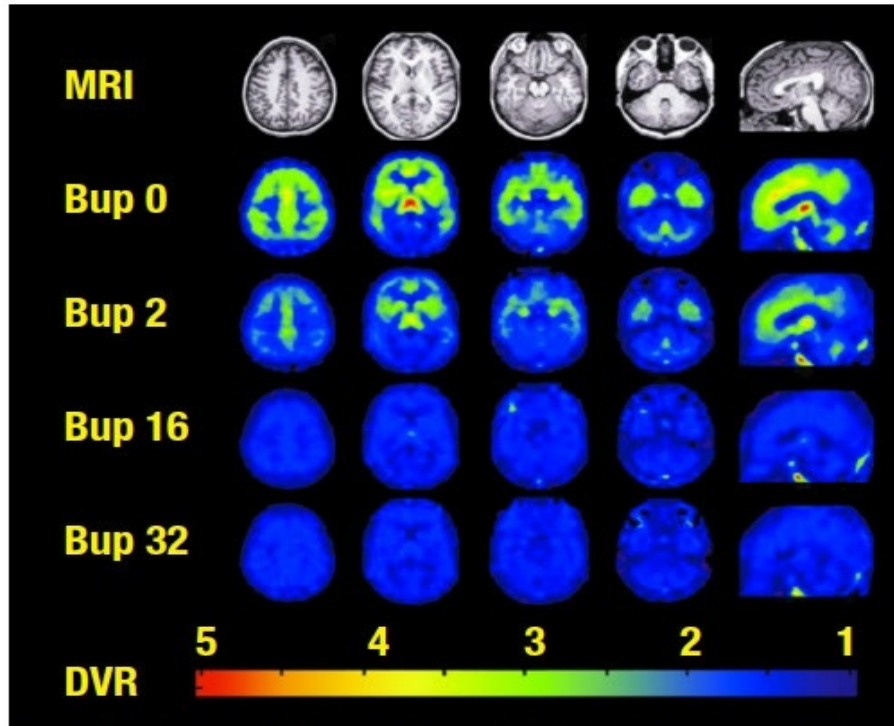


Figure 3. MRI and PET scan of the binding of buprenorphine to MOR in human brain. Full receptor occupancy is only attained at doses within or above analgesic doses. **Bup**, buprenorphine; **DVR**, distribution volume ratio; **MOR**, μ -opioid receptor; **MRI**, magnetic resonance imaging; **PET**, positron emission tomography
Reprinted with permission from MacMillan Publishers Ltd: *Neuropsychopharmacology*. 2003;28(11):2000-2009, copyright 2003.

Buprenorphine
Dosing Goal:

To suppress
withdrawal:

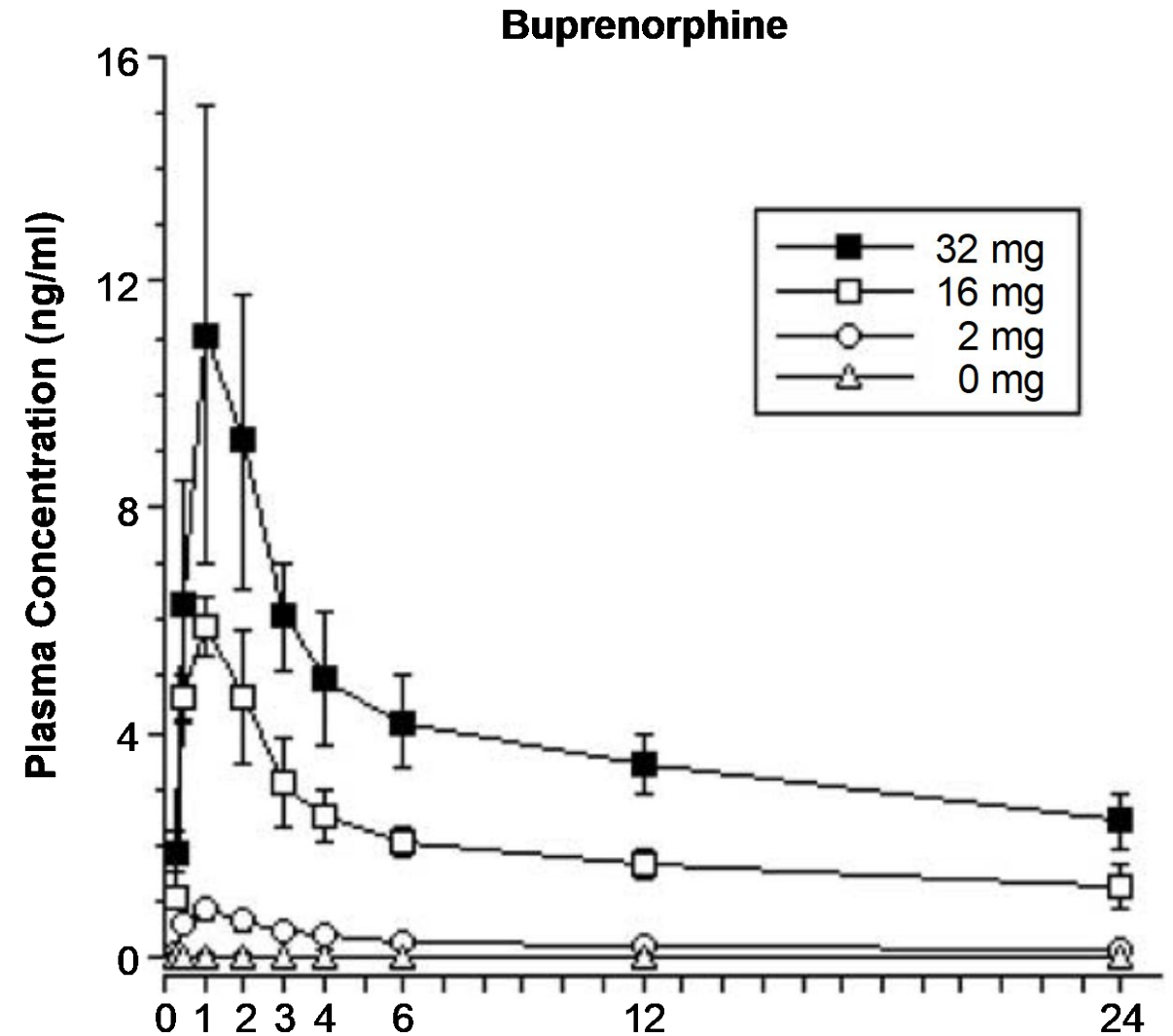
To block
opioids:

- ◆ Need enough buprenorphine to bind to 50% of mu-opioid receptors
- ◆ For most patients this requires ~4 mg (1 ng/ml)

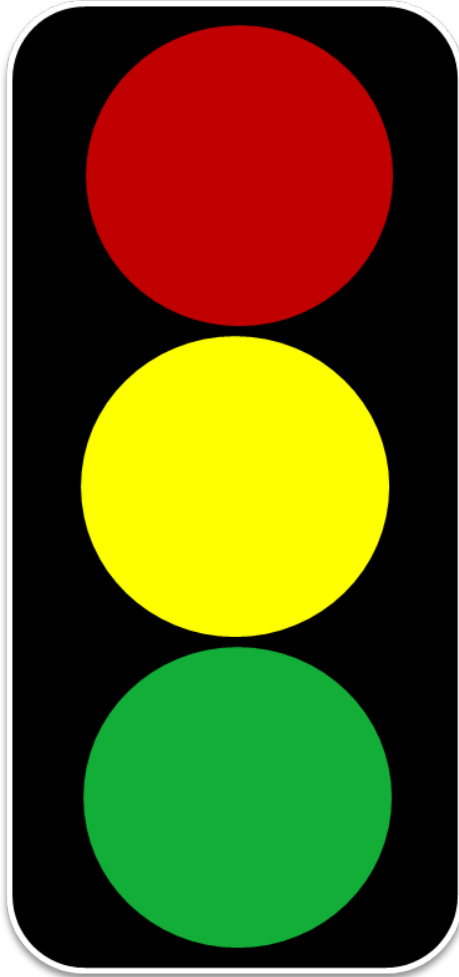
- ◆ Need enough buprenorphine to bind to 80% of mu-opioid receptors
- ◆ For most patients this requires ~16 mg (3 ng/ml)

Buprenorphine Concentrations (non-pregnant)

- Concentrations, buprenorphine dose over 24 hours
- 1 ng/dl minimum dose that suppressed cravings (50-60% receptor occupancy)
- 32 mg not significantly different than 16 mg



Buprenorphine Dosing



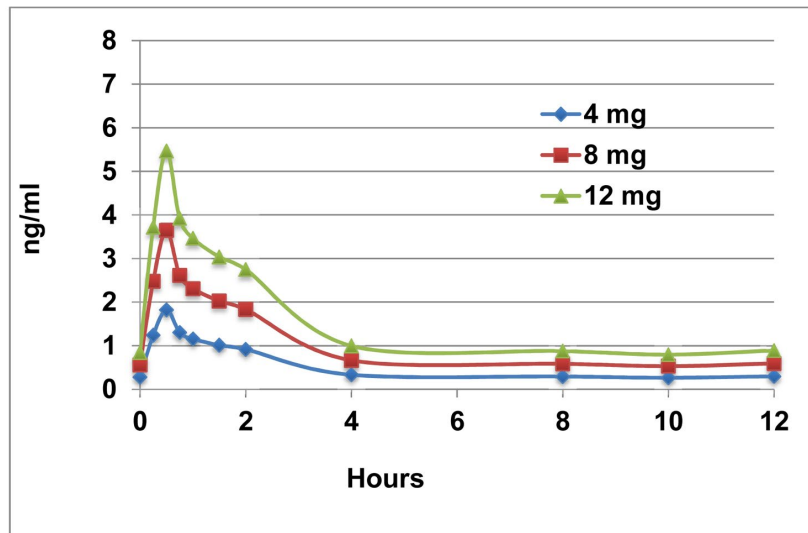
> 24-32 *mg/day* (**Unusual:** Full Review of Medical/Behavioral Issues) (Unusual: Full Review of Medical/Behavioral Issues) May be needed for persons who have been using fentanyl; 24-32 mg is now an acceptable dose for people with high tolerance (especially with fentanyl usage) and/or pain syndrome.

> 16-24 *mg/day* (**Possible:** Consider Patient Difference)

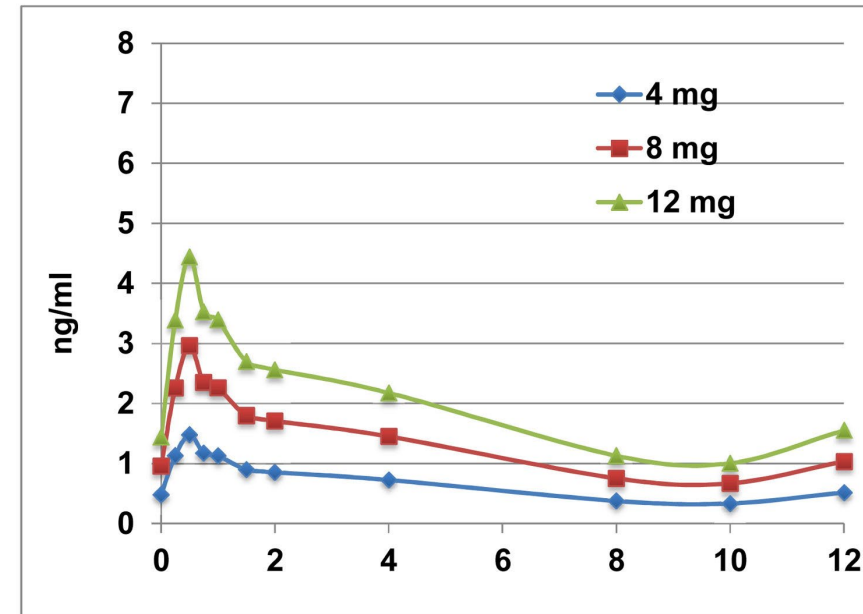
≤ 16 *mg/day* (**Typical**)

Pregnant Persons Benefit From Split Dosing

Figure 1a.



*Concentration per dose
2nd trimester.*



*Concentration per dose
3rd trimester.*

Buprenorphine Dosing and NOWS/NAS

- There does not appear to be a relationship between dose at delivery and the risk of NOWS/NAS
- Maternal dose alone may not fully represent the fetal exposure to buprenorphine.
- There does appear to be a relationship between the quantity of buprenorphine in meconium and the risk of NOWS/NAS
- No correlation between maternal opioid maintenance therapy dose and the duration or severity of NOWS/NAS.
- The patient should be encouraged to report any withdrawal symptoms through their pregnancy without fear a dose increase will affect their baby's hospital stay or need for NOWS/NAS treatment.
- Tobacco use is strongly associated with NOWS/NAS and NOWS/NAS severity.

Dosing in Pregnancy

- Buprenorphine dosing guidelines based on studies done on a small number of persons using heroin.
 - The studies did not control for gender, nicotine exposure, body weight, co-occurring pain, pregnancy.
- Pregnant persons have definitively been shown to need increased doses of buprenorphine and more frequent dosing intervals.
- Pregnancy dosing does not seem to affect NOWS/NAS rates.

Outpatient Follow-up During Pregnancy

Frequent visits allow for frequent feedback/intervention for noncompliance (we have found this really helpful)

See patient within 1-3 days after initiation of buprenorphine.

Ask about symptoms (checklist) and counseling (confirm) (if you do not provide OB care, confirm she is receiving care).

Provide witnessed urine for drug screen.

Provide prescription for 1 week.
Weekly follow-up visit

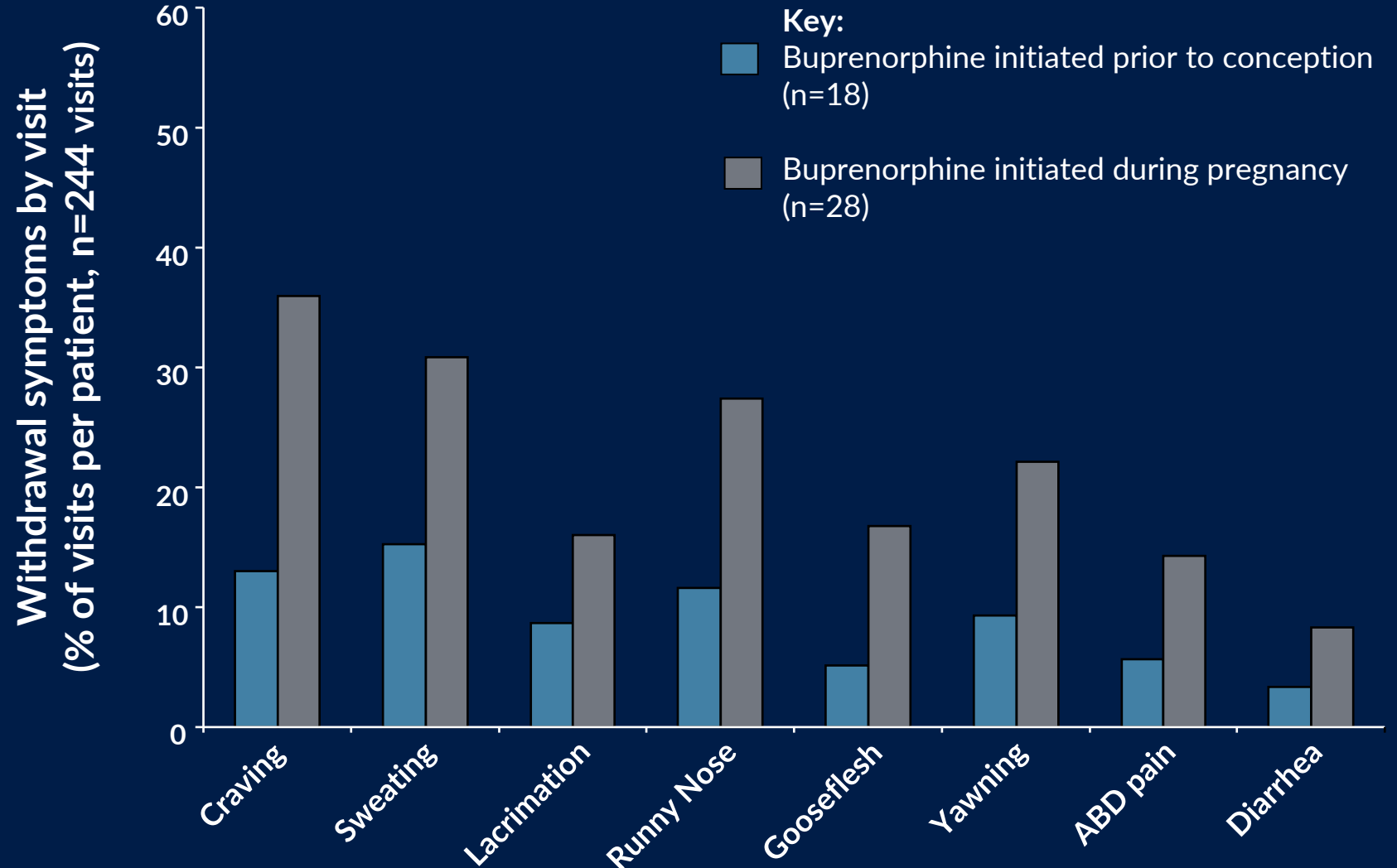
For patients that have been quite stable and compliant, we reduce frequency to every two weeks and longer may be appropriate if stable prior to pregnancy.

Take-Home Message About Buprenorphine Inductions

- Induction can occur in the outpatient setting or overnight stay.
- Moderate withdrawal symptoms are well-tolerated by pregnant people.
- The degree of maternal withdrawal may be important inpatient satisfaction with medication.
- Dosing in smaller incremental doses may be important inpatient satisfaction with medication.
- Compassionate and patient-centered care and regular follow-up facilitate ongoing safe care and timely dose adjustment.

