Substance Use Disorder and Its Effects on Pregnancy and Newborns December 8, 2021

Leslie Hayes, MD

No disclosures

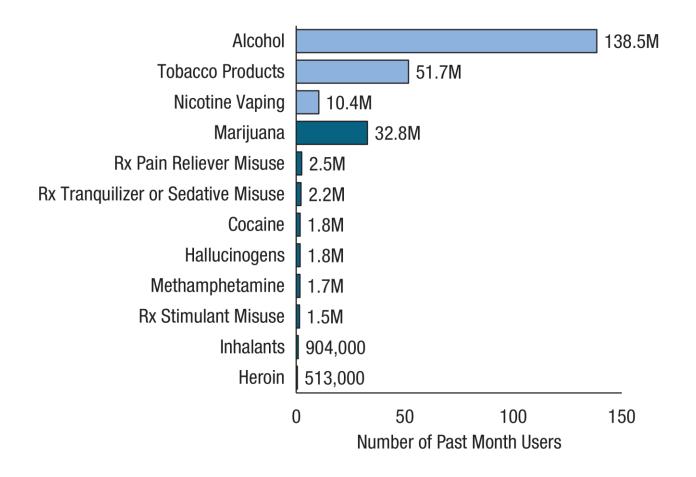
A few words on terminology

- I will use substance use disorder in this presentation, rather than addiction. Addiction tends to be somewhat stigmatizing, and the word addict is quite stigmatizing. The preferred term is person with substance use disorder.
 - A specific substance use disorder will be referred to as heroin use disorder or alcohol use disorder.
- If at all possible, you should never use the terms clean and dirty, especially not to refer to a person.
- In general, in speaking about people with substance use disorder, it is good to remember that these are people with an illness and often people who have been through a significant amount of trauma. Compassion and respect will go a long way.

General information on substance use disorder

- Substance use disorder is often defined by what we refer to as the 4 C's.
- Compulsion
 - People with SUD have compulsions to use the substance.
- Cravings
 - People with SUD have cravings around the substance.
- Consequences
 - People with SUD continue to use despite adverse consequences.
- Control
 - People with SUD have lost control over their use.

Past Month General Substance Use and Nicotine Vaping: Among People Aged 12 or Older; 2020



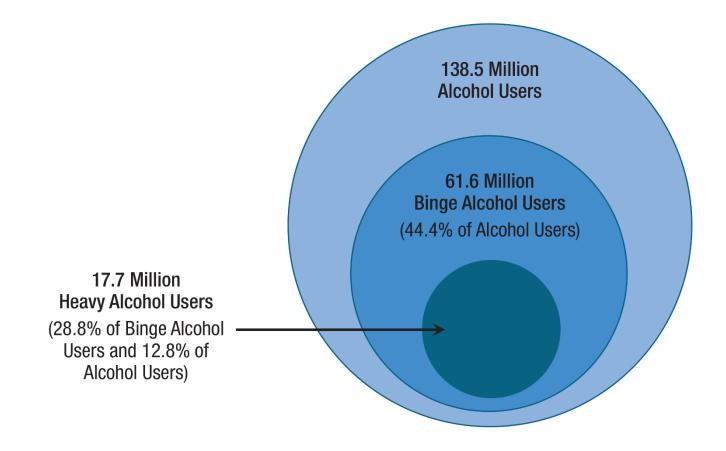
Rx = prescription.

Note: General Substance Use includes any illicit drug, alcohol, and tobacco product use. Tobacco products are defined as cigarettes, smokeless tobacco, cigars, and pipe tobacco.

Note: The estimated numbers of current users of different substances are not mutually exclusive because people could have used more than one type of substance in the past month.

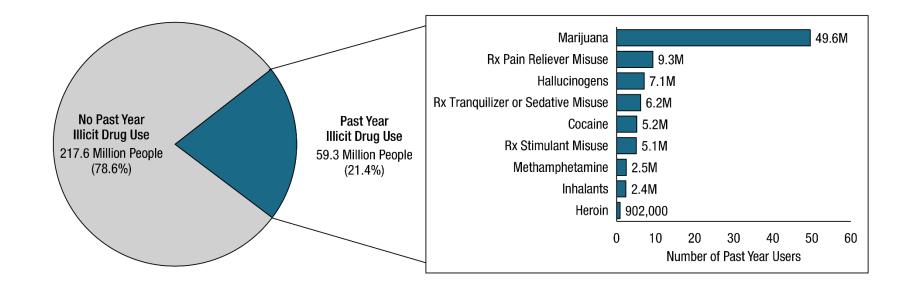


Current, Binge, and Heavy Alcohol Use: Among People Aged 12 or Older; 2020

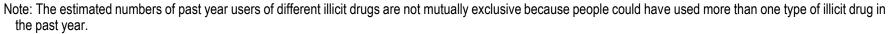




Past Year Illicit Drug Use: Among People Aged 12 or Older; 2020

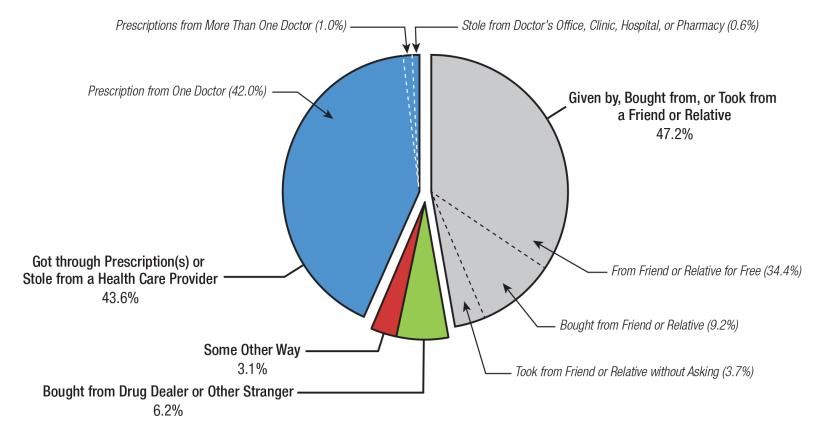


Rx = prescription.





