Substance Use Disorders in Pregnancy and Postpartum: Principles of Management

Seetha Ramanathan, MD, MPA
Associate Professor,
Department of Psychiatry and Behavioral Sciences
Division Chief of Women's Mental Health,
Norton College of Medicine at
SUNY Upstate Medical University

Tolani Ajagbe, MD, FASAM
Associate Professor,
Department of Psychiatry and Behavioral Sciences
Int Division Chief, Division of Pain and Addiction Med
Program Director, Addiction Psychiatry Fellowship
Chief, Department of Psychiatry
Medical Director, Addiction Treatment Services,
Crouse Health

Disclosures

Drs Ramanathan & Ajagbe do not have any relevant financial relationship with a commercial interest to disclose.

Learning Objectives

1. Understand the problem of SUD in the perinatal period.

2. Describe general strategies to systematically address SUD in the perinatal setting.

3. Discuss management of OUD in the perinatal setting.

AGENDA

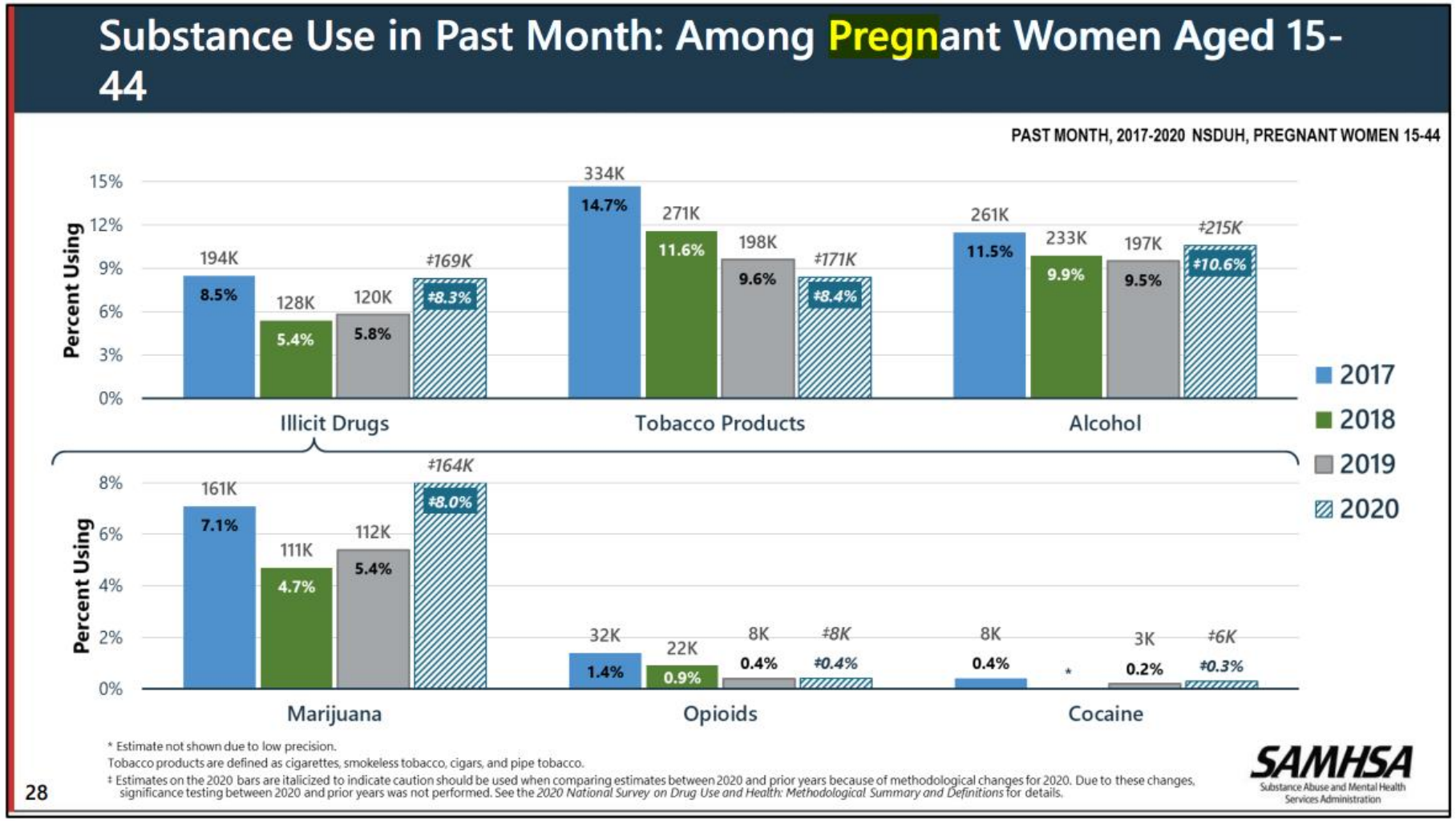
- Seetha Ramanathan, MD
- Tolani Ajagbe, MD, FASAM

- *Discussion between Drs Ramanathan and Ajagbe*
- Q&A

Perinatal Period and SUD

- 22.3 percent of pregnant women reported using at least one substance in the previous month
- Women often cut down or discontinue during pregnancy (decreases by trimester)
- Increased rates in postpartum
- Risk of OD in postpartum – heightened at 7-12 months (late postpartum period)

Without Maternal Mental Health and Substance Use Interventions, We Can't Address the Maternal Mortality Crisis | SAMHSA,
Smid and Terplen, 2022, Kim , 022



Source: https://www.samhsa.gov/data/sites/default/files/reports/slides-2020-nsduh/

SUD is a leading cause of perinatal death

- Leading cause of pregnancy related deaths in the United States.
- 1 in 5 deaths in the perinatal period are because of MH and SUDs.
- #1 preventable cause of death.

Condition					AI/AN		Asia
	Number of pregnancy-related deaths	%	Number of pregnancy-related deaths	%	Number of pregnancy-related deaths	%	Number o pregnancy related deaths
Mental health conditions[c]	224	22.7	34	24.1	2	-	1
Hemorrhage[d]	135	13.7	30	21.3	2	-	10
Cardiac and coronary conditions[e]	126	12.8	15	10.6	1	-	7
Infection	91	9.2	15	10.6	1	-	0
Embolism-	86	8.7	9	6.4	0	-	2

Trost, Beauregard, Chandra, Njie, Berry, et al., 2022

November 2023

Spotlight on Perinatal Substance Use Disorder

Issue Brief from the New York State Maternal Mortality Review Board

- 2018 deaths, substance use disorder caused more than one in four statewide pregnancy-associated deaths.
- Of these, 13% occurred during pregnancy, 18% occurred within 42 days of the end of pregnancy, and 69% occurred between 43 days and one year after the end of the pregnancy.
- Ninety-two percent (92%) of pregnancy-associated deaths caused by substance use disorder occurred outside of New York City, and these deaths comprised nearly half (48%) of all pregnancy-associated deaths in the rest of state.
- Preliminary analyses of review results from 2019 and 2020 suggest that substance use disorder remained one of the most common causes of pregnancy-associated deaths.

Source: https://www.health.ny.gov/community/adults/women/maternal_mortality/docs

From: **Pregnancy and Postpartum Drug Overdose Deaths in the US Before and During the COVID-19 Pandemic**

JAMA Psychiatry. 2024;81(3):270-283. doi:10.1001/jamapsychiatry.2023.4523

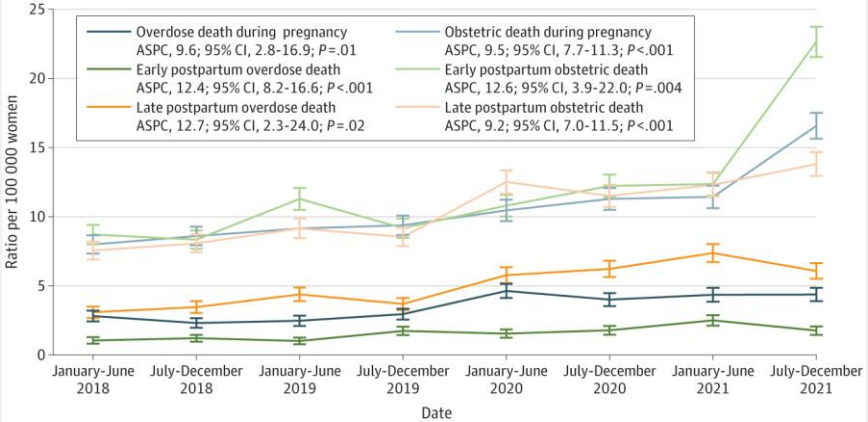


Figure Legend:

US Trends in Pregnancy-Associated Drug Overdose or Obstetric Mortality Ratio Among Women Aged 10 to 44 Years by Pregnancy TimingData were collected from the National Vital Statistics System, including 2018-2021 final mortality data and 2018-2021 final birth data. Mortality ratio was calculated as the number of deaths among pregnant or recently pregnant women aged 10 to 44 years by causes divided by the number of women aged 10 to 44 years who gave live birth during the corresponding time period (per 100 000 mothers). Error bars indicate 95% CIs. ASPC indicates average semiannual percentage change.