Withdrawal Symptoms By Visit

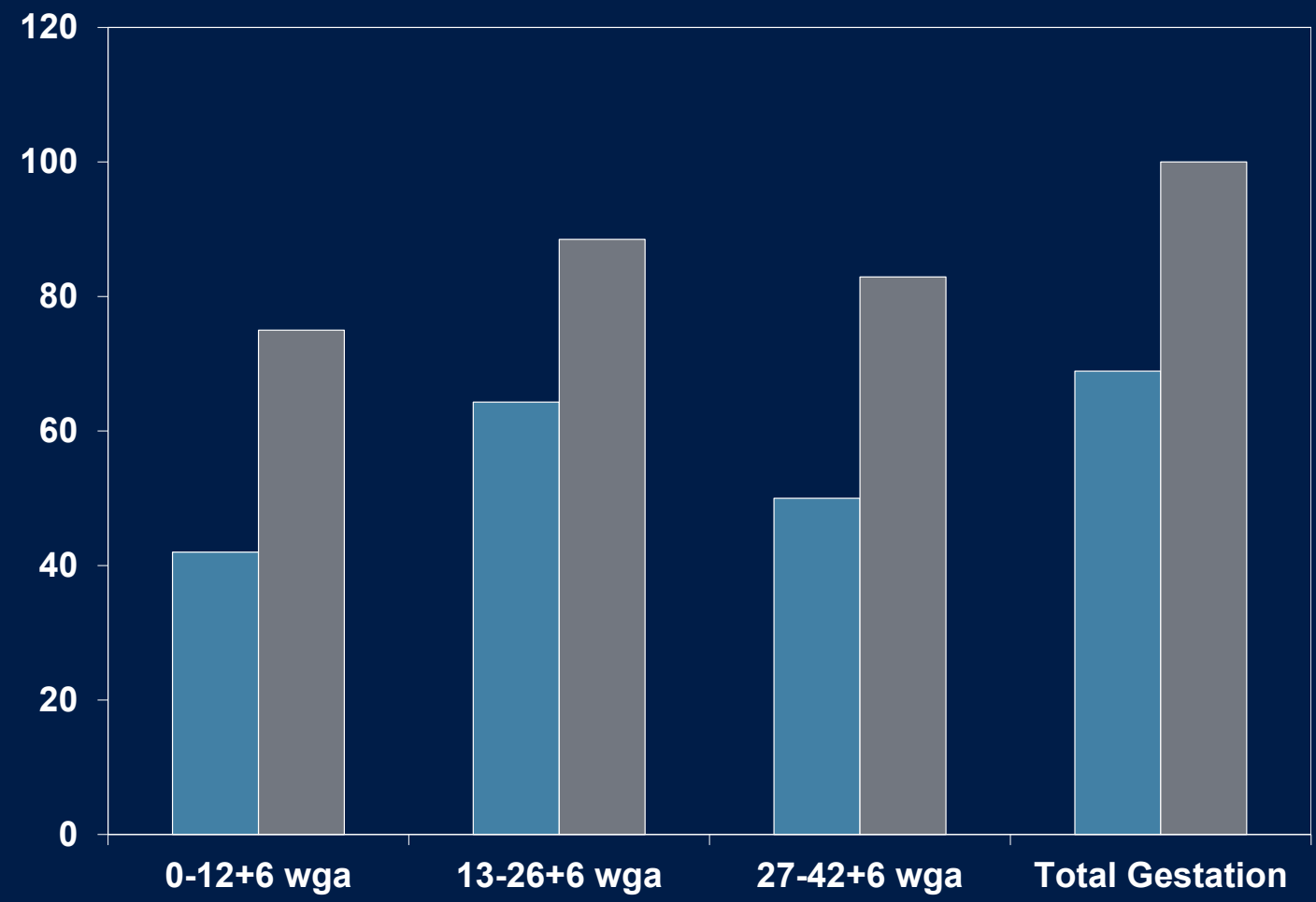
Complaints are frequent; more so when buprenorphine initiated during pregnancy



% Requiring Dose Change by Trimester

About 2/3 of birthing people on a stable dose prior to pregnancy will need an increase in dose during gestation

Key:
■ Buprenorphine initiated prior to conception (n=18)
■ Buprenorphine initiated during pregnancy (n=28)



Birthing Parent Dose and NOWS/NAS Severity

No correlation between maternal opioid maintenance therapy dose and the duration or severity of NOWS/NAS

Individual should be encouraged to report any symptoms of withdrawal through their pregnancy without fear a dose increase will affect their baby's hospital stay or need for NOWS/NAS treatment

Tobacco use is strongly associated with NOWS/NAS and NOWS/NAS severity

Managing Your Patient in Labor



Managing Your Patient in Labor

Interpreting the nonstress test (NST) of a patient on buprenorphine or methadone

Avoiding opioid antagonists: butorphanol and nalbuphine

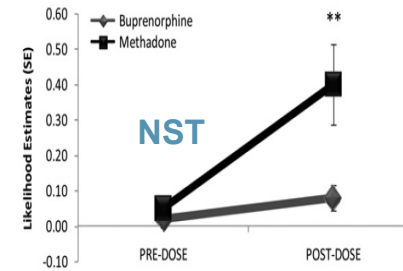
Managing pain intrapartum and postpartum SVD and cesarean

Fetal Assessment in Pregnant Persons Treated With Methadone or Buprenorphine

Patients:

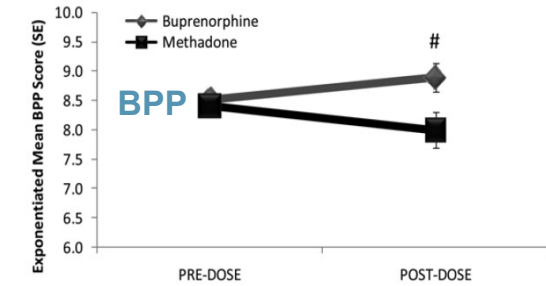
- MOTHER study
- Maintained on methadone or buprenorphine (blinded)
- BPP/NST 2 hrs prior to a dose; repeated 2 hrs after the dose (peak effect)

Interpret antenatal testing cautiously when a few hours after a dose.



Group: $p=.002$; Time: $p=.001$; Group x Time: $p=.21$, $**p<.01$

Figure 3 Likelihood estimates for a non-reactive fetal non-stress test in the pre- and post-dose assessments. ******Pairwise comparison with a Bonferonni correction, $P<.01$



Group: $p=.02$, Time: $p=.20$, Group x Time: $p=.05$; # $p>.09$ ns

Figure 4 Exponentiated mean biophysical profile score (BPP) in the pre- and post-dose assessments. #Pairwise comparison with a Bonferonni correction, $P>.05$, not significant (NS)

	<i>Predose NST</i>	<i>Post dose NST</i>	<i>Predose BPP</i>	<i>Post dose BPP</i>
Methadone	No Difference Meth vs. Bup	More likely non-reactive than pre-dose	No difference*	Both meth and bup: Significant chance reduced movement;
Buprenorphine		More likely reactive than methadone	*if pre- and post-scores are combined, bup BPP scores higher ($8.7\pm$ vs 8.2 ± 0.2)	Non-sig increased chance of no breathing

Alert!

Nalbuphine and butorphanol are partial opioid agonists and can precipitate acute withdrawal in opioid dependent patients.

Patient maintained
on methadone
requested
medication for pain



Neonatal Opioid Withdrawal Syndrome (NOWS)



Maintenance Therapy in Pregnancy: Neonatal Opioid Withdrawal Syndrome (NOWS)/NAS

Generalized disorder with dysfunction of the autonomic nervous system, GI tract and respiratory system

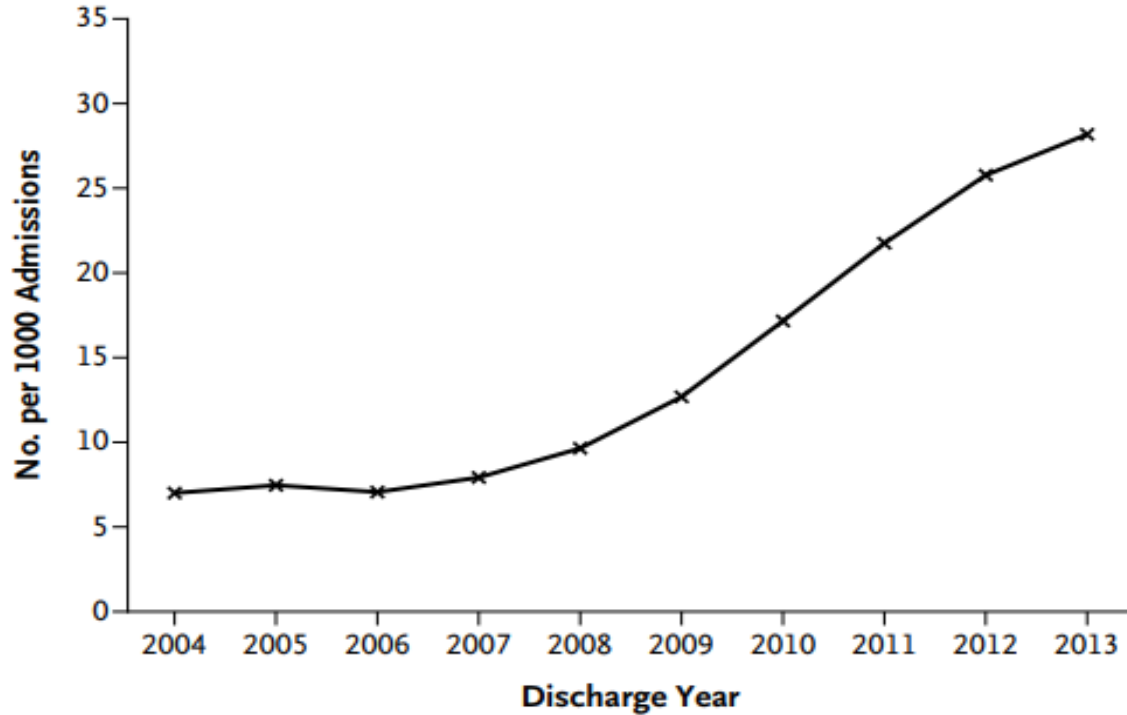
Occurs in 60-80% of infants with intrauterine exposure to opioid maintenance therapy

Onset: majority present within 72 hours after delivery

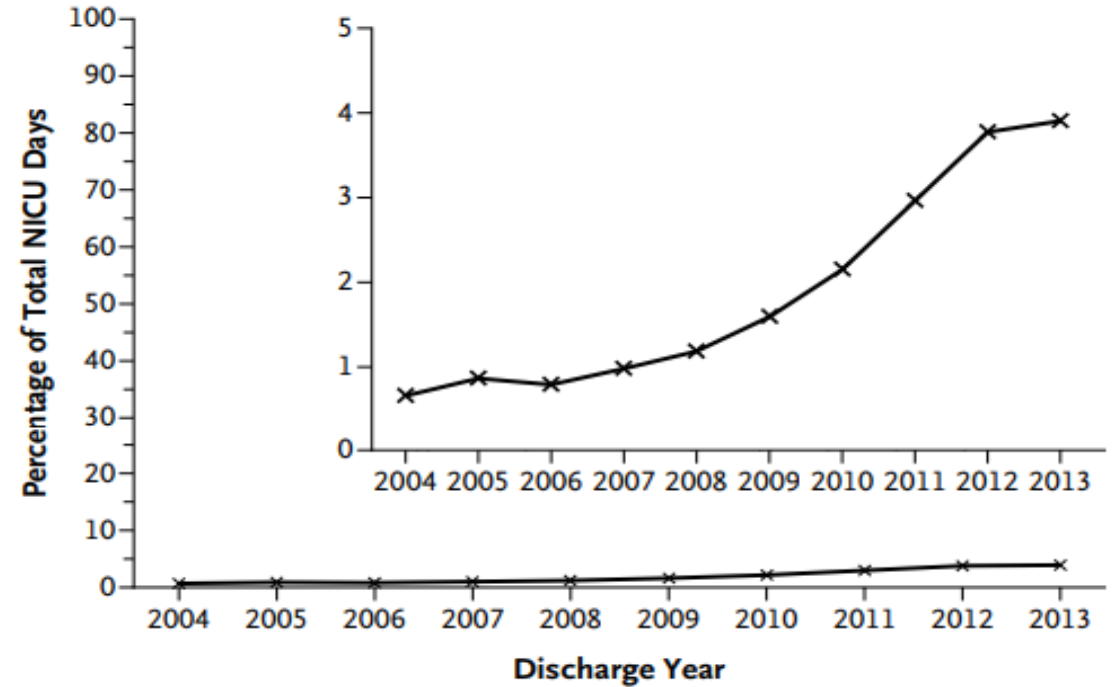
Duration: up to 4 weeks (prolonged if exposed in-utero to more than one substance associated with NOWS)

NOWS Trends

Admissions for the Neonatal Abstinence Syndrome



Percentage of Total NICU Days Attributable to the Neonatal Abstinence Syndrome, According to Year

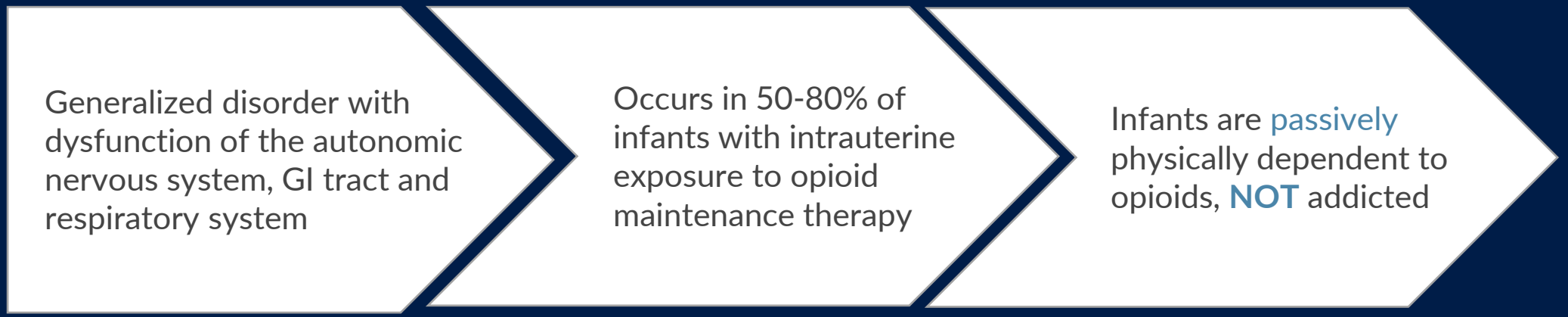


- 2004 - 2013, rate of NICU admissions for NOWS increased from 7 to 27 cases /1000 admissions; median length of stay increased from 13 to 19 days
- In US, total % of NICU days attributed to the NOWS increased from 0.6% to 4.0%



Stop labeling babies as 'born addicted' — it stigmatizes them and is inaccurate

BY DR. LYNN WEBSTER, OPINION CONTRIBUTOR — 06/19/18 07:00 AM EDT
THE VIEWS EXPRESSED BY CONTRIBUTORS ARE THEIR OWN AND NOT THE VIEW OF THE HILL



NOWS Management

Non-Pharmacologic Approaches

- Quiet dimly lit room, handled gently, swaddling, pacifier, gentle rocking
- Rooming In by keeping mother and baby together - reduction in NOWS/NAS length of stay and cost
- Non-insertive acupuncture
- Breastfeeding recommended as it soothes agitated infants

Pharmacotherapy

- Oral morphine or oral methadone are preferred first-line medication

An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome

Matthew R. Grossman, Adam K. Berkowitz, Rachel R. Osborn, Yaqing Xu, Denise A. Esserman, Eugene D. Shapiro and Matthew J. Bizzarro

Pediatrics June 2017, 139 (6) e20163360; DOI: <https://doi.org/10.1542/peds.2016-3360>

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Info & Metrics

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Abstract

BACKGROUND AND OBJECTIVES: The incidence of neonatal abstinence syndrome (NAS), a constellation of neurologic, gastrointestinal, and musculoskeletal disturbances associated with opioid withdrawal, has increased dramatically and is associated with long hospital stays. At our institution, the average length of stay (ALOS) for infants exposed to methadone in utero was 22.4 days before the start of our project. We aimed to reduce ALOS for infants with NAS by 50%.

METHODS: In 2010, a multidisciplinary team began several plan-do-study-act cycles at Yale New Haven Children's Hospital. Key interventions included standardization of nonpharmacologic care coupled with an empowering message to parents, development of a novel approach to assessment, administration of morphine on an as-needed basis, and transfer of infants directly to the inpatient unit, bypassing the NICU. The outcome measures included ALOS, morphine use, and hospital costs using statistical process control charts.

RESULTS: There were 287 infants in our project, including 55 from the baseline period (January 2008 to February 2010) and 44 from the postimplementation period (May 2015 to June 2016). ALOS decreased from 22.4 to 5.9 days. Proportions of methadone-exposed infants treated with morphine decreased from 98% to 14%; costs decreased from \$44 824 to \$10 289. No infants were readmitted for treatment of NAS and no adverse events were reported.

CONCLUSIONS: Interventions focused on nonpharmacologic therapies and a simplified approach to assessment for infants exposed to methadone in utero led to both substantial and sustained decreases in ALOS, the proportion of infants treated with morphine, and hospital costs with no adverse events.