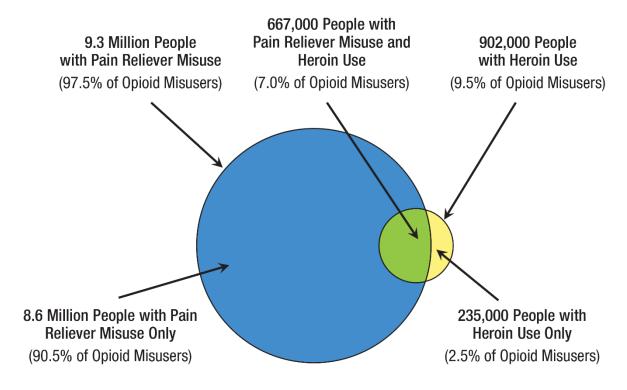
Source Where Pain Relievers Were Obtained for Most Recent Misuse: Among People Aged 12 or Older Who Misused Pain Relievers in the Past Year; 2020



9.3 Million People Aged 12 or Older Who Misused Pain Relievers in the Past Year



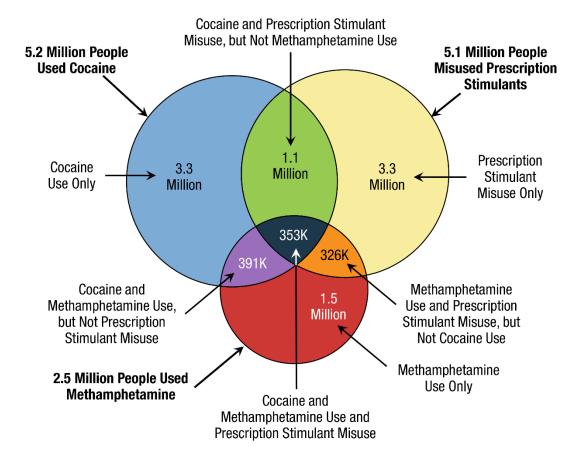
Past Year Opioid Misuse: Among People Aged 12 or Older; 2020



9.5 Million People Aged 12 or Older with Past Year Opioid Misuse



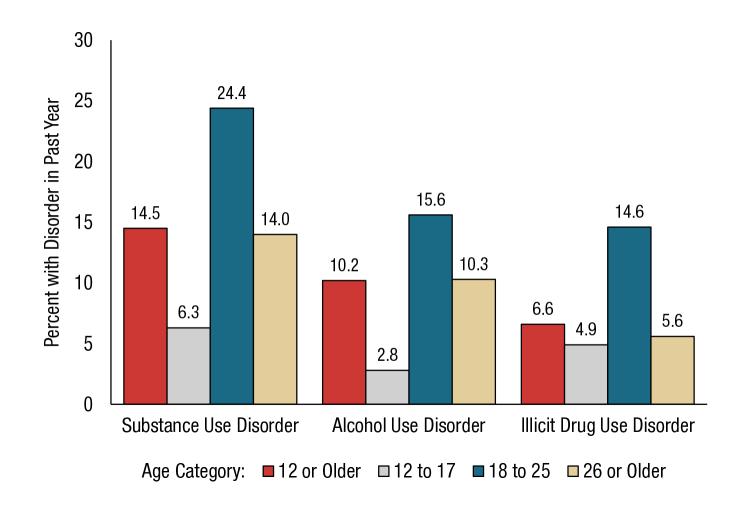
Past Year Central Nervous System (CNS) Stimulant Misuse: Among People Aged 12 or Older; 2020



10.3 Million People Aged 12 or Older with Past Year CNS Stimulant Misuse

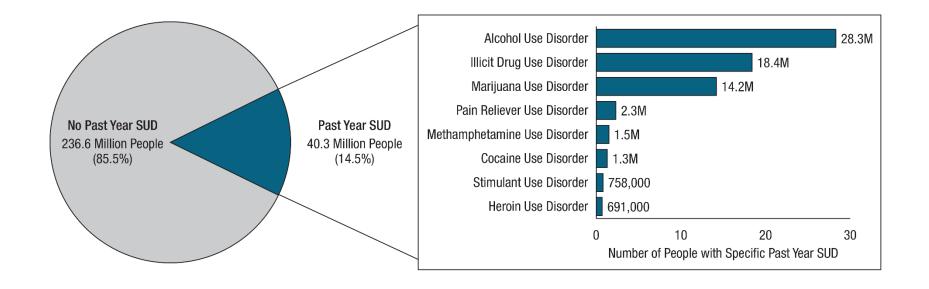


Substance Use Disorder, Alcohol Use Disorder, and Illicit Drug Use Disorder in the Past Year: Among People Aged 12 or Older; 2020



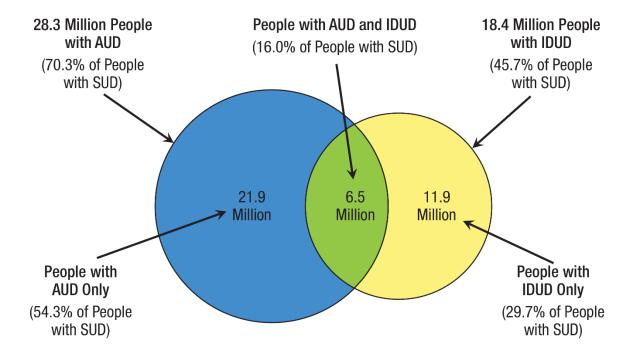


People Aged 12 or Older with a Past Year Substance Use Disorder (SUD); 2020





Alcohol Use Disorder (AUD) and Illicit Drug Use Disorder (IDUD) in the Past Year: Among People Aged 12 or Older with a Past Year Substance Use Disorder (SUD); 2020



40.3 Million People Aged 12 or Older with Past Year SUD



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

Definition of terms for providers not regularly doing obstetric care

- IUGR = Intrauterine growth restriction = fetal weight by ultrasound < 10th percentile
- SGA = small for gestational age = weight of newborn baby < 10th percentile for gestational age
- 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 #1:

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.



Case study #1:

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 #2

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 egnatal Opioid Withdrawal Syndrome at birth. Currently 7 years old, doing well.



Gender differences in substance use disorder

Gender differences and substance use disorder

 Women are more likely to be introduced to injection drug use by their male sexual partner, whereas men are more likely to be injected by a friend.¹

^{1.} Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355

Gender differences and substance use disorder

- Women are more likely to use prescription opioids to selfmedicate for anxiety or stress.¹ Men are more likely to use prescription opioids for experimentation or to get high.²
- Women are more likely to drink in response to stress and negative emotions whereas men are more like to drink to enhance positive emotions or conform to a group.³

^{1.} Final Report: Opioid Use, Misuse, and Overdose in Women.. Office on Women's Health. July 19, 2

^{2.} Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355

Women and violence and SUD

- Girls with a history of childhood sexual abuse are 3 times as likely to develop an addictive disorder as girls without that history.¹
- One study showed lifetime intimate partner violence victimization was reported by 46.7% of women and 9.5% of men entering SUD treatment.
- Zweben. Special Issues in Treatment: Women in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 p. 532
- 2. Schneider et al. Violence and Victims, Volume 24, Number 6, 2009 744 © 2009 Prevalence and Correlates of Intimate Partner Violence Victimization Among Men and Women Entering Substance Use Disorder Treatment