Maternal Consequences

- Poor prenatal care.
- Increased risk of infections such as Hep B.
- Other comorbid conditions such as poverty, IPV.
- Greater risk of complications such as placental abruption, PROM.

Simmons & Austin, 2023; Pallantino et al, 2021, Forray &Foster, 2016

Fetal Consequences

- Small for gestational age.
- Behavioral consequences.
- Cognitive issues.

Forray &Foster, 2016

What we know about treatment?

- Postpartum period is a high-risk period.
- Only 9.3 % reproductive age women received treatment.
- Pregnant and parenting women were not more likely to receive treatment – *therapeutic orphans.*
- Black and Hispanic women were less likely to receive treatment.
- Pregnant and postpartum individuals face a lot of barriers to care/ treatment.

Martin, Scialli, Terplen, 2020

Principles of Treatment

- Language – nonjudgmental, non-stigmatizing
- SBIRT
- Recognize the role of TRAUMA
- Recognize and address comorbid mental health issues
- Specific pregnancy related changes that affect prescribing strategies

Language

BEST PRACTICES TO AVOID USING STIGMATIZING LANGUAGE

Don't Use	Do Use	Why
"addict" *"abuser"* *"junkie"*	*"person who uses heroin"* *"person with cocaine use disorder"*	*Using "person-first" language demonstrates that you value the person, and are not defining them by their drug use.*
"got clean"	*"no longer uses drugs"*	*"Clean," although a positive word, implies that when someone is using they are "dirty."*
"addicted newborn" *"born addicted"* *"crack baby"*	*"newborn opioid withdrawal (NOW)"* *"baby with prenatal cocaine exposure"*	*Infants are not addicted; they have prenatal substance exposure and/or physiological dependence.*
"medication replacement therapy (MRT)" *"medication assisted therapy (MAT)"*	*"opioid agonist therapy (OAT)"* *"medication for opioid use disorder (MOUD)"* *"medication for alcohol use disorder"*	*These categories are value-neutral and precise.* *When discussing a specific medication, refer to it by both its generic and brand names.*

Deficits-Based	Strengths-Based
Addict	Person with a substance use disorder
Frequent Flyer	Utilizes services and supports when necessary
Hostile, Aggressive	Protective
Helpless/Hopeless	Unaware of capabilities/ opportunities
Mentally ill	Person with a mental illness
Lazy	Ambivalent, Working to build hope
Manipulative	Resourceful
Unfit parent	Person experiencing barriers to successful parenting
Resistant	Chooses not to, Isn't ready for, Not open to
Suffering with	Working to recover from; experiencing; living with
Abuses the system	Good self-advocate
Weaknesses	Barriers to change or needs

[Ambulatory Patient Groups (APG) Clinical and Medicaid Billing Guidance - October 2024 (ny.gov)]

NIDA Quick Screen

NIDA *Quick Screen* Question: In the past year, how often have you used the following?	Never	Once or Twice	Monthly	Weekly	Daily or Almost Daily
Alcohol • For men, 5 or more drinks a day • For women, 4 or more drinks a day					
Tobacco Products					
Prescription Drugs for Non-Medical Reasons					
Illegal Drugs					

OMS - ASSIST V3 (nih.gov)

5 Ps

Peers: Do any of your friends have a problem with drug or alcohol use?
Partner: Does your partner have a problem with alcohol or drugs?
Parents: Did either of your parents ever have a problem with alcohol or drugs?
Past Use: Before you knew you were pregnant, how often did you drink beer, wine, wine coolers, or liquor? *Not at all, rarely, sometimes, or frequently?*
Present Use: In the past month, how often did you drink beer, wine, wine coolers, or liquor? *Not at all, rarely, sometimes, or frequently?*
Smoke: How many cigarettes did you smoke in the month prior to pregnancy?

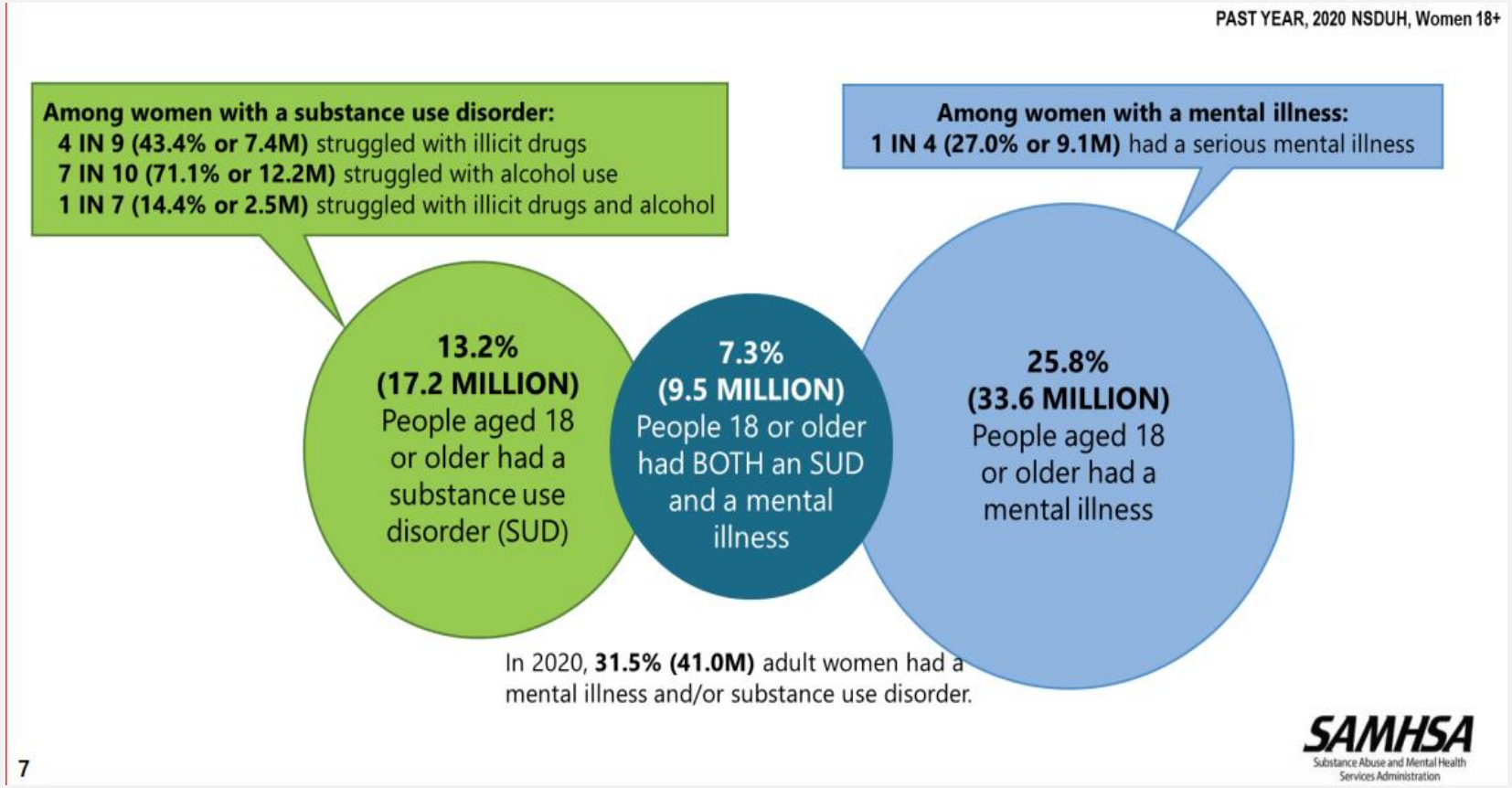
Morse et al. 1997; Chasnoff et al. 2001

Trauma

- Cope with trauma.
- The rates of at least one ACE ranges from 85.4% to 100%.
- Dose-response relationship between ACEs and SUDs.
- ACEs affect emotion regulation, causing an inability to modulate distressing emotions in a healthy and adaptive way.

