ASAM REVIEW COURSE 2024

Pregnancy and Newborns: Considerations from Science to Systems

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LEARNING OBJECTIVE

Describe the effect of substance use disorder on pregnancy and evidence-based treatment strategies for pregnant patients and newborns.

Presentation Outline

Pregnancy and SUD

The postpartum patient with SUD

Effects of substance use during pregnancy on the newborn

Neonatal opioid withdrawal syndrome

Pregnancy and Substance Use Disorder

Definition of terms for providers not regularly doing obstetric care

- G = Gravida = total number of pregnancies
- P = Para = total number of deliveries
- XX weeks = weeks since last menstrual period or weeks since conception + 2
- Full-term = 37-41 weeks gestation
- IUGR = Intrauterine growth restriction = fetal weight by ultrasound < 10th percentile
- SGA = small for gestational age = weight of newborn baby < 10th percentile for gestational age

Definition of terms for providers not regularly doing obstetric care

- Preterm labor = labor at < 37 weeks
- Preterm delivery = delivery at < 37 weeks
- Placental abruption = placenta pulls away from the wall of the uterus. Small abruptions can cause IUGR or preterm labor. Large abruptions can be fatal for mother and baby.

Case Study

33 yo G4P3 had been stable on buprenorphine-naloxone for 4 years. Presented to her buprenorphine provider for routine appointment and was discovered to be pregnant. Her buprenorphine provider did not give her a script because of this. She relapsed to heroin. She presented to our clinic at 25 weeks gestation, but because of transportation difficulties, she was unable to get restarted on buprenorphine and delivered a premature infant at 31 weeks. She restarted buprenorphine postpartum, and both she and baby did well.

Case Study

22yo G1P0 presents @ 9 weeks gestation. Actively using heroin. Desperately wanted to keep this pregnancy and this child. Started on buprenorphine maintenance, did well. Child with no signs of Neonatal Opioid Withdrawal Syndrome at birth. Currently 10 years old, doing well.

Substance use in pregnancy

- Use of alcohol, tobacco, and drugs during pregnancy is the leading preventable cause of mental, physical, and psychological impairments in children.
- Opioid-dependent pregnant women have an unintended pregnancy rate of 86%.[1]
  - Please provide or refer for contraception if you are treating patients with OUD who can get pregnant and don't want to do so.
  - Also, please start them on folate, 0.4 – 0.8 mg daily, even if they are not planning to get pregnant.[2]

1. *Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 P. 1315*
2. *https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/folic-acid-for-the-prevention-of-neural-tube-defects-preventive-medication accessed 4/14/2024*

Rate of opioid use disorder in pregnancy is increasing

- Between 1998-2011, there was a 127% increase in opioid-dependent pregnant women presenting for delivery.[1]
- The estimated Maternal Opioid-related Diagnosis rate significantly increased from 2010 - 2017 from 3.5 per 1000 delivery hospitalizations (95% CI, 3.0-4.1) to 8.2 per 1000 delivery hospitalizations (95% CI, 7.7-8.7).[2]

1. *McCarthy et al. Opioid dependence and pregnancy: minimizing the stress on the fetal brain. American Journal of Obstetrics and Gynecology. 3 December 2016. pp 1-6*
2. *Hirai AH, Ko JY, Owens PL, Stocks C, Patrick SW. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017. JAMA. 2021;325(2):146–155. doi:10.1001/jama.2020.24991*

Perinatal SBIRT: 4 Ps Plus

Parents	Did either of your parents ever have a problem with alcohol or drugs?
Partner	Does your partner have a problem with alcohol or drugs?
Past	Have you ever had a problem with alcohol or drugs in the past?
Past 30 days	In the past month, have you drunk any alcohol or used any substances?