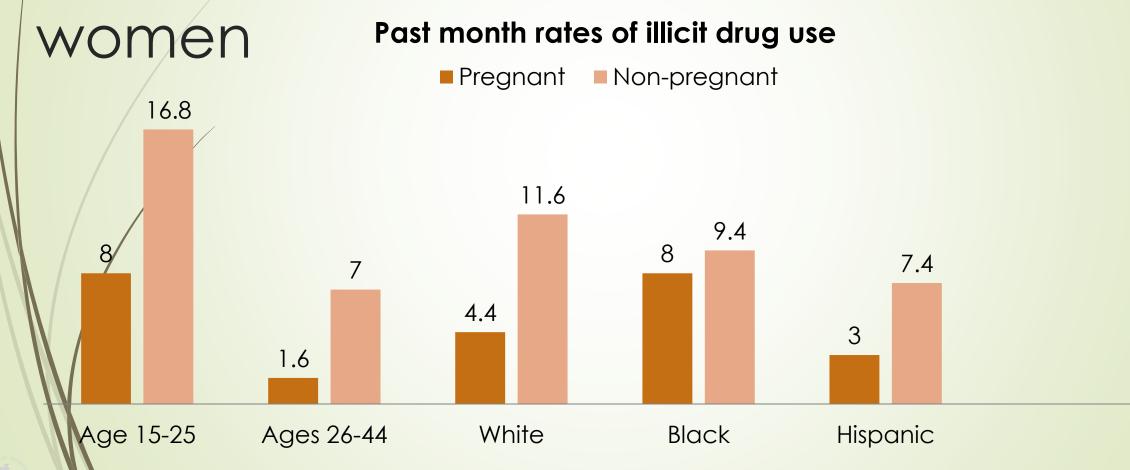
Substance use in pregnancy

- Use of alcohol, tobacco, and drugs during pregnancy is the leading preventable cause of mental, physical, and psychological impairments in children.
- Between 1998-2011, there was a 127% increase in opioid-dependent pregnant women presenting for delivery.¹
- Opioid-dependent pregnant women have an unintended pregnancy rate of 86%.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. 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

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

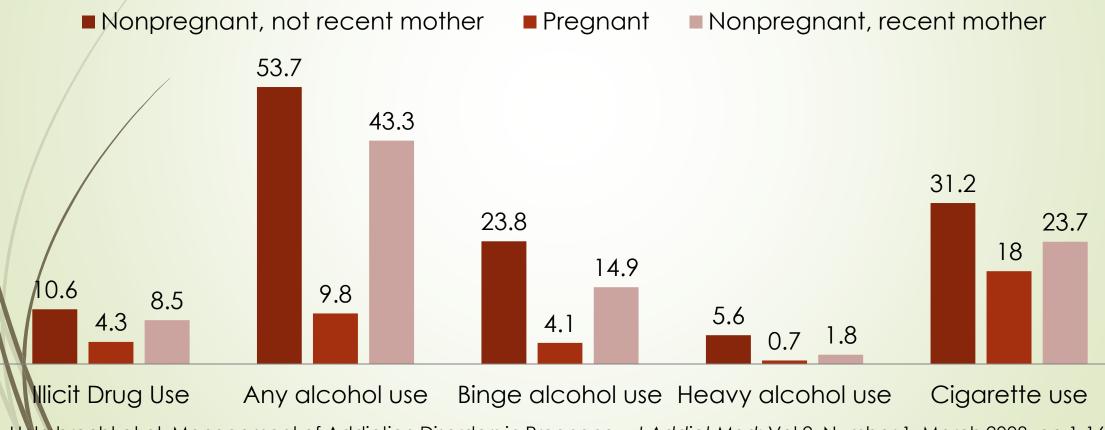
Percentages of past-month illicit druguse in pregnant and non-pregnant



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

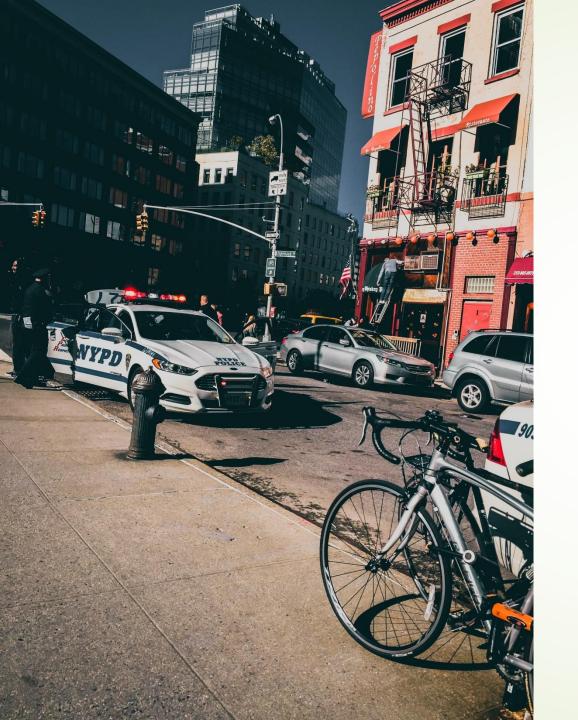




Helmbrecht et al. Management of Addiction Disorders in Pregnancy. J Addict Med; Vol 2, Number 1, March 2008, pp 1-16

Implications of opioid use disorder with pregnancy

- 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.



Case study #3

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.

Case study #4

23 yo G2P1 presented using heroin. \$tarted on buprenorphine with good response. Metabolite testing confirmed patient was taking medication. Incarcerated. Patient found with large quantities of methamphetamine and heroin and drug paraphernalia in her cell/Jail wished to stop buprenorphine. Told it needed to be continued. She was placed in solitary because of this.



 What are psychosocial implications of substance use disorder with pregnancy?

implications of substance use disorder with pregnancyCo-occurring disorders

- - Depression.
 - Both substance use disorder and depression cause poor self-care.
 - Domestic violence
 - Second-leading cause of trauma-related death in pregnancy.

Implications of substance use disorder with pregnancy

- Psychosocial:
 - Most mothers have a high motivation to change.
 - Lot of guilt/shame for many women
 - Legal implications around custody of baby and older children
 - Most substance-using pregnant women 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 abuse drugs start using because their partners abuse drugs. If they are still with that partner, it can be difficult for them to quit unless he quits as well.

Case Study #5

25 yo G2P1 presents at 26 weeks, stating, "I'm addicted to heroin." 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 heroin 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 women 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
- Women 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 Imapce 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

Medication therapy and pregnancy

- Medication therapy can be done with either methadone or buprenorphine.
 - Methadone has been used longer, but most providers prefer to start with buprenorphine if available.
- Data regarding naltrexone is limited, but it is probably safe to continue in pregnancy if patient wishes. It should not be started in pregnancy.