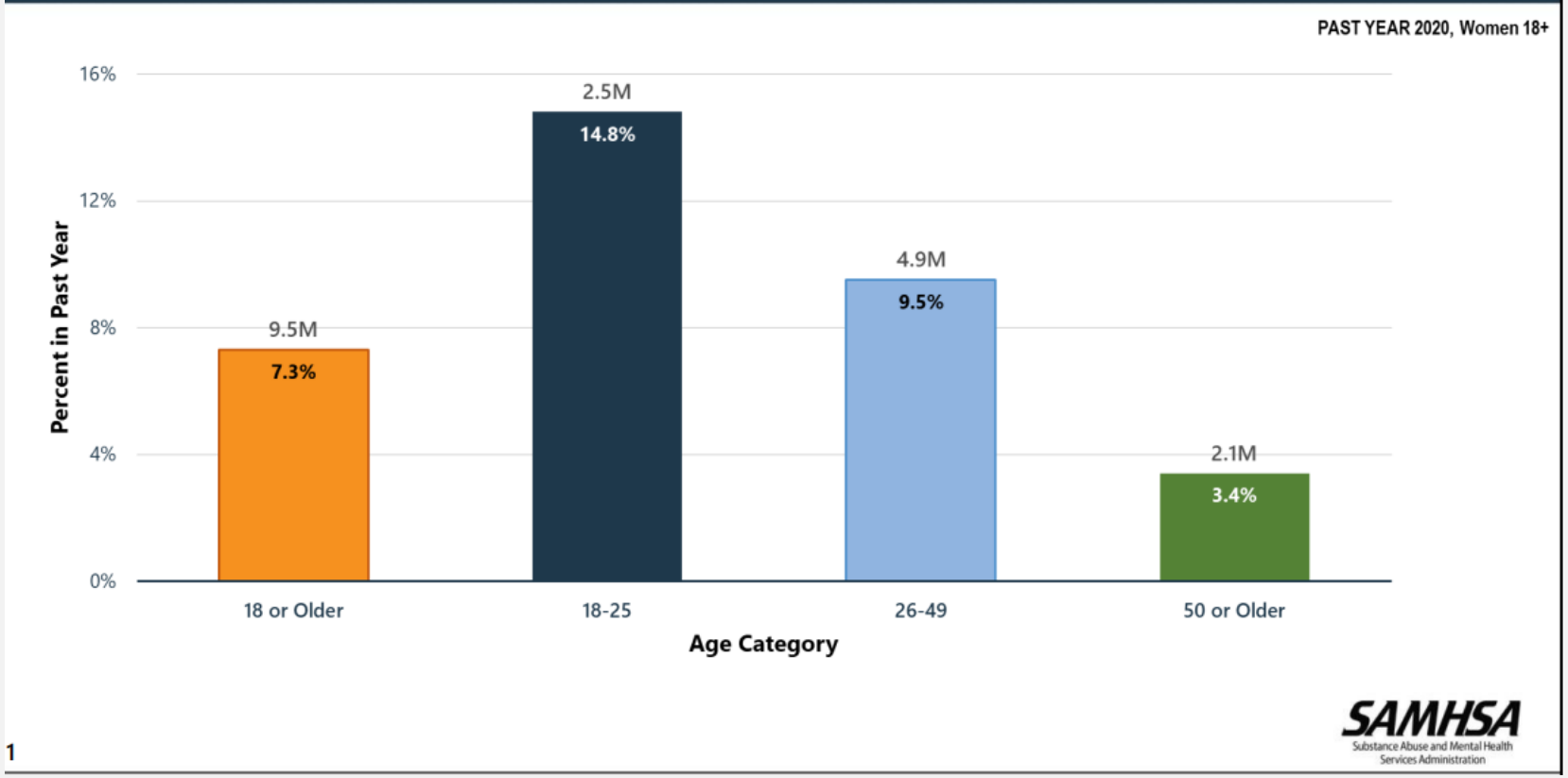
Bryant et al, 2020

Mental Illness and Substance Use Disorders in the Past Year: Among Women Aged 18+



Source: NSDUH2020

Co-Occurring Substance Use Disorder and Any Mental Illness in Past Year: Among Adult Women Aged 18+



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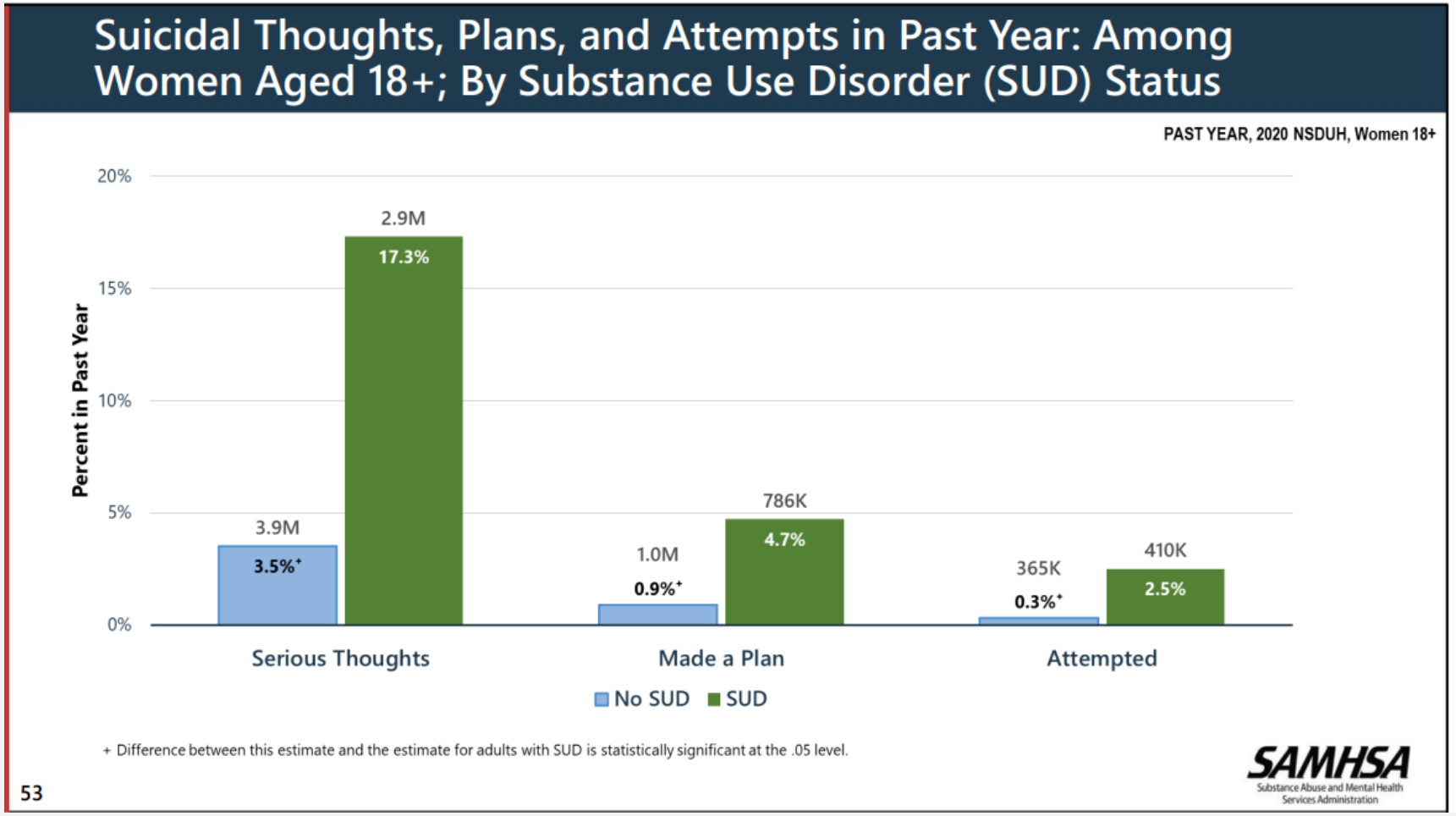
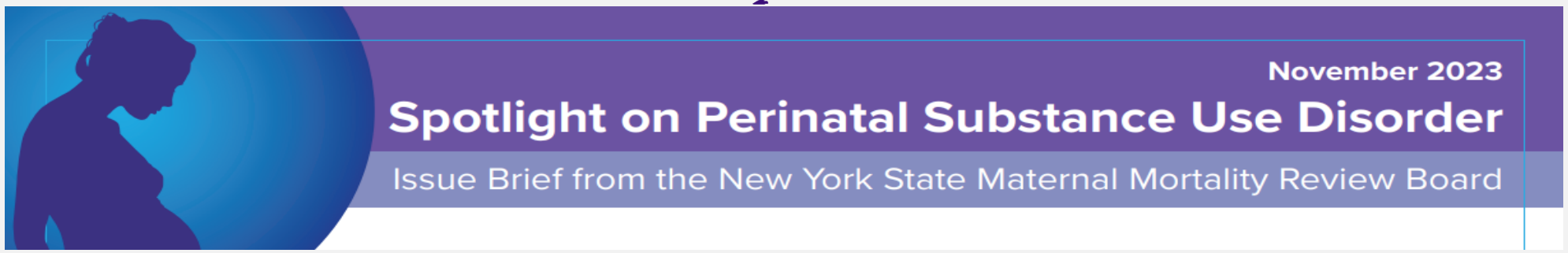
Source: NSDUH2020