In this issue

Pediatrics

Vol. 139, Issue 6

1 Jun 2017

[Table of Contents](#)

[Index by author](#)



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[Table of Contents](#)

Jump to section

[Article](#)

[Abstract](#)

[Methods](#)

[Results](#)

[Discussion](#)

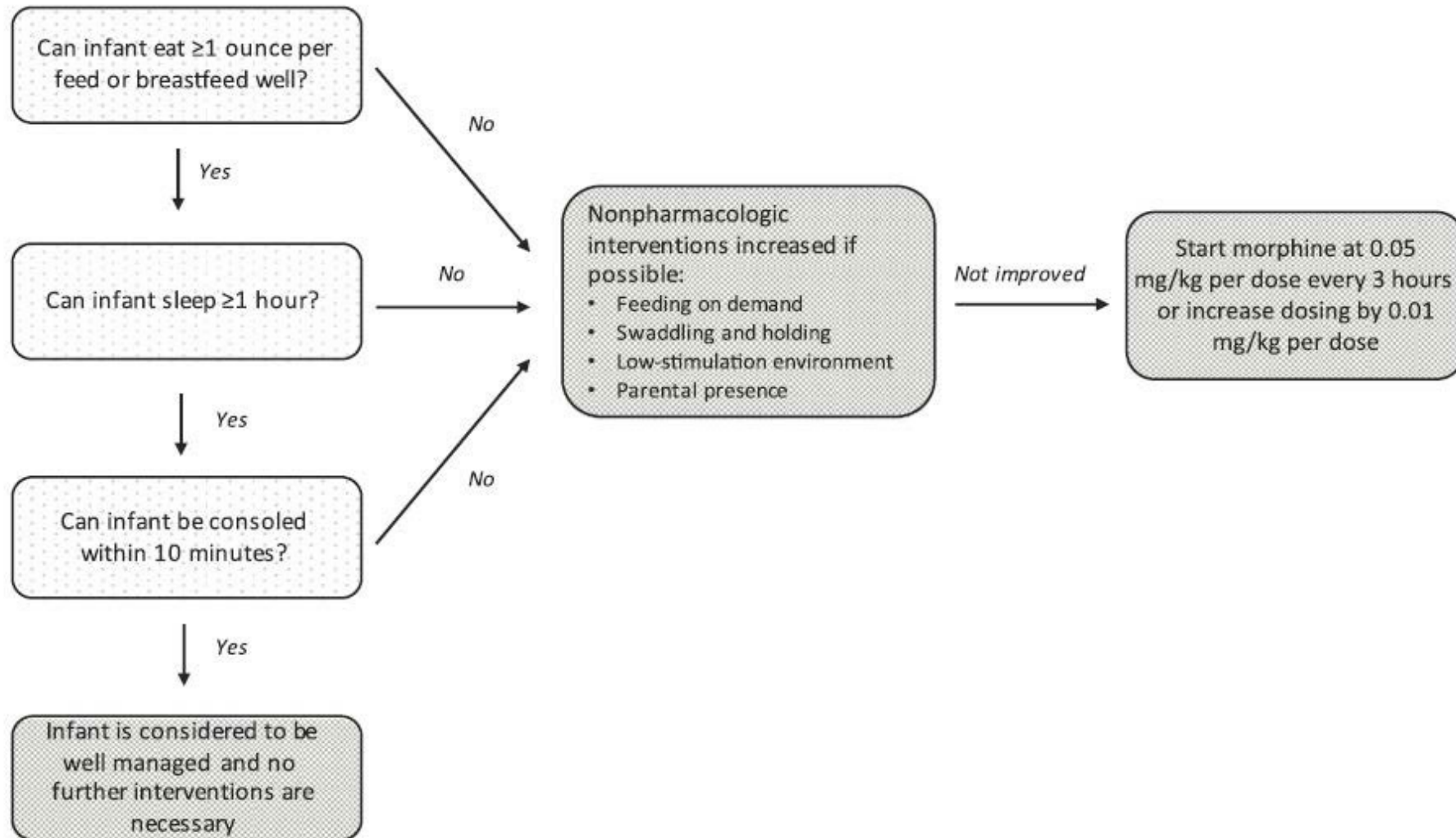
[Conclusions](#)

Yale's Eat, Sleep, Console

- Historically, the number of infants exposed to methadone in-utero increased by 74% from 2003 – 2009
 - ALOS – 22.4
 - Average Cost – \$44, 800
- 98% of these infants were treated with morphine
- ***Goals of Eat, Sleep, Console program:***
 - Decrease ALOS 50 %
 - Decrease morphine 50 %



Decision Tree - Eat, Sleep, Console



Yale's Results

- 287 infants met inclusion criteria.
- Length of Stay (LOS) decreased from 22.4 days to 5.9 days.
- The number of infants treated with morphine decreased from 98% to 14%.
- The max dose of morphine for that group decreased from 1.04 mg/kg/day to 0.5 mg/kg/day.
- Breastmilk feeds increased from 20-45%
- Decrease cost of stay from about \$45,000 to about \$11,000 per case.
- Estimated decrease of 2,618 patient days from 2011-2015 for a cost savings of \$1.2 million per year or \$5.4 million total.

Breastfeeding / Chestfeeding



Benefits of Breastfeeding/Chestfeeding for Newborns with NOWS

30% decrease in the development of NOWS

50% decrease in length of neonatal hospital stay

Improved mother-infant bonding

Positive reinforcement for maternal recovery

Opioid Use Disorder and Breastfeeding/Chestfeeding

The transfer of methadone and into human milk is minimal and unrelated to maternal doses

Buprenorphine has poor oral bioavailability and is also compatible with breastfeeding

The amount of buprenorphine in human milk is small and unlikely to have negative effects on the infant

Both are considered Category L3 (probably compatible)

Breastfeeding/Chestfeeding and NOWS/NAS: Benefits for Newborns

- 30% decrease the development of NOWS/NAS
- 50% decrease in neonatal hospital stay
- Improved mother-infant bonding
- Positive reinforcement for maternal recovery

Breastfeeding/Chestfeeding

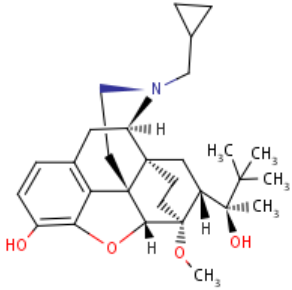
HCV infection is not a contraindication to breastfeeding/chestfeeding

- Unless she develops cracked or bleeding nipples
 - Recommend to pump/dump until healed

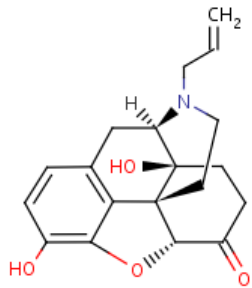
Contraindications to breastfeeding/chestfeeding

- Maternal HIV infection
- Current maternal substance use
 - Mother currently under the influence of illicit substance
- Recent heavy marijuana use
 - Lipophilic, concentration in breast milk
 - Recent study found little THC in breast milk (Baker et al. Ob Gyn. 2018)

Both Buprenorphine and Naloxone Are Compatible With Breastfeeding/Chestfeeding



Buprenorphine
CASRN:
52485-79-7



Naloxone
CASRN:
465-65-6

Summary of Use during Lactation:

- Because of the low levels of buprenorphine in breastmilk, its poor oral bioavailability in infants, and the low drug concentrations found in the serum and urine of breastfed infants, its use is **acceptable in nursing mothers**. Monitor the infant for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants. Although unlikely, if the baby shows signs of increased sleepiness (more than usual), difficulty breastfeeding, breathing difficulties, or limpness, a physician should be contacted immediately. Observe infants for withdrawal signs if breastfeeding is stopped abruptly. The breastfeeding rate among mothers taking buprenorphine for opiate addiction may be lower than in other mothers.

Summary of Use during Lactation:

- No information is available on the excretion of naloxone into breastmilk. Because it is not orally bioavailable, it is unlikely to affect the breastfed infant. Studies in nursing mothers have shown that naloxone does not affect lactation hormone levels. **If naloxone is required by the mother, it is not a reason to discontinue breastfeeding.**

What About Non-Obstetric Pain?

“Opioid Debt”

Patients with an opioid use disorder who are physically dependent on Opioid Agonist Treatment (i.e., methadone or buprenorphine) must be maintained on a daily equivalence before ANY analgesic effect is realized with opioids used to treat acute pain.

Opioid analgesic requirements are often higher due to increased pain sensitivity and opioid cross tolerance.

Buprenorphine Maintenance Treatment: *Theoretical Concern*

- May antagonize effects of previously administered opioids.
- May block the effects of subsequent administered opioids.
- However, experimental mouse and rat pain models.
 - Combination of buprenorphine and full opioid agonists (morphine, oxycodone, hydromorphone, fentanyl) resulted in additive or synergistic effects
 - Receptor occupancy by buprenorphine does not appear to cause impairment of mu-opioid receptor accessibility

Buprenorphine Maintenance Treatment: *Options*

- Continue buprenorphine and titrate short-acting opioid analgesic.
- D/c buprenorphine, use opioid analgesic, then re-induce.
- Divide buprenorphine to every 6-8 hours.
- Use supplemental doses of buprenorphine*
- If inpatient:
 - D/c buprenorphine
 - Start methadone 20-40mg (or other long-acting opioid) for opioid debt
 - Use short-acting opioid analgesics
 - Then re-induce w/ buprenorphine when acute pain resolves

Buprenorphine Maintenance: *Treatment*

- Systematic review
- 10 trials involving 1,190 patients
- Due to heterogeneity of studies, pooling results and meta-analysis not possible
- All studies reported effectiveness in treating chronic pain
- Majority of studies were observational and low quality
- Current evidence insufficient to determine effectiveness of SL buprenorphine for treatment of chronic pain
- Expert opinion supports the use of buprenorphine for chronic pain in patients diagnosed with an opioid use disorder
- Needs to be dosed 6-8 hours; does not have a ceiling effect for pain.

Methadone Maintenance Treatment (MMT) and Acute Pain

Methadone maintenance dosed every 24 hours does not confer analgesia beyond 6-8 hours

The addition of short-acting opioid analgesics in addition to MMT will not cause excessive CNS or respiratory depression due to opioid cross-tolerance

Increased pain sensitivity may necessitate higher doses at shorter intervals

Scheduled dosing or PCA not “prn” during the severe acute pain

A short course of opioid analgesics during severe acute pain is unlikely to compromise patient’s recovery

Compassionate, nonjudgmental language and trauma-informed care is important!

MMT and Acute Pain: Clinical Recommendations

Continue usual verified
methadone dose

Treat pain aggressively with
conventional analgesics,
including opioids at higher
(1.5 times) doses and shorter
intervals

Avoid using mixed
agonist/antagonist opioids
(e.g., buprenorphine (Stadol))
as they will precipitate acute
withdrawal

Careful use and
monitoring of
combination products
containing
acetaminophen

After obtaining patient
written consent,
communicate with the MMT
program at time of
admission and prior to
discharge

MMT & Chronic Pain

- Analgesia from methadone lasts 6-8 hours while treatment of OUD lasts over 24 hours
- MMT programs typically dose methadone once per day which will not treat pain beyond 6-8 hours
- Daily MMT dosing can be a good test for pain opioid responsiveness based on the patient's response to: *"Do you get any pain relief from your once-a-day methadone dose?"*
 - *"Yes, all day but not enough."* (pain likely opioid withdrawal-mediated pain)
 - *"Yes, but it only lasts 8 hours."* (pain may be opioid responsive)
 - *"No, not at all."* (pain may be opioid resistant)

MMT & Chronic Pain

While most methadone programs only administer methadone once daily, some clinics will administer split doses (a 2nd or 3rd dose for unsupervised self-administration later in the day) which would allow for simultaneous treatment of OUD and pain

Note that it is illegal for a clinician outside of a MMT program to prescribe methadone for the treatment of OUD whether or not the patient has concurrent pain

It is possible to prescribe chronic opioid analgesics for a patient's chronic pain while he/she is on MMT

Standardization of split methadone dose is in progress.

MMT & Chronic Pain

Some considerations regarding prescribing opioid analgesics for chronic pain to a patient on MMT.

- MMT program can closely monitor patient for opioid analgesic misuse e.g., drug testing, pill counts
- Methadone maintenance doses (>80 mg per day) should block euphoric effects of co-administered opioid analgesics
- Opioid analgesic may interfere with the MMT program's ability to monitor patients for illicit opioid use as prescribed opioid analgesics may interference with drug testing
- Patients may be tempted at the MMT program to divert (e.g., sell) prescribed opioid analgesics to other patients
- Whole person, integrative medicine modalities, mindfulness and non-opioid multimodals

Acute Pain: Overcoming Naltrexone Blockade

Hot plate test after XR-NXT or placebo, rats treated with opioid agonist (morphine, fentanyl, hydrocodone)

Naltrexone blocks analgesic effects of opioids at conventional doses

Naltrexone blockade can be overcome at 6-20x usual dose resulting in analgesia without significant respiratory depression or sedation

NMT and Emergent Acute Pain

- Discontinue naltrexone (no need for taper)
- Consult anesthesia
- Need to have healthcare providers specifically trained in the use of anesthetic drugs and management of respiratory effects of potent opioids
- Opioid analgesics (high dose) administered under close observation
- Need setting that is equipped and staffed for cardiopulmonary resuscitation.
- Need to be prepared to establish and maintain a patient airway with assisted ventilation if needed
- Consider nonopioids and regional anesthesia

*For more info on naltrexone and pain management,
can call pharmaceutical company at 1-888-235-8008*

NMT and Perioperative Pain Management

Naltrexone will block the effects of co-administered opioid analgesic.

- ***PO naltrexone***
 - $t_{1/2}$ is 14 hours, d/c for at least 72 hours preoperatively
 - 50% of blockade effect is gone after 72hrs
- ***IM depot naltrexone***
 - Peak plasma within 2-3 days, decline begins in 14 days
 - If possible, delay elective surgery for a month after last dose

Overdose Prevention

Naloxone should be prescribed to everyone with an opioid use disorder

Pregnant persons should receive naloxone in cases or overdose to prevent death to mother and fetus

Available formulations

Families also need to have it available

Billing / Coding

- Pregnant persons can bill E:M code in addition to global Ob. Usually time-based.
- Screening, brief intervention, referral to treatment has separate E:M code
 - 99408 and 99409
 - H0049 and H0050-Medicare
- If not pregnant, use E:M coding

Billing / Coding

Initial visit: usually can bill
for a 45 min or 60 min
level visit
99204-5

Follow up visits document
at an appropriate E:M
code
99213-4

Can also document
counseling for
smoking, 99406, if
relevant

Follow up 1-2 weeks until
stable, then q 4 weeks.
Based on time.
99213-4

Case Reports



Case: L.K.

- L.K. is a 29 y/o G2P0 schoolteacher at 7 weeks with history of chronic pelvic pain presumed to be secondary to endometriosis.
- On oxycodone extended-release 20 mg bid given to her by pain specialist. Also history of depression on venlafaxine XR 150 mg
- Per patient, she was told to stop oxycodone extended-release and wean off venlafaxine by genetic counselor/MFM consult



Case: L.K. Cont.

- Counseled on pain control, weaning, etc.
- Able to wean down to 10 mg every other day, but not able to stop (Pain improved with pregnancy)
- Baby born full term, no NOWS/NAS
- Breast fed for 1 ½ years

Case: W.S.



- W.S. is a 25 y/o G3P2 at 16 weeks referred because of illicit extended-release oxycodone use
- Pt started use about 3 years ago because of low-back pain, but then noticed that it helped her deal with life
- Currently using between 30-120 mg a day. Attempted to stop, but after two days had extreme nausea/vomiting/diaphoresis

Question

Which patient has an opioid use disorder?



Case: L.K. Cont.

- Pain med needs continued to increase after pregnancy (up to 60 mg bid with hydrocodone/acetaminophen for “breakthrough pain”)
- Hospitalized for severe depression. Admitted to chewing oxycodone extended release for high

Case: L.K. Cont.

- Switched to bup/nlxn. Pain better controlled
- Counseling/therapy for severe PTSD
- SSRI-fluoxetine 100 mg
- Quit smoking
- Menses return and she gets pregnant (planned and desired)
- During pregnancy has hepatitis flare.
 - Chronic congenital hepatitis b infection, stopped tenofovir during pregnancy



Case: L.K. Cont.

- Baby born at 37 weeks (cholestasis of pregnancy) by C-section for breech
- Didn't breast feed (pediatrician didn't feel comfortable with the tenofovir)
- Baby without NOWS/NAS

Case: W.S.



- Uneventful induction onto buprenorphine while pregnant
- Delivered at term
- Healthy baby. No NOWS/NAS.
- Still my patient 10 years later 2 returns to use
- Oxycodone x 6 months
- Meth-brief
- 1 unintended pregnancy-TAB with LNG IUS
- 1 planned uncomplicated pregnancy with term delivery
- Another LNG IUS

Questions?





Session 4: Treating Adolescents and Young Adults; Managing Medical and Psychiatric Co-Morbidities

In this session, we will review:



Adolescents and Young
Adults



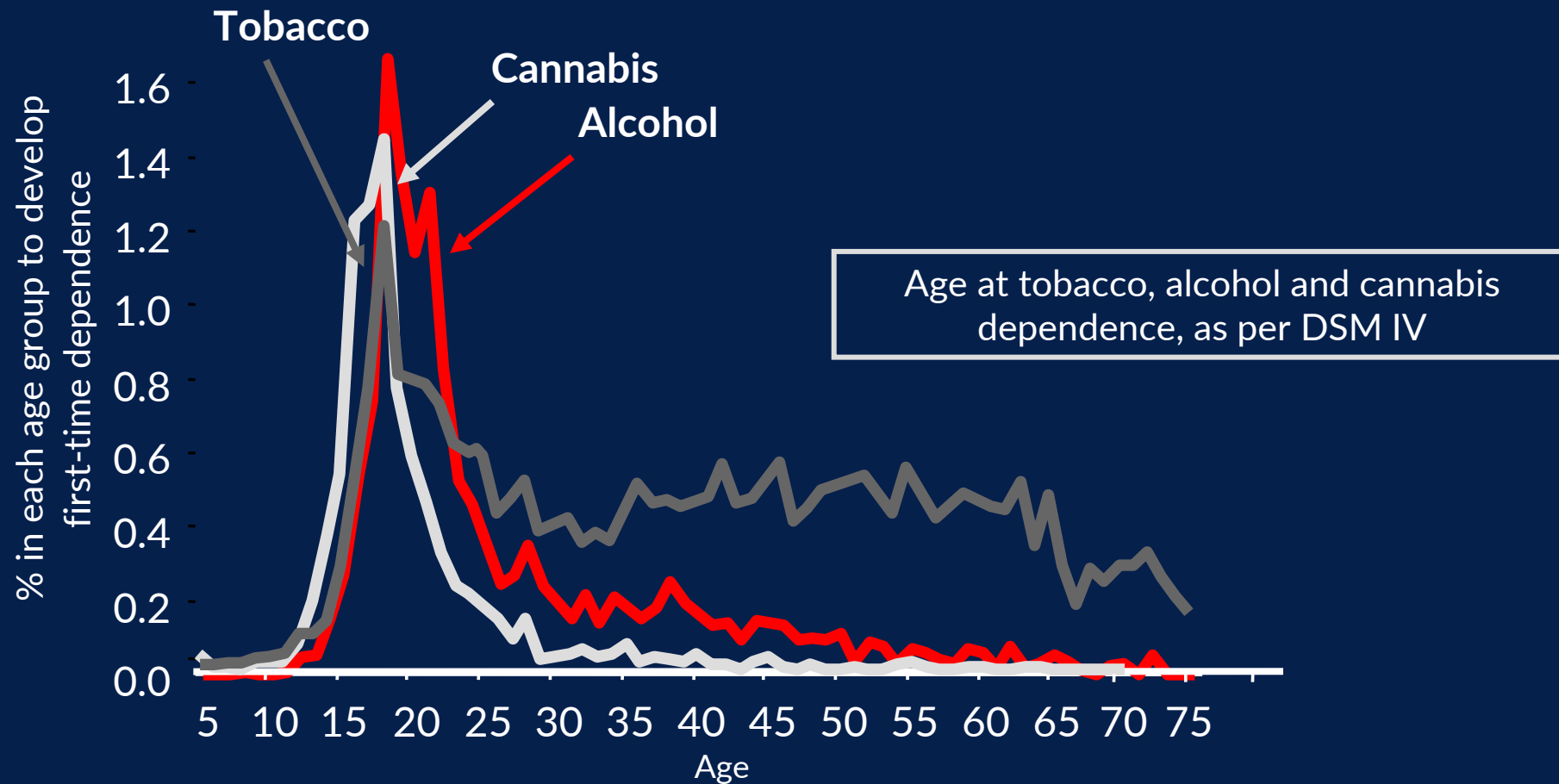
Medical Co-morbidities



Psychiatric Co-morbidities



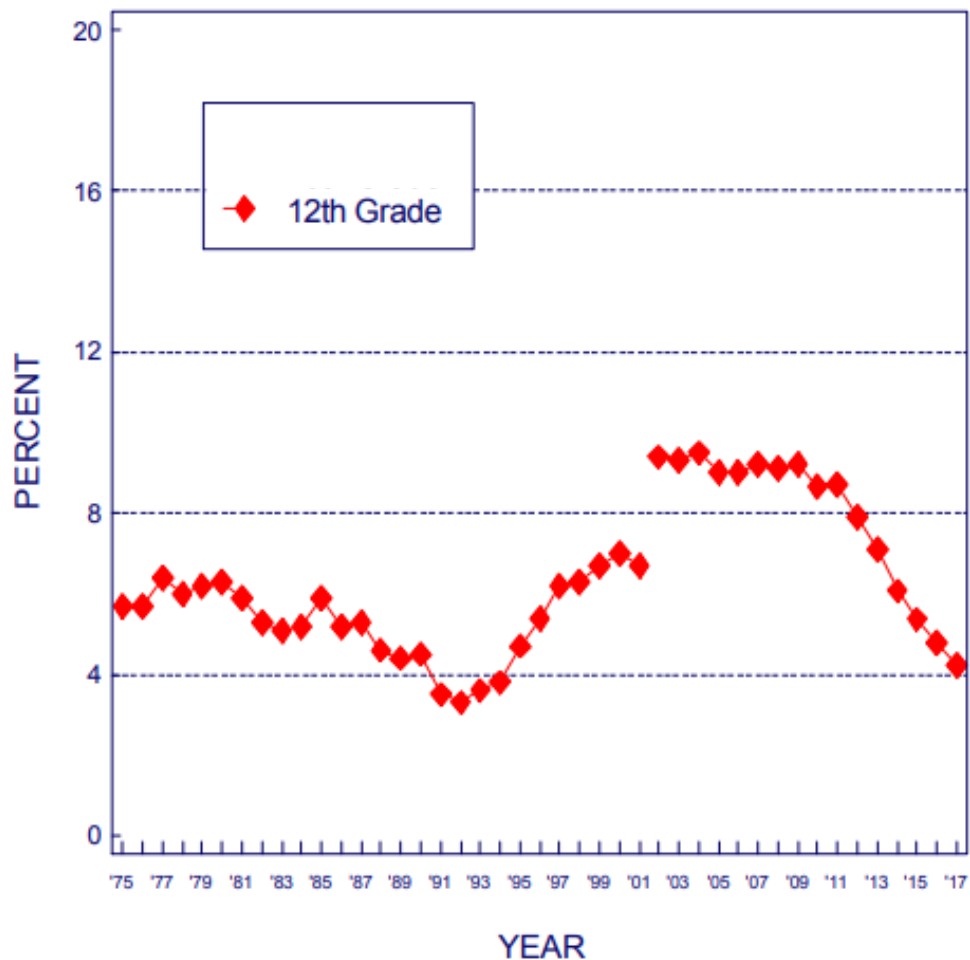
Addiction is a Developmental Disease: Often Starts in Childhood and Adolescence



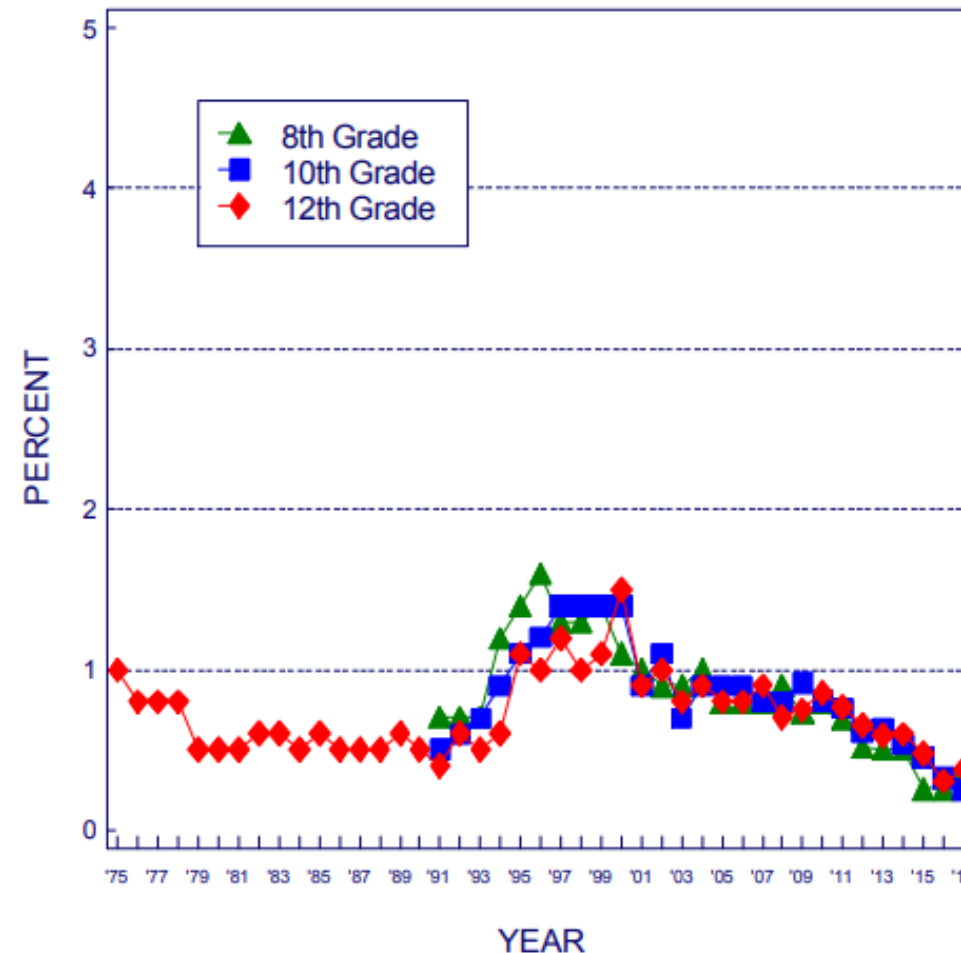
National Epidemiologic Survey on Alcohol and Related Conditions, 2003

Teens and Opioid Use in Past Year

Prescription Opioids

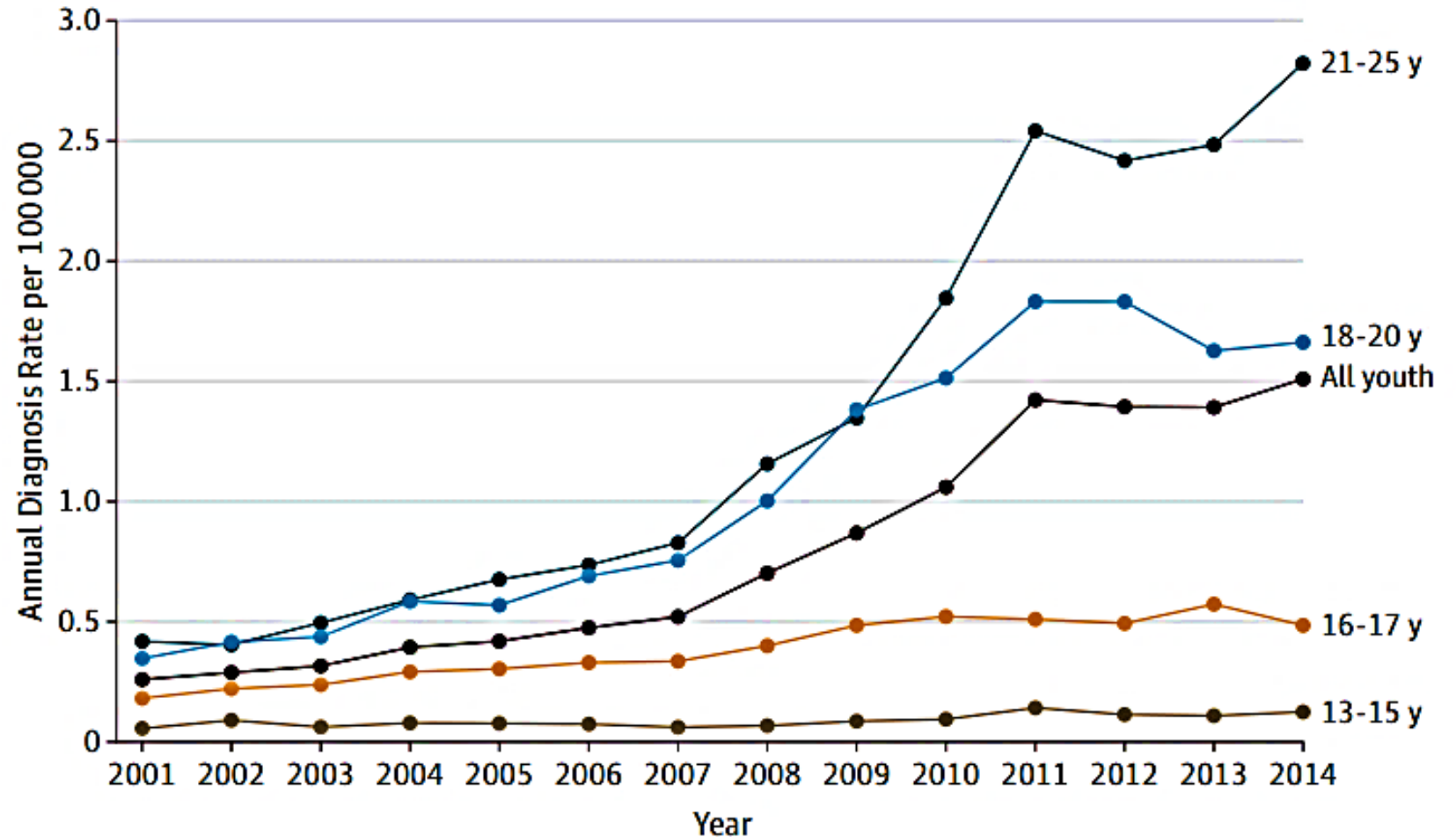


Heroin



Trends in New OUD Diagnoses Among Youth and Young Adults

The diagnosis rate of OUD increased nearly 6-fold from 2001 to 2014 (from 0.26 per 100 000 person-years to 1.51 per 100 000 person-years).

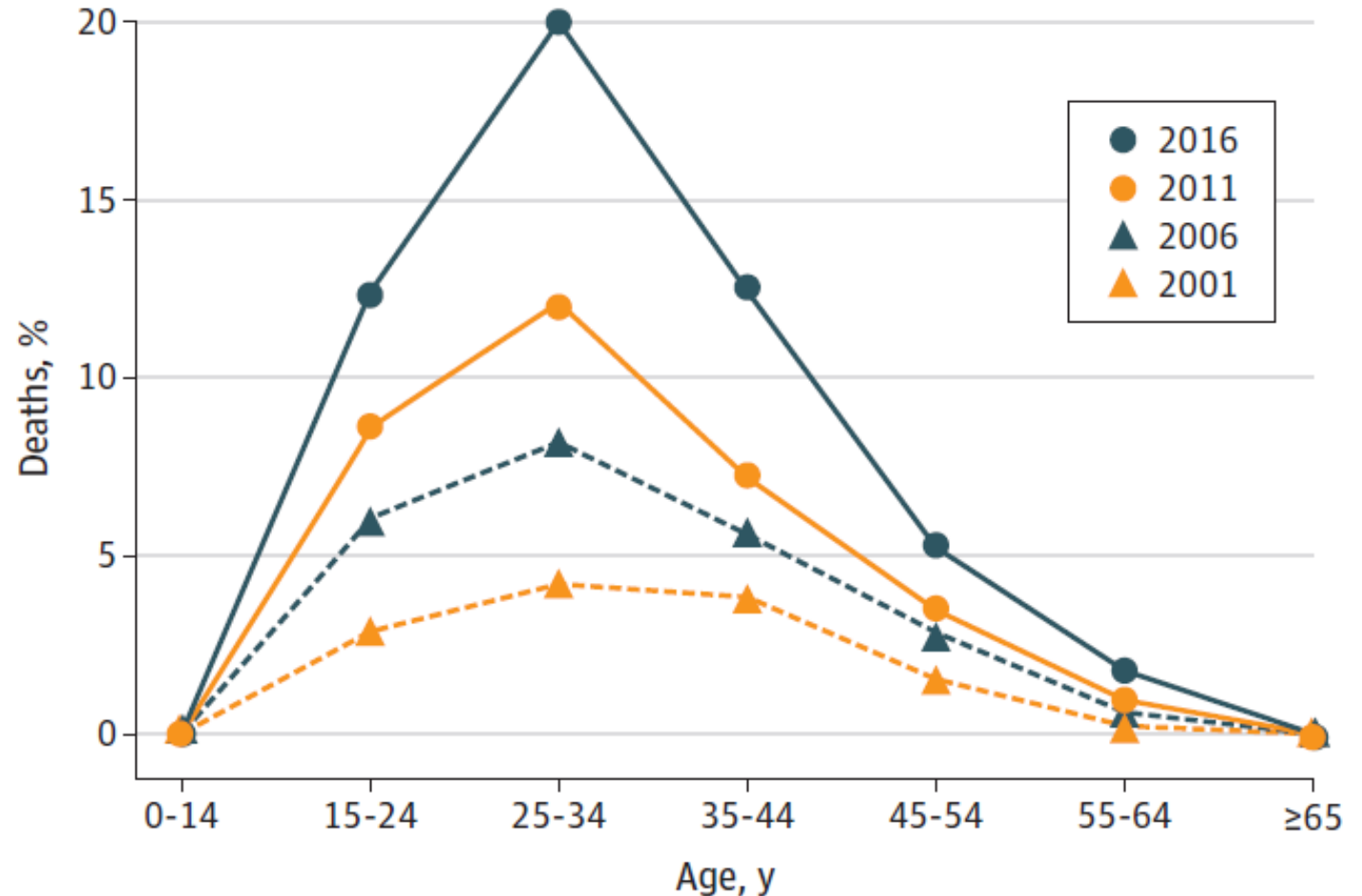


Proportion of Young Adult Deaths Related To Opioids

Between 2001–2016, opioid-related deaths increased by 345%

Aged 15 to 24 yrs, 12.4% of deaths were attributable to opioids in 2016

- ◆ greater than 3-fold increase from 2001 to 2016
- ◆ alcohol, cocaine, or benzodiazepines were also present in 45% of deaths



Age & Buprenorphine Retention

Emerging adults more likely to drop out, return to use, and test positive for illicit opioids

It is important that adolescents and young adults are treated by clinicians that are experienced in working with this age group.

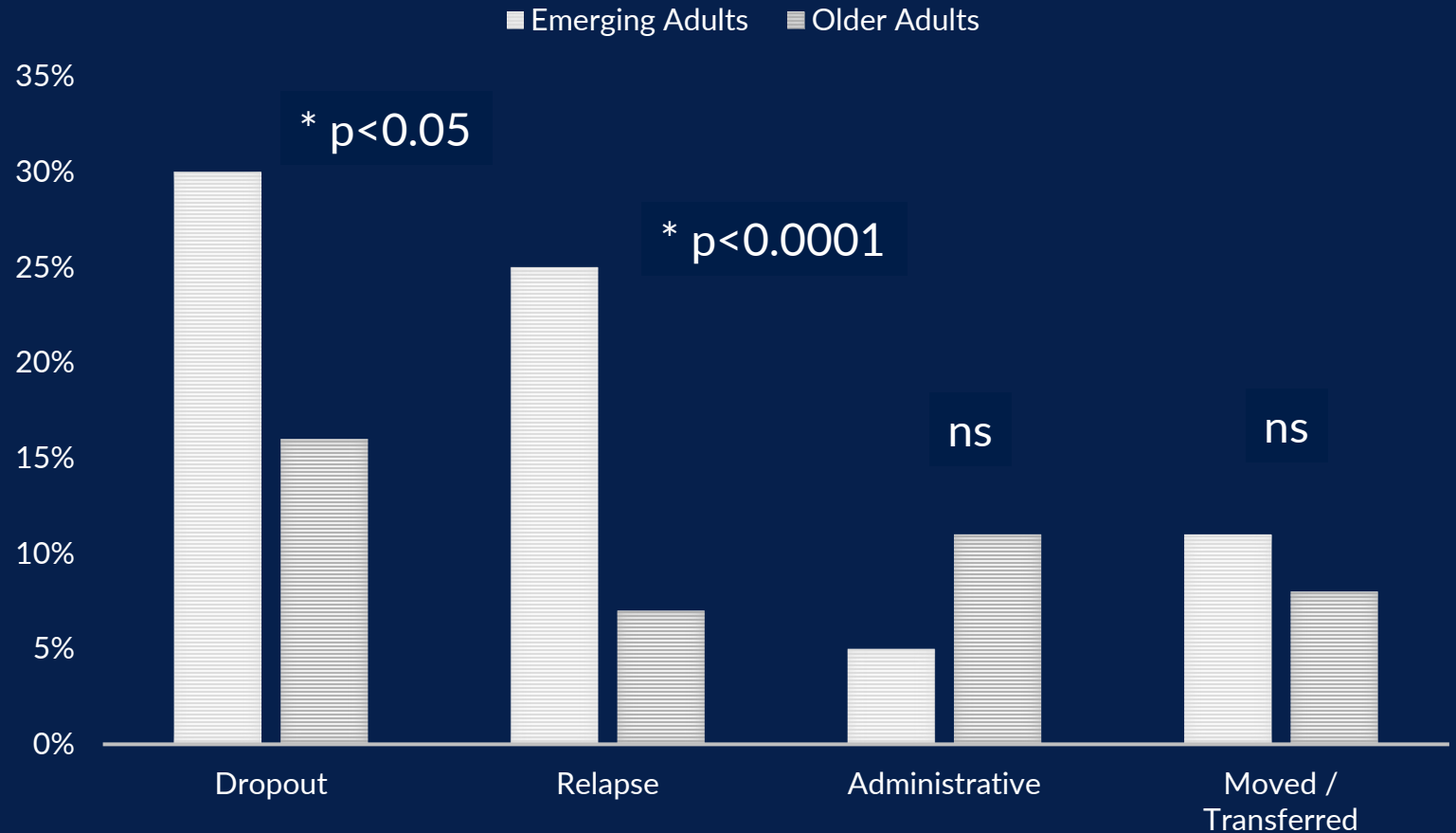


Fig. 3. Emerging adults versus older adults compared on reasons for program disenrollment by 12 months after admission.

Medications for Adolescents with OUD

Compared buprenorphine versus clonidine for 28-day opioid detoxification

RCT; double-blind, double-dummy design

Participants 13-18 years old, N=36

All participants received counseling in addition to medications

Compared to clonidine, patients who received 4 weeks of buprenorphine treatment:

- ◆ Had fewer positive opioid drug tests
- ◆ Stayed in treatment longer
- ◆ Were more likely to continue pharmacologic treatment after the 4-week trial period

Extended vs. Short-Term Buprenorphine

Naloxone for Treatment of Youth with OUD

RCT, 2-week detox
versus 12-week
treatment

N=156 participants
15-21 years old

All received 2
counseling sessions for
12 weeks

Compared to 2 week detox,
those who received 12
weeks of buprenorphine
had better treatment
retention and had fewer
positive opioid drug tests at
4 and 8 weeks and fewer
positive opioid tests overall

There was no
difference in the rates
of opioid-positive drug
tests at 12 weeks
(when both groups
had completed tapers).