Buprenorphine vs methadone in Pregnancy

- 2010 NEJM study showed significantly less neonatal abstinence syndrome in buprenorphine group than the methadone group¹
 - Required less morphine. Neonates exposed to buprenorphine needed 89% less morphine than neonates exposed to methadone.
 - Shorter hospital stay. Neonates exposed to buprenorphine spent 43% less time in the hospital.
 - Shorter duration of treatment

^{1.} Jones, H. et al. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. *NEJM*. Vol 363, 12/9/10 pp 2320-31

Buprenorphine vs methadone in Pregnancy

2016 UC-Davis study split dosage of methadone for all pregnant women. It showed much better outcomes, with rate of neonatal abstinence syndrome = 29%.¹

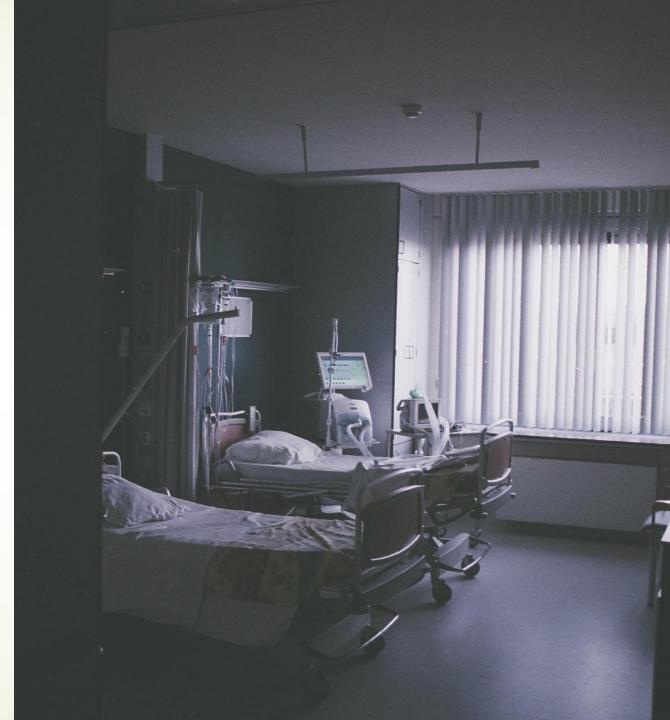
1. McCarthy, J et al. The Effect of Methadone Dose Regimen on Neonatal Abstinence Syndrome. *J Addict Med;* Vol 9, Number 2, March/April 2015. pp 105-110.

Maternal methadone dose does not correlate with severity of NOWS. 1,2

- 1. Weaver et all. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Kies et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2014 p. 1260
- Cleary et al. Methadone dose and neonatal abstinence syndromesystematic review and meta-analysis. <u>Addiction</u> 2010 Dec;105(12):2071-84

What about medically monitored withdrawal?

Patient is a 36 yo G2P1 at 36 weeks. Wanted to start on buprenorphine. Told to stop heroin 12 hours before coming into hospital to start. She stopped 48 hours before. Came into hospital in florid withdrawal. Noted to be having contractions. Cervix was completely dilated on exam. Delivered 30 minutes later.



Medically Assisted Withdrawal

- Some studies have shown it can be done with low risk of fetal mortality^{1,2}
 - However, fetal monitoring only shows life-threatening distress³
 - It does not show chronic stress which may lead to epigenetic changes or increased risk of substance use disorder in fetus⁴
 - Dashe et al. Opioid detoxification in pregnancy. Obstetrics and Gynecology. Volume 92, Issue 5, November 1998, pp 854-858
 - 2. Bell et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6
 - 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
 - 1. Ibid.

Medically Assisted withdrawal

- Most studies show a high rate of relapse to opioid^{1,2}
 - Rates range from 17-96%^{3,4,5}
 - Relapse rate is lower on medication-assisted therapy⁶

- 1. Dashe et al. Opioid detoxification in pregnancy. Obstetrics and Gynecology. Volume 92, Issue 5, November 1998, pp 854-858
- 2. Bell et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6
- 3. Dashe et al. pp. 854-858
- Jones et al. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. J Addict Med 2017 DOI 10.1097 Accessed 2/18/17
- 5. Bell et al. Ibid.
- Jones et al. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. J Addict Med 2017 DOI 10.1097

Medically Assisted Withdrawal

- Although currently, about 50% of cases of neonatal opioid withdrawal syndrome result from medicationassisted therapy, medically assisted withdrawal does not decrease rates of NOWS because of the high rates of relapse¹
- No study of medically-assisted withdrawal has examined maternal outcomes postpartum²
 - Jones et al. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. J Addict Med 2017 DOI 10.1097
 - 2. Ibid.

Postpartum period

Post-partum mothers and substance use disorder

- High risk of relapse. Encourage them to continue with recovery behaviors and medication.
- Often, do not have good parenting skills. Consider home nursing, parenting classes.
- May have a more fussy baby than average need a lot of support.

34 yo G2P1 had been on buprenorphinenaloxone 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 bøby with negative urine drug screens throughout pregnancy. Died of an verdose about 1 year post-partum.



Maternal mortality and opioid use disorder

- Maternal death = death of a woman while pregnant or within 42 days of termination of pregnancy from any cause related to or aggravated by pregnancy or its management but not from accidental or incidental causes.
- Pregnancy-associated death = death of a woman while pregnant or within 365 days of pregnancy conclusion, regardless of cause
- Pregnancy-related death = death of a woman while pregnant or within 365 days of pregnancy conclusion from any cause related to or aggravated by her pregnancy or its management but not from accidental or incidental causes

Maternal mortality and opioid use disorder

Studies from Maryland, Tennessee, Colorado, Utah, Ohio, and Massachusetts have found that postpartum overdose is one of the top causes of maternal mortality, causing 15-33% of deaths.

- 1. <a href="https://phpa.health.manyland.gov/mch/Documents/Health-General%20Article%20%C2%A713-1207.%20Annotated%20Code%20of%20Manyland%20-%20119%018-20App.ndf%018-proff%018-pr
- 2. Tennessee Maternal Mortality Review of 2Maryland Maternal Mortality Review. 2014 Annual Report. MD Dept of Health and Mental Hygiene. Prevention and Health Promotion Administration.
- 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
- Smid et al. Pregnancy-Associated Death in Utah: Contribution of Drug-Induced Deaths. Obstet Gynecol. 2019 Jun; 133(6): 1131-1140
- 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



Maternal mortality and opioid use disorder

- Suicide is also a substantial contributor to postpartum mortality.¹
- Risk factors for postpartum opioid overdose and postpartum suicide have significant overlap.²
- Three of the most common include depression, intimate partner violence, and substance use disorder.
- Screen for depression postpartum. Use Edinburgh Postpartum Depression Screen or another tool.

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.