[1]*ACOG committee opinion 711, 2017*

[2] *J Perinatol. 2005 Jun;25(6):368-74.*

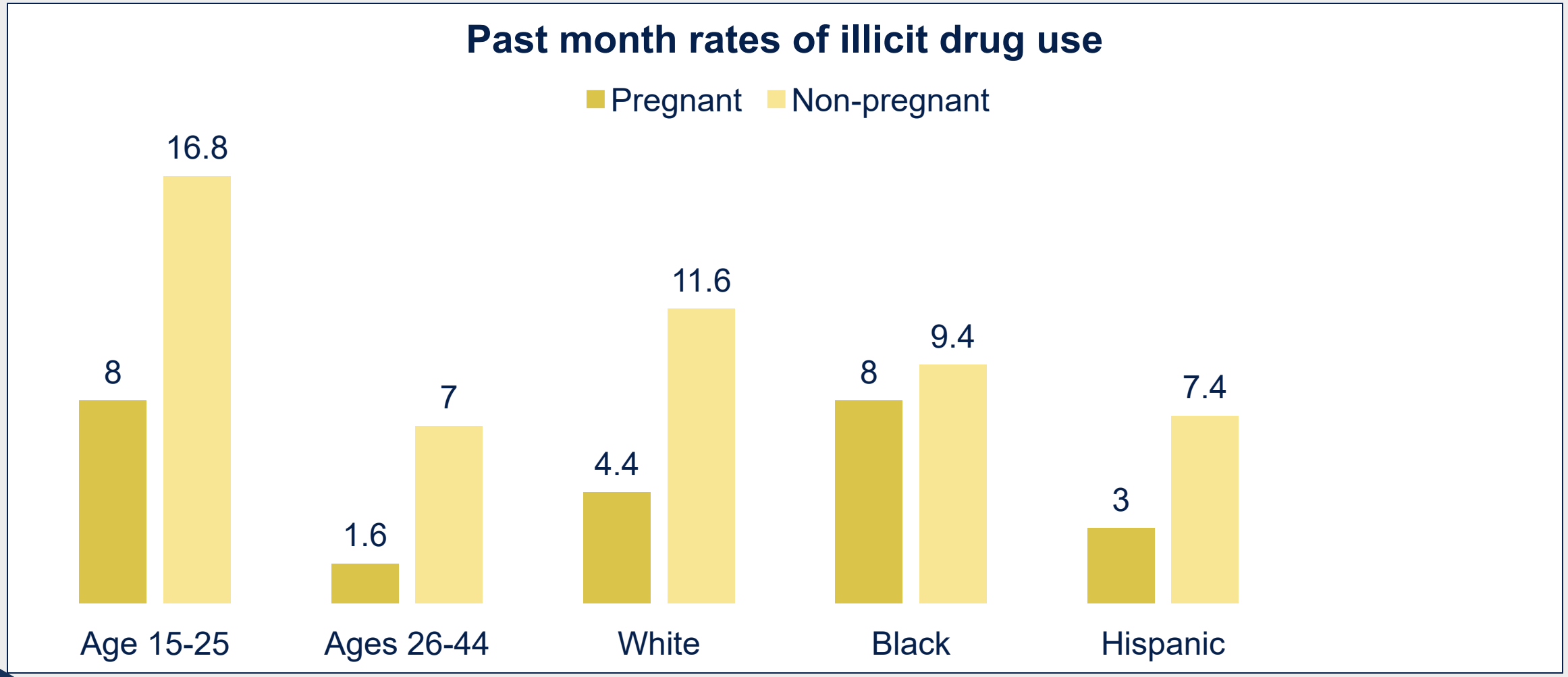
PERINATAL SBIRT: 4P'S PLUS

- ***A positive on the 4 P's does not mean that a patient has a substance use disorder, but it does mean that you need to ask more questions***

[1]*ACOG committee opinion 711, 2017*
[2] *J Perinatol. 2005 Jun;25(6):368-74.*

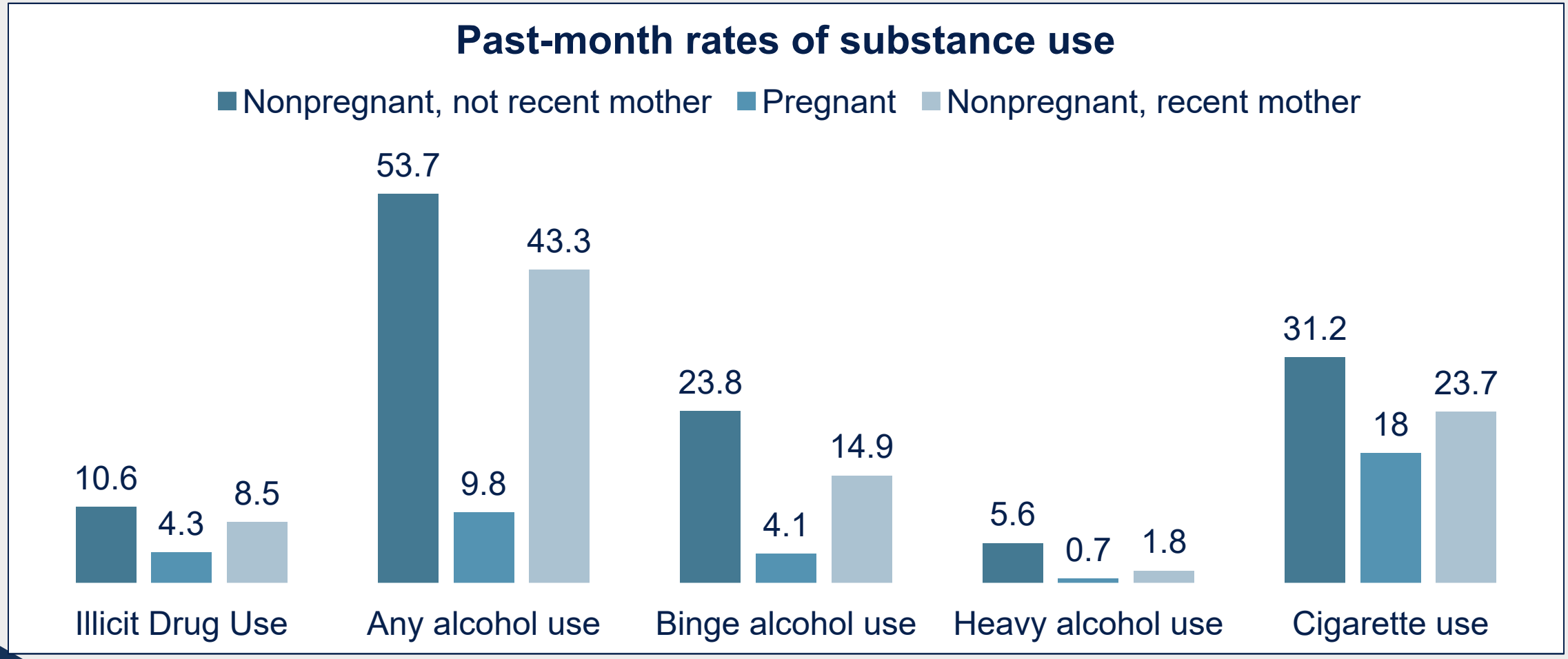
- What are medical implications of substance use disorder with pregnancy?
- What is the significance of pregnancy for any substance use disorder?

Percentages of past-month illicit drug use in pregnant and non-pregnant women



Helmbrecht et al. Management of Addiction Disorders in Pregnancy. J Addict Med; Vol 2, Number 1, March 2008, pp 1-16

Percentages among women aged 15-44 years who reported past-month substance use by pregnancy and recent motherhood status



Helmbrecht et al. Management of Addiction Disorders in Pregnancy. J Addict Med; Vol 2, Number 1, March 2008, pp 1-16