The authors
concluded, longer-
term medication
maintenance seems
superior to short term

Pharmacologic Treatment of Young Adults

Methadone (OTP)

may be a good option for young adults with unstable living arrangements as daily visits provide structure and eliminate the need to manage medications at home.

Naltrexone

is also an option for adolescents and also may be clinically useful for adolescents/young adults living away from home, or patients with co-occurring alcohol use disorders.

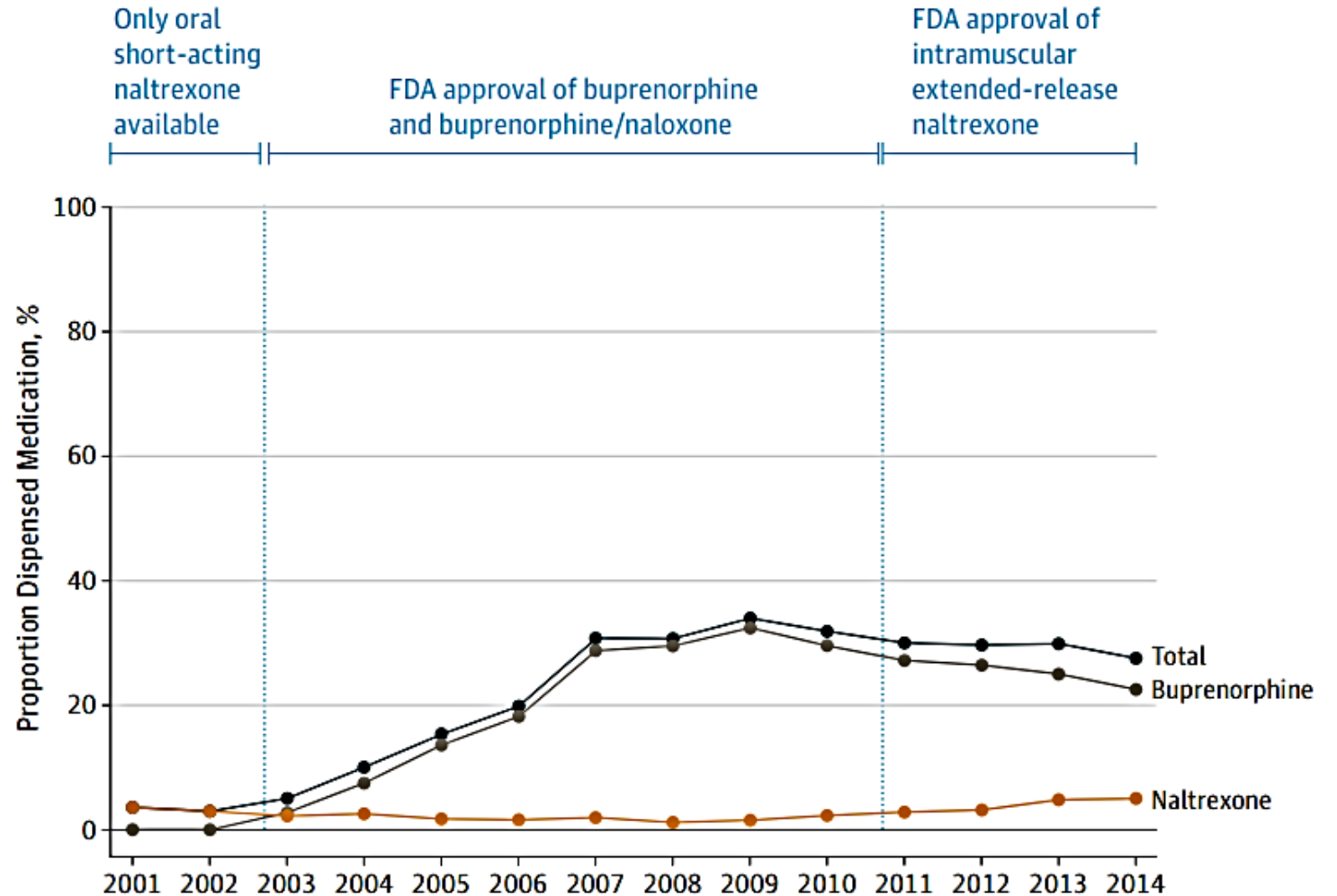
There are no published studies on the efficacy of naltrexone for OUD in adolescent patients.

Trends in New OUD Diagnoses Among Youth and Young Adults

27% dispensed a medication within 6 m of diagnosis (89% buprenorphine and 11% naltrexone)

Increased more than 10-fold, from 3% (2002) to 32% (2009), but declined in subsequent years to 28% in 2014

Younger, female, black and Hispanic youth were less likely to receive medications





Medication-Assisted Treatment of Adolescents With Opioid Use Disorders

COMMITTEE ON SUBSTANCE USE AND PREVENTION

OAD is a leading cause of morbidity and mortality among US youth

Effective treatments are underutilized

Resources to disseminate available therapies...for this age group are needed to save and improve lives of youth with OUD

Pregnancy: Barriers to Treatment

Stigma

Significant misinformation about what medication treatment is and its benefits.

Lack of Training

Only 1% of waived providers identify as pediatricians.

Coordination of Care

These cases are complicated, involve state agencies, families, children → can be hard to ensure that a consistent plan is being offered and implemented.

Treatment Duration

- The optimal length of time for medication treatment in adolescents and young adults is not known.
- Studies in adults have found that patients continued to improve over the course of the first six years of treatment.
- The impact of exposure to long term agonists/antagonists on the developing brain are unknown although the negative effects of ongoing drug use are well known.

Maintaining Engagement in School

Substance use disorders often interfere with education.

Maintaining education with the most effective combination of pharmacotherapy and psychosocial treatment is important.

If adolescents and young adults discontinued schooling, then when stabilized should be encouraged to return to school.

Buprenorphine, methadone, and naltrexone, properly administered do not impair cognitive function.

Teens Presenting with Parents

- In many cases, adolescents will present for treatment with the knowledge, and often with the support of parents
- Parents are often the first people teens turn to for help
- In these cases, managing confidentiality is a clinical decision of what information to share with parents in the context of parents already being aware of the “big picture”

Teens Presenting without Parents

- Teens may present for treatment without the knowledge or consent of their parents
- In most states adolescents above a certain age may consent for treatment for an SUD without their parents, though details vary

Managing Teens Who Refuse to Involve Parents

- Ask adolescent their reasons for excluding parents. Many teens could benefit from the support of parents, but are too embarrassed to discuss the problem
- In these cases, offer to treat confidentially and leave the decision of how to proceed up to the teen
- Ask what would happen if a parent learned about a drug problem by accident
- Emphasize that teens who enter treatment should be proud of their decision to get help
- Offer to help “break the news” to parents
- Offer overdose education and naran prescription as a standard to all teens using opioids.

Confidentiality

Parental request to see their child's chart.

In some settings, the parent of a minor may have the right to see the chart. Check with a legal expert. If the parent does have the right, discuss the pros and cons.

Pros

May find out more detailed information about teen.

Cons

- ◆ May make teen angry and less willing to share other information in the future.
- ◆ May damage the therapeutic relationship between provider and teen.
- ◆ Teen may drop out of treatment.
- ◆ Chart may not contain information sought.

If parents insist on viewing chart, have them make a formal medical records request.

Managing Teens That Refuse to Involve Parents

- If the teen fears that revealing a SUD would put him/her at risk, or if teen decides not to involve parents, proceed with confidential treatment
- Seek legal expertise to insure that “mature minor” or “emancipated” status will allow you to treat an adolescent for a SUD without consent in your state
- Review plans for keeping treatment a secret; ask the teen how likely his/her plan is to succeed
- Discuss issues of confidentiality with the rest of the treatment team (counselors, psychiatrists or other professionals)
- Ensure all documentation is in place for treating an adolescents as an “emancipated” or “mature” minor



Medical Co-Morbidities

Medical Co-Morbidities: Background

Persons with OUD frequently have or are at risk of other comorbid medical conditions

Office-based OUD treatment provides an opportunity to combine substance use treatment with medical care

Routine Healthcare

Blood pressure, lipids,
weight, physical activity,
diabetes, bone density

Age-appropriate screening
(colorectal, breast, cervical,
lung, +/- prostate, skin)

Tuberculin skin test

Vaccines—Influenza, tetanus-
diphtheria, pneumococcal
(PCV13, PPSV23), hepatitis A,
B, zoster, human papillomavirus
(HPV)

Needle-Related Systemic Bacterial Infections

Soft tissue infection

Vascular endothelium

- E.g., infective endocarditis,
infected (mycotic) arterial
aneurysm, septic
thrombophlebitis

Epidural abscess or
discitis

Cellulitis; abscess

Sepsis

Osteomyelitis

Hepatitis C Virus (HCV) Infection

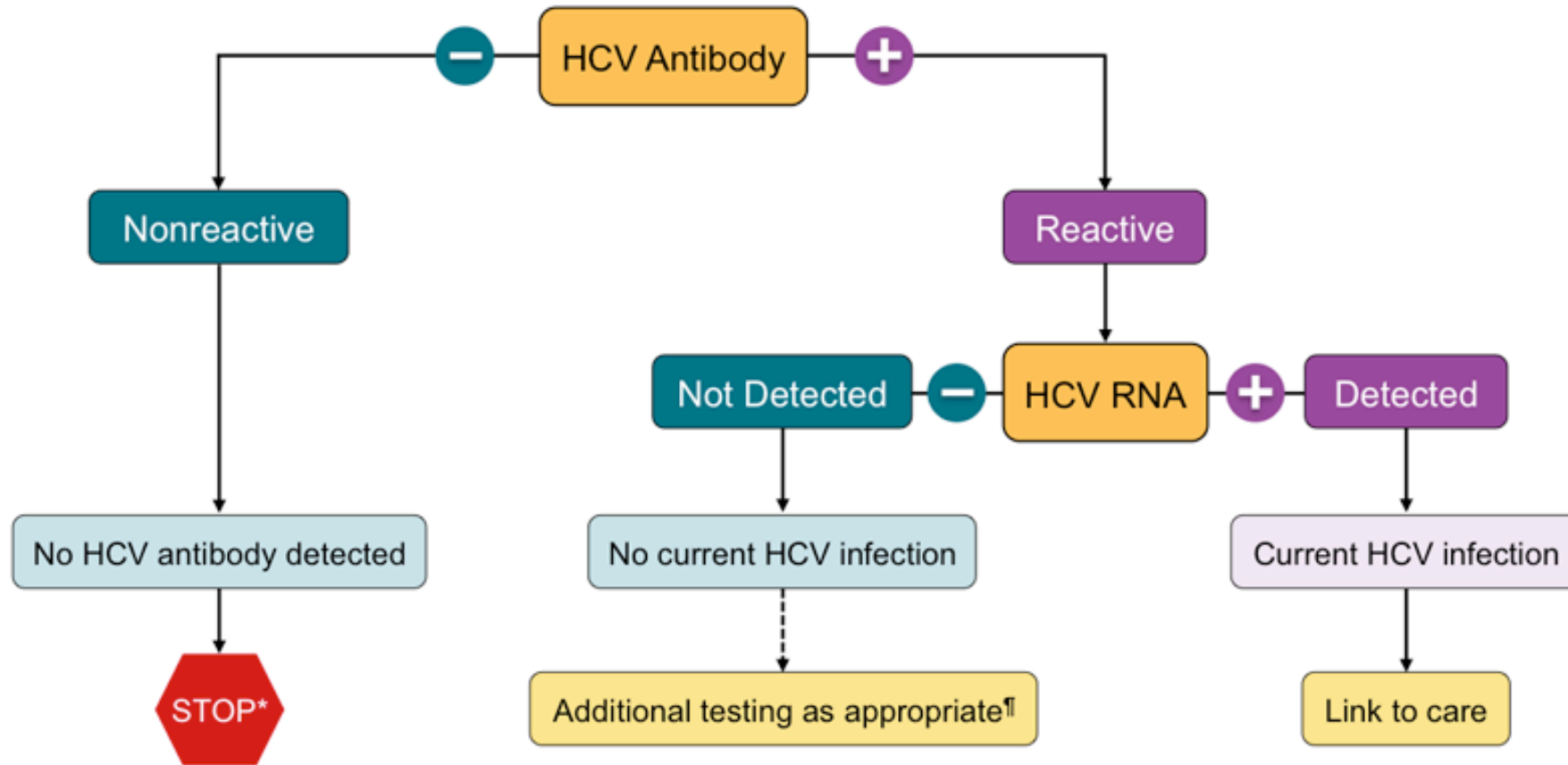
Most common blood-borne infection in U.S., 3.2 million people (70-90% people who inject drugs (PWID); ~30% <age 30)

Acute process is self-limited, rarely causes hepatic failure, and leads to chronic infection up to 85% of time

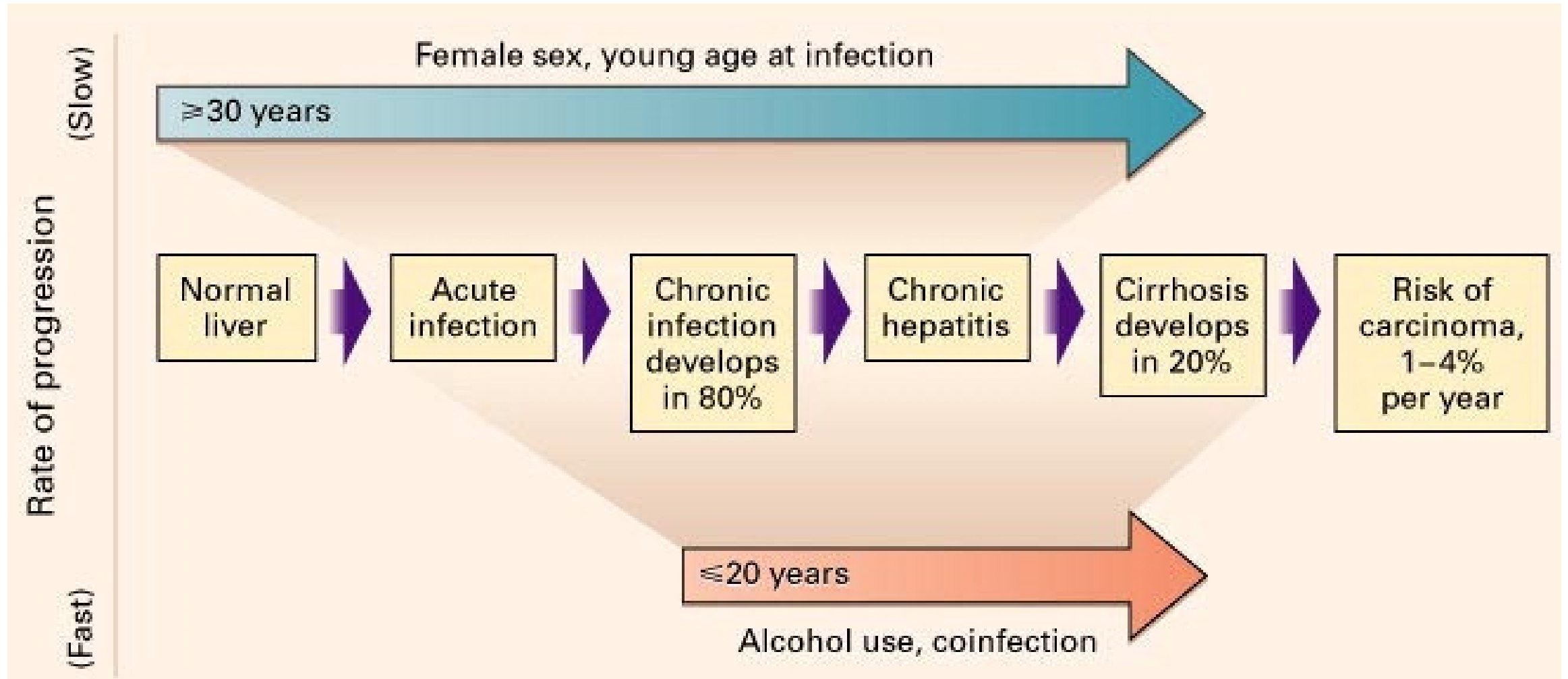
Chronic HCV infection often follows a progressive course over many years and can ultimately result in cirrhosis, hepatocellular carcinoma, and the need for liver transplantation

HCV-related deaths outnumber deaths due to HIV

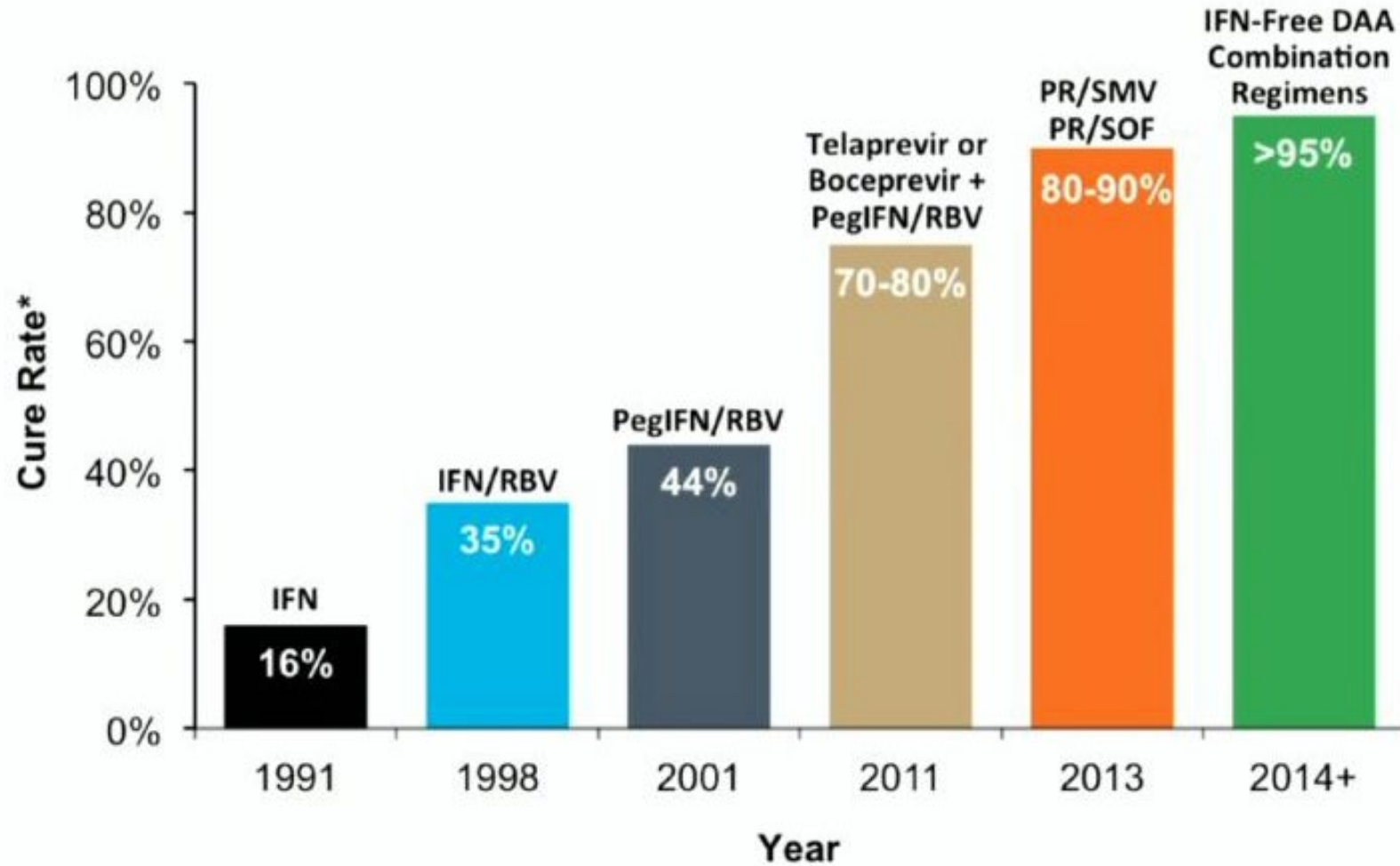
Recommended Testing Sequence for Identifying Current HCV Infection



HCV Natural History



Rising Cure Rates for Chronic HCV (G1)



Buprenorphine & HCV

- Buprenorphine undergoes hepatic metabolism, primarily by the CYP450 3A4 system.
- A large (n=1269) trial of bup/nx- and methadone-maintained patients found no evidence of elevated transaminases with buprenorphine. Only HCV or recent HCV seroconversion predicted elevated transaminase levels. (Saxon et al. 2013)
- Patients with impaired hepatic function should be monitored, but buprenorphine may be prescribed without major concern for liver injury.