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.



Birth Defects with substances

Birth defects with substances

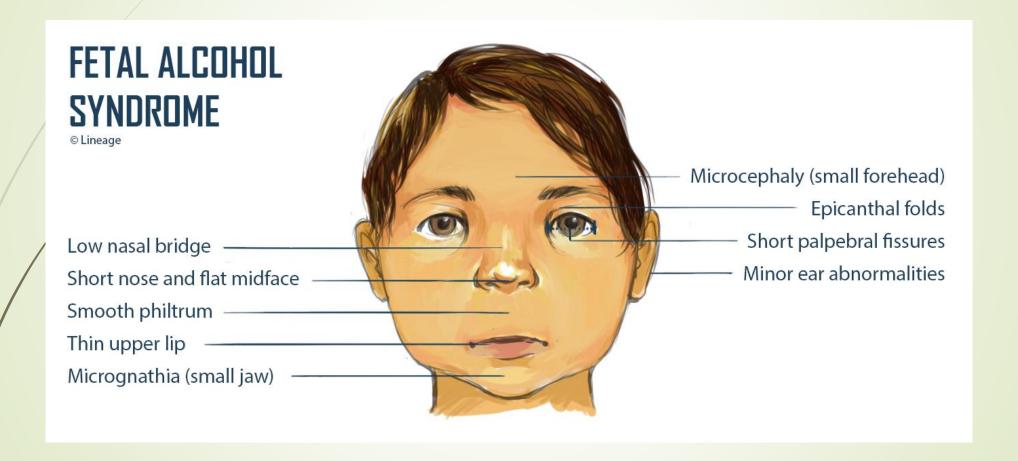
 The drug with the most teratogenic potential is alcohol.¹

 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





- Incidence of fetal alcohol syndrome = 6-9/1000 children¹
- Incidence of partial fetal alcohol syndrome = 11-17 per 1000 children²
- Incidence of fetal alcohol spectrum disorder = 24-48 per 1000 children³
 - 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. 1319

Fetal alcohol spectrum disorders

- Fetal alcohol syndrome with and without confirmed maternal alcohol exposure
- Partial fetal alcohol syndrome: face and growth retardation or structural brain disorders
- Alcohol related brain damage
- Alcohol related neurodevelopmental disorder– complex pattern of behavior or cognitive abnormalities

- Incidence of fetal alcohol syndrome = ½ 2/1000 live births¹
- Incidence of fetal alcohol spectrum disorder up to 1% of live births¹
 - Recent epidemiological studies suggest combined prevalence of FAS/FASD of up to 5% of US population. Diagnosis quite difficult without facial abnormalities.²

- 1. Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Kies et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2014 p. 1260
- 2. Grant et al. The Impact of Prenatal Alcohol Exposure on Addiction Treatment. J Addict Med. Volume 7, Number 2, March/April 201

- Small amounts of prenatal alcohol exposure may harm some fetuses, while others may be impervious to high levels.¹
- Women at highest risk of producing a child with FAS seem to be those who binge drink.²

1. Grant et al. The Impact of Prenatal Alcohol Exposure on Addiction Treatment. J Addict Med. Volume 7, Number 2, March/April 2013 2. Ibid

- IQ generally > 70 with FAS, so it is not classified as an intellectual disability.
 - Learning problems and functional deficits quite common.
 - Executive functioning is significantly affected: Inhibition, emotional control, initiating tasks, planning/organization, self-monitoring.
- Facial features and growth deficits may attenuate over time.
- People with FASD are at high risk of Substance Use Disorder.
 - Children with FASD living in a stable and nurturing home for most of childhood strongly protected against Alcohol Use Disorder.

Grant et al. The Impact of Prenatal Alcohol Exposure on Addiction Treatment. J Addict Med. Volume 7, Number 2, March/April 2013

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
- 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

Marijuana and pregnancy

No teratogenic pattern to cannabis.¹

Weaver et al. Ibid.

- Recent meta-analyses have disagreed as to whether cannabis affects birthweight.^{2,3,}
 - The meta-analysis that adjusted for tobacco and alcohol use did not show an effect.²
- There do seem to be neurodevelopmental deficits associated with cannabis use.⁴

- 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
- 2. 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.
- 3. 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.00000000001649.

Methadone and buprenorphine

No known risk of increased birth defects associated with the use of buprenorphine or methadone¹

Neonatal opioid withdrawal syndrome

30 yo G3P3, stable social situation, no medical problems, delivered 2 days prior by C/S. Urine drug screen on admission had been positive for opiates, but not addressed. At 48 hours, baby went into withdrawal. Mother initially admitted to having taken "a Lortab" from aunt, then on questioning, admitted to taking regularly. Baby treated with methadone, did well. Mother remorseful, seemed genuinely surprised that Lortab could harm baby.

Patient is a 28yo G4P4, stable on methadone for several years. She was on 140 mg of methadone at the time of delivery. Baby was born by vaginal delivery. We watched for several days. Baby breastfed well, had normal tone, slept for 3 hours at a time, and was calm and happy in mother's arms. Discharged home without any problems.

Patient is a newborn baby born to a G1P0 who had gotten on methadone during her pregnancy because she had been using heroin when she got pregnant. She had done well with the pregnancy. After the baby was born, he developed increasing fussiness and had trouble breastfeeding. By day 3 of life, he was inconsolable at times and sleeping poorly. He was started on morphine with immediate improvement. He required six days of medication and went home afterwards. He is currently in first grade and both mother and baby are doing well.

Neonatal Opioid Withdrawal Syndrome

- Neonatal Abstinence Syndrome or Neonatal Opioid Withdrawal Syndrome is poorly-defined.
 - Different authors use the term to mean
 - Babies who have been exposed to opioids in pregnancy
 - Babies who show symptoms of opioid withdrawal
 - Babies who require treatment with medication
- In addition, treatment is not standardized, so it is very hard to compare studies as different institutions have vastly different lengths of stay and numbers of babies requiring medication.

Neonatal opioid withdrawal syndrome definition

- Neonatal opioid withdrawal syndrome = physical withdrawal.
- Neonatal opioid withdrawal syndrome ≠
 baby is addicted to drugs.

Case Study #11

• 12 yo boy came with his mother to a community session on pregnancy and opioid use disorder. He had had neonatal withdrawal himself. I mentioned in the talk that neonatal withdrawal did not mean an addicted baby. Afterward, he told his mother that he had always thought he was an addict because he had been born addicted, but now he realized he wasn't an addict, and he wanted to pursue schooling so that he could help people who were addicted. The term NOWS is often used interchangeably with the more established term, neonatal abstinence syndrome (NAS). More recently, the term NOWS has been used to refer to infants born to opioid-using mothers, whereas NAS has been used by some professionals to refer to infants born to mothers with polysubstance use.