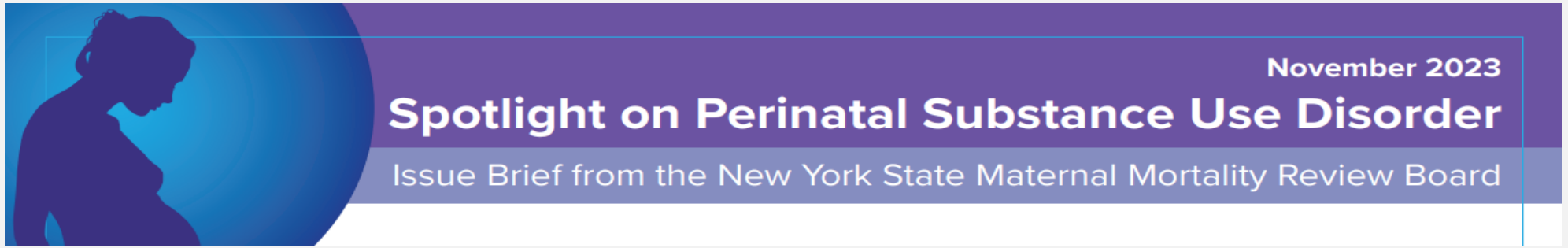


Source: NSDUH2020

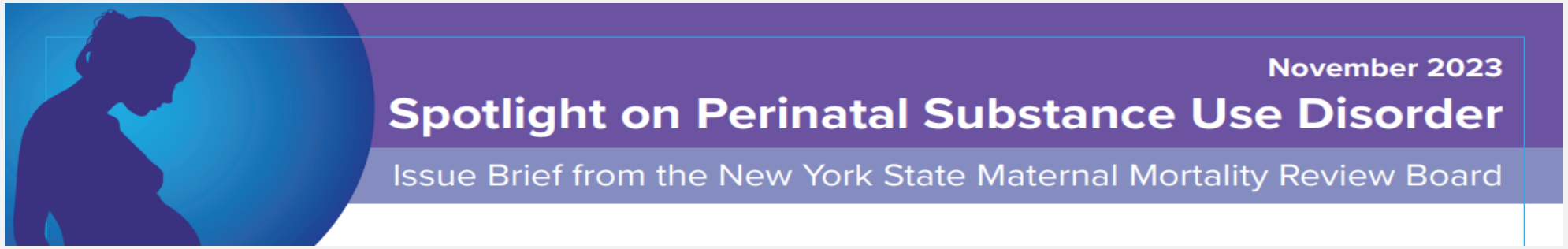


- **Recommendation 1:** Provide early, universal verbal screening for substance use utilizing appropriate standardized tools.
  - Biological testing (toxicology testing) is not recommended universally.
  - When biological testing (toxicology testing) is used:

• Informed consent should be obtained prior to testing;
• Biological testing should NOT be used to assess the severity of substance use, as the test only captures one moment in time;
• Medical professionals should be aware of what is included in the panel;
• All toxicology panels should be comprehensive enough to include substances of concern (e.g., fentanyl), medications prescribed (e.g., buprenorphine), and their metabolites (e.g., norfentanyl and norbuprenorphine); and
• All positive results from point of care or immunoassay tests should have confirmatory testing.



- **Recommendation 2:** A naloxone prescription should be provided at the first prenatal visit and on discharge following an emergency department visit or hospitalization (including the birth hospitalization), and the patient's support system should be educated on the use and administration of naloxone.
- **Recommendation 3:** Obstetric providers should engage community resources and treatment programs and provide closed-loop referrals particularly at discharge after delivery
- **Recommendation 4:** Substance use disorder treatment providers caring for birthing people should develop expertise for treatment in the perinatal and postpartum (up to one year after the end of pregnancy) periods.



- **Recommendation 5:** Substance use alone, whether disclosed through a self-report, verbal screening, toxicology testing, Plan of Safe Care, medical record note, or newborn symptoms is not evidence of child neglect.

- **Recommendation 6:** Patients with substance use disorder, especially those taking buprenorphine or methadone, should have an anesthesia consult during pregnancy to discuss pain management during labor or cesarean birth and the postpartum course.

Pregnancy

- Increased blood volume and volume of distribution
- Enhanced hepatic metabolism – CYP3A4
- Changes in serum protein binding
- Increased GFR and renal clearance
- Prolonged GI transit time

Implementation: Management of OUD in the peripartum setting

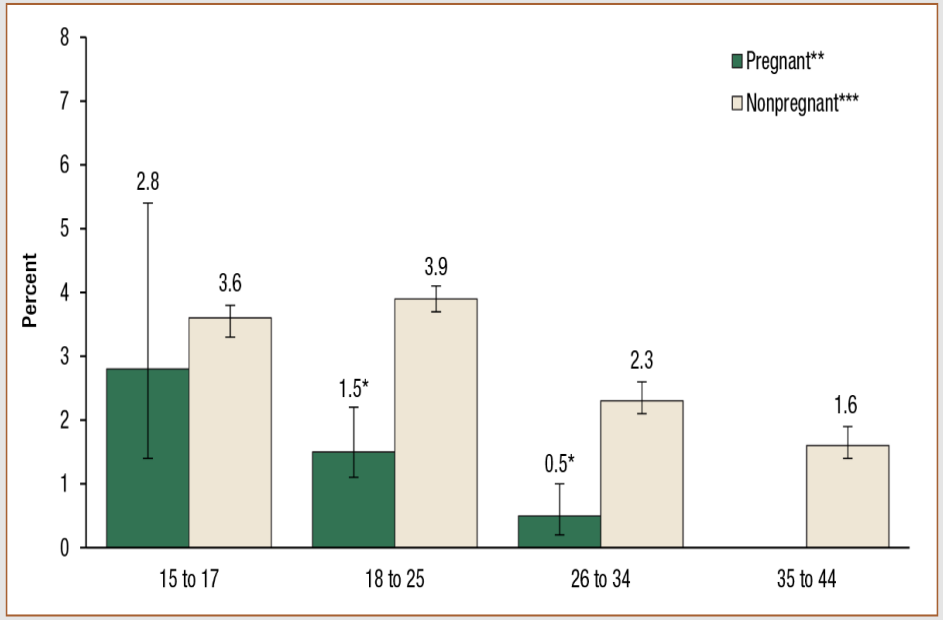
Tolani Ajagbe, MD, FASAM

OPIOID USE IN PREGNANCY

Opioid Use in Pregnancy

- Recent estimates of opioid use disorder (OUD) range from 0.4% to 0.8% during pregnancy; 2% among women of reproductive age.
- CDC: 7% of women reported using prescription opioid pain relievers during pregnancy; 21% report misuse.
- The prevalence of opioid use disorder (OUD) among pregnant women in the United States quadrupled from 1.5 to 6.5 per 1,000 delivery hospitalizations from 1999-2014.

