Opioid Use Disorder in Pregnancy

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Objectives

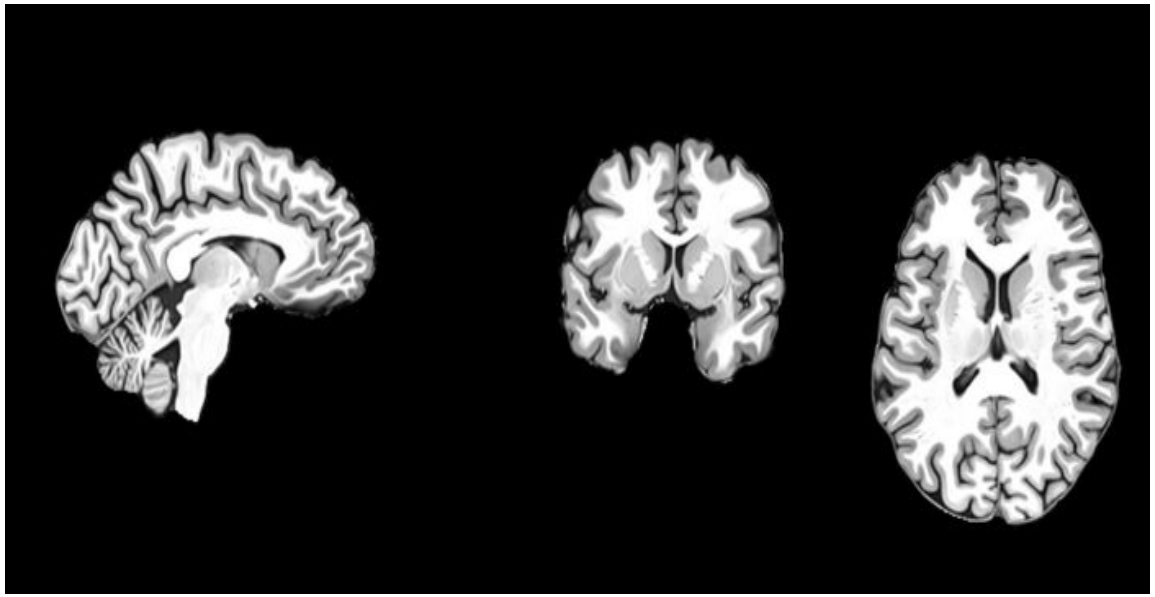
- Physiological Changes of Pregnancy
- Understanding Opioid Use Disorder
- Scope and Impact of the Problem
- Screening Practices
- Consequences and Complications
- Treatment and Medications

Physiological Changes of Pregnancy[1]

- Physiological Changes occur in nearly every organ system in pregnancy.
  - Increased renal blood flow increases drug clearance
  - Increased maternal blood and plasma volume
  - Cardiac output increases 30-50%
  - There is an increase in total body water to 6-8 liters
  - Progesterone stimulates hepatic microsomal enzyme activity
- These changes can lead to an increase or a decrease in the effectiveness of different drugs

Changes in The Brain during Pregnancy[2]

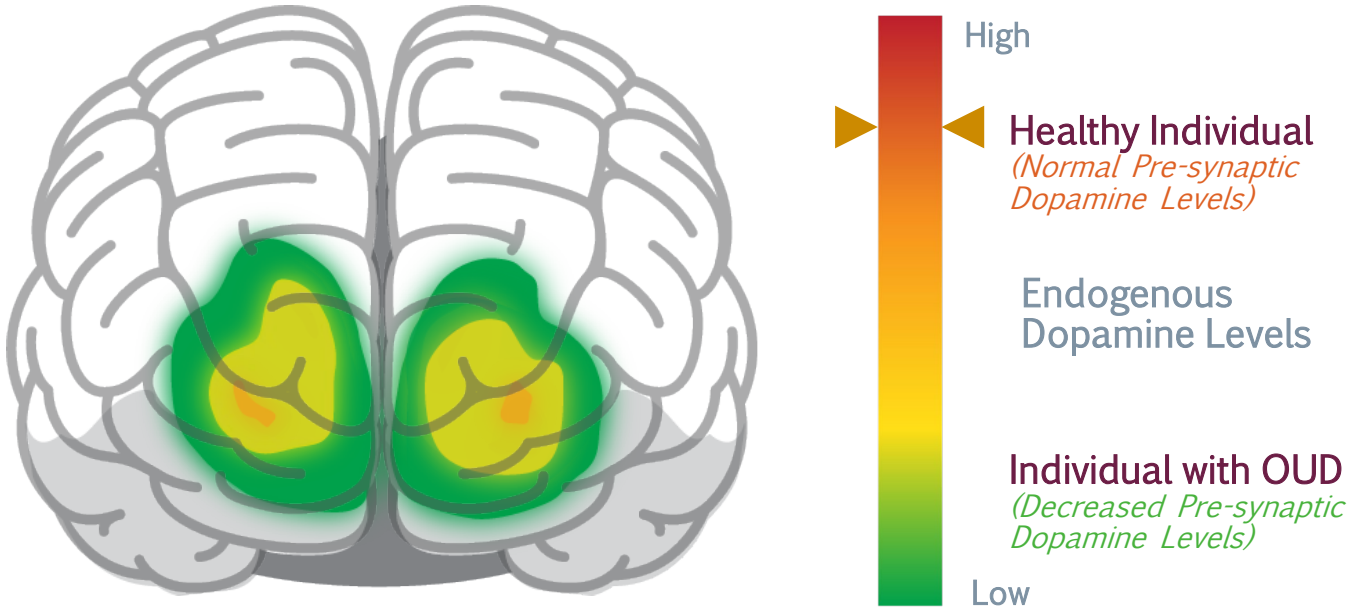
- **Cognitive changes**
  - Memory problems and decrease comprehension
  - "Pregnancy brain"
- **Emotional Changes and Hormonal Imbalance**
  - Higher Cortisol Levels
  - Estrogen and progesterone flood are 100 to 1000 times greater than pre-pregnancy levels
- **Neuroanatomical Changes**:
  - While total brain volume decreases, white matter in the brain strengthens.
  - These white matter changes are suspected to aid in the development of the bond between the mother and infant.
- **Persistent Effects**
  - Sensitive period of neurodevelopment



https://www.wsj.com/science/pregnancy-brain-0aa642c5?st=qy242t9nsvro3m2&reflink=article_imessage_share