Birth defects with substances

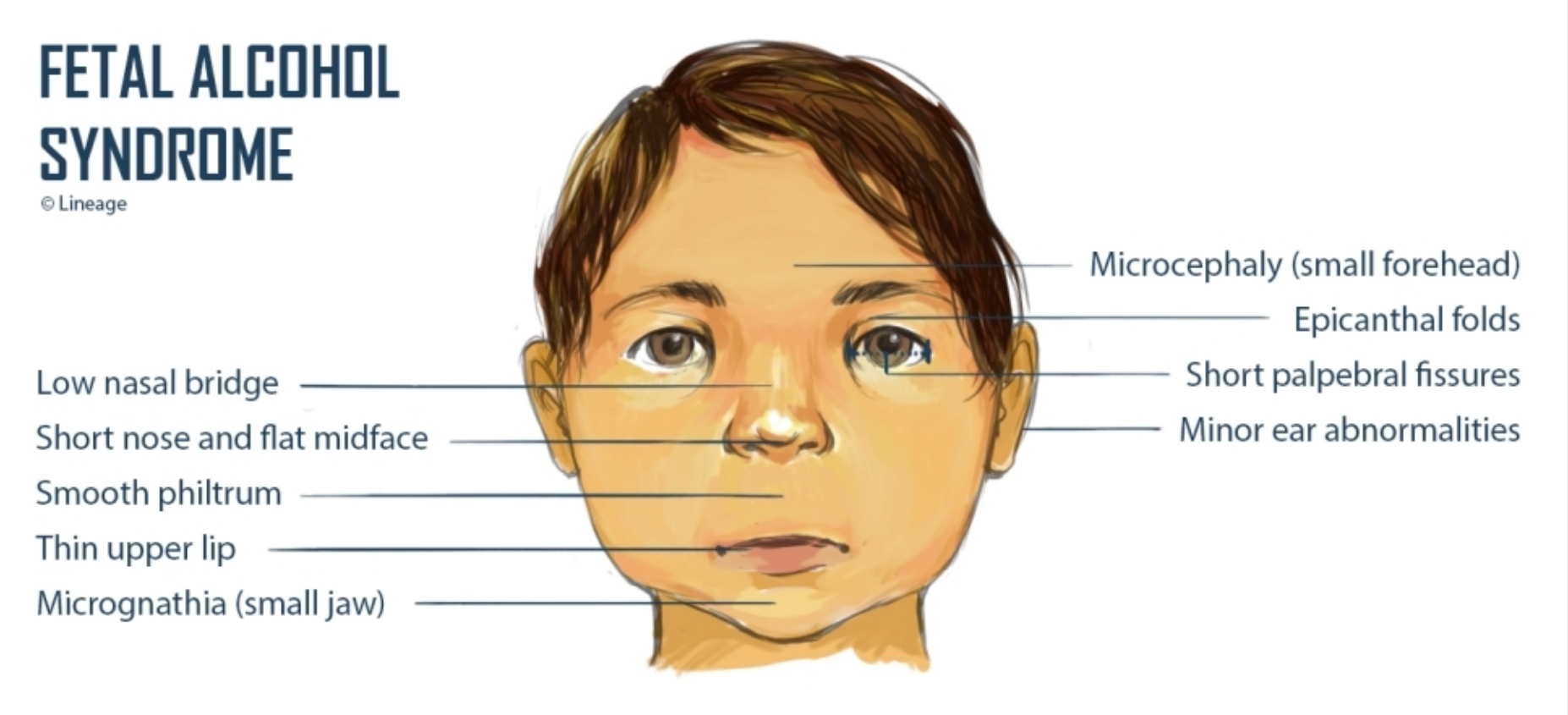
- The drug with the most teratogenic potential is alcohol. [1]

[1] *Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 P 1317*

Fetal alcohol syndrome

- Evidence of growth restriction (prenatal and/or postnatal)
  - Height and/or weight <= 10th percentile
- Evidence of deficient brain growth and/or abnormal morphogenesis
  - Structural brain anomalies or head circumference <=10th percentile
- Characteristic pattern of minor facial anomalies
  - Short palpebral fissures, thin vermillion border upper lip, smooth philtrum

Fetal alcohol syndrome



Tobacco and pregnancy

- Neonates born to mothers who smoke weigh an average of 200 gm less than neonates born to mothers who don't smoke. [1]
- 22% of SUIDs (Sudden Unexpected infant deaths) can be directly attributed to maternal smoking during pregnancy. [2]

[1]Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019P 1318

[2]Anderson TM, Lavista Ferres JM, Ren SY, et al. Maternal Smoking Before and During Pregnancy and the Risk of Sudden Unexpected Infant Death. Pediatrics. 2019; 143(4):e20183325

Cannabis and pregnancy

- Difficult to get definitive answers on effects:
  - Women often using other substances, especially alcohol and tobacco
  - Psychosocial variables, such as income, age, and education, vary
  - Pre-existing conditions, such as ADHD or anxiety
  - Many studies done before level of THC was as high as now
- Cannabis use is common – the prevalence of self-reported marijuana use is 2-5%, and it increased from 2.37% in 2002 to 3.85% in the 2014 NSDUH.[1]

[1] *Thompson R, DeJong K, Lo J. Marijuana Use in Pregnancy: A Review. Obstet Gynecol Surv. 2019 Jul;74(7):415-428*

Cannabis and pregnancy

- Most common reasons to use cannabis in pregnancy are morning sickness and to manage anxiety/depression
  - Use of cannabis for morning sickness can lead to cannabinoid hyperemesis syndrome. [1]

[1] *Badowski S, Smith G. Cannabis use during pregnancy and postpartum. Can Fam Physician. 2020;66(2):98-103.*

Cannabis and pregnancy

- Data is mixed on effect of cannabis on pregnancy. [1]
  - Studies have given varied results on effect on birthweight [2,3], birth defects [4], and other outcomes.
  - There does seem to be a pattern of neurobehavioral effects on the fetus, with hyperactivity and sleep problems in toddlers, ADHD in pre-teens, and emotional dysregulation in adolescents. [5-7]

[1] *Sheryl A. Ryan, Seth D. Ammerman, Mary E. O'Connor, COMMITTEE ON SUBSTANCE USE AND PREVENTION, SECTION ON BREASTFEEDING, Lucien Gonzalez, Stephen W. Patrick, Joanna Quigley, Leslie R. Walker, Joan Younger Meek, IBCLC, Margreete Johnston, Lisa Stellwagen, Jennifer Thomas, Julie Ware; Marijuana Use During Pregnancy and Breastfeeding: Implications for Neonatal and Childhood Outcomes. Pediatrics September 2018; 142 (3): e20181889. 10.1542/peds.2018-1889*

[2] *Badowski S, Smith G. Cannabis use during pregnancy and postpartum. Can Fam Physician. 2020;66(2):98-103.*

[3] *Gunn JK et al. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. BMJ Open. 2016 Apr 5;6(4):e009986. doi: 10.1136/bmjopen-2015-009986.*

[4] *Conner et al. Maternal Marijuana Use and Adverse Neonatal Outcomes: A Systematic Review and Meta-analysis. Obstet Gynecol. 2016 Oct;128(4):713-23. doi: 10.1097/AOG.0000000000001649.*

[5] *Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019P 1325*

[6] *Thompson R, DeJong K, Lo J. Marijuana Use in Pregnancy: A Review. Obstet Gynecol Surv. 2019 Jul;74(7):415-428*

[7] *Nashed et al. Cannabinoid Exposure: Emerging Evidence of Physiological and Neuropsychiatric Abnormalities Frontiers in Psychiatry. 11/2021*

[8] *Roncero et al. Cannabis use during pregnancy and its relationship with fetal developmental outcomes and psychiatric disorders. A systematic review. Reprod Health. 2020;17(1):25. 2020 Feb 17.*

Cannabis and pregnancy –what we need to tell our patients

- Pregnant complain about hearing mixed messages from healthcare providers. They also state that want more research on the safety and effects of cannabis with pregnancy. [1]
- There is no recognized “safe” amount of marijuana with pregnancy.
  - Although marijuana hasn’t been found definitively to be dangerous, it has also most definitely not been found to be safe.
  - It is also likely much more dangerous if combined with tobacco and alcohol.
- There is very likely a risk of long-term neurocognitive effects.
- While it may help with morning sickness, it can lead to cannabinoid hyperemesis syndrome, which is way worse, and there are better treatments.