Figure 1. Past month opioid misuse among women aged 15 to 44, by pregnancy status and age: 2007 to 2012



Substance Use During Pregnancy | Maternal Infant Health | CDC , Ko et al 2019, Haight et al, 2018

Opioid Use in Pregnancy

- More than 85% of pregnancies in women with OUD may be unintended
- From 2010-2017: 131% increase in opioid dependent pregnant women hospitalized for delivery.
- CDC: Neonatal abstinence syndrome (NAS) diagnosed in 6 out of 1,000 newborn hospital stays.
- CDC: The number of babies born with NAS in the United States increased by 82% from 2010 to 2017.

Substance Use During Pregnancy | Maternal Infant Health | CDC , Heil et al

Opioid Use in Pregnancy

Other Contributing Factors to morbidity:

- Poor nutrition
- Poor prenatal care
- Intimate partner violence/trauma
- Dangers from drug seeking (e.g., violence and incarceration)
- Social issues:
  - Poverty
  - Inadequate housing
  - Poor family and social supports etc.

Opioid Effects in Pregnancy

Placental insufficiency

Placental abruption

Intrauterine meconium passage

Spontaneous abortion

PROM/Preterm birth

Fetal distress/Intrauterine death

Preeclampsia/Eclampsia

IUGR

Low Apgar Score

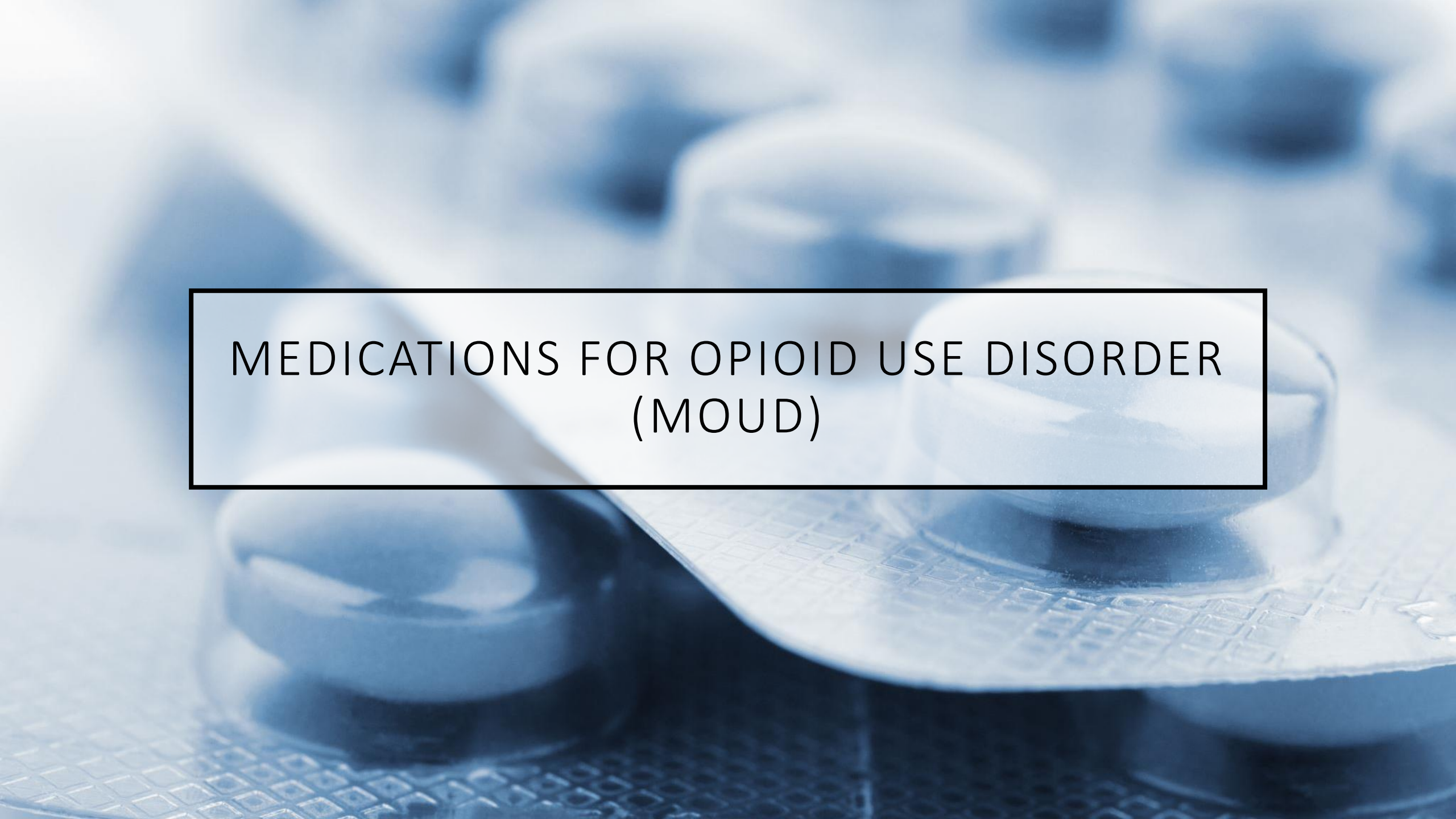
Neonatal Abstinence Syndrome

? Congenital Anomalies

Dangers of Intrauterine Withdrawal

- Norepinephrine surge and uterine contractions
- Decreased placental blood flow and oxygen supply
- Fetal motor hyperactivity with increased oxygen demands
- Potential outcome: fetal distress, preterm labor, fetal demise

McCarthy et al, 2017



MEDICATIONS FOR OPIOID USE DISORDER (MOUD)

Medications for Opioid Use Disorder (MOUD)

Opioid addiction treatment involving the use of a safe, effective, long-acting opioid, with a plan to develop cross-dependence with the abused opioid.

Treatment Goals:

- elimination of withdrawal symptoms
- reduction/elimination of cravings
- improved functioning

Medications for Opioid Use Disorder (MOUD)