HCV and Opioid Agonist Therapy (OAT)

A meta-analysis demonstrated good treatment outcomes in patients with active drug injection who are eligible and committed to starting HCV treatment

- ◆ Current guidelines recommend that active injection drug use should not exclude patients from HCV treatment

No significant pharmacodynamic interactions have been reported between approved direct anti-viral agents (DAAs) and buprenorphine or methadone

Dose adjustments are not recommended; therefore, DAAs appear to be the "perfect" therapy for patients on OAT

Acute HIV

Acute HIV infection may present as a mononucleosis type of syndrome with nonspecific symptoms. In some cases, early HIV infection may be asymptomatic

Up to 60% of individuals with early HIV infection will not experience symptoms

Time to positivity of HIV diagnostic tests

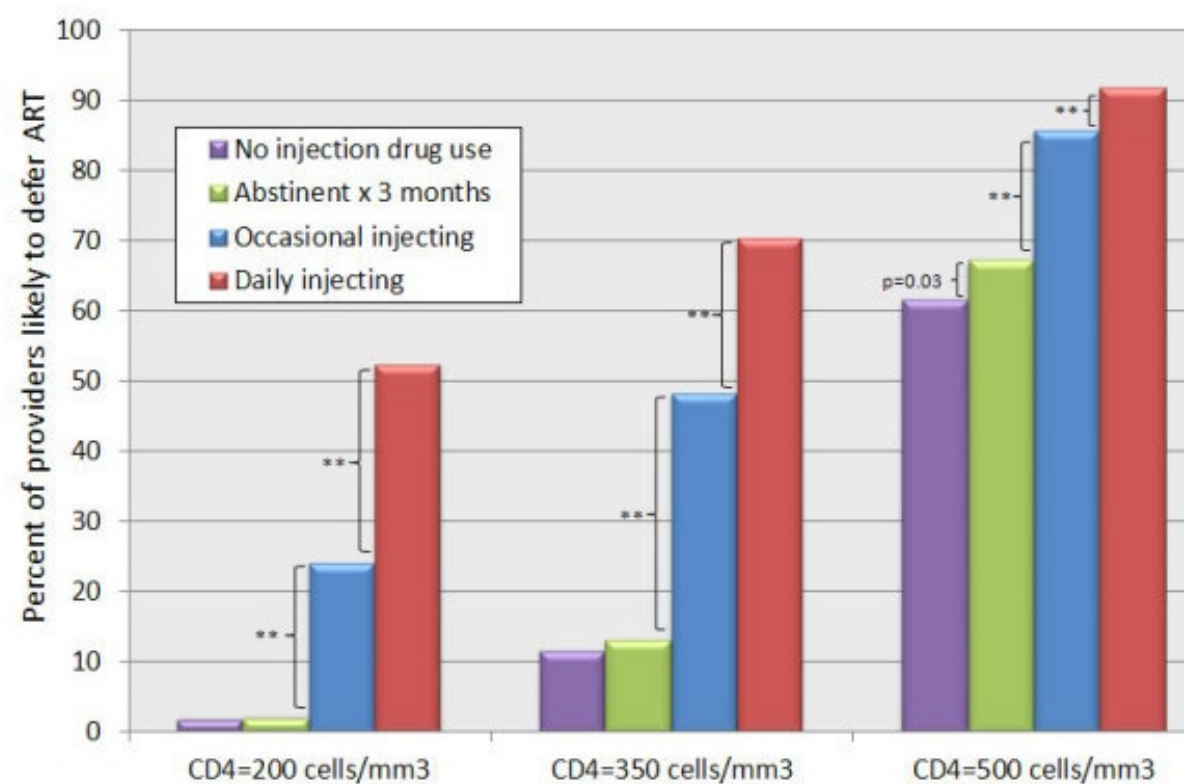
Test	Target of detection	Approximate time to positivity (days)
Enzyme-linked immunoassay		
First generation	IgG antibody	35 to 45
Second generation	IgG antibody	25 to 35
Third generation	IgM and IgG antibody	20 to 30
Fourth generation	IgM and IgG antibody and p24 antigen	15 to 20
Western blot		
	IgM and IgG antibody	35 to 50 (indeterminate)
		45 to 60 (positive)
HIV viral load test		
Sensitivity cutoff 50 copies/mL	RNA	10 to 15
Ultrasensitive cutoff 1 to 5 copies/mL	RNA	5

HIV Treatment Goals

- Improve individual health outcomes.
- Restore health, prolong life in a manner indistinguishable from uninfected persons
- Lower community viral load and HIV transmission

Persons Who Inject Drugs (PWID) Less Likely to Receive ART

- Predictors of deferring.
- Physician vs. non-physician (AOR 2.6, 95% CI 1.4-4.9)
- Fewer years of HIV care experience
- Regularly caring for <20 HIV+ patients
- Clinic with low prevalence of PWID



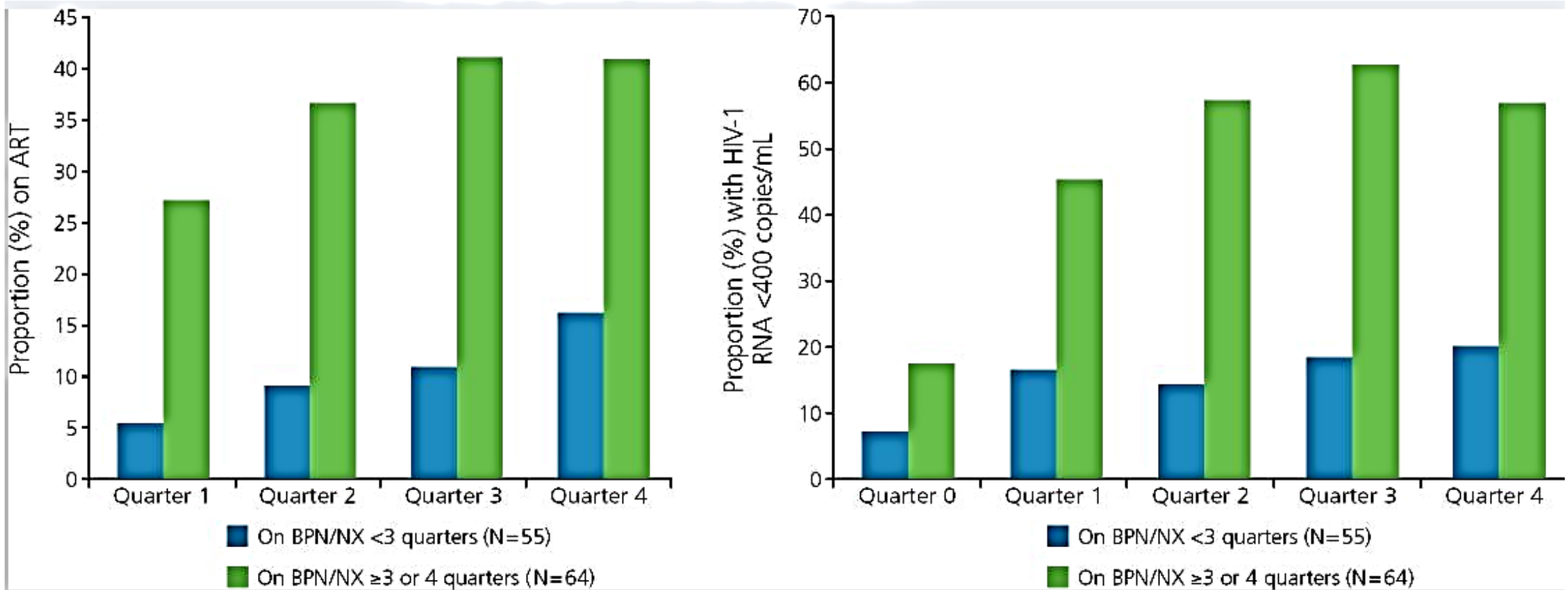
Percentage of HIV providers (n=662) who would defer prescribing ART by CD4+ count and injection drug use status

Buprenorphine and HIV Outcomes

HIV-infected patients treated with office-based buprenorphine in the Buprenorphine-HIV Evaluation and Support (BHIVES) national demonstration project:

- Decreased opioid use
- Increased HIV ART use
- Experienced higher quality of HIV care
- Reported better quality of life

Buprenorphine Retention and HIV Outcomes

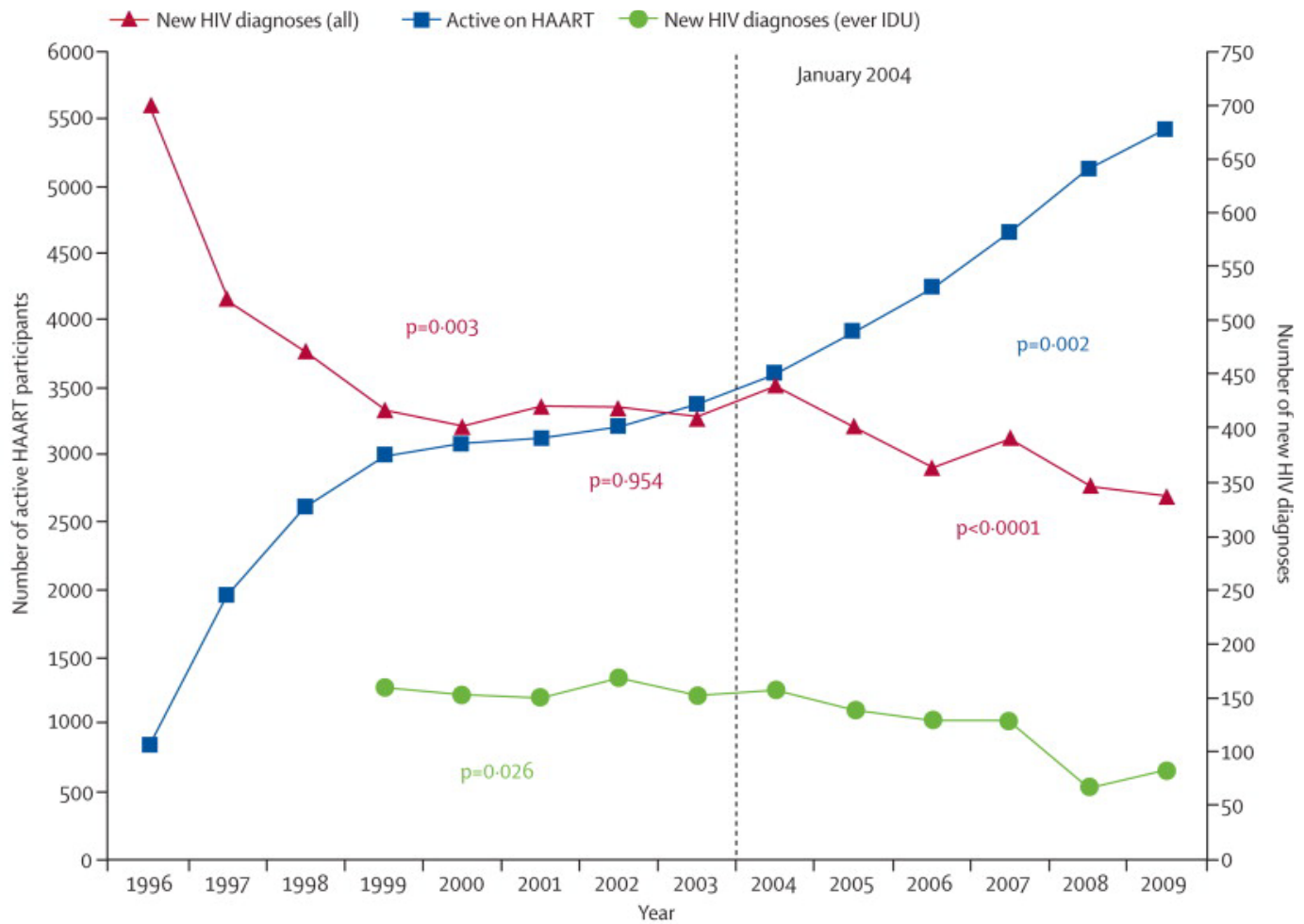


HIV outcomes are improved with retention on buprenorphine treatment ($p \leq .05$ for all comparisons with baseline)

Opioid Agonist Treatment as HIV Prevention

Methadone-maintained patients report less needle and syringe sharing

Methadone-maintained patients are 3-6 times less likely to become HIV positive as compared to out-of-treatment heroin users, including among those who continue to use drugs



Treatment Expansion
(Increases in methadone maintenance)

Parallels Drop in New HIV Cases in PWID

Number at risk	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Active on HAART	837	1960	2597	2994	3079	3120	3211	3356	3585	3913	4255	4654	5123	5413
New HIV diagnoses (all)	702	519	471	416	400	420	418	408	441	400	361	391	346	338
New HIV diagnoses (ever IDU)	NA	NA	NA	159	152	149	168	149	156	137	128	128	65	80
HIV tests done in BC (per 1000)	138	140	137	135	135	135	145	142	154	161	172	176	182	NA



HIV Pre-Exposure Prophylaxis (PrEP)

For HIV-uninfected patients, PrEP using antiretroviral medications is an evidence-based way to prevent new infections among those at greatest risk

Fixed-dose combination of the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) emtricitabine and tenofovir alafenamide (TDF-FTC) should be administered once daily for as long as the risk of infection persists

PrEP has been associated with a reduction in HIV transmission in PWID

PrEP

- ✓ *Pre-exposure prophylaxis:*
when people who don't have HIV take HIV medicine every day to reduce their chances of getting HIV.
- ✓ *Reduces risk of getting HIV:*
from sex by ~88%.
from injection drug use by >74%.



Current FDA-Approved Medications

- Emtricitabine (200mg)/Tenofovir Disoproxil Fumarate (300mg): Truvada®.
- Emtricitabine (200mg)/Tenofovir Alafenamide (25mg): Descovy®.

Which is best?

- Truvada® vs Descovy® based on individual risk factors.
- Descovy® not for use in people assigned female at birth who are at risk of getting HIV through vaginal sex (effectiveness not yet studied).

PEP



Post-exposure prophylaxis:

when a patient takes HIV medicine very soon after possible exposure to HIV in order to prevent HIV infection.



Not meant for regular use:

PEP intended for emergency situations.

Must be started within 72 hours after a possible exposure to HIV. The sooner, the better.



PEP

Current preferred medication regimen:

- Tenofovir disoproxil (300 mg)/emtricitibine (200 mg) QD, PLUS.
- Raltegravir (400 mg) BID or dolutegravir (50 mg) QD.

Length of treatment:

- If prescribed PEP, patient will take HIV medicine every day for 28 days.

Safer Sex

- *People under the influence of drugs are more likely to engage in risky sex and could get HIV.*
 - Those who share needles/syringes are more likely to have unprotected sex.
 - Provider should educate patient on: contraception options, condoms, PrEP and PEP, regular STI testing.
 - Be aware of “club drug” use leading to unsafe sex.



Psychiatric Co-Morbidities

Induced vs. Independent Disorder

Distinguish between substance-induced disorders versus independent psychiatric disorders.

Substance-Induced

Disorders related to the use of psychoactive substance; typically resolve with sustained abstinence

Independent

Disorders which arise during times of abstinence; use of psychoactive substances not the etiology

Substance-Induced Psychiatric Disorders

- Patient's history suggests symptoms occur only when he/she is actively using substances
- Symptoms are related to intoxication, withdrawal, or ongoing neurobiological perturbation from substances
- Onset and/or offset of symptoms are preceded by increases or decreases in substance use
- Goal should be sustained abstinence followed by re-evaluation of symptoms

Substance-Independent Psychiatric Disorders

- Earliest psychiatric symptoms often precede onset of substance use disorder
- Patient's history suggests symptoms occur during periods when not using psychoactive substances
- May also find a family history of the disorder
- Goal of substance use disorder treatment should still be cessation of substance use, but treatment must also address psychiatric symptoms simultaneously

General Treatment Principles

- Patients with OUD and independent depressive, anxiety, or stress disorders
 - Can respond to medication and/or psychotherapy treatments for depression, anxiety, and PTSD
 - Anxiety disorders and PTSD typically treated with antidepressants
- Generally, avoid use of benzodiazepines
 - Risk of misuse
 - Possibility of interactions with buprenorphine AND methadone
 - Prescribed benzos are not a reason not to start buprenorphine.