Situations in which a baby can develop neonatal opioid withdrawal syndrome

- 1. Mother using methadone** or buprenorphine for opiate use disorder
- 2. Mother using opiate pain pills for chronic pain
- 3. Mother using methadone** or buprenorphine + illicit opiates
- 3. Mother with untreated opiate use disorder*
- **most severe neonatal opioid withdrawal syndrome
- *next most severe

Epidemiology of Neonatal Opioid Withdrawal Syndrome

- From 2000 to 2016, the incidence of NOWS increased from 1.2 to 8.8 per 1000 hospital births.
 - These increases have been steeper in rural and tribal areas and among infants enrolled in the Medicaid

Epidemiology of Neonatal Opioid Withdrawal Syndrome

- According to CDC data, among 28 states with available data, the overall incidence of NOWS increase 300% from 1.5/1000 births in 1999 to 6.0/1000 live births in 2013.¹
 - Lowest incidence in Hawaii at 0.7/1000 hospital births.
 - Highest incidence in West Virginia at 33.4/1000 hospital births.
 - New Mexico was fifth at 8.5/1000 hospital births.

Social determinants of neonatal opioid withdrawal syndrome

Long-term unemployment and a shortage of mental health clinicians are associated with higher rates of neonatal abstinence syndrome on a county level.¹

Poverty is also associated with excess length of stay for NOWS.²

States with potentially punitive policies toward pregnant women around substance use (policies considering it child abuse or neglect) showed a significant increase in rates of NOWS in the years after the policies were put in place.³

- 1. Patrick, Stephen et al. Association Among County-Level Economic Factors, Clinician Supply, Metropolitan or Rural Location, and Neonatal Abstinence Syndrome. JAMA. 2019; 321 (4): 385-393.
- Vesoulis et al. Poverty and Excess Length of Hospital Stay in Neonatal Opioid Withdrawal Syndrome. J. Addict Med. Volume 14, Number 2, March/April 2020
- 3. Flaherty, Laura et al. Association of Punitive and Reporting State Policies Related to Substance Use in Pregnancy With Rates of Neonatal Abstinence Syndrome. JAMA Network Open. 2019; 2(11): e1914078.



Neonatal opioid withdrawal syndrome symptoms

- Gastrointestinal symptoms:
 - emesis
 - diarrhea
 - poor feeding babies often have very disorganized suck
- Autonomic over-reactivity
 - sneezing
 - rhinorrhea
 - Yawning
 - tachycardia
 - increased metabolic rate

Neonatal opioid withdrawal syndrome symptoms

- CNS symptoms
 - Irritability
 - increased tone
 - high-pitched cry
 - hypersensitivity to stimuli
 - seizures if untreated
- All of the above can lead to significant weight loss.
- The diarrhea and excessive movement can also cause severe excoriation the perianal region.

Neonatal opioid withdrawal syndrome symptoms

- Babies often have poor weight gain due to all of the above
- Symptoms are traditionally measured using Finnegan score

Neurochemistry of NOWS

- The most important center of activity in opioid withdrawal is the locus ceruleus of the pons.
 - This is the noradrenergic nucleus of brain.
 - It is very sensitive to opioid status.
- A lack of opioids causes increased production of norepinephrine, which causes most of the symptoms of NOWS.

Finnegan Scale

SYSTEM	SIGNS AND SYMPTOMS SCO	ORE	Par.			6W			COMMENTS
'RAL NERVOUS SYSTEM DIST	Continuous High Pitched (or other) Cry Continuous High Pitched (or other) Cry	2							Daily Weight
	Sleeps <1 Hour After Feeding	3							
	Sleeps <2 Hours After Feeding	2							
	Sleeps <3 Hours After Feeding	1							
	Hyperactive Moro Reflex	2							
	Markedly Hyperactive Moro Reflex	3							
	Mild Tremors Disturbed	1							
	Moderate-Severe Tremors Disturbed	2							
	Mild Tremors Undisturbed	3							
	Moderate-Severe Tremors Undisturbed	4					 42		
	Increased Muscle Tone	2							
	Excoriation (Specific Area)	1							
	Myoclonic Jerks	3							
	Generalized Convulsions	5		 	1				
IETABOLIC/VASOMOTOR/RESPIRATOR DISTURBANCES	Sweating	1		 					
	Fever 100.4*-101*F (38*-38.3*C)	1							
	Fever > 101°F (38.3°C)	2							
	Frequent Yawning (>3-4 times/interval)	1							
	Mottling	1							
	Nasal Stuffiness	1							
	Sneezing (>3-4 times/interval)	1							
	Nasal Flaring	2		 _					
	Respiratory Rate >60/min	1							
	Respiratory Rate > 60/min with Retractions	2							
GASTRO-INTESTIONAL DISTURBANCES	Excessive Sucking	1							
	Poor Feeding	2							
	Regurgitation	2							
	Projectile Vomiting	3							
	Loose Stools	2							
	Watery Stools	3							
	TOTAL SCORE								

Finnegan Scale

- Calculate the Finnegan Scale when baby is at their best.
- Generally, the indication to start morphine is any 3 combined scores
 >= 24.

Most important symptoms

- Can baby eat?
 - Can baby take in at least an ounce per feed or breastfeed for at least 10 minutes?
- Can baby sleep?
 - Can baby sleep undisturbed for at least an hour?
- Can baby be consoled?
 - Can crying baby be consoled in 10 minutes or less?
- Babies who were measured on these criteria rather than the Finnegan or similar scales were given significantly less morphine with decreased length of stay and no adverse outcomes.¹

Treatment of neonatal opioid withdrawal syndrome

Non-pharmacologic treatment

Non-pharmacologic interventions are first-line treatment of NOWS.¹

^{1.} Grossman et al. Neonatal Abstinence Syndrome: Time for a Reappraisal. Hospital Pediatrics Volume 7, Issue 2, February 2017 pp 115-116

Non-pharmacologic treatment of neonatal opioid withdrawal syndrome

- Dartmouth study showed use of non-pharmacologic treatments decreased percentage of babies needing treatment with morphine from 46% to 27%.
- Length of stay decreased from 16.9 days to 12.3 days.
- Average hospital cost per infant decreased from \$19,737 to \$8,735.
- No adverse effects

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

Non-pharmacologic treatment of neonatal opioid withdrawal syndrome

■ Yale Study showed the proportion of methadone exposed-infants treated with morphine decrease from 98% to 14% with institution of non-pharmacologic care and some changes in way medication was dosed. Hospital costs decreased from \$44,824 to \$10,289. Average length of stay decreased from 22.4 to 5.9 days.¹

Non-pharmacologic and drug-limiting treatment of neonatal opioid withdrawal syndrome

- Interventions included the following:
 - Prenatal counseling of parents
 - Empowering messages to parents
 - Simplified assessment (ESC)
 - Rapid morphine weans
 - Morphine given as needed
 - Rooming in.