mu opioid receptor <u>full agonist</u>

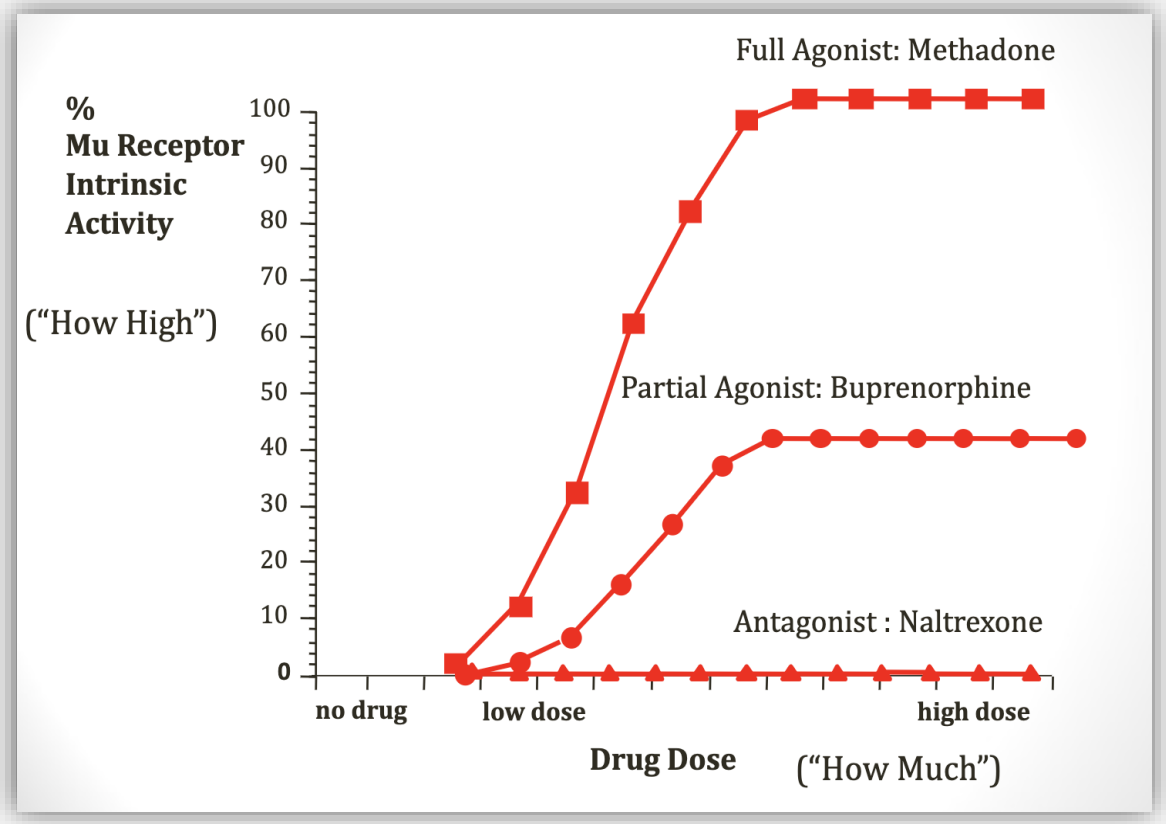
-Methadone-Oral

mu opioid receptor <u>partial agonist</u>

-Buprenorphine (Suboxone; Subutex) Sublingual

mu opioid receptor <u>antagonist</u>

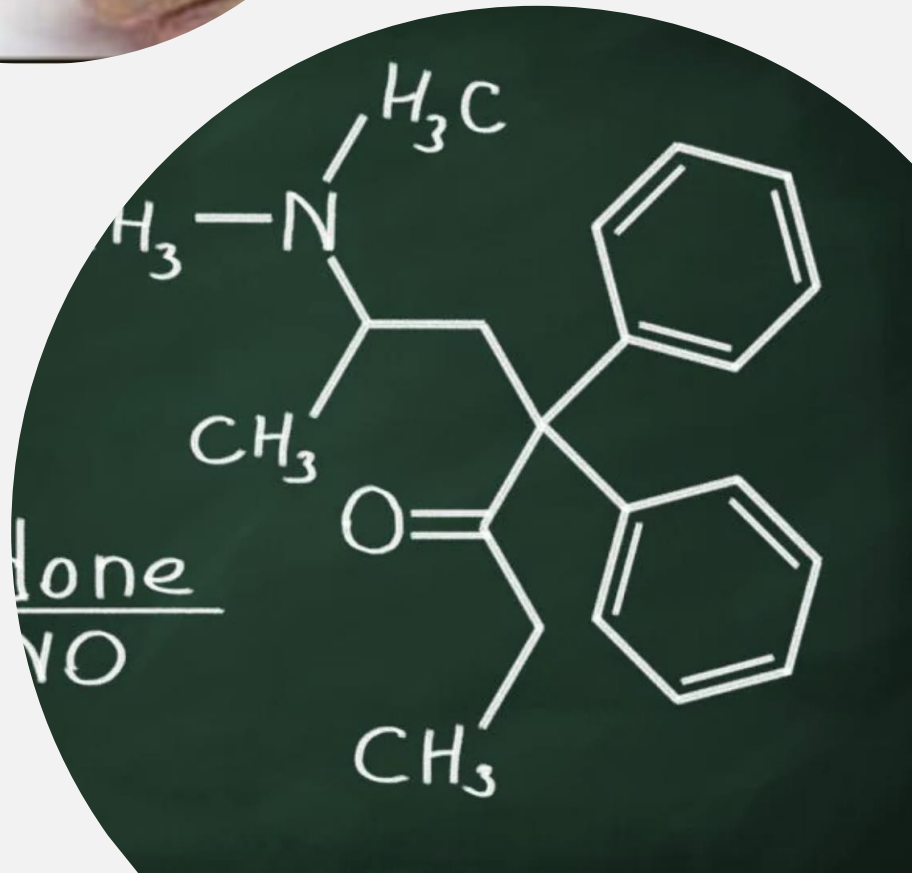
-Naltrexone XR (Vivitrol) Monthly intramuscular injections



Methadone

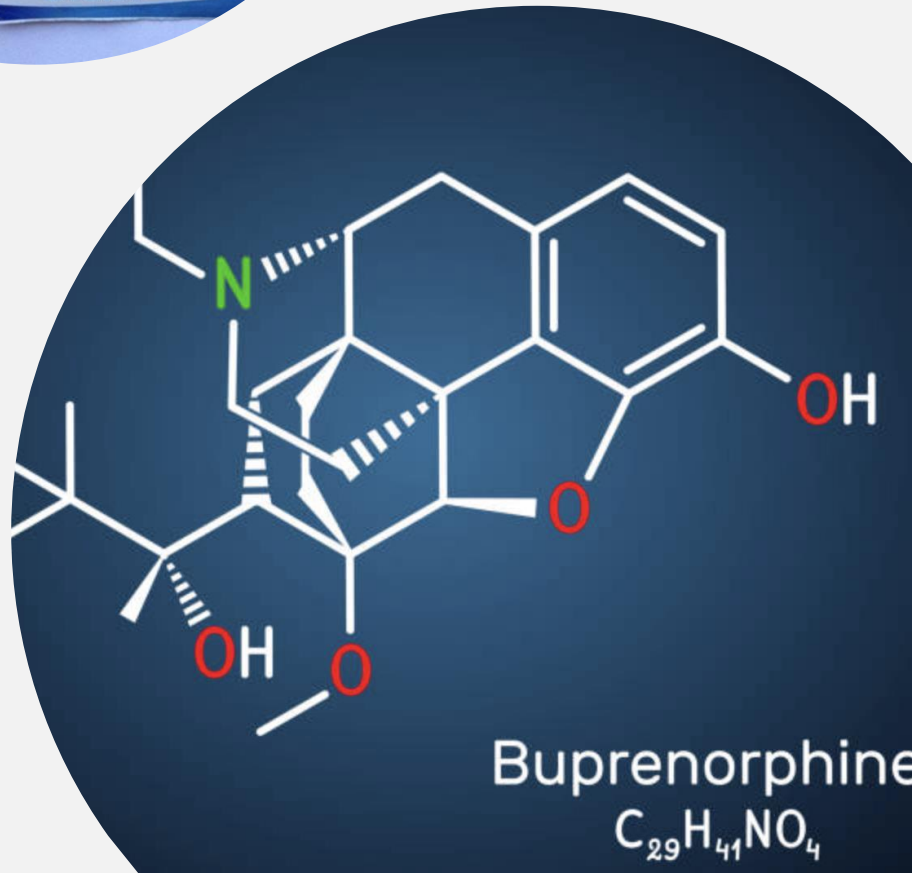
- Synthetic, full agonist opioid
- Schedule II medication
- Synergistic effect with other opioids
- Blocks other opioids from binding to the opioid receptor
- Half-life: average 24-36 hours
  - Daily administration of methadone ensures a

    24-hour asymptomatic state
- Individualized dosing:
  - Average daily dose: 60mg-120mg
  - Higher doses more effective



Buprenorphine

- Synthetic, partial agonist opioid
- Schedule III medication
- High affinity for opioid receptors
- Blocks other opioids from binding to the opioid receptor
- DATA 2000 waiver no longer required
- Half-life: average 24-48 hours
- Individualized dosing:
  - Average daily dose: 8mg-16mg
  - Ceiling effect at 32mg



MOUD Benefits in Pregnancy

Maternal

- Relapse prevention
- Reduction in substance use
- Lower risk of relapse
- Decreases risk of HBV/HCV/HIV horizontal and vertical transmission
- Increases engagement with health care system

Zedler, 2014, Krans et al, 2021

MOUD Benefits in Pregnancy

Neonatal

- Reduces fetal exposure to illicit substances
- Protects fetus from repeated withdrawal episode
- Decreases risk of spontaneous abortion, preterm labor, and IUGR
- Decreases NICU admissions
- Decreases morbidity and mortality
- Reduces neonatal medical complications, including NAS

Zedler, 2014, Krans et al, 2021

MOUD Adjustments in Pregnancy

Maintenance dosing considerations:

- Total blood volume: Increases by 45% by 28 weeks
- Cardiac function: Pulse increases by 10-15 bpm and CO increases by 30-50% by second trimester
- Elimination half-life decreases in 2nd and 3rd trimesters due to increased metabolism
- Increased renal clearance
- More prone to withdrawal symptoms, especially at trough levels
- May require dose increase and/or dose splitting

Source: Opioid Use and Opioid Use Disorder in Pregnancy | ACOG

Neonatal Abstinence Syndrome

Timeline

- Onset: Heroin (24-36 hours); Methadone (5-15 days)
- Duration: Heroin (>1-2 weeks); Methadone (>2-3 weeks)