The Nature of Opioid Use Disorder (OUD): A Chronic, Relapsing Brain Disease[4]

- Chronic use of opioids and the resulting opioid dependence produces:
  1. **Structural and functional changes** in brain regions implicated in regulating impulse control, reward, and motivational functions[5]
  2. **Physiological changes** that result in distressing withdrawal symptoms in the absence of opioids[5]
- The structural, functional, and physiological changes to the brain in OUD are persistent and cause challenges to daily functioning[6]



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Medication-Assisted Treatment for Opioid Use Disorder – MAT for OUD

- MAT Services that integrating medical, behavioral, and psychosocial programs can reduce mortality from OUD by 50%.[3]
- Methadone, Buprenorphine, and Naltrexone are the three main FDA approved medications for OUD[3]
- MAT is recommended during pregnancy as it helps reduce the risk of complications, including preterm birth and neonatal abstinence syndrome (NAS).

DSM-5 CRITERIA FOR SUBSTANCE USE[7]

11 criteria outlined in the DSM-5-TR can be grouped into 4 primary categories

1. IMPAIRED CONTROL	2. SOCIAL IMPAIRMENT	3. RISKY USE	4. PHYSICAL DEPENDENCE
1. Use of larger amount and for longer than intended 2. Repeated attempts to quit and/or control use 3. Much time spent using 4. Craving to use	5. Neglected major role obligations to use 6. Social/interpersonal problems related to use 7. Activities given up for use	8. Use in hazardous situations 9. Continued use despite physical or psychological problems	10. Tolerance 11. Withdrawal

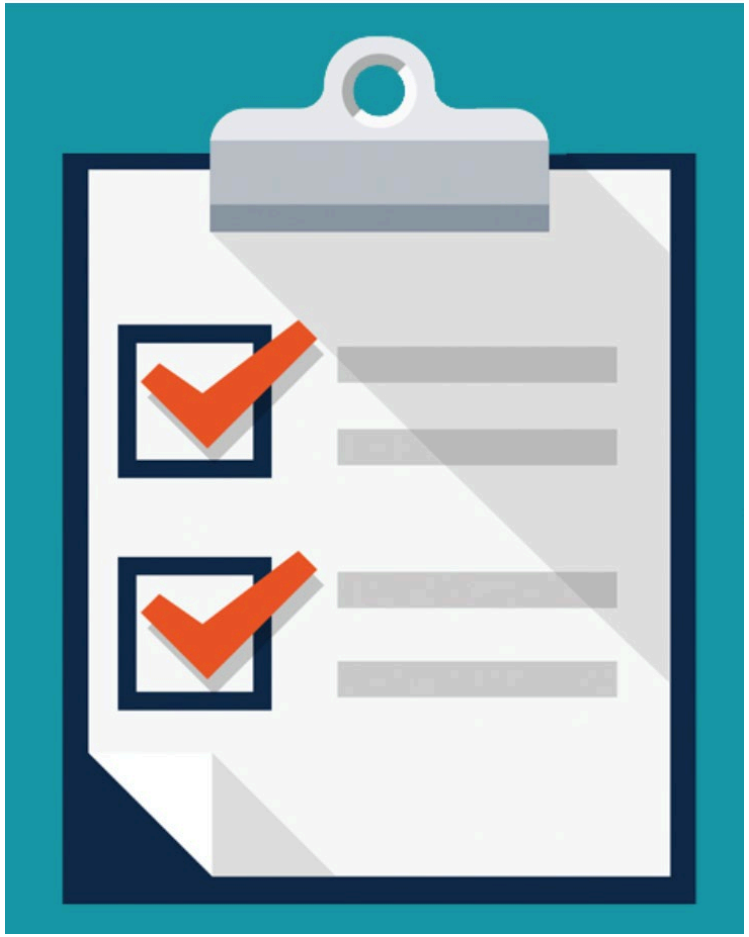
DSM-5: Three Levels of Severity[7]

Depending on how many symptoms are identified:

- **Mild**: 2-3
- **Moderate**: 4-5
- **Severe**: 6+

Further describe the state of SUD

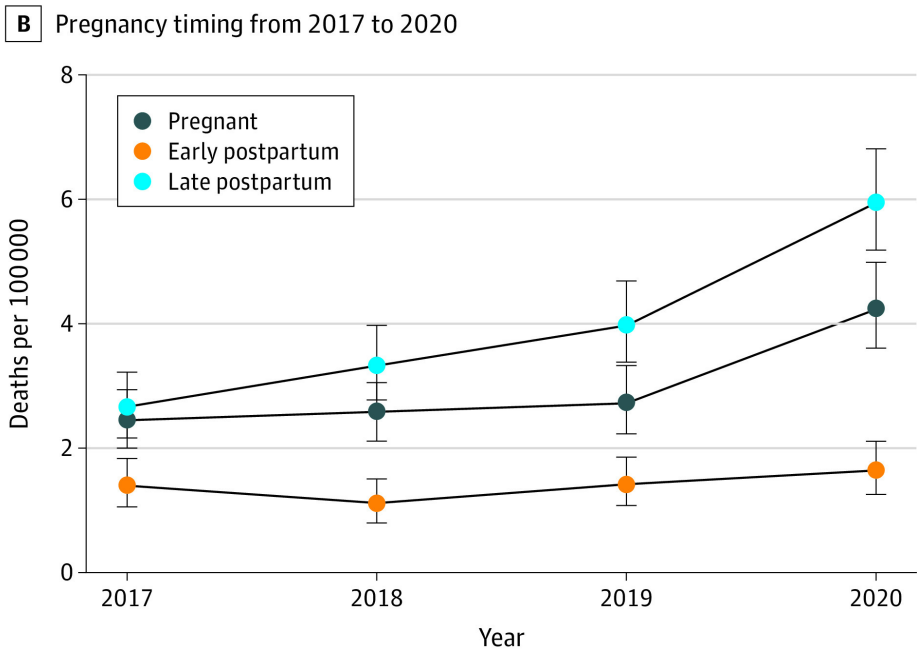
- Early remission
- Sustained Remission



Incidence of Opioid Overdose Deaths have Increased in Mothers

2017-2020 Data[10]