Barbosa-Leiker et al. ***Daily Cannabis Use During Pregnancy and Postpartum in a State With Legalized Recreational Cannabis****, Journal of Addiction Medicine: November/December 2020 - Volume 14 - Issue 6 - p 467-474*

Stimulant use and pregnancy

- Methamphetamine [1] and cocaine [2] use are associated with the following:
  - Preterm delivery
  - Low birth weight
  - Small for gestational age infants

1. *Kalaitzopoulos et al.* ***Effect of Methamphetamine Hydrochloride on Pregnancy Outcome: A Systematic Review and Meta-analysis****, Journal of Addiction Medicine: May/June 2018 - Volume 12 - Issue 3 - p 220-226*
2. *Smid MC et al.* ***Stimulant Use in Pregnancy: An Under-recognized Epidemic Among Pregnant Women****. Clin Obstet Gynecol. 2019;62(1):168-184.*

Implications of opioid use disorder with pregnancy – fetus

- Medication: Both use and withdrawal have fetal effects. **Withdrawal effects usually considered more serious.**
  - Withdrawal causes a hyperadrenergic state which causes constriction of blood vessels in placenta. Exacerbated by cocaine and methamphetamine use. Can cause preterm labor and placental abruption.
  - Biggest direct effect of opioid use is Neonatal Opioid Withdrawal Syndrome at birth.

Maternal complications of opioid use with pregnancy

- A 2014 study found that opioid abuse or dependence increased the odds of major obstetrical morbidity and mortality:
  - In-house mortality aOR 4.6
  - Maternal cardiac arrest aOR 3.6
  - IUGR aOR 2.7
  - Placental abruption aOR 2.4
  - Preterm labor aOR 2.1
  - Oligohydramnios aOR 1.7
  - Transfusion aOR 1.7
  - Stillbirth aOR 1.5

Maeda, Ayumi et al. "Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes." Anesthesiology vol. 121,6 (2014): 1158-65. doi:10.1097/ALN.0000000000000472

Case Study
Pregnancy and Substance Use Disorder

28 yo G5P4, on methadone maintenance, disappeared from care at about 20 weeks, returned at 38 weeks in labor. Stated she had been at a methadone clinic in another community, but urine was negative for methadone, + for opiates. Baby went into horrible withdrawal at birth, child protective services involved and took child. Mother was arrested when she and her cousin, who was foster mother, got in fight on OB floor.

- What are psychosocial implications of substance use disorder with pregnancy?

Implications of substance use disorder with pregnancy

- Co-occurring disorders
  - Depression and other mental illness [1,2]
    - Both substance use disorder and depression cause poor self-care.
  - Domestic violence
    - Second-leading cause of trauma-related death in pregnancy.

1. *Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240*
2. *Schiff et al. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018*

Implications of substance use disorder with pregnancy

- Psychosocial:
  - Most mothers/birthers have a high motivation to change.
  - Lot of guilt/shame for many individuals
  - Legal implications around custody of baby and older children
  - Most substance-using pregnant peopl have very poor self-care behaviors. If they continue to use drugs, they are unlikely to take good care of themselves during the pregnancy.

Implications of substance use disorder with pregnancy

- Psychosocial:
  - Often have history of childhood sexual abuse or physical abuse (with implications for parenting)
  - High incidence of PTSD
  - Most women who use drugs start using because their partners use drugs. If they are still with that partner, it can be difficult for them to quit unless he quits as well.

Comorbid Medical Conditions Case Study Pregnancy and Opioid Dependence

25 yo G2P1 presents at 26 weeks, stating, “I’m addicted to fentanyl.” Scared that she will lose baby to child protective services or have medical complications. She wants to get into treatment.

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

Prenatal Care

- In a study in the Journal of Perinatology, it was found that pregnant people with illicit drug use and no prenatal care had the highest risk for prematurity, low-birth weight and small for gestational age infants. As prenatal care increased, risk for prematurity, low birth weight and small for gestational age babies dropped. [1]
- Pregnant people will often delay or not get prenatal care because of stigma and fear of consequences, including being reported to child protective services. [2]

[1]*El-Mohandes et al. Prenatal Care reduces the Impact of Illicit Drug use on Perinatal Outcomes. Journal of Perinatology. 2003; 23:354-360*

[2]*Bishop et al. Pregnant Women and Substance Use. Overview of Research and Policy in the United States. Bridging the Divide: A Project of the Jacobs Institute of Women's Health. February 2017*

- Abstinence-based therapy is not recommended during pregnancy for anyone who is actively using opioids.[1]

[1]*Kampman and Jarvis. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med 2015;9 358-367*

Medication therapy and pregnancy

- Medication therapy for opioid use disorder (MOUD) is standard of care for pregnancy[1]

SAMHSA Advisory. Evidence-Based, Whole-Person Care for Pregnant People who have Opioid Use Disorder. March, 2024

Benefits of MOUD during pregnancy

- A recent study of 10,741 pregnant persons with OUD on Medicaid with 13,320 pregnancies showed the following benefits to Medication for Opioid Use Disorder:
  - Decreased rate of overdose
  - Decreased preterm birth
  - Decreased low birthweight
- All of the above outcomes improved with longer duration of MOUD during the pregnancy

Krans EE, Kim JY, Chen Q, Rothenberger SD, James AE 3rd, Kelley D, Jarlenski MP. Outcomes associated with the use of medications for opioid use disorder during pregnancy. Addiction. 2021 Dec;116(12):3504-3514. doi: 10.1111/add.15582. Epub 2021 Jun 9. PMID: 34033170; PMCID: PMC8578145.