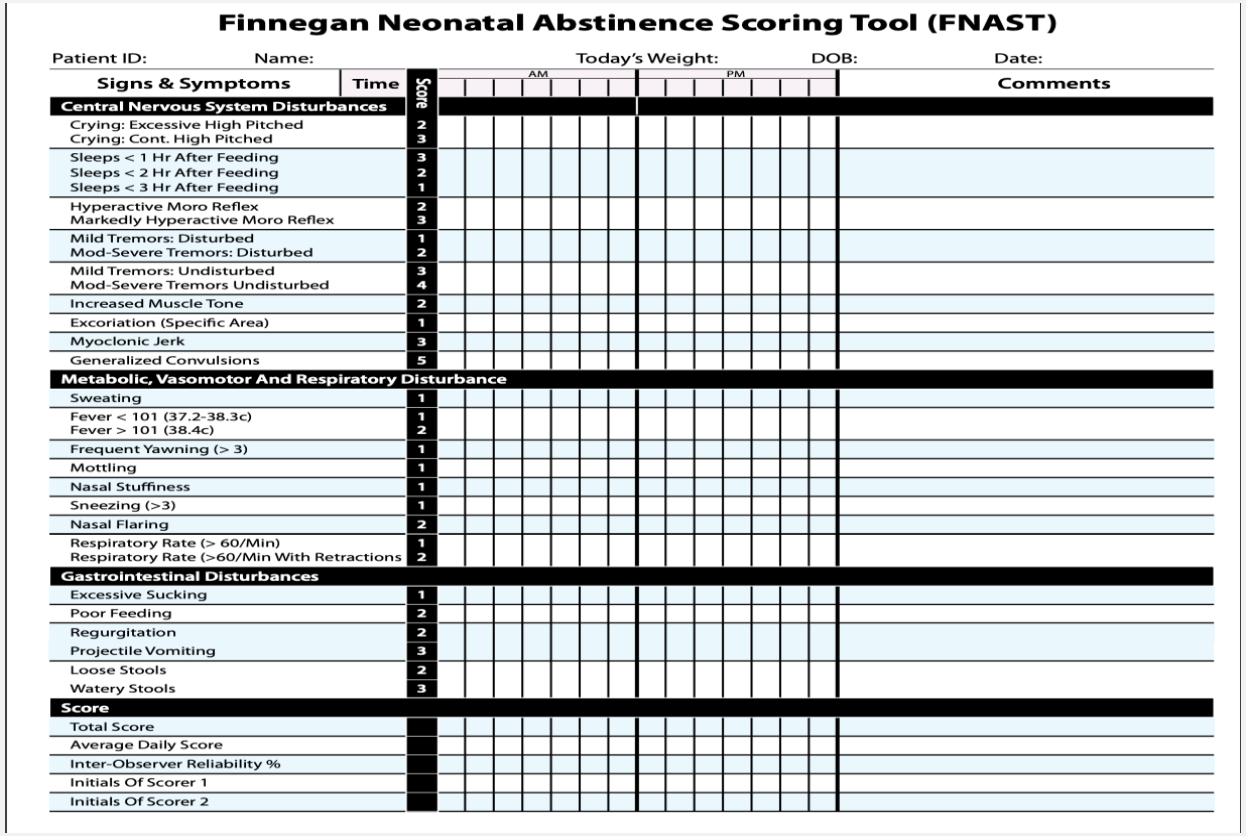
Signs and symptoms

- CNS: High pitched cry, tremor, muscle spasms, myoclonic jerks, seizures
- Respiratory: sneezing, yawning, nasal flaring, stuffiness, tachypnea, resp. distress
- GI: poor feeding, excessive sucking, regurgitation, projectile vomiting, diarrhea
- Autonomic instability: Heart rate, respiratory rate, and temperature

Neonatal Abstinence Syndrome

Finnegan Neonatal Abstinence Scoring Tool (FNAST)

- 19-item scale
- Assessment 2 hours after birth and then every 4 hours.
- Medications indicated for:
- score ≥9 for 2 consecutive evaluations or
- ≥13 on a single evaluation
- until the score remains ≤8 for 48 hours



Finnegan Neonatal Abstinence Scoring Tool (FNAST)

Patient ID: Name: Today's Weight: DOB: Date:

Signs & Symptoms	Time	Score	AM	PM	Comments
Central Nervous System Disturbances					
Crying: Excessive High Pitched Crying: Cont. High Pitched		2 3			
Sleeps < 1 Hr After Feeding Sleeps < 2 Hr After Feeding Sleeps < 3 Hr After Feeding		3 2 1			
Hyperactive Moro Reflex Markedly Hyperactive Moro Reflex		2 3			
Mild Tremors: Disturbed Mod-Severe Tremors: Disturbed		1 2			
Mild Tremors: Undisturbed Mod-Severe Tremors Undisturbed		3 4			
Increased Muscle Tone		2			
Excoriation (Specific Area)		1			
Myoclonic Jerk		3			
Generalized Convulsions		5			
Metabolic, Vasomotor And Respiratory Disturbance					
Sweating		1			
Fever < 101 (37.2-38.3c) Fever > 101 (38.4c)		1 2			
Frequent Yawning (> 3)		1			
Mottling		1			
Nasal Stuffiness		1			
Sneezing (>3)		1			
Nasal Flaring		2			
Respiratory Rate (> 60/Min) Respiratory Rate (>60/Min With Retractions		1 2			
Gastrointestinal Disturbances					
Excessive Sucking		1			
Poor Feeding		2			
Regurgitation		2			
Projectile Vomiting		3			
Loose Stools		2			
Watery Stools		3			
Score					
Total Score					
Average Daily Score					
Inter-Observer Reliability %					
Initials Of Scorer 1					
Initials Of Scorer 2					

Mehta et al, 2013

Neonatal Abstinence Syndrome

Treatment:

- Pharmacological intervention is required for 50 to 70% of infants.
- Sustained symptom escalation requires treatment with an opioid agonist: morphine or methadone.
- Treatment guided by NAS assessment/scoring (FNAST).
- Others/adjuncts: buprenorphine; phenobarbital and clonidine.
- Nurse in quiet environment and minimize stimuli.
- Once NAS symptoms resolve, opioid is slowly tapered on a modified protocol that can extend for 2 or more weeks.

Anbalagan, 2024

Methadone vs Buprenorphine as MOUD in Pregnancy

Methadone	Buprenorphine
Well studied	Limited Studies
Safe, reduces maternal and fetal morbidity and mortality	Safe, reduces maternal and fetal morbidity and mortality
NAS (MOTHER Project): - higher symptom severity - required more medication - Required longer Tx duration - longer hospital stays	NAS (MOTHER Project): - Lower severity of symptoms - 89% less morphine needed - 58% shorter Tx duration - 43% shorter hospital stay
More drug-to-drug interactions	Fewer drug-to-drug interactions
Higher treatment retention	Lower treatment retention

Jones et al, 2015

Methadone vs Buprenorphine as MOUD in Pregnancy

A recent meta-analysis showed:

- Methadone is associated with higher treatment retention
- Buprenorphine resulted in:
  - 10 percent lower incidence of NAS
  - Decreased neonatal treatment time by 8.46 days
  - Less morphine needed for NAS treatment by 3.6 mg

Brogly SR, et al

MOUD AND PERIPARTUM PAIN MANAGEMENT

MOUD and Peripartum Pain Management

- Goal: provide adequate analgesia while avoiding both overmedication and withdrawal.
- Provision of analgesia for the pregnant woman with OUD can be complex and challenging.
- There is a tendency for clinicians to under-medicate pain with opioid analgesics, and this tendency is exaggerated when treating women with OUD.

Carroll et al 2004; Alford et al 2006

MOUD and Peripartum Pain Management

- Health care professionals concerned about drug-seeking behavior and overmedication may make the erroneous assumption that the daily maintenance dose of methadone or buprenorphine alone provides analgesia.

- Although pharmacotherapy for OUD provides analgesia, long-term opioid exposure leads to tolerance and opioid-induced hyperalgesia .

- Pain management in women with OUD should be similar to that in women without OUD and include both pharmacologic (opioid and nonopioid) and nonpharmacologic approaches.

Huxtable et al 2011; Carroll et al 2004

MOUD and Peripartum Pain Management

- Acute intrapartum pain should NOT be treated with additional doses of methadone or buprenorphine.