General Treatment Principles

- Common for patients with OUD to report high rates of depressive and anxiety symptoms at time of treatment entry
- Symptoms often resolve within a few days after entry (i.e., substance-induced)
- *“Sick and tired of being of being sick and tired”*
- Conduct routine mental health screening (PHQ, etc. Every 6-12 months)

Confidentiality

Epidemiology in OUD

- Lifetime rates: 15-50%
- Current rates: 3-25%

*Conduct routine SI screening
with each visit.*

Features

- Depressed mood
- Anhedonia
- Weight/appetite change
- Sleep change
- Psychomotor agitation/retardation
- Loss of energy
- Feeling worthless/inappropriate guilt
- Decreased concentration
- Thoughts of death/suicidal ideation

Assess: Suicidal Ideation

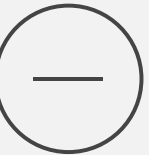
- Assess level of intent, level of lethality, risk factors
 - Male gender
 - Older
 - Major depression
 - Active substance use
 - Serious medical problems
 - Recent loss (e.g., of employment, relationship, death of family member)
- Consider referral to emergency services
 - e.g., crisis service, emergency department
- Recognize low-intent patients can make high-lethality attempts

Pharmacologic Treatment of Depression in OUD: SSRIs / SNRIs



Advantages

- No overdose risk
- Minimal dose titration needed (except venlafaxine)
- Sedation and anticholinergic side effects rare
- SNRIs may have anti-nociceptive effects



Disadvantages

- High rates of sexual side effects
- Increased risk of GI bleed due to anti-platelet activity

Pharmacologic Treatment of Depression: TCAs

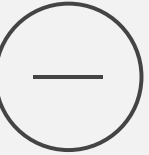
Advantages

- Sedation (sometimes helpful for patients with insomnia)
- Demonstrated anti-nociceptive effects



Disadvantages

- Potentially lethal in overdose due to effects on cardiac conduction
- Require careful dose titration
- Sedation, anticholinergic, and hypotensive side effects



Anxiety Disorders

Epidemiology in OUD

- Most common anxiety disorders are phobias, followed by Generalized Anxiety Disorder
 - Lifetime rates: 8-27%
 - Current rates: 5-17%



Phobia Features

- Excessive and unreasonable fear
 - Can be of an object (animal), situation (flying)
- Exposure produces intense anxiety and distress
- Avoidance as coping mechanism

Anxiety Disorders

Generalized Anxiety Disorder Features

Excessive anxiety and worry, difficult to control

Restlessness / feeling keyed up

Easy fatigue

Difficulty concentrating

Irritability

Muscle tension

Sleep disturbance

Panic Disorder Features

- Panic attacks - discrete periods of intense fear or discomfort, with:
 - Palpitations, pounding heart, increased HR
 - Sweating, trembling, shaking
 - Shortness of breath / smothering feeling
 - Feeling of choking
 - Chest pain / discomfort
 - Nausea / abdominal distress
 - Feeling dizzy, lightheaded, unsteady, faint
 - Derealization or depersonalization

Social Anxiety Disorder

- Features
 - Fear or anxiety about social situations
 - Fear of being negatively evaluated, humiliated
 - Social situations avoided or endured with anxiety
 - Fear out of proportion to actual threat
 - Fear or avoidance lasts ≥ 6 months
- Epidemiology
 - Occurs in ~ 10% of SUD patients
- Challenges
 - Can make attendance at group meetings challenging

Post-Traumatic Stress Disorder (PTSD)

- Common across the sexes in individuals with OUD (exact percentages are undetermined)
- Patients rarely volunteer the history
- Suspect in individuals of all sexes with Antisocial Personality Disorder or Borderline Personality Disorder
- Sexual abuse history is common
- Adverse Childhood Experiences (ACEs)

Adverse Childhood Experiences (ACEs)

ABUSE



Physical



Emotional



Sexual

NEGLECT



Physical



Emotional

INSTABILITY IN THE HOUSEHOLD



Mental Illness



Incarcerated Relative



Mother treated violently



Substance Misuse



Divorce

Adverse Childhood Experiences (ACEs)

Study Findings- Of 17,000 Participants:

- 🔍 64% reported at least one ACE
- 🔍 22% reported 3 or more ACEs
- 🔍 Strongly predictive of negative outcomes later in life:
 - *Each ACE associated with 2-4 fold increased risk of early initiation of drug use*
- 🔍 Findings replicated in cohort of urban, poor, non-white patients in 2013



ACEs: Common Adverse Outcomes

- Development of addiction to alcohol or other substances
- Chronic diseases (e.g., ischemic heart disease, chronic pulmonary disease)
- Social outcomes (e.g., exposure to domestic violence, adolescent pregnancy)
- Mental Illness (e.g., depression)

Discussing Childhood Trauma in Clinical Care

- Trauma-Informed Care (including welcoming, safe clinical structure)
- Trauma-Informed Communication
- Motivational Interviewing Tools

Person-Centered Language

- Importance of Non-stigmatizing Language
- Use gender/sexuality-inclusive language.
- Be mindful of gender use in language, specifically during anecdotes and question responses. Avoid assumptions.
- Use "they," "one," and "who" as opposed to "he" or "she."
- Avoid jokes at the expense of patients and stigmatizing/offensive language.

Buprenorphine and Benzodiazepines and Non-Pharmacological Treatment

Buprenorphine and Benzodiazepines

Among 34 reported buprenorphine-associated overdoses in France, 31 also had benzodiazepines

Risks of benzodiazepines

- ◆ Tolerance and withdrawal
- ◆ Excess sedation and falls
- ◆ Cognitive impairment
- ◆ Reinforcement/reward/addiction

Effects of benzodiazepines

- ◆ Rapid elimination of anxiety symptoms or insomnia when used short-term

Buprenorphine and Benzodiazepines

Double-blind, placebo-controlled, RCT show all types of antidepressants effective for all anxiety disorders and should be first line treatment

Benzodiazepines may also be effective for anxiety disorders, but rare patients respond only to benzodiazepines

Intermittent use for panic attacks possible, but better strategy is to optimize antidepressants to minimize frequency of attacks

Benzodiazepines not contraindicated in buprenorphine treatment if appropriately prescribed in moderate doses (≤ 40 mg diazepam equivalents/day)

FDA Communication (9/2017) “The combined use of these drugs (buprenorphine, benzodiazepines) increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks...”

Non-Pharmacological Treatment

- Don't overlook importance of non-pharmacological treatments
 - E.g., cognitive behavioral therapy
- Especially in patients with mild / moderate anxiety
- Integrative Approaches for Anxiety/Depression/PTSD:
 - Mindfulness
 - Visualization
 - Imagery
 - BRT
 - DBT
 - CBT

Antisocial Personality Disorder

Epidemiology

- Personality disorders highly prevalent in patients with OUD
- Most common is Antisocial Personality Disorder (ASP) particularly in men
 - Rates (any personality disorder): 14-68%
 - Rates (ASP): 14-55%



Management of Personality Disorder Patients

- Distinguish between behaviors that occur as part of drug use lifestyle versus personality disorder
- If needed establish limits and boundaries calmly but firmly
- Recognize limitations to treatment in office based setting
- Refer to specialized services once cessation of illicit substance use is achieved, if patient is distressed

Epidemiology of Other Psychiatric Co-Morbidities and OUD

Schizophrenia

Relatively rare

Bipolar Disorder

Less common than major depression (unipolar disorder)

Eating Disorders

Lifetime history not uncommon, but rare as a current problem

Attention Deficit Hyperactivity Disorder (ADHD)

Considerable interest, but little information about prevalence



Questions? Answers.



Session 5: Keeping Your Patient Safe & Interactive Clinical Cases

Drug Diversion and Misuse

XYZ Medical Practice

Sample Office-Based Opioid Use Disorder Policy and Procedure Manual

Policy Title: **Diversion Control for Patients Prescribed Transmucosal
(Sublingual) Buprenorphine**

Effective Date: **Month, Day, Year**

This Diversion Control Policy is provided for educational and informational purposes only. It is intended to offer physicians guiding principles and policies regarding best practices in diversion control for patients who are prescribed buprenorphine. This Policy is not intended to establish a legal or medical standard of care. Physicians should use their personal and professional

ASAM Sample Diversion Control Plan

Available online: <http://bit.ly/diversionpolicy>



Diversion

People self-treating with diverted buprenorphine reported:

- 97% take it to prevent cravings
- 90% take it to prevent withdrawal
- 29% take it to save money

Why? Limited access to treatment, lack of health insurance.

Potential Diversion

Common Signs

- Requests for early refills (medication lost or stolen).
- Inconsistent laboratory testing (e.g., bup negative).
- Claims of being allergic to naloxone and requesting monotherapy.
- Police reports of patient selling in streets.
- Reports of concerning behavior.
- Inconsistent appointments (e.g., missed).

Risk Management: *Educate Patients about Harms of Diversion of Misuse*

Misuse and Diversion

- Can lead to harmful medical and social consequences, overdose, and an increase in stigma for patients and providers.

Legislation

- Periodically re-evaluated by DEA and SAMHSA for risks and benefits.

What patients do with their medications matters for us all!

Ways to Mitigate Diversion Risk

- Tabs/film must dissolve under the tongue to maximize bioavailability for at least 10 minutes.
- Mouth checks to prevent diversion.
- The patient eats crackers and drinks water after tabs dissolve.
- Monitor urine bupe/norbupe levels.
- If possible, use a monthly injectable form of buprenorphine.

Responding to Misuse and Diversion



Evaluate
and reassess
treatment plan and
patient progress.



*Intensify
Treatment*
or refer to higher
Level of Care.



Document and Describe
clinical thinking that supports a clinical response,
should be aimed at minimizing risk and treating
patient at the level of care needed.



Harm Reduction

1. Naloxone and Overdose Education
2. Syringe Service Programs
3. Polysubstance Use
4. HIV, PrEP and PEP
5. Safer Sex

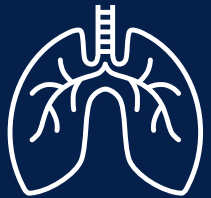
Opioid Mu Receptor Agonist Drug Effects

- *Acute Exposure*
 - Euphoria, nausea, vomiting, depressed respiration, sedation, analgesia.
- *Large Dose Acute Exposure*
 - Non-responsive, pinpoint pupils, hypotension, skin cyanotic, pulmonary edema.
- *Chronic Use Effects*
 - Physical dependence, withdrawal, tolerance, lethargy, constipation.



Opioid-induced Respiratory Depression

Opioids depress the brain stem's response.



- Depression of the medullary respiratory center.
- Decreased tidal volume and minute ventilation.
- Decreased respiratory response to elevated CO₂.
- Hypercapnea, hypoxia and decreased oxygen saturation.
- Life threatening hypoxia.
- Sedation occurs before significant respiratory depression, and, therefore, is a warning sign.

Naloxone Formulations



Injection

1 dose =
0.4mg/1ml
Intramuscular



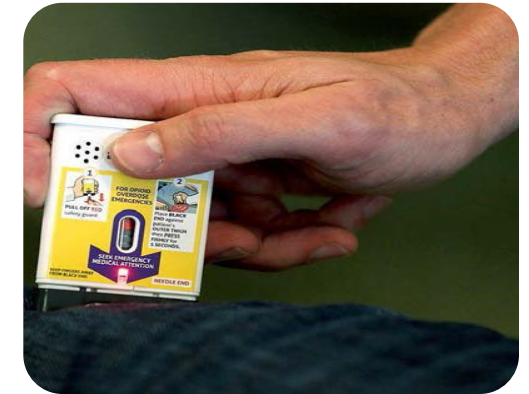
Nasal w/atomizer

“Multi-step”
1 dose =
2mg/2ml
Intranasal



Nasal spray

“Single-step”
1 dose =
4mg/0.1ml
Intranasal



Auto-injector

1 dose =
0.4mg/1ml
Intramuscular

Naloxone

Prevent Overdose

- Broader provision of naloxone has been shown to prevent opioid overdose morbidity and mortality.

Co-Prescribe

- U.S. Department of Health and Human Services urges that all patients receiving medications for OUD be co-prescribed naloxone.

Coffin PO, Behar E, Rowe C, Santos GM, Coffa D, Bald M, Vittinghoff E. Nonrandomized intervention study of naloxone coprescription for primary care patients receiving long-term opioid therapy for pain. *Annals of Internal Medicine*. 2016;165(4):245–252.

Evaluations of Overdose Education and Naloxone Distribution (OEND) Programs

- Feasibility
- Increased knowledge and skills
- No increase in use, increase in drug treatment
- Reduction in overdose in communities
- Cost-effective

Piper et al. *Subst Use Misuse* 2008; Doe-Simkins et al. *Am J Public Health* 2009; Enteen et al. *J Urban Health* 2010; Bennett et al. *J Urban Health*. 2011; Walley et al. *JSAT* 2013

Green et al. *Addiction* 2008; Tobin et al. *Int J Drug Policy* 2009; Wagner et al. *Int J Drug Policy* 2010

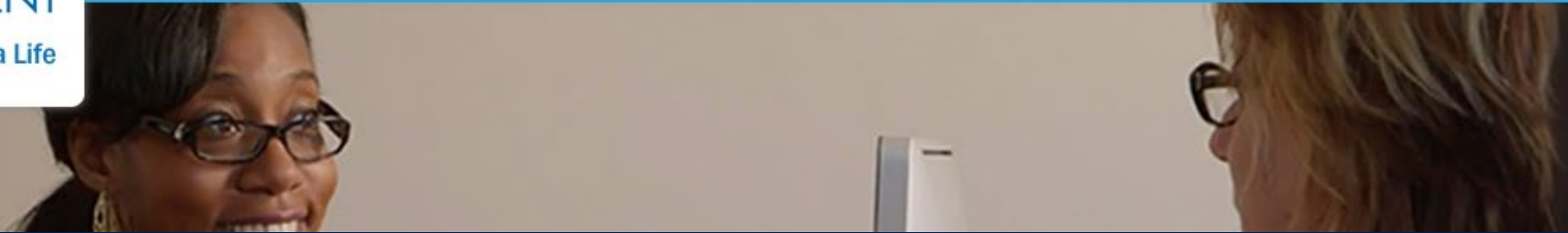
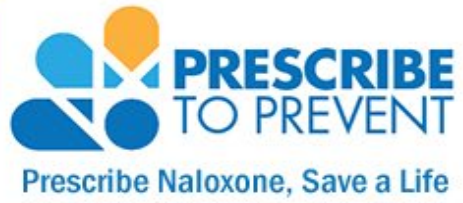
Seal et al. *J Urban Health* 2005; Doe-Simkins et al. *BMC Public Health* 2014; Jones et al. *Addictive Behaviors* 2017

Maxwell et al. *J Addict Dis* 2006; Evans et al. *Am J Epidemiol* 2012; Walley et al. *BMJ* 2013; Coffin et al. *Ann Intern Med* 2016

Coffin & Sullivan. *Ann Intern Med*. 2013

Overdose Education and Naloxone *Communicate to Patients*

- ***Don't use opioids alone. Beware of fentanyl.***
 - Known overdose risk factors: mixing substances, abstinence, using alone, unknown source.
 - Opportunity window: heroin overdoses take minutes to hours; fentanyl takes seconds to minutes.
 - Call 911 before administering naloxone.



*Overdose Education
Education for Providers and Patients*



Overdose education is important for which of the following groups?

- a. Injection opioid users themselves
- b. Family and friends of opioid users
- c. Community members who may be exposed to opioid use
- d. All of the above

Polysubstance Use

Tobacco, Alcohol, Cannabis

<i>Substance</i>	<i>Medication Options</i>	<i>Psychosocial Treatment</i>
Tobacco	Nicotine replacement therapy (patch, gum, lozenge); bupropion; varenicline	Cognitive behavioral therapy (CBT); mindfulness; telephone support and quitlines; mutual help
Alcohol	Naltrexone; acamprosate; disulfiram	CBT; motivational enhancement therapy; marital/family counseling; mutual help
Cannabis	No FDA-approved medications	CBT; contingency management; motivational enhancement therapy; mutual help

Polysubstance Use

Cocaine, Methamphetamine, Benzodiazepines

<i>Substance</i>	<i>Medication Options</i>	<i>Psychosocial Treatment</i>
Cocaine	No FDA-approved medications	CBT; contingency management; therapeutic communities; mutual help
Methamphetamine	No FDA-approved medications	CBT; contingency management; mutual help
Benzo-diazepines	No FDA-approved medications	CBT; contingency management; mutual help

Tobacco



~480,000 Deaths

Leading cause of preventable death (CDC)



~67% smoke
Smoking rates among SUD patients who enter treatment



2-4 times higher
Smoking rates higher in patients with SUD than general public



Death from tobacco
SUD patients more likely to die from tobacco than other substances



Activity

Sandra, Katie, Susan, Charlie

Assess the assigned cases and identify an appropriate treatment approach for each case in groups. Determine if the patient meets DSM-5 criteria for an opioid use disorder.

Prompting Questions

What more information do you need to decide on a diagnosis(es) and treatment plan? Is the patient a suitable candidate for OBOT? Was your group in agreement or did you disagree? If you decide the patient is a good candidate for OBOT, what will the treatment plan include?

35 minutes

After the discussion, one member of each group shares key takeaways with the whole class.



SANDRA'S CASE

Sandra:

25-year-old G2P1 female,
referred for treatment at 28
weeks pregnant.

- She was hospitalized for alcohol, benzodiazepines, and opioid withdrawal.
- When Sandra was pregnant with her first son, two years ago, she attended residential treatment for alcohol use disorder, opioid use disorder, and benzodiazepine use disorder.
- Sandra has co-occurring bipolar I.



Case Discussion – Sandra

Discuss:

- How should Sandra be treated while in the hospital?
- Is her benzo use a contraindication to buprenorphine?
- What should her follow up be?

Sandra:

25-year-old G2P1 female,
referred for treatment at 28
weeks pregnant.

- Sandra underwent three-day withdrawal for benzodiazepines and was then started on buprenorphine.
- She was on Hope Probation, so she was released to jail, then residential treatment.
- She had an uneventful pregnancy and delivered at 39 weeks.
- Baby developed mild NOWS/NAS and was treated for seven days



Case Discussion – Sandra

Discuss:

- How should Susan's labor pain be managed?
- How should Susan be treated postpartum?

Sandra:

25-year-old G2P1 female,
referred for treatment at 28
weeks pregnant.

- While in IOP postpartum, Sandra returned to using alcohol for one day.
- She turned herself into her PO and was incarcerated for two weeks. She did not receive MOUD and completely withdrew.
- She went to her OBGYN and received XR naltrexone injection x 1 dose.
- She didn't like the side effects, so she didn't continue past one month.
- She graduated IOP and went back to work until she returned to use.
 - *How could we help prevent her return to use?*

KATIE'S CASE

Katie:

35-year-old woman who presents for follow-up care. She has diagnoses of severe opioid use disorder and moderate cocaine use disorder.