Benefits of MOUD during pregnancy

- In addition to the medical benefits, infants with NOWS are significantly (odds ratio 3.9) more likely to be discharged to the parent, rather than foster or relative, care if the mother received prenatal MOUD

Singleton, Rosalyn et al. "Assessing the Impact of Prenatal Medication for Opioid Use Disorder on Discharge Home With Parents Among Infants With Neonatal Opioid Withdrawal Syndrome." Journal of addiction medicine vol. 16,6 (2022): e366-e373. doi:10.1097/ADM.0000000000000987

Medication therapy and pregnancy

- 2010 NEJM study showed significantly less severe Neonatal Opioid Withdrawal Syndrome in buprenorphine group than the methadone group[1]
  - Babies exposed to buprenorphine required 89% less morphine, had a 43% shorter hospital stay, and shorter duration of treatment than babies exposed to methadone[1]
- 2022 study showed significantly lower rates of NOWS in babies exposed to buprenorphine than methadone.[2]

1. *Jones, H. et al. Neonatal Opioid Withdrawal Syndrome after Methadone or Buprenorphine Exposure. NEJM. Vol 363, 12/9/10 pp 2320-31.*
2. *Suarez et al. Buprenorphine versus Methadone for Opioid Use Disorder in Pregnancy NEJM Vol 387 12/1/2022 Pages: 2033-2044*

Medication therapy and pregnancy

- Most providers prefer to start with buprenorphine.
- However, if buprenorphine does not work for patient, it is essential to switch them to methadone quickly. Having the patient on a successful treatment for Opioid Use Disorder is the most essential part of treatment.
- “ANY OPIOID AGONIST THERAPY IS RECOMMENDED OVER UNTREATED OPIOID USE DISORDER IN PREGNANCY.” [1]

Suarez et al. Buprenorphine versus Methadone for Opioid Use Disorder in Pregnancy NEJM Vol 387 12/1/2022 Pages: 2033-2044

Neonatal Opioid Withdrawal Syndrome definition

- Neonatal Opioid Withdrawal Syndrome is highly treatable if diagnosed early, limited in duration, and, as far as we know, has limited long-term effects compared to the effects of untreated opioid use disorder.
- We should never use the possibility of NOWS to justify not properly treating opioid use disorder.
- We should also make sure that all pregnant women who are under treatment with medication facing the possibility of a baby with NOWS understand that they are doing the best possible thing for their baby.

Split dosing recommended for both buprenorphine and methadone during pregnancy

- A recent SAMHSA alert stressed the importance of split dosing of both methadone and buprenorphine during pregnancy to help manage the impact of metabolic changes.[1]

https://www.samhsa.gov/sites/default/files/split-dose-guidance-sotas-csat.pdf
Accessed 4/24/2023

Starting buprenorphine in a pregnant person

- Very little data or consensus recommendation
- Most clinicians are doing micro-dosing as an outpatient or rapid micro-dosing in an inpatient setting
- Macrodosing may be considered if the patient presents in active withdrawal

Access to MOUD while pregnant

- A 2020 study of obstetricians showed that only a third of obstetricians always recommend MOUD and a fourth never recommend it. [1]
- MOUD providers are far less likely to accept pregnant patients than non-pregnant patients. [2]
  - Methadone 97% vs 91%
  - Buprenorphine 83% vs 51%
- Maternal mortality reviews have found MOUD rates ranging from 0-60% for pregnant patients with OUD who died of overdoses.[3,4,5,6,7]

1. *Ko, J.Y., Tong, V.T., Haight, S.C. et al. Obstetrician–gynecologists' practice patterns related to opioid use during pregnancy and postpartum—United States, 2017. J Perinatol 40, 412–421 (2020).*
2. *Stephen W. Patrick et al. (2018): Barriers to accessing treatment for pregnant women with opioid use disorder in Appalachian states, Substance Abuse*
3. *Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240*
4. *Schiff et al. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018*
5. *Kountanis JA, Roberts M, Admon LK, et al. Maternal deaths due to suicide and overdose in the state of Michigan from 2008 to 2018. Am J Obstet Gynecol MFM 2023;5:100811.*
6. *Smid et al. Pregnancy-Associated Death in Utah: Contribution of Drug-Induced Deaths. Obstet Gynecol. 2019 Jun; 133(6): 1131-1140*
7. *Maryland Maternal Mortality Review. 2020 Annual Review. Health – General Article 13-1207 – 13-1208 and 13-1212.*

Morning sickness and methadone

- Both ondansetron and methadone cause QT prolongation, so use other treatments first.
- Lifestyle changes:
  - Small frequent meals
  - Avoid fluids with meals
  - Eat something before getting out of bed
  - Popsicles
- Ginger
- Pyridoxine, 10 mg + Doxylamine, 10mg tid

What about medically monitored withdrawal?

Medically monitored withdrawal

- **THERE ARE NO GOOD STUDIES ON MEDICALLY MONITORED WITHDRAWAL. THE AVAILABLE STUDIES ARE OF POOR TO FAIR QUALITY AND HAVE CONFLICTING RESULTS.**
- Recent meta-analysis reviewed 15 studies with 1,997 participants, of whom 1,126 went detoxification
  - Study quality was fair to poor with no randomized control trials
  - Mostly inpatient or residential setting with 3 incarceration studies
- Detoxification completion ranged from 9-100%.
- Relapse ranged from 0-100%
- 2 maternal deaths from postpartum overdose in one study

Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE, Meyer MC, Jones HE, Krans EE. Opioid Detoxification During Pregnancy: A Systematic Review. Obstet Gynecol. 2018 May;131(5):803-814. doi: 10.1097/AOG.0000000000002562. PMID: 29630016; PMCID: PMC6034119.

Medically monitored withdrawal

- Rates of fetal demise and birthweights were similar between women who underwent detoxification and comparison group
- Rates of neonatal abstinence syndrome ranged from 0-100%

Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE, Meyer MC, Jones HE, Krans EE. Opioid Detoxification During Pregnancy: A Systematic Review. Obstet Gynecol. 2018 May;131(5):803-814. doi: 10.1097/AOG.0000000000002562. PMID: 29630016; PMCID: PMC6034119.

