



**UW PACC**

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# TREATING OPIOID USE DISORDER IN PREGNANCY

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# SPEAKER DISCLOSURES

Nadejda Besspalova, MD has no relevant financial relationships.

# GOALS AND OBJECTIVES

- Summarize the epidemiology of opioid use disorder in pregnancy
- Explain the role of medications for OUD (MOUD) during pregnancy
- Compare the relative risks and benefits of MOUD options in pregnancy
- Identify the logistics of MOUD for pregnant people

# ACRONYMS

- Pre-term labor – PTL
- People who use drugs – PWUD
- Neonatal Opioid Withdrawal Syndrome – NOWS
- Neonatal Abstinence Syndrome – NAS
- Intrauterine Fetal Demise – IUFD

# POP QUIZ!

- Remember pregnancy risk categories A, B, C, D, X (no longer used and replaced with Pregnancy and Lactation Labeling Rule)
- Think of a medication that was Category A
- What category was RhoGAM?

# CASE

- Jennifer is a 28 year old G3P0021 woman who comes to you see after finding out she is 7 weeks pregnant. Her first OB visit is scheduled in 3 weeks. She does not have a PCP.
- She comes to see you because she is currently using heroin daily, multiple times per day, has difficulty quantifying amounts. She suspects her supply has fentanyl in it. She has a history of injecting but not recently.
- She also uses cannabis and cigarettes, rarely alcohol, has tried meth but doesn't use it regularly
- She has been diagnosed with various psychiatric conditions including anxiety, depression, bipolar disorder. One hospitalization for psychosis in the context of meth use.

# CASE CONTINUED

- She wants to stop using and asks you about detox. She is hesitant about MOUD because she heard it can cause NAS and she is worried about CPS involvement. Has been on both methadone and buprenorphine in the past, both successfully
- Her longest period of abstinence was about a year on Suboxone but she relapsed in the context of moving to get away from IPV relationship and struggling with depression
- What do you want to know? How you counsel her?

# THE CHALLENGES FACED BY PREGNANT PEOPLE WITH OUD AND THOSE WHO CARE FOR THEM

- STIGMA
- Difficulties obtaining MOUD
- Psychiatric comorbidities
- Fragmented care
- Supports/recovery environment
- Risk of Neonatal Opiate Withdrawal Syndrome/Neonatal Abstinence Syndrome



# SOURCES OF STIGMA