- She has been treated with buprenorphine/ naloxone 16/4 mg daily for 6 months and has stopped using heroin, which is confirmed by urine drug testing.
- However, her urine drug tests show evidence of continuous cocaine use.
 - *How will you respond to Katie's continued cocaine use?*

SUSAN'S CASE

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She started using oxycodone with her roommate and has been using intranasal heroin (1 gram) daily for the last 15 months.
- Some of her friends are now switching to intravenous use because it takes less heroin to keep from getting sick.
- She does not want to inject drugs but may be “forced” to because she cannot keep paying the “extra cost” of sniffing heroin.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She has used all the money her parents gave her for school expenses to buy heroin, her credit cards are maxed out, and she has borrowed money from her friends.
- Until last semester, she had an overall B average, but this semester she is struggling academically and has been told she will be put on academic probation if her grades don't improve.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- When she doesn't use heroin, she has anxiety, muscle aches, diarrhea, and can't sleep.
- She recognizes the symptoms as heroin withdrawal. She was surprised because she thought she could not develop withdrawal from only sniffing drugs.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She smokes one pack of cigarettes per day.
- She drinks alcohol on the weekends, up to 3 drinks per occasion.
- She denies other drug use.
- She has no prior history of addiction treatment.

Case Discussion – Susan

Discuss:

- Does she meet the criteria for DSM-5 moderate to severe OUD?
- Is she a candidate for office-based opioid treatment with buprenorphine/naloxone?
- What additional information would you need to make that decision?
- If you decide to treat Susan, what are your treatment plan and goals?



Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She was induced on buprenorphine in the office and given a prescription for 6-day supply of bup/nx (16/4 mg/day) and was told to participate in the clinic's 2x per week return to use prevention group and to schedule individual counseling at an off-site program.
- She was told she needed to attend the return to use prevention group in order to get her next bup/nx prescription.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She returns in 6 days for her next bup/nx refill.
- She has not attended the return to use prevention group nor arranged for counseling.
 - *What will be your treatment approach at this time?*

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She was only partially adherent with the recommended counseling for 3 weeks including attending all but 1 of the return to use prevention groups but never started counseling.
- She states she has been too busy to go to counseling. She goes to school 5 days a week and has a new job working evenings as a waitress at a pub.
 - *Should you require Susan to attend counseling? Why? Why not?*

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She then returns in 4 days (3 days before her follow up appointment) and states that one of her friends stole her bup/nx tablets.
- Her urine is buprenorphine negative and opiate positive. She states she is sniffing heroin again to prevent withdrawal after running out of bup/nx.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She has been missing too many classes and has had to change her status to part-time student. She told her parents that she needs time away from school to figure out what her major should be.
- She wants “one more chance” to restart bup/nx treatment.
 - *What would you recommend for Susan at this point?*

CHARLIE'S CASE

Charlie:

25-year-old G2P1 female is seeking treatment at 26 weeks pregnant.

- Charlie states, “I’m addicted to heroin.”
- She is scared that she will lose her baby to child protective services or have medical complications.
- She wants to get into treatment and has come to you for help.



Case Discussion – Charlie

Discuss:

- Is medication-assisted therapy an option for her?
- Which is better, buprenorphine or methadone?
- What about weaning off the heroin and using abstinence-based therapy?
- Does she need any special care for her pregnancy?

Activity

End of Course Reflection

Take five minutes to put in the chat what you found most valuable from the course, where you could use the knowledge gained in your work, and challenges you anticipate in treating OUD.

Prompting Questions

- What are some strategies and solutions for overcoming challenges when treating opioid use disorder?

10 minutes

Share your key takeaways with the class.

Entering a 30 Patient Notification
Buprenorphine Waiver
Notification Form

Go to this link: <http://buprenorphine.samhsa.gov/forms/select-practitioner-type.php>



System Use Notification

- You are accessing a U.S. Government information system, which includes (1) this computer, (2) this computer network, (3) all computers connected to this network, and (4) all devices and storage media attached to this network or to a computer on this network. This information system is provided for U.S. Government-authorized use only.
- Unauthorized or improper use of this system is prohibited and may result in disciplinary action, as well as civil and criminal penalties.
- Personal use of social media on this system may result in disciplinary action unless otherwise authorized.
- By using this information system, you understand and consent to the following:
 - You have no reasonable expectation of privacy regarding any communication or data transiting or stored on this information system. At any time, and for any lawful Government purpose, the government may monitor, intercept, and search and seize any communication or data transiting or stored on this information system.
 - The government may record and audit your information system usage, including usage of personal email systems to conduct HHS businesses.
 - Any communication or data transiting or stored on this information system may be disclosed or used for any lawful Government purpose.

Submit 275-Patient Annual Reports Using This Same Interface

Before you begin

Before starting this application, please make sure you have

- Your DEA Number
- Your State Medical License Number
- Your Training Certificate Information (Only Required for new Waivers)

After submitting application waiver, submit your training certificate to csatbupinfo@dsgonline.com

Do you work for the US military, Veterans Administration, or Indian Health Service?

Yes No

Next

For more information, contact the SAMHSA Center for Substance Abuse Treatment's (CSAT's) Buprenorphine Information Center at 866-BUP-CSAT (866-287-2728) or send an email to infobuprenorphine@samhsa.hhs.gov.

Select "Yes" or "No."
Click "Next."

Look up your DEA number and address on file here: <https://apps.deadiversion.usdoj.gov/webforms/validateLogin.jsp>

Check your waiver eligibility

Enter your information below to check your waiver eligibility and get started.

Select your practitioner type:

MD/DO APRN (NP/CNS/CRNA/CNM) PA

Licensing State:

~select

State Medical License Number:

Letters and numbers only. No spaces or dashes.

DEA Registration Number:

Letters and numbers only. No spaces or dashes.

Back

Submit

Select type.

Select state.

Enter ML
number.

Enter DEA
number.

You will receive a prompt to apply for the 100-patient level if you meet certain criteria.

buprenorphine.samhsa.gov says

Please apply for the 100-patient level if you meet either of the following criteria:

1) You hold a board certification in addiction medicine or addiction psychiatry by the American Board of Preventive Medicine or the American Board of Psychiatry and Neurology.

OR

2) You provide medication-assisted treatment in a qualified practice setting.

Click here for next screen

OK

What is a Qualified Practice Setting?

- A qualified practice setting is a practice setting that:
 - i. provides professional coverage for patient medical emergencies during hours when the practitioner's practice is closed;
 - ii. provides access to case-management services for patients including referral and follow-up services for programs that provide, or financially support, the provision of services such as medical, behavioral, social, housing, employment, educational, or other related services;
 - iii. uses health information technology systems such as electronic health records;
 - iv. is registered for their State prescription drug monitoring program (PDMP) where operational and in accordance with Federal and State law; and
 - v. accepts third-party payment for costs in providing health services, including written billing, credit, and collection policies and procedures, or Federal health benefits.

Please note, all five criteria must be met.

We encourage eligible providers to apply for the 100-patient waiver. This does not mean you have to treat 100 patients.

New Applicant Eligible For Waiver Level 30 or 100

Based on the credentials entered, you appear to be a new applicant. If this is not the case and you have previously submitted a waiver application, please recheck your data and resubmit so that we can link your new activity to your existing account. If you need further assistance, please contact our help desk at 866-BUP-CSAT (866-287-2728). You can also email us at infobuprenorphine@samhsa.hhs.gov.

Starting at the 100-Patient Level
New legislation makes it possible for practitioners to apply for a waiver at the 100-patient level if they meet the following condition(s):

No Yes I am board certified in addiction medicine or addiction psychiatry by the American Board of Preventive Medicine or the American Board of Psychiatry and Neurology.
OR
 No Yes I provide medication-assisted treatment with covered medications (as such terms are defined under 42 C.F.R. § 8.2) in a qualified practice setting as described under 42 C.F.R. § 8.615.

Select your practitioner type:
 MD/DO APRN (NP/CNS/CRNA/CNM) PA

Licensing State:
Maryland

State Medical License Number:
1234567

DEA Registration Number:
AB1234567

Make applicable selections

New Applicant Eligible For Waiver Level 30 or 100

Based on the credentials entered, you appear to be a new applicant. If this is not the case and you have previously submitted a waiver application, please recheck your data and resubmit so that we can link your new activity to your existing account. If you need further assistance, please contact our help desk at 866-BUP-CSAT (866-287-2728). You can also email us at infobuprenorphine@samhsa.hhs.gov.

Starting at the 100-Patient Level
New legislation makes it possible for practitioners to apply for a waiver at the 100-patient level if they meet the following condition(s):

No Yes I am board certified in addiction medicine or addiction psychiatry by the American Board of Preventive Medicine or the American Board of Psychiatry and Neurology.
OR
 No Yes I provide medication-assisted treatment with covered medications (as such terms are defined under 42 C.F.R. § 8.2) in a qualified practice setting as described under 42 C.F.R. § 8.615.
 Although I am eligible for the 100-patient level, I wish to only apply for the 30-patient level.

You appear to be eligible to apply for the 100-patient waiver. Press Next to begin your 100-patient waiver application.

You can apply for the 30-patient waiver, even if you are eligible for a 100 patient waiver. Check this box to apply for the 30-patient waiver.

Click here for next screen

- 1A. Type in name.
- 1B. (Auto populated).
- 1C. Select professional discipline.
- 1D. (Auto populated).

1A. NAME OF PRACTITIONER

First Name

Middle Name

Last Name

Suffix

1B. State Health Professional License Number

License State

1C. Professional Discipline

1D. DEA Registration Number ⓘ

2. Type in primary/service address where you intend to practice.
3. Type in primary/service phone number.
4. Type in fax number (optional).
5. Type in e-mail twice. (This e-mail is where you will receive your approval letter.)

Only one address should be specified. For the practitioner to dispense the narcotic drugs or combinations to be used under this notification, the primary address listed here must be the same primary address listed in the practitioner's registration under § 823(f).

2. ADDRESS OF PRIMARY LOCATION

Address Line 2

City

State

Zip Code

3. TELEPHONE NUMBER

Extension (if applicable)

4. FAX NUMBER

5. EMAIL ADDRESS

Confirm Email Address

New Notification - an initial notification for a waiver submitted for the purpose of obtaining an identification number from DEA for inclusion in the registration under 21 USC § 823(f).

***New Notification 100** - an initial notification for a waiver

New Notification, with the intent to immediately facilitate treatment of an individual (one) patient - an initial notification submitted for the purpose described above, with the additional purpose of notifying the Secretary and the Attorney General of the intent to provide immediate opiate addiction treatment for an individual (one) patient pending processing of this waiver notification.

Second Notification - For physicians who submitted a new notification not less than one year ago and intend and need to treat up to 100 patients. (See Office of National Drug Control Policy Reauthorization Act of 2006.)

6. PURPOSE OF NOTIFICATION

- New Notification to treat up to 30 patients
- Second notification of need and intent to treat up to 100 patients
- New Notification, with the intent to immediately facilitate treatment of an individual (one) patient
- New notification to treat up to 100 patients*

*NOTE: In order to treat up to 100 patients in the first year, practitioners must either hold additional credentialing as defined under 42 C.F.R. § 8.2, or provide medication-assisted treatment with covered medications (as such terms are defined under 42 C.F.R. § 8.2) in a qualified practice setting as described under 42 C.F.R. § 8.615.

7. CERTIFICATION OF USE OF NARCOTIC DRUGS UNDER THIS NOTIFICATION

- When providing maintenance or detoxification treatment, I certify that I will only use Schedule III, IV, or V drugs or combinations of drugs that have been approved by the FDA for use in maintenance or detoxification treatment and that have not been the subject of an adverse determination.

6. (Auto selected for 30 or 100).

7. Check off box.

8. CERTIFICATION OF QUALIFYING CRITERIA

I certify that I meet at least one of the following criteria and am therefore a qualifying physician (Check and provide copies of documentation for all that apply):

- Subspecialty board certification in Addiction Psychiatry or Addiction Medicine from the American Board of Medical Specialties
- Addiction certification or board certification from the American Society of Addiction Medicine or American Board of Addiction Medicine
- Subspecialty board certification in Addiction Medicine from the American Osteopathic Association

Completion of not less than eight hours of training for the treatment and management of opioid-dependent patients that included training on the following topics: opioid maintenance and detoxification; appropriate clinical use of all drugs approved by the Food and Drug Administration for the treatment of opioid use disorder; initial and periodic patient assessments (including substance use monitoring); individualized treatment planning, overdose reversal, and relapse prevention; counseling and recovery support services; staffing roles and considerations; and diversion control; and that was provided by the following organization(s):

- American Society of Addiction Medicine (ASAM)
- American Academy of Addiction Psychiatry (AAAP)
- American Medical Association (AMA)
- American Osteopathic Association (AOA)/American Osteopathic Academy of Addiction Medicine (AOAAM)
- American Psychiatric Association (APA)
- SAMHSA Providers' Clinical Support System (PCSS)
- Other (Specify, include date and location)

Date and location of training (Use "Web" for city if web training was received):

Date	City	State
<input type="text"/>	<input type="text"/>	<input type="text" value="Maryland"/>

- Participation as an investigator in one or more clinical trials leading to the approval of a narcotic medication in Schedule III, IV, or V for maintenance or detoxification treatment.
 - State medical licensing board-approved experience or training in the treatment and management of patients with opioid dependency.
 - Graduated in good standing from an accredited school of allopathic medicine or osteopathic medicine in the United States during the last five (5) years, and during which I successfully completed a comprehensive allopathic or osteopathic medicine curriculum, or accredited medical residency, that included at least 8 hours of training on treating and managing opioid-dependent patients that included training on the following topics: opioid maintenance and detoxification; appropriate clinical use of all drugs approved by the Food and Drug Administration for the treatment of opioid use disorder; initial and periodic patient assessments (including substance use monitoring); individualized treatment planning, overdose reversal, and relapse prevention; counseling and recovery support services; staffing roles and considerations; and diversion control.
 - Other
- Specify**

Check off which training you completed.

Type in date and city and state of training.

Leave "For Second Notifications" unchecked.

For 100-patients, select the "New Notifications for 100" and the applicable selection below. Leave blank for 30-patient Notifications

- For Second Notifications - I certified qualifications in my initial notification and these qualifications have not changed
 - Subspecialty board certification in Addiction Psychiatry or Addiction Medicine from the American Board of Medical Specialties
 - Addiction certification or board certification from the American Society of Addiction Medicine or American Board of Addiction Medicine
 - Subspecialty board certification in Addiction Medicine from the American Osteopathic Association
 - Provide medication-assisted treatment in a "qualified practice setting" as defined in 42 C.F.R. § 8.615

- New Notification for 100 Patients – I certify that I meet at least one of the following criteria and am therefore a qualifying physician.
 - Subspecialty board certification in Addiction Psychiatry or Addiction Medicine from the American Board of Medical Specialties
 - Addiction certification or board certification from the American Society of Addiction Medicine or American Board of Addiction Medicine
 - Subspecialty board certification in Addiction Medicine from the American Osteopathic Association
 - Provide medication-assisted treatment in a "qualified practice setting" as defined in 42 C.F.R. § 8.615

Upload completed training certificate and a copy of your medical license.

You may upload any documentation of your training here. If you do not provide a copy of your certificate, this may result in delayed processing of your waiver. Please retain a copy of the training certificate for your records as proof of required training completion.

Choose files To Upload

Choose Files

9. Check off both boxes.

9B. (Auto selected for 30 or 100).

9. CERTIFICATION OF CAPACITY

- I certify that I have the capacity to provide patients with appropriate counseling and other appropriate ancillary services, either directly or by referral.
- I certify that I have the capacity to provide, directly or through referral, all drugs approved by the Food and Drug Administration for the treatment of opioid use disorder, including for maintenance, detoxification, overdose reversal, and relapse prevention.

9B. CERTIFICATION OF MAXIMUM PATIENT LOAD

- I certify that I will not exceed 30 patients for maintenance or detoxification treatment at one time.
- Second Notification – I have provided treatment at the 30 patient limit for one year and need to treat up to 100 patients and I certify that I will not exceed 100 patients for maintenance or detoxification treatment at one time if I meet the criteria under 21 U.S.C. 823(g)(2)(B)(iii)(II)(aa)-(cc).
- New Notification for 100 Patients – I will not exceed 100 patients for maintenance or detoxification treatment at one time.

The SAMHSA Treatment Locator Web site is publicly accessible at http://buprenorphine.samhsa.gov/bwns_locator. The Locator Web site lists the names and practice contact information of physicians with DATA waivers who agree to be listed on the site. The Locator Web site is used by the treatment-seeking public and health care professionals to find physicians with DATA waivers. The Locator Web site additionally provides links to many other sources of information on substance abuse. No physician listings on the SAMHSA Treatment Locator Web site will be made without the express consent of the physician.

Check a box indicating whether or not you consent.

10A. CONSENT

- I consent to the release of my name, primary practice address, and phone number to the SAMHSA Treatment Locator Web site.
- I do not consent to the release of my name, primary practice address, and phone number to the SAMHSA Treatment Locator Web site.

Check "yes" or "no"—whichever applies to you.

10B. CONSENT Do you also want to be identified on the SAMHSA Treatment Locators as providing treatment with:

- | | Yes | No |
|--|-----------------------|-----------------------|
| 1. Long-acting injectable naltrexone | <input type="radio"/> | <input type="radio"/> |
| 2. Long-acting injectable buprenorphine | <input type="radio"/> | <input type="radio"/> |
| 3. Long-acting implantable buprenorphine | <input type="radio"/> | <input type="radio"/> |

11.

I certify that the information presented above is true and correct to the best of my knowledge. I certify that I will notify SAMHSA at the address below if any of the information contained on this form changes. Note: Any false, fictitious, or fraudulent statements or information presented above or misrepresentations relative thereto may violate Federal laws and could subject you to prosecution, and/or monetary penalties, and or denial, revocation, or suspension of DEA registration. (See 18 USC § 1001; 31 USC §§ 3801–3812; 21 USC § 824.)

Check off box.

Please type your name to sign this electronic form. Submission Date: 10/10/2019

Sign.

Re-enter DEA number.

Please re-enter your DEA Registration Number to verify:

Hit the "submit" button.

Submit

Please note the following:

DATA Waiver Team Email Address: InfoBuprenorphine@samhsa.hhs.gov

Confirmation e-mails are sent immediately after your application is submitted.

Approval Letters are e-mailed within 45 days of your complete application submission.

*Please check your junk and spam folders if you have not already added InfoBuprenorphine@samhsa.hhs.gov to your contacts.

Any questions or inquiries should be directed to InfoBuprenorphine@samhsa.hhs.gov or call 1-866-287-2728.

Q&A

KEEPING YOUR PATIENTS SAFE

End of Session 5

Contact Us



Address

11400 Rockville Pike,
Suite #200
Rockville, MD 20852



Phone

Phone: (301) 656 – 3820
Fax (301) 656 - 3815



Online

www.ASAM.org
education@asam.org