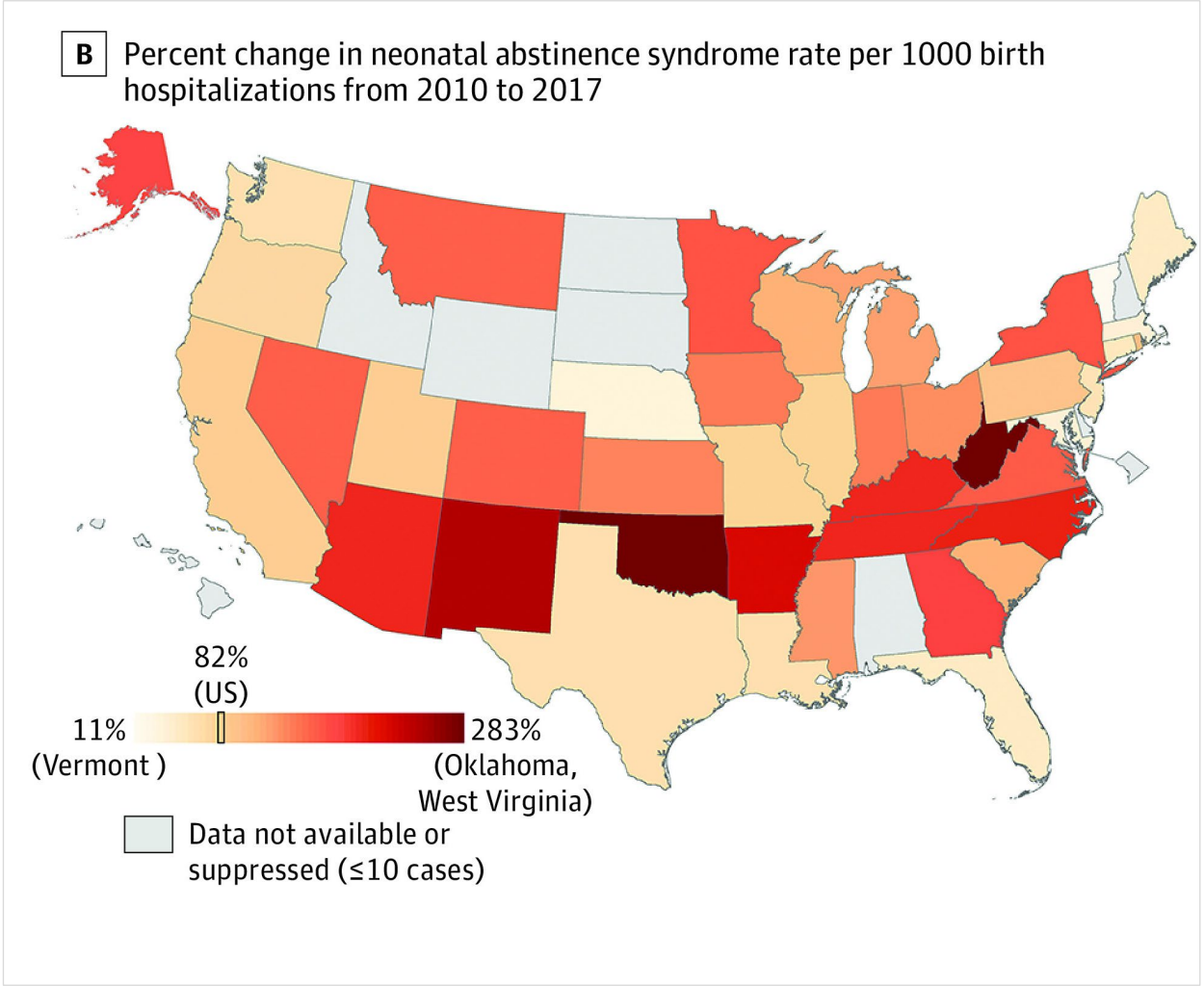
- Overdose-related deaths in pregnancy: 1,249
- 81% increase in overdose deaths in pregnant/postpartum women
- Highest overdose rates during late postpartum (6-30 weeks after delivery)
  - This is likely due to stress, changes in tolerance, and sleep deprivation[11]