Non-pharmacologic treatment of neonatal opioid withdrawal syndrome

- Small and frequent feeds. Frequent burping.¹
- Quiet, dim light. Soft slow manner. Swaddling.²
- Skin-to-skin. Family involvement with rooming in.³
- Prenatal education about neonatal opioid withdrawal syndrome.⁴
- Frequent feeds and high calorie formulas may help with nutritional needs.⁵

- Vekez et Jansson. The Opioid Dependent Mother and Newborn Dyad: Nonpharmacologic Care. J. Addict Med. 2008:2 113-120
- 2. Ibic
- 3. Ibid
- 4. Holmes et al. Rooming-In to Treat Neonatal Abstinence Syndrome: Improved Family-Centered Care at Lower Cost. Pediatrics 1026; pp
- Kocherlota. Neonatal Abstinence Syndrome. Pediatrics. Volume 134, Number 2, August 2014. pp e547-e561

Rooming-in

Rooming-in is standard of care and should be offered to every mother-infant dyad.¹

Swaddling

- Infants should only be swaddled at home if caregivers have been given training¹
 - Swaddled infants should always be placed on their backs
 - When an infant attempts to roll, swaddling should be discontinued

Non-pharmacologic treatment of neonatal opioid withdrawal syndrome

Mothers may have a lot of guilt and anxiety which may lead to maladaptive behaviors, including relapse, aggressive behavior, and neglect. It is important to support the mother.¹

> Vekez et Jansson. The Opioid Dependent Mother and Newborn Dyad: Nonpharmacologic Care. J. Addict Med. 2008;2 113-120

Case Study #12

■ Patient is 28 yo G2P2. She was using pain pills off the street when she presented with her first pregnancy. She got on buprenorphine and has done quite well. She has not had a single relapse in 6 years. Recently, her son was due to start kindergarten. I did a school physical on him. I always bring in past medical history. Mother came back to the office in tears and told me that she couldn't give the physical form to his teachers because it said that he had had neonatal abstinence syndrome, and "The teachers will judge me and think I am nothing but a junkie."

Shame

Shame is rarely therapeutic for substance use disorder. It is far more likely to precipitate relapse than it is to motivate someone into recovery. This is especially true for a new mother who used drugs during her pregnancy and has a baby with Neonatal Opioid Withdrawal Syndrome.

Pharmacologic treatment of neonatal opioid withdrawal syndrome

- When non-pharmacologic treatment is not adequate, the babies are usually treated with medication.
- This is usually morphine or methadone.

Maternal experiences

- Mothers can feel profound guilt about using illicit drugs during pregnancy.¹
- The mothers felt they had little knowledge of how quickly addiction could occur and the power it could have over their lives.²
- They felt the nurses lacked necessary education about substance addiction.³

3 Ibid

^{1.} Fraser et al. Caring, chaos, and the vulnerable family: Experiences in caring for newborns of drug-dependent parents. Int J of Nursing Studies, Vol 44 (2007) pp 1363-1370

Cleveland and Bonugli Experiences of Mothers of Infants with Neonatal Abstinence in the Neonatal Intensive Care Unit. JOGNN Vol 43, 2014. pp 318-329.

Maternal experiences

- They felt the nurses took their frustration in attempting to care for their babies out on the mothers.¹
- They felt judged by the nurses.²
- They feared being exposed as bad parents.³
- They feared losing their children to Child Protective Services.^{4, 5}
- They feared that being on medication-assisted therapy would result in contact with Child Protective Services.⁶

^{1.} Cleveland and Bonugli Experiences of Mothers of Infants with Neonatal Abstinence in the Neonatal Intensive Care Unit. JOGNN Vol 43, 2014. pp 318-329.

^{2.} Ibid

Murphy-Oikonen et al. The Experience of NICU Nurses in Caring for Infants with Neonatal Abstinence Syndrome. Neonatal Network Vol 29, No 5, September/October 2010, pp 307-313

^{4.} Ibic

Howard. Experiences of opioid-dependent women in their prenatal and postpartum care: Implications for social workers in health care. Social Work in Health Care Vol 55 No. 1. 2016. pp 61-85

⁶ Ibio

Nursing attitudes

- Caring for babies with NOWS is time consuming and difficult.¹
- The parents of babies with NOWS are a demanding group.²
- NICU nurses are highly technically skilled. Caring for infants with NOWS is frequently mundane and highly time-consuming. It is hard to balance the many needs of the infant with NOWS while providing critical care to infants who are at higher risk medically.³
- They worry about the infant's welfare after discharge.⁴

^{1.} Fraser et al. Caring, chaos, and the vulnerable family: Experiences in caring for newborns of drug-dependent parents. Int J of Nursing Studies, Vol 44 (2007) pp 1363-1370

^{3.} Murphy-Oikonen et al. The Experience of NICU Nurses in Caring for Infants with Neonatal Abstinence Syndrome. Neonatal Network Vol 29, No 5, September/October 2010, pp 307-313

^{4.} Ibid

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 opiate use disorder.
- We should never use the possibility of NOWS to justify not properly treating opiate use disorder.

Neonatal opioid withdrawal syndrome

We should also make sure that all pregnant women who are under treatment with opiate-replacement therapy facing the possibility of a baby with NOWS understand that they are doing the best possible thing for their baby.

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 who are in a treatment program and have had negative drug screens for 2 months prior to delivery.^{1,2,3,4,5}
 - This includes women on MOUD.
- Jansson, L. et al, Methadone Maintenance and Breastfeeding in the Neonatal Period PEDIATRICS Vol. 121 No. 1 January 2008, pp. 106-114
- 2. Reece-Stretman et al. ABM Clinical Protocol #21: Guidelines for Breastfeeding and Substance use or Substance Use Disorder, Revised 2015 Breastfeeding Medicine; Vol 10, November 3, 2015, pp 135-141
- 3. Substance Use, Misuse, and Use Disorders During and Following Pregnancy, with an Emphasis on Opioids. ASAM Policy Statement. January 18, 2017
- Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. SAMHSA. HHS Publication No. (SMA) 18-5054 ACOG Committee Opinion. Opioid Use and Opioid Use Disorder in Pregnancy. Number 711. August 2017.

Intermediate effects

Babies may have hyperirritability, poor sleep, and other minor symptoms of withdrawal for weeks to months.

Long-term effects on baby of maternal methadone and buprenorphine use

Neonatal outcome is improved if mothers get on methadone early in pregnancy or even before pregnancy.¹

Long-term effects on baby of maternal methadone and buprenorphine use

Infants born to mothers who received methadone or buprenorphine were found as toddlers to have no more problems than those from a sample without SUD¹

Long-term effects on baby of maternal methadone and buprenorphine use

- Very hard to control for other factors
 - Other drug use
 - Poor socioeconomic status
 - Inadequate prenatal care
- It is also hard to tease out the direct effects of drug use versus adverse effects related to poor pregnancy outcomes related to drug use.