- Higher than usual opioid analgesic doses may be required because tight binding to the mu-opioid receptor (buprenorphine) blocks the analgesic effects of full opioid agonists.

- Monitor for respiratory depression; although acceptable analgesia can be achieved in clinical practice without respiratory or CNS depression.

Hernandez, 2005

MOUD and Peripartum Pain Management

Intrapartum	Postpartum
Continue MAT daily dosing	Remain on same dose of methadone or buprenorphine during L&D
Treat intrapartum pain like in any other patient	Reassure post-op & postpartum pain will be treated like in any other patient
Avoid opiate agonist-antagonist therapy, if possible	
Consider non-opiate pain management	
Dose adjustments per individual needs	

MOUD and Peripartum Pain Management

Non-Pharmacologic	Pharmacologic
Exercise/Physical Therapy	Acetaminophen
Heat (spasm); Cold (joint inflammation)	NSAIDS
Yoga/Mindfulness/Meditation/Hypnosis	Tricyclic Antidepressants (amitriptyline, imipramine, desipramine)
Massage	Other antidepressants (duloxetine)
Acupuncture	Anticonvulsants (gabapentin, pregabalin, carbamazepine)
Psychotherapy (CBT)	Muscle relaxants (baclofen, tizanidine)
	Topical analgesics (capsaicin, lidocaine)
	Interventional procedures (regional nerve block)

MOUD AND BREASTFEEDING

MOUD and Breastfeeding

Maintenance dosing considerations:

- The transfer of methadone and buprenorphine into mother's milk is minimal (<1% of maternal dosing)
- Concentration of methadone in mother's milk is unrelated to maternal dosing
- 30% decrease in NAS; 50% decrease in NAS-related hospital stay

Harris et al, 2023

MOUD and Breastfeeding

Benefits seen in newborns:

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

Harris et al, 2023

Medically Supervised Withdrawal

- Not recommended due to high rates of relapse: 50-90%.
- Associated with poorer outcomes.
- Only recommended if opioid agonist treatment is declined or unavailable.
- May require prolonged inpatient care and intensive outpatient addiction treatment follow up.

[Opioid Use and Opioid Use Disorder in Pregnancy | ACOG]

OPIOID OVERDOSE IN PREGNANCY

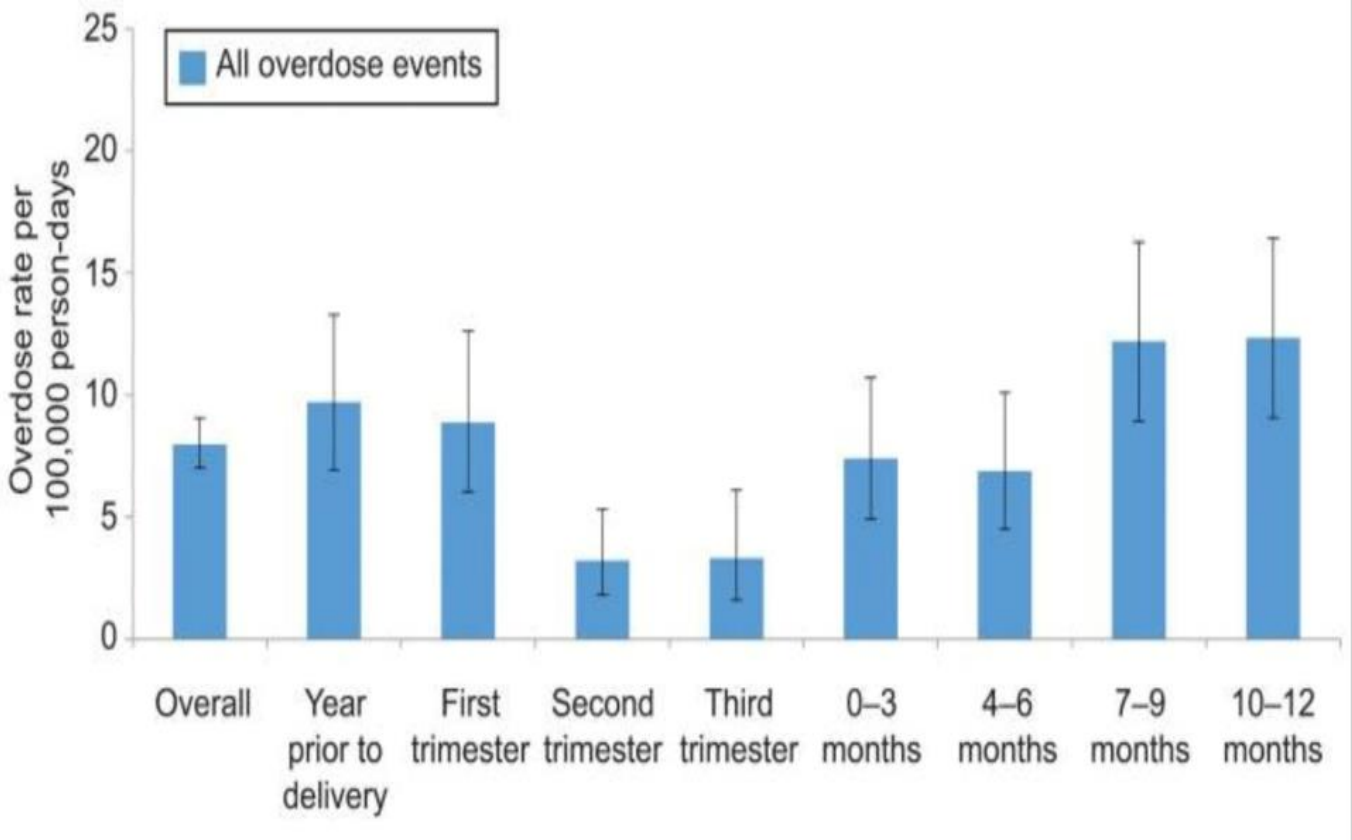
Opioid Overdose in Pregnancy

Among all pregnancy associated deaths, 11–20% were due to opioid-overdose

- Overdose events were lowest in the third trimester but increased after delivery, with the **highest rates 7–12 months postpartum.**
- Overdose rates among women on MAT in the month of overdose **were significantly lower** compared with those not receiving MAT.
- Naloxone crosses the placenta and therefore may precipitate withdrawal in the fetus and increased risk of spontaneous abortion, premature labor, or stillbirth.

Bruzelius & Martins, 2022, Schiff et al, 2018

Opioid Overdose in Pregnancy



Schiff et al, 2018

Opioid Overdose in Pregnancy

- Nausea, vomiting in opioid naïve individuals
- Drowsiness
- Stupor
- Cool, moist skin
- Bradycardia/Hypotension
- Hypothermia
- Non-cardiogenic pulmonary edema
- Pinpoint pupils (may dilate with hypoxia)
- Coma
- Respiratory depression: slow, deep breathing (2-7 breaths/min) – usual cause of death
- Generalized seizures: Meperidine/Demerol

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Treatment:

- Naloxone (Narcan) 0.4-2 mg (1ml) IV/IM/SC, Q2-3 min. PRN
- Intranasal Naloxone 1mg in each nostril; may repeat Q3-5 minutes if symptoms recur
- If no response after giving the maximum dose of 10mg, consider sedative/hypnotic OD
- Monitor methadone (or other LA opioids) overdose patients for 24- 48 hrs.
- Continuous 24-hour IV infusion of Naloxone for patient's who overdose on long-acting opioids e.g. methadone, OxyContin. Monitor for up to 72 hrs.
- Naloxone may not work well for buprenorphine. May require 15-20x normal dose + M. Ventilation

DISCUSSION QUESTIONS

- How do we pick the right treatment strategy for the patient?
- What would be appropriate dosing strategies in pregnancy?
- How has Fentanyl changed recommendations for Buprenorphine dosing?
- Tell us about low dose and high dose initiations in pregnancy?
- Hospitalization for initiation?
- Any recommendations that Obs can follow in the postpartum period?
- Any recommendations on the long-acting preparations?
- How would you recommend that comorbid substance use is taken care of?
- We spoke a lot about opioids: Any other substances that we should discuss? Amphetamines?
- Recent papers on cannabis use in pregnancy.
- Any resources you would recommend? Care for Pregnant and Postpartum People with Substance Use Disorder | AIM (saferbirth.org)