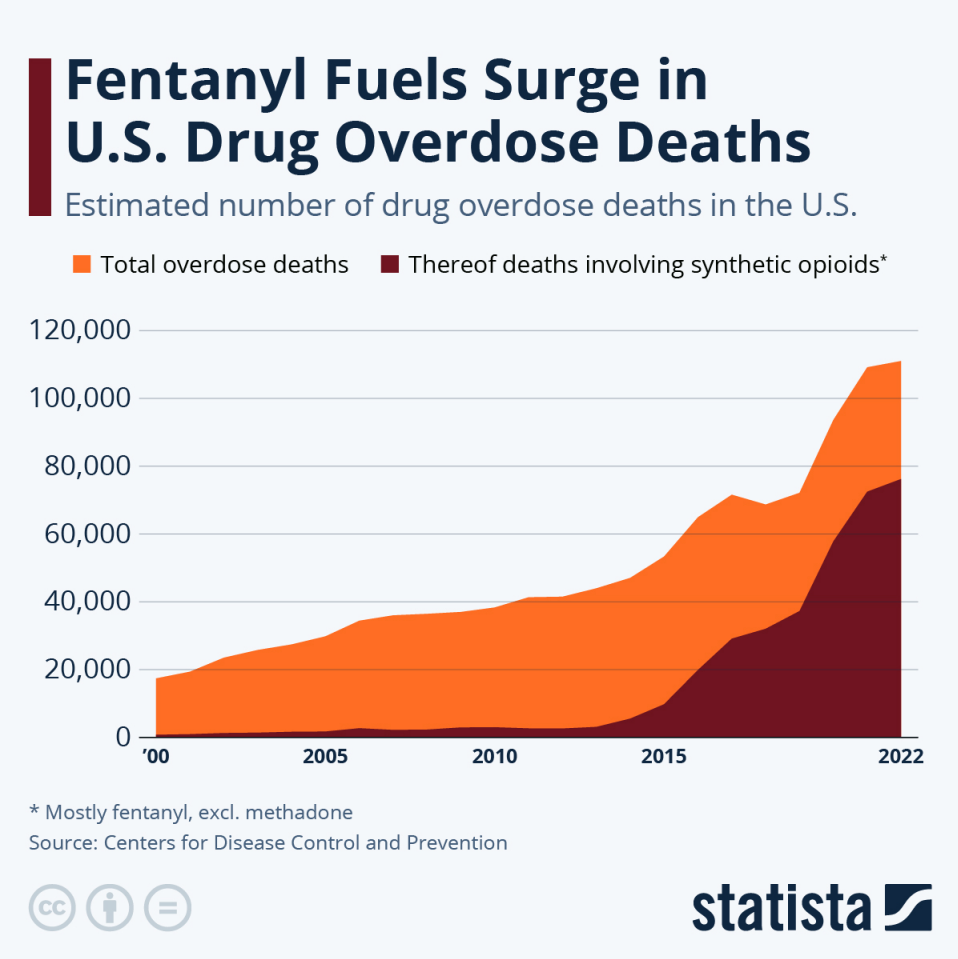
MATERNAL OPIOID USE HAS INCREASED SIMULTANEOUSLY

- From 2010-2017 Maternal Opioid-Related Diagnosis (MOD) rate increased from 3.5 to 8.2 per 1,000 deliveries.[9]
- In urban center, rates are much higher
- This value can be underreported due to early discharge of the baby before they develop symptoms

NAS Reporting by State



Incidence Overdose Has Increased Exponentially



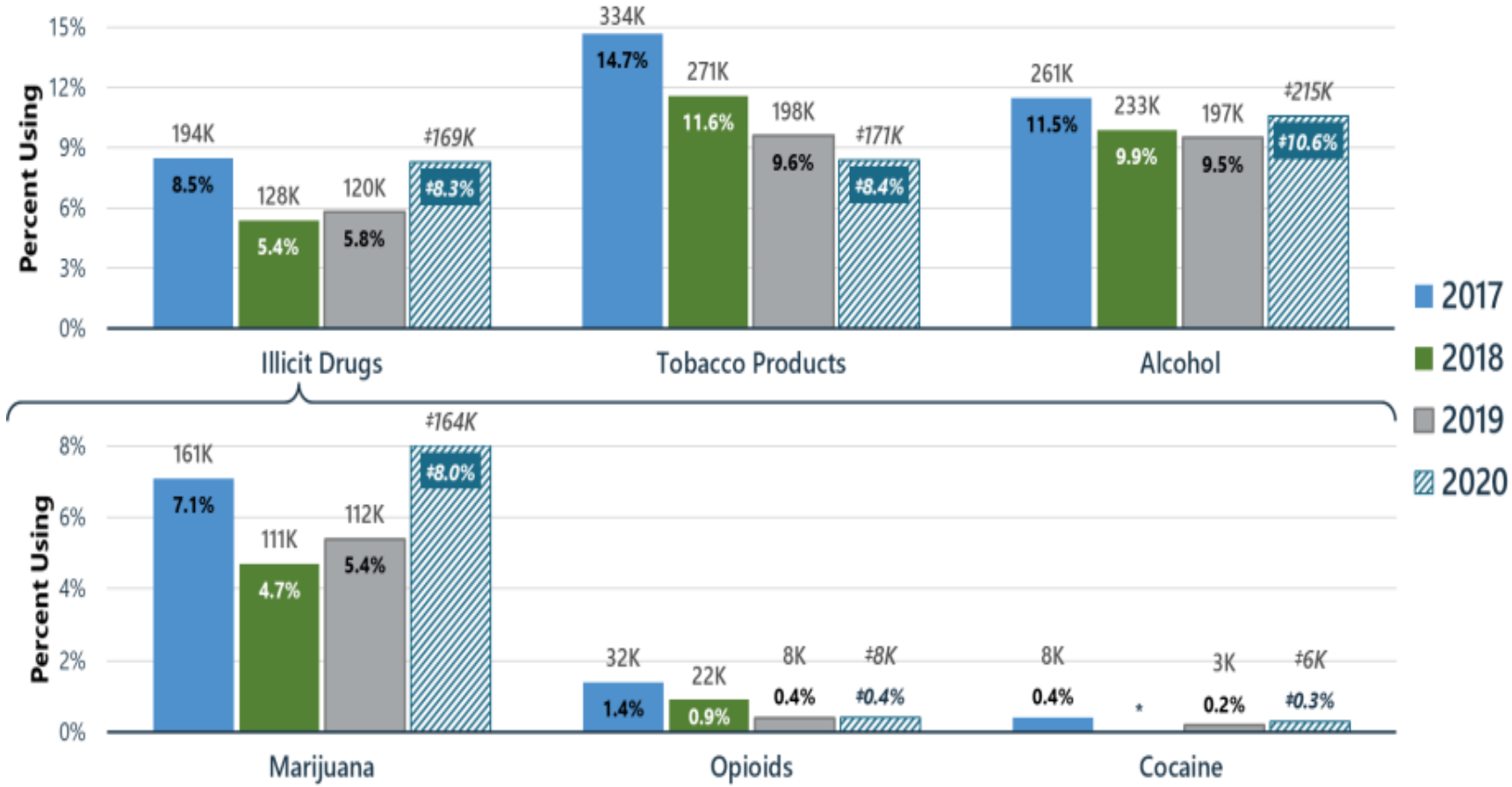
- Drug overdose deaths exceeded 110,000 in 2022 with synthetic opioids involved in 76,000 of those deaths.[8]
- Fentanyl is up to 50 times more potent than heroin.[8]

Impact of Systemic Issues and Medical Intervention

- The "war on drugs" and mass incarceration disproportionately affect people of color, leading to increased scrutiny and biased treatment in pregnancy care.[12]
- Black birthing individuals with positive urine toxicology are ten times more likely to be reported to child protective services.[13]
- In 2020, 1 in 5 Black women did not receive adequate prenatal care compared to 1 in 10 White women.[14]
- From 2018-2021, U.S. maternal deaths nearly doubled to 33 per 100,000 births, with Black patients facing a three times higher risk of pregnancy-related death compared to White patients.[15,16]