Medically Monitored withdrawal

- No study of medically monitored withdrawal has examined maternal outcomes postpartum[1]

1. Jones et al. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. J Addict Med 2017 DOI 10.1097

Comorbid Medical Conditions Case Study: Pregnancy and Opioid Dependence

34 yo G2P1 had been on buprenorphine-naloxone for heroin use disorder. She moved away and got pregnant and weaned herself off the buprenorphine. Moved back and declined to restart buprenorphine because “I am not going to ever go back to drugs.” NSVD of healthy baby with negative urine drug screens throughout pregnancy. Died of an overdose about 1 year post-partum.

MATERNAL MORTALITY AND OPIOID USE DISORDER

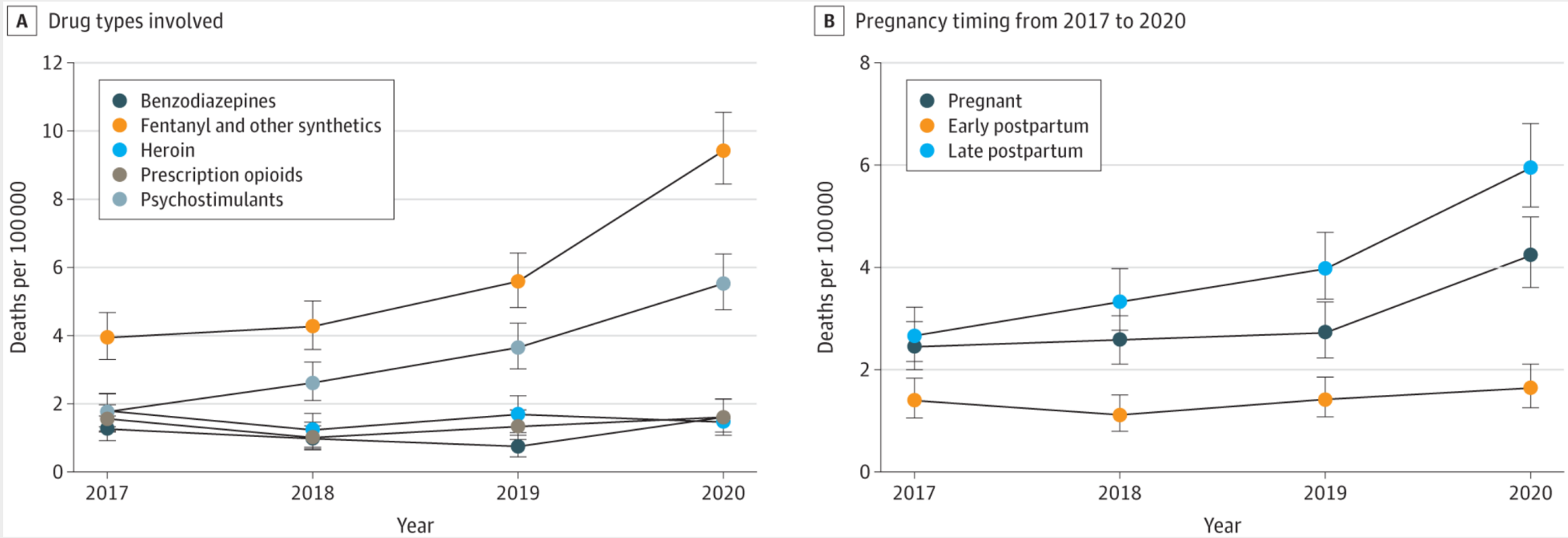
- Studies from Maryland[1], Tennessee[2], Colorado[3], Utah[4], Ohio[5], Massachusetts[6], California[7], Michigan[8], Virginia[9], Philadelphia[10], and New Mexico,[11] have found that postpartum overdose is one of the top causes of maternal mortality, causing 15-38% of deaths.

MATERNAL MORTALITY AND OPIOID USE DISORDER

1. Maryland Maternal Mortality Review. 2020 Annual Review. Health – General Article 13-1207 – 13-1208 and 13-1212.
2. Tennessee Maternal Mortality. Maternal Mortality in Tennessee 2021. 2023 Report to the Tennessee General Assembly Tennessee Department of Health | Family Health and Wellness | October 2023
3. Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240
4. Smid et al. Pregnancy-Associated Death in Utah: Contribution of Drug-Induced Deaths. Obstet Gynecol. 2019 Jun; 133(6): 1131-1140
5. Hall et al. Pregnancy-Associated Mortality Due to Accidental Drug Overdose and Suicide in Ohio, 2009-2018. Obstetrics and Gynecology. Vol 136, No 4 October 2020
6. Schiff et al. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018
7. Goldman-Mellor S, Margerison CE. Maternal drug-related death and suicide are leading causes of postpartum death in California. Am J Obstet Gynecol 2019;221:489.e1-9
8. :Kountanis JA, Roberts M, Admon LK, et al. Maternal deaths due to suicide and overdose in the state of Michigan from 2008 to 2018. Am J Obstet Gynecol MFM 2023;5:100811.
9. Virginia Maternal Mortality Review Team Annual Report. Report To The Governor And The General Assembly 2023
10. Mehta PK, Bachhuber MA, Hoffman R, Srinivas SK. Deaths From Unintentional Injury, Homicide, and Suicide During or Within 1 Year of Pregnancy in Philadelphia. Am J Public Health. 2016 Dec;106(12):2208-2210. doi: 10.2105/AJPH.2016.303473. Epub 2016 Oct 13. PMID: 27736205; PMCID: PMC5105012
11. New Mexico Maternal Mortality Review Committee. Pregnancy-Associated Deaths 2015 – 2018. New Mexico Department of Health.