For neonatal abstinence syndrome, it is very hard to distinguish risks of drug use vs NAS

- Long-term follow-up of infants born with NOWS is difficult because of limited retention in treatment and psychosocial stressors as experienced by the children's families. However, some studies show that NOWS affects cognitive, behavioral, and motor development, as well as academic performance.
- Children 5–12 years of age born to heroin-dependent mothers, whether they were raised at home by their mothers or they were adopted by another family, showed lower performance IQ scores on the Wechsler Intelligence Scale for Children—Revised (WISC-R) compared to controls.
- An Australian cohort study following birth, hospitalization, and death records for all children born in New South Wales between 2000 and 2011 to a maximum of 13 years of age found that children with a history of NOWS were significantly more likely to be hospitalized for "mental and behavioral disorders" when compared to children born without a NOWS diagnosis. This includes speech/language disorders, autism, and behavioral and emotional disorders including ADHD, oppositional defiant disorder (ODD), and conduct disorder (CD)
- At this time, longitudinal studies have inconsistent findings on the effects of fetal methadone and buprenorphine exposure on motor development in neonates

Weller et al. Neonatal Opioid Withdrawal Syndrome (NOWS): A Transgenerational Echo of the Opioid Crisis. Cold Spring Harb Perspect Med.; 11(3):. doi:10.1101/cshperspect.a039669

Newborns with hepatitis C

- A large percentage of pregnant women with heroin use disorder also have hepatitis C.
- Their babies need to be tested at 18 months of age. About 5% will be positive.

Urine drug testing and newborns

Patient is a 28 yo G3P2 at term. Does not have custody of her older children. History of heroin use disorder, started on buprenorphine early in pregnancy. All negative drug screens throughout pregnancy, following with counseling and meetings. At the time of delivery, she tested negative for any illicit drugs. Her baby tested positive on a urine drug screen for amphetamines. This was not confirmed. Meconium screen was negative for amphetamines, positive only for buprenorphine. Child protective services were notified. They took custody. Patient continued attending meetings and doing well for about six months, but child protective services refused to give her custody because of issues with her house. She eventually relapsed and disappeared from care.

Patient is a 23 yo G2P1, presented at 38 weeks for labor check. She had been on buprenorphine since about 14 weeks. All urine drug screens during pregnancy were negative for drugs, including one 3 days before and another 3 days after the labor check. At the time of her labor check, she tested positive for amphetamines. No one asked her about it at the time, and it was not confirmed. The baby's doctor noticed at the time of delivery and notified child protective services. She was allowed to keep custody but was required to give drug screens for child protective services. She continued to have negative drug screens in the office. However, when the baby was about a month old, she tested positive for amphetamines again and lost custody. Again, this urine was not confirmed. She became so upset with this that she decided she might as well start using methamphetamines, and she took 6 months to stop. She still has not regained custody.

Drug testing of newborns

- Urine drug screen
 - Available quickly
 - Relatively non-invasive, easy to collect
 - Only shows recent exposures
 - Immunoassay test –there may be false positives.
 - MUST COMPLETE CONFIRMATORY TESTING FOR ANY POSITIVE RESULTS

Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. SAMHSA. HHS Publication No. (SMA) 18-5054

Drug testing of newborns

- Meconium drug test
 - This shows any drug use from about 32 weeks on
 - May be harmful for women with abstinence closer to term
- Umbilical cord test
 - Easy to collect
 - Accurately reflects fetal drug exposure

Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. SAMHSA. HHS Publication No. (SMA) 18-5054 Child protective services and substance-exposed newborns

To call Child Protective Services or not

- Reasons to think about calling Child Protective Services:
 - There is a high incidence of child abuse among women addicted to drugs. (30% serious neglect, 22.5% physically or sexually abused.)¹
- Reasons to think about not calling Child Protective Services:
 - Not all parents who use drugs are abusing their kids.
 - Calling Child Protective Services often places a severe stress on what is a vulnerable family situation.
 - Losing a child to Child Protective Services can be devastating to the mother's mental health

Certain racial and ethnic groups tend to be over-represented in the child welfare system

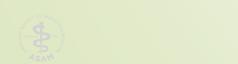
- A significant body of research has documented the overrepresentation of certain racial and ethnic groups in the child welfare system relative to their representation in the general population.
 - In 2019, American Indian and Alaska Native children made up 1 percent of the child population and accounted for 2 percent of the foster care population, while African-American children accounted for roughly 14 percent of the and 23 percent of the foster care population.
 - That same year, White children made up half of the child population and just 44 percent of the foster care population.
- Drug-positive newborns of African-American mothers were more likely than White mothers to be reported to CPS, despite the similarity of the overall health characteristics of their infants.
- Children from diverse racial and ethnic backgrounds with head injuries were almost twice as likely to be reported for abusive head trauma than White children with similar symptoms

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.





Three conclusions from study about mother who had lost a baby to child protective services

- 1. Be aware of the effect on the mother and whole family unit.
- 2. Treat these women with compassion.
- 3. Don't ever retrospectively justify the decision to take a child away from a mother by the mother's actions after losing custody.

Comprehensive addiction and recovery act

CARA requires states to identify and report on the following:

Number of substance-exposed infants born

Number of substance-exposed infants for whom a Plan of Care was created

Number of infants with a Plan of Care for whom referrals were made to appropriate services, including services for affected family members or caregivers



New Mexico Law and Substance-Exposed Newborns

- New Mexico has passed a law supporting CARA amendments to CAPTA. The new law...
- Gives CYFD until January 1, 2020 to develop rules that guide stakeholders in the care of newborns who exhibit physical, neurological, or behavioral symptoms consistent with prenatal drug exposure or fetal alcohol spectrum disorder.
- Specifies that the rules are to include guidance on the creation of a Plan of Care for any substance-exposed newborn.
- Pregnant women who communicate use of drugs or alcohol will be offered supports through a Plan of Care at time of delivery.
- Women whose substance use during pregnancy was not identified will be offered supports through a Plan of Care at time of delivery.

Counseling around Child Protective Services

- 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

Take home points

- Medication treatment of opioid use disorder is standard of care for pregnant women.
- Post-partum is a high risk time for relapse and overdose.
- There is no such thing as an addicted newborn.
- Non-pharmacologic measures are standard of care for neonatal opioid withdrawal syndrome.
- Make sure baby is evaluated for fetal alcohol syndrome if mother was drinking alcohol.
- Talk to patients about child protective services. Be honest and compassionate, not punitive.