SUD Among Pregnant Women$_{20}$

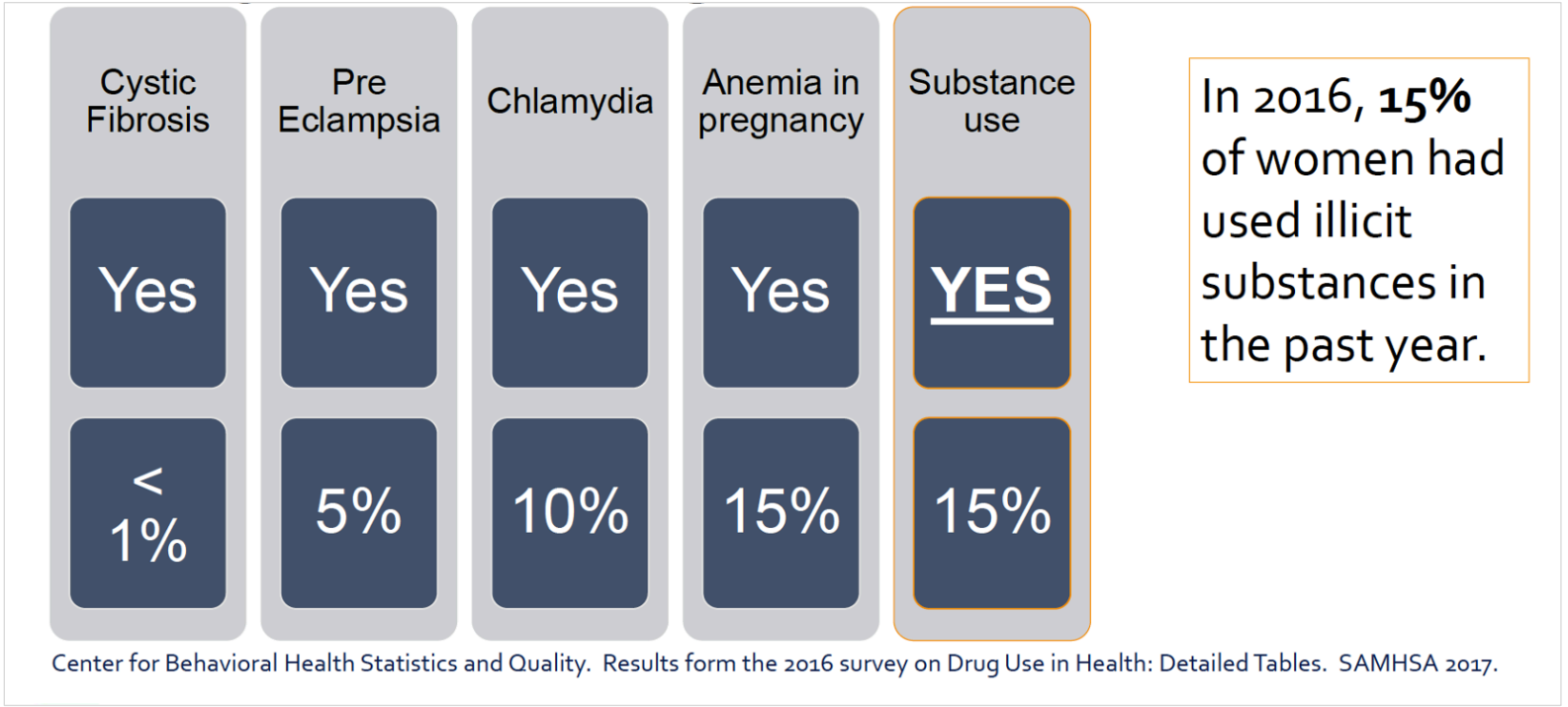
In 2020, between **8% and 15%** of pregnant women aged 15-44 used illicit drugs, tobacco products, or alcohol.



https://www.samhsa.gov/data/sites/default/files/reports/rpt37925/2020NSDUHWomenSlides072522.pdf

SHOULD WE SCREEN FOR SUBSTANCE USE IN PREGNANCY?

- ACOG recommends universal screening for substance use due to the prevalence of OUD in the general population.[17]
- Additionally, early identification and intervention improves outcomes and can be cost effective[18,19]



Center for Behavioral Health Statistics and Quality. Results form the 2016 survey on Drug Use in Health: Detailed Tables. SAMHSA 2017.