From: **US Trends in Drug Overdose Mortality Among Pregnant and Postpartum Persons, 2017-2020**

JAMA. 2022;328(21):2159-2161. doi:10.1001/jama.2022.17045



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Maternal mortality and opioid use disorder

- Studies in New Mexico, Philadelphia, and Maryland found that about half of maternal deaths were connected to substance use.[1,2,3]
  - Maryland[3] and Tennessee[4] found that about 3/4 of deaths where SUD contributed had a co-occurring mental health problem.
- Around 40% are associated with serious mental illness.[1,2]
- About 20% are associated with Intimate Partner Violence.[1,2]
  - 54.3% of suicides and 45.3% of homicides involved IPV.[5]

1. *New Mexico Maternal Mortality Review Committee. Pregnancy-Associated Deaths 2015 – 2018. New Mexico Department of Health.*
2. *Mehta PK, Bachhuber MA, Hoffman R, Srinivas SK. Deaths From Unintentional Injury, Homicide, and Suicide During or Within 1 Year of Pregnancy in Philadelphia. Am J Public Health. 2016 Dec;106(12):2208-2210. doi: 10.2105/AJPH.2016.303473. Epub 2016 Oct 13. PMID: 27736205; PMCID: PMC5105012*
3. *Maryland Maternal Mortality Review. 2020 Annual Review. Health – General Article 13-1207 – 13-1208 and 13-1212.*
4. *Tennessee Maternal Mortality. Maternal Mortality in Tennessee 2021. 2023 Report to the Tennessee General Assembly Tennessee Department of Health | Family Health and Wellness | October 2023*
5. *Glazer, Kimberly B, and Elizabeth A Howell. "A way forward in the maternal mortality crisis: addressing maternal health disparities and mental health." Archives of women's mental health vol. 24,5 (2021): 823-830. doi:10.1007/s00737-021-01161-0*

Maternal mortality and opioid use disorder

- Suicide and homicide are also a substantial contributors to postpartum mortality.[1]
- Risk factors for postpartum opioid overdose, postpartum suicide, and pregnancy-associated homicide have significant overlap.[2]
- Three of the most common include depression, intimate partner[3] violence, and substance use disorder.[2]

1. *Campbell et al. Pregnancy- Associated Deaths from Homicide, Suicide, and Drug Overdose: Review of Research and the Intersection with Intimate Partner Violence. Journal of Women's Health. Volume 30, Number 2, 2021.*
2. *Mangla et al. Maternal self-harm deaths: an unrecognized and preventable outcome. American Journal of Obstetrics and Gynecology. October 2019.*
3. *Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240*

Maternal mortality and opioid use disorder

- Discontinuing psychiatric medications is associated with suicide.[2,3]
  - Roughly half of women on psychiatric medications discontinue them with pregnancy[1]
- Not taking or discontinuation of MOUD is a significant risk factor for overdose.[3,4]
  - Methadone discontinuation rate in the first six months postpartum was found to be 56% in one systematic review.[4]

1. *Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240*
2. *Smid MC, Maeda J, Stone NM, Sylvester H, Baksh L, Debbink MP, Varner MW, Metz TD. Standardized Criteria for Review of Perinatal Suicides and Accidental Drug-Related Deaths. Obstet Gynecol. 2020 Oct;136(4):645-653. doi: 10.1097/AOG.0000000000003988. PMID: 32925616; PMCID: PMC8086704.*
3. *Trost et al. Preventing Pregnancy-Related Mental Health Deaths: Insights From 14 US Maternal Mortality Review Committees, 2008–17 Health Affairs 2021 40:10, 1551-1559*
4. *Wilder et al Medication assisted treatment discontinuation in pregnant and postpartum women with opioid use disorder. Drug and Alcohol Dependence 149 (2015) 225–231*

Increased maternal mortality continued for many years after delivery in 2019 study

Mothers in Ontario and England with babies who had neonatal abstinence syndrome have a mortality rate that is over ten times as high as mothers who did not have an affected baby.

Roughly 1 in 20 mothers died over the next decade.

Top cause of death was unintentional injuries, but there were also high rates of murder and suicide, drug-related deaths, and unavoidable deaths.

Guttmann A et al. Long-term mortality in mothers of infants with neonatal abstinence syndrome: A population-based parallel-cohort study in England and Ontario, Canada. PLoS Med 16(11): e1002974. November 26, 2019.

What can be done

- Screen for depression postpartum. Use Edinburgh Postpartum Depression Screen or another tool.
- Screen for relapse.
- Talk about seatbelts.
- Distribute Narcan.
- Make sure every postpartum patient has a follow up appointment with primary care, postpartum care, and addiction medicine.
- Use home nursing liberally.

Neonatal Opioid Withdrawal Syndrome

Neonatal Opioid Withdrawal Syndrome definition

- Neonatal Opioid Withdrawal Syndrome = physical withdrawal.
- Neonatal Opioid Withdrawal Syndrome baby is ≠ addicted to drugs.

Clinical definition of opioid withdrawal in the neonate from the AAP

- Presence of clinical elements 1 and 2
- (1)In utero exposure to opioids with or without other psychotropic substances (recommended to be collected via confidential maternal self-report; toxicology testing also acceptable with maternal informed consent)
- (2)Clinical signs characteristic of substance withdrawal; any 2 of the following 5 signs qualify:
  - Excessive crying (easily irritable)
  - Fragmented sleep (<2-3 h after feeding)
  - Tremors (disturbed or undisturbed)
  - Increased muscle tone (stiff muscles)
  - Gastrointestinal dysfunction (hyperphagia, poor feeding, feeding intolerance, loose or watery stools)

Jilani et al. Standardizing the Clinical Definition of Opioid Withdrawal in the Neonate. The Journal of Pediatrics. September/October 2020 - Volume 14 - Issue 5

Neonatal Opioid Withdrawal Syndrome

- Neonatal Opioid Withdrawal Syndrome is highly treatable if diagnosed early, limited in duration, and, as far as we know, has limited long-term effects compared to the effects of untreated opioid use disorder.
- We should never use the possibility of NOWS to justify not properly treating opioid use disorder.
- We should also make sure that all pregnant women who are under treatment with medication facing the possibility of a baby with NOWS understand that they are doing the best possible thing for their baby.

Non-pharmacologic treatment of Neonatal Opioid Withdrawal Syndrome

- Non-pharmacologic treatment includes the following:
  - Small, frequent feeds.
  - Quiet, dim light.
  - Swaddling or skin-to-skin.
  - Prenatal education for parents.
- Studies from Dartmouth [1] and Yale [2] showed substantial improvements in cost and length of stay using non-pharmacologic treatment.