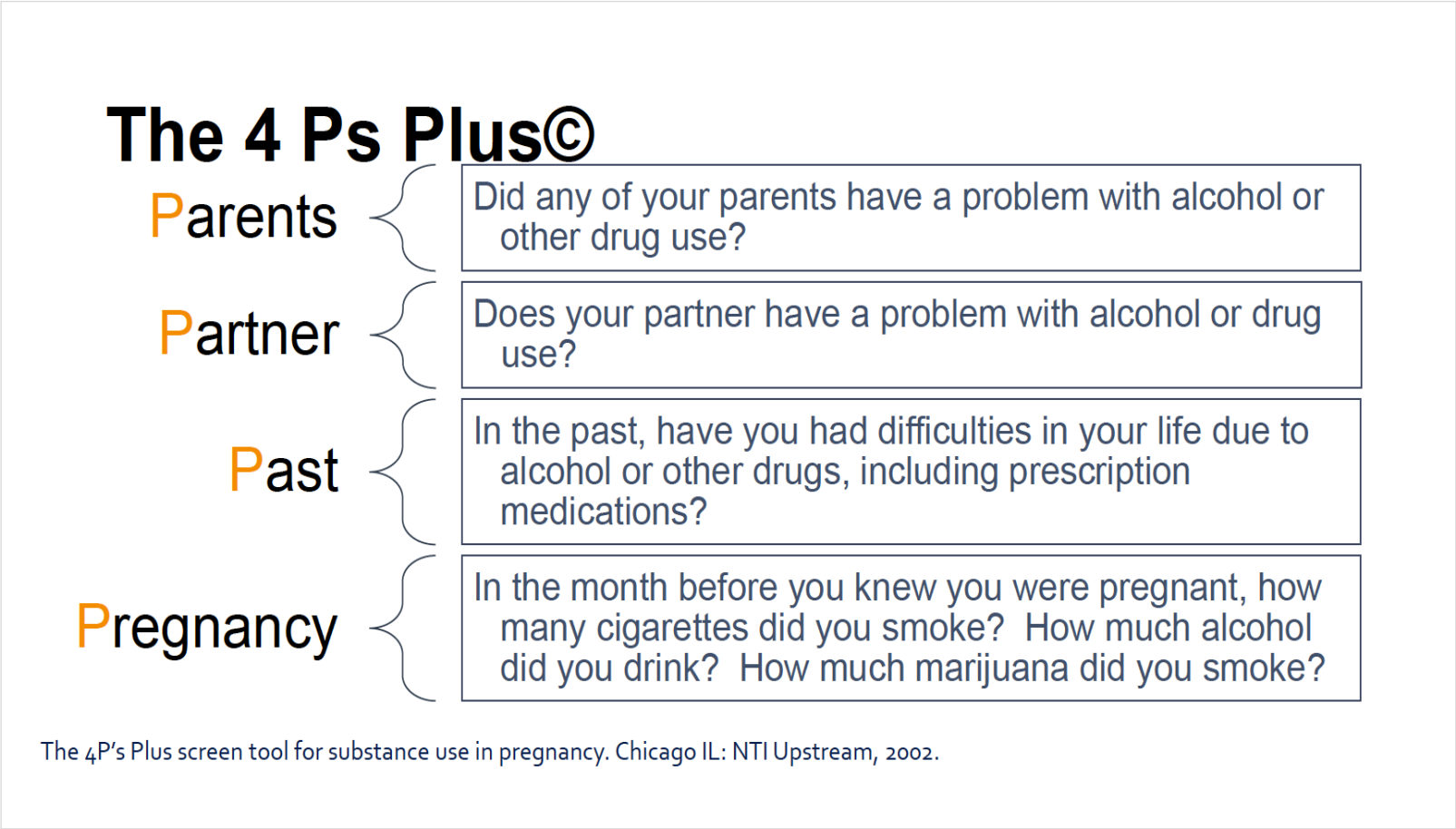
In 2016, **15%** of women had used illicit substances in the past year.

Strategies for Screening[21]

- Use validated verbal screening tools
  - i.e. NIDA quick screen, 4Ps Plus, DAST-10 and the CRAFFT
- Maternal urine toxicology with intentions of improving clinical decision-making
  - False positive
- Selective newborn biological toxicology testing to ensure the child receives the necessary care from a multidisciplinary team.
- SUD screening should be performed at intake of prenatal care to identify needs as early as possible

SCREENING QUESTIONNAIRE

- If lab screening is unavailable, questionnaires can be reliable[22]
- Identified pregnant women at risk for SUD
- Validated across race, ethnicity, language



The 4P's Plus screen tool for substance use in pregnancy. Chicago IL: NTI Upstream, 2002.

Positive Screening

- **If positive**, there's a follow up questionnaire to gather further information
  - frequency of use
  - all the various substances that the women are using
- The 4 Ps Plus screen + Brief Intervention can:
  - Reduce substance use
  - Save lives
  - Save money

TN Obstetrical reporting requirements related to OUD

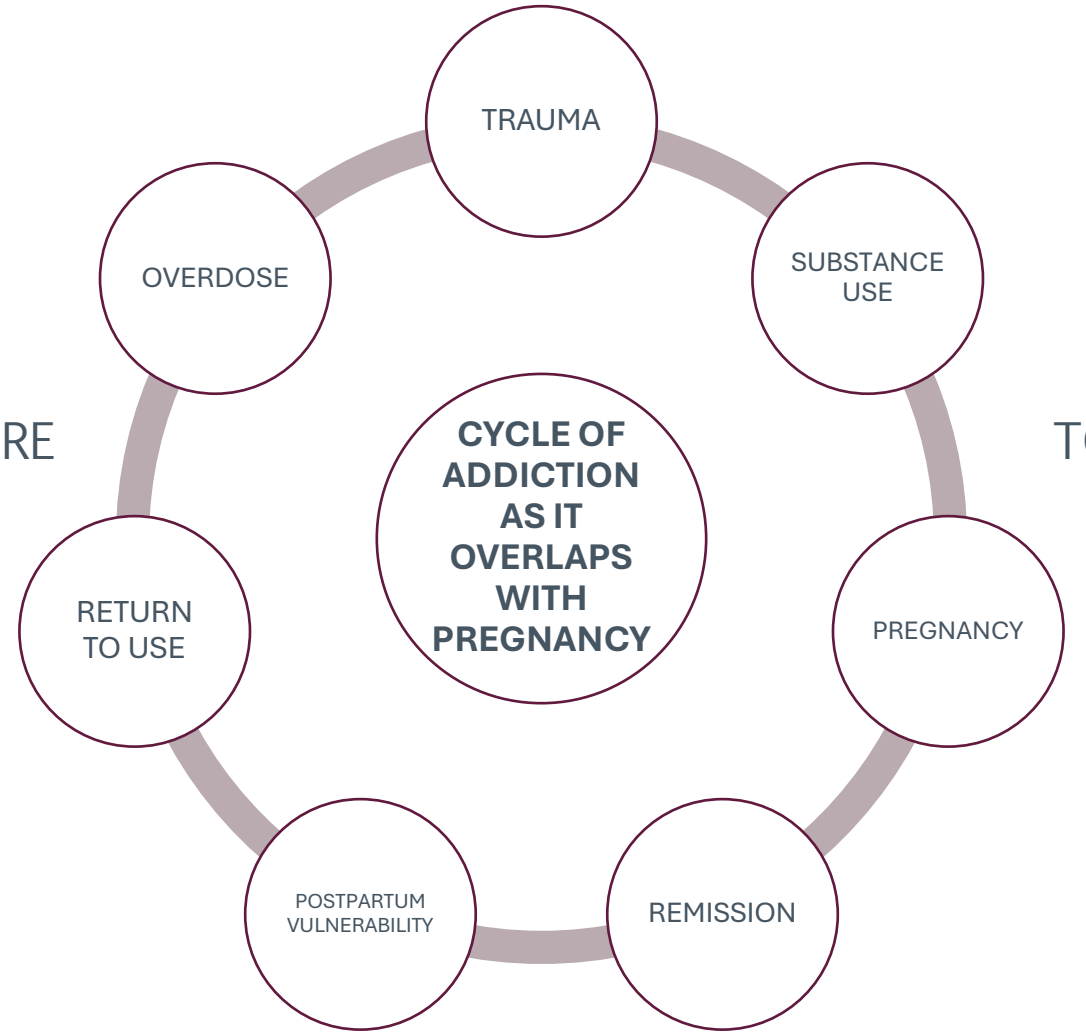
- Since January 1, 2013**, all cases of Neonatal Abstinence Syndrome (NAS) in Tennessee must be reported to the Department of Health** at the time of diagnosis.[23]
- **Fetal Assault Law (2014):** Tennessee enacted a law allowing the prosecution of pregnant women for drug use that harms their newborns.
  - The law faced significant criticism for violating human rights and discouraging prenatal care. It was allowed to expire in 2016 without renewal due to ongoing controversy and lack of clear effectiveness.[24]

CONSEQUENCES AND COMPLICATIONS

- OUD consequences are characterized by financial, social, and psychological issues the lead to psychosocial stress and exposure to violence
- Limit treatment and other life options
- Difficulties distinguishing which problems are due to opioids, other drugs, withdrawals vs coexistent maternal issues
- Cycle of addiction as it overlaps with pregnancy

FOR PEOPLE WITH CHEMICAL DEPENDENCY, **PREGNANCY IS A RISK FACTOR** FOR LOSS OF TOLERANCE, RELAPSE, OVERDOSE, AND DEATH

TOLERANCE DECREASE HERE



TOLERANCE INCREASE HERE

Obstetrical Complications, Polysubstance Use[25]

- **Maternal Complications**:
  - Maternal death
  - Poor fetal growth
  - Preterm birth
  - Stillbirth
  - Specific birth defects
  - Neonatal abstinence syndrome (NAS)

Unknown Long-Term Effects:

- Potential developmental impacts on children with or without NAS.

TREATMENTS FOR OUD[20]

1. Medically-Supervised Withdrawals (Detoxification)
2. Abstinence-Based Therapy
    1. Counseling
    2. Peer Support
    3. Social Services
3. Opioid Antagonist Therapy
    1. Naloxone and Naltrexone
4. Opioid Agonist Therapy
    1. Buprenorphine and Methadone

Inpatient admission for stabilization, detoxification for patients with polysubstance use disorder.

Inpatient residential or partial hospitalization admission for patients who fail outpatient management

Medication Treatment Stages

Induction

Process of initial dosing with medication for OUD treatment until the patient reaches a state of stability; also called initiation.

Stabilization

This stage involves close monitoring and dose adjusting to ensure the treatment is working.

Maintenance

This stage is where a prescription is written, recovery is supported, and co-morbid conditions are treated.

Buprenorphine[26]

- Buprenorphine's partial agonism at the μ-opioid receptor creates a ceiling effect, reducing adverse effects like respiratory depression and euphoria compared to full-agonist opioids like methadone.
- Compared to placebo, buprenorphine, at any dosage, improves treatment retention by an absolute 21% to 28% (NNT = 4-5)
- Patients receiving high-dose buprenorphine (≥ 16 mg/d) had fewer evident cases of illicit opioid use.

Buprenorphine – Overview[26]

- Partial opioid agonist
- Exerts its analgesic effect via high-affinity binding to mu opiate receptors in the CNS
- **Ceiling effect**-Due to it being a partial mu agonist, its pain-relieving effects level off at higher does, then behaves like an antagonist Peak effect one hour after administration
- Typical Doses range from 12-24 mg SL divided BID
- Lower risk of overdose
- Fewer drug interactions
- Prescriptions visible through PDMP

METHADONE[27]

- Full opioid agonist
- Less likely to lead to a euphoric sensation
- Alleviates withdrawal and craving symptoms
- Half-life 8 to 59 hours
- Typical doses range from 40-180 mg daily
- Split dosing is common in pregnancy

Methadone: Split Dose in Pregnancy[28]

Pregnancy Adjustments:

•Split dosing is recommended for all pregnant patients.

•Half-life decreases from 24 to 8 hours in pregnancy

Dosing Adjustments:

•Increased dosing required as pregnancy progresses to account for expanded volume of distribution and enhanced metabolism.

•Discontinue split dosing 2-3 weeks postpartum.

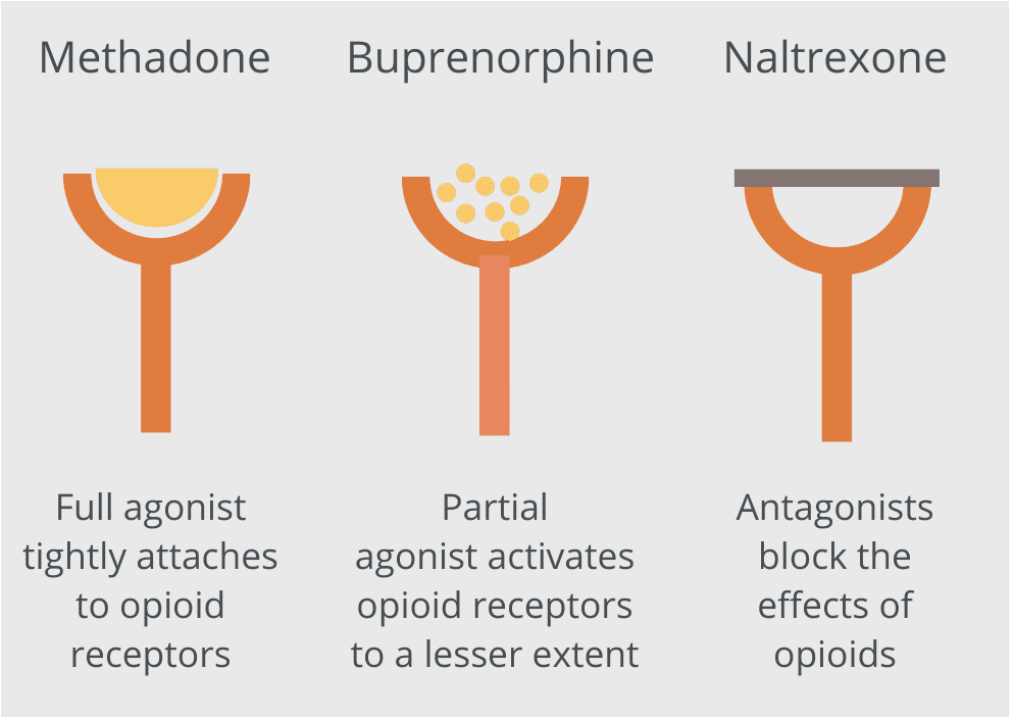
Postpartum Management:

•Prescriber must reassess patient 2-3 weeks after birth.

•Transition to single daily dose

Naltrexone[29, 31]

- Attaches to the opioid receptor to prevent the high from taking opioids
- Mostly used for individuals with mild OUD
- Patients must go through a withdrawal before initiating treatment
- After an initial test (25 mg), 50 mg maintenance doses can be used
- 380 mg extended-release IM injection every 4 weeks is easier to enforce
- There are not enough studies for Naltrexone in pregnancy to determine efficacy. Buprenorphine and Methadone are first line.



Methadone and Buprenorphine Dosing in Pregnancy

Methadone:[29]

- **Initial Dosing**:
  - Start with 20-30 mg orally.
  - Incremental doses of 5-10 mg every 3-6 hours as needed.
  - Average maintenance dose: ~120 mg.
- **Maintenance Dosing**:
  - Increase by 5-10 mg per week if needed.
  - Twice-daily dosing at 12-hour intervals may be more effective.
  - Continue usual dose intrapartum.
  - Monitor with weekly urine drug screens.
  - Check methadone serum trough levels if symptoms persist despite dose increase.

Buprenorphine:[29]

- **Candidates**:
  - Initiate only when showing moderate opioid withdrawal signs.
- **Dosing**:
  - Dose similar to nonpregnant patients; average increase ~3 mg with advancing gestation.
  - Maintain usual dose intrapartum and postpartum.

Suboxone vs Subutex in Pregnancy[30]

- Evidence supports using buprenorphine/naloxone (Suboxone) over buprenorphine monotherapy (Subutex) in pregnancy.
  - Switching to monotherapy increases risks of abuse and diversion without clear benefits.
  - Many patients struggle with switching postpartum due to anxiety and concerns about efficacy.

Effect Of Methadone And Buprenorphine On Fetal Biophysical Parameters[31]

- **Methadone**: Decreases fetal heart rate reactivity, variability, and increases time to achieve reactive NST and complete BPP.
- **Buprenorphine**: Reduces fetal heart rate and variability, but effects are less pronounced than methadone. More reactive NSTs and higher BPP scores compared to methadone.
- **Ultrasound Monitoring**:
  - MOUD has no consistent effect on fetal growth.
  - Single ultrasound between 28-32 weeks to monitor fetal growth.
  - Additional ultrasounds if growth restriction is suspected.

LABOR AND DELIVERY AND POSTPARTUM MANAGEMENT CONSIDERATION

Neuraxial Anesthesia is ideal for patients for MOUD patients.[31]

- Buprenorphine and methadone do not interfere with anesthetics.

Important Principles:

- Maintenance doses of methadone/buprenorphine are not sufficient for acute pain[32, 33]
- Acute pain management should mimic non-OUD patients, using pharmacologic and nonpharmacologic methods.
- Avoid additional doses of methadone or buprenorphine for acute intrapartum pain.
- Higher opioid doses may be needed due to receptor binding and tolerance[34]
- Morphine (6-10 mg IV) can be used in early labor for patients dilated <6 cm, with careful monitoring.

Opioid Antagonists:

- Avoid drugs like nalbuphine, pentazocine-naloxone, butorphanol, and naloxone to prevent withdrawal [34,32]
- If given, reverse withdrawal with a full opioid agonist[32]

Breastfeeding with OUD[21]

- Multiple sources have indicated benefits of breastfeeding for mothers on MAT and their newborns:
  - Decreased length of stay
  - Decreased need for initiation and duration of pharmacotherapy
  - Lower chance of NOWS (Neonatal Opioid Withdrawal Syndrome)[39]
- There are a few cases in which breastfeeding is not recommended for mothers with OUD
  - HIV Positive
  - Active Tuberculosis
  - Active Herpes Simplex Lesions
  - Hepatitis B or C with cracked or bleeding nipples
  - Return to illicit drug use

POST-PARTUM RISK CONSIDERATIONS

- **Overdose Risk**:
  - Leading cause of pregnancy-related deaths in the year post-birth.[37]
- **Continue Medication-Assisted Treatment (MOUD)**:
  - Reduces postpartum opioid overdose death by 60%.[38]
- **Pain Management**:
  - Use a multimodal approach starting with nonopioid analgesia.[32]
  - Significant variability in opioid dose requirements.[36, 32]

Buprenorphine vs. Methadone:

- Managing acute pain is more challenging with buprenorphine due to its higher mu-opioid receptor affinity.[31]

- **Follow-Up Care**:
  - Pregnant patients with OUD need more follow-up to prevent relapse.

SUMMARY

- Opioid use has been increasing globally.
- For pregnant patients with opioid use disorder, treatment with buprenorphine or methadone should be offered.
- Neither drug is superior per se but there are more recent data suggesting some benefits for those receiving buprenorphine.
- Medications for OUD are associated with fewer neonatal complications and side effects than detoxification or continued use of nonprescribed opiates.
- Neonatal opioid withdrawal is typically less severe in neonates exposed to buprenorphine compared with methadone.
- Hormonal changes and maternal attachment during pregnancy can facilitate lasting recovery from opioid use disorder.
- Encouraging breastfeeding and continuing medication-assisted treatment supports this process and promotes both maternal and infant health.

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ANY QUESTIONS