1Holmes et al. Rooming-In to Treat Neonatal Opioid Withdrawal Syndrome: Improved Family-Centered Care at Lower Cost. Pediatrics 2016; pp 2015-2029

2Grossman et al. An Initiative to Improve the Quality of Care of Infants with Neonatal Opioid Withdrawal Syndrome. Pediatrics 2017;139(6)

Breastfeeding

- The Academy of Breastfeeding Medicine, the American Academy of Pediatrics, the American College of OB-GYN, the Substance Abuse and Mental Health Services Administration, and the American Society for Addiction Medicine recommend breastfeeding for women with substance use disorder.[1,2,3,4,5]
  - This includes women on MOUD.
- The recommendations from the Academy of Breastfeeding Medicine are the most recent. They recommend mothers breastfeed if they have discontinued use by the or during the delivery hospitalization.[2]
  - Women who were using at the time of delivery or who relapse should express and discard milk. There should be a multidisciplinary discussion about risks and benefits in this situation and when to start or restart breastfeeding.

1. *Jansson, L. et al, Methadone Maintenance and Breastfeeding in the Neonatal Period PEDIATRICS Vol. 121 No. 1 January 2008, pp. 106-114*
2. *Harris et al. Academy of Breastfeeding Medicine Clinical Protocol #21: Breastfeeding in the Setting of Substance Use and Substance Use Disorder (Revised 2023). BREASTFEEDING MEDICINE Volume 18, Number 10, 2023*
3. *Substance Use, Misuse, and Use Disorders During and Following Pregnancy, with an Emphasis on Opioids. ASAM Policy Statement. January 18, 2017*
4. *Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. SAMHSA. HHS Publication No. (SMA) 18-5054*
5. *ACOG Committee Opinion. Opioid Use and Opioid Use Disorder in Pregnancy. Number 711. August 2017*

Child protective services and mental health

Study in Manitoba showed that losing custody of a child-to-child protective services is associated with significantly worse maternal mental health outcomes than experiencing the death of a child

Risk of depression was 1.90 times greater for women who had lost a child to child protective services.

Risk of substance use was 8.54 times greater for women who had lost a child to child protective services.

Wall-Wieler, Elizabeth et al. Maternal Mental Health after Custody Loss and Death of a Child: A Retrospective Cohort Study Using Linkable Administrative Data. The Canadian Journal of Psychiatry. 2018, Vol. 63(5) 322-328.

To Call Child Protective Services or not

- Know your state laws and hospital policies
- Discuss child protective service involvement during pregnancy
  - What will trigger a referral
  - What will likely happen with a referral
- Discuss with your patient what to do if a referral is made:
  - Be honest with child protective services
  - Have a plan for SUD treatment
  - Have a plan to ensure the baby is safe

In Summary

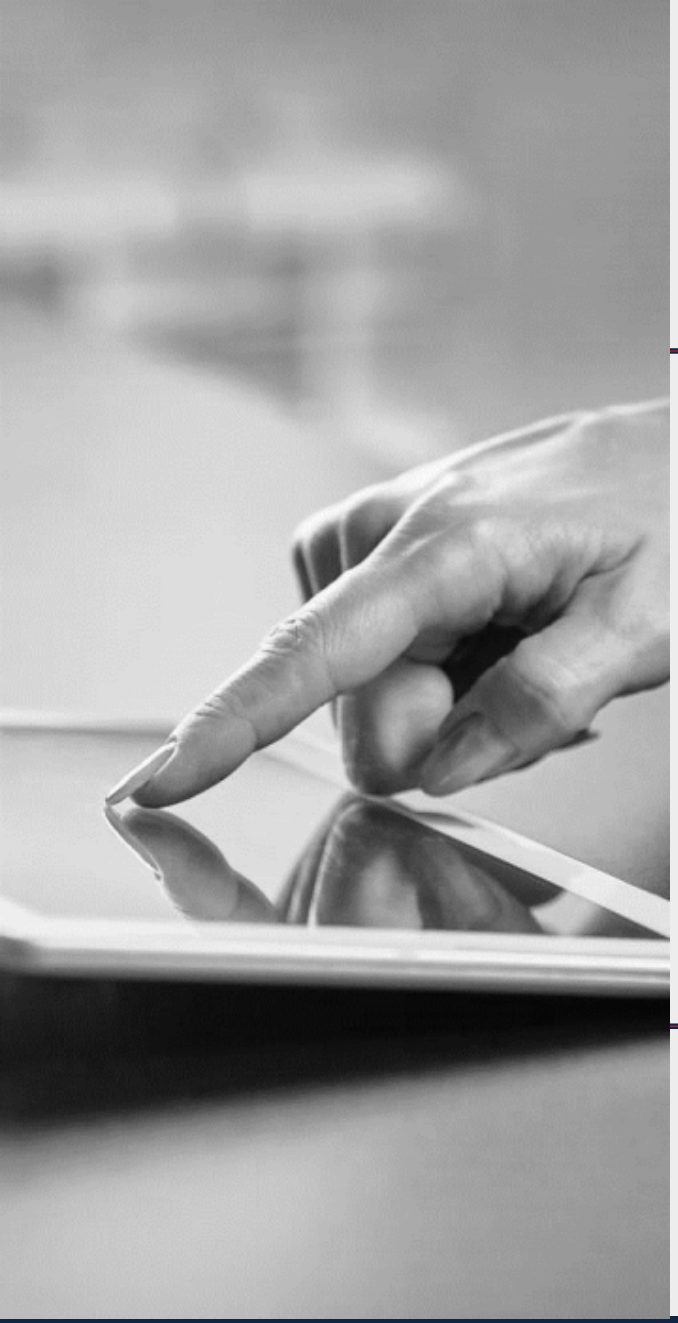
1. Alcohol and tobacco are the most dangerous drugs for the fetus in pregnancy.
2. Medication treatment is recommended for opioid use disorder in pregnancy.
3. The postpartum period and after is a high-risk time for relapse and death in birthers with SUD.
4. Use non-medical treatments first for neonatal opioid withdrawal syndrome.

Which of the following is correct about opioid use disorder and pregnancy?

A. The highest risk time for relapse is postpartum
B. Medically-assisted withdrawal should be done during the second trimester to reduce the risk of neonatal opioid withdrawal syndrome
C. C-section is recommended for anyone actively using opioids
D. There is a high risk of congenital anomalies with opioid use

Which of the following is an example of an epigenetic phenomenon?

A. Children in a household with high levels of alcohol consumption are more likely to drink alcohol
B. Children in a high-stress environment are more likely to have certain genes expressed, some of which will predispose them to substance use disorder
C. Some alleles of the ADH2 gene will cause flushing and nausea with alcohol ingestion, and thus are protective against alcohol use disorder
D. People who are ultra rapid metabolizers of methadone don't do well on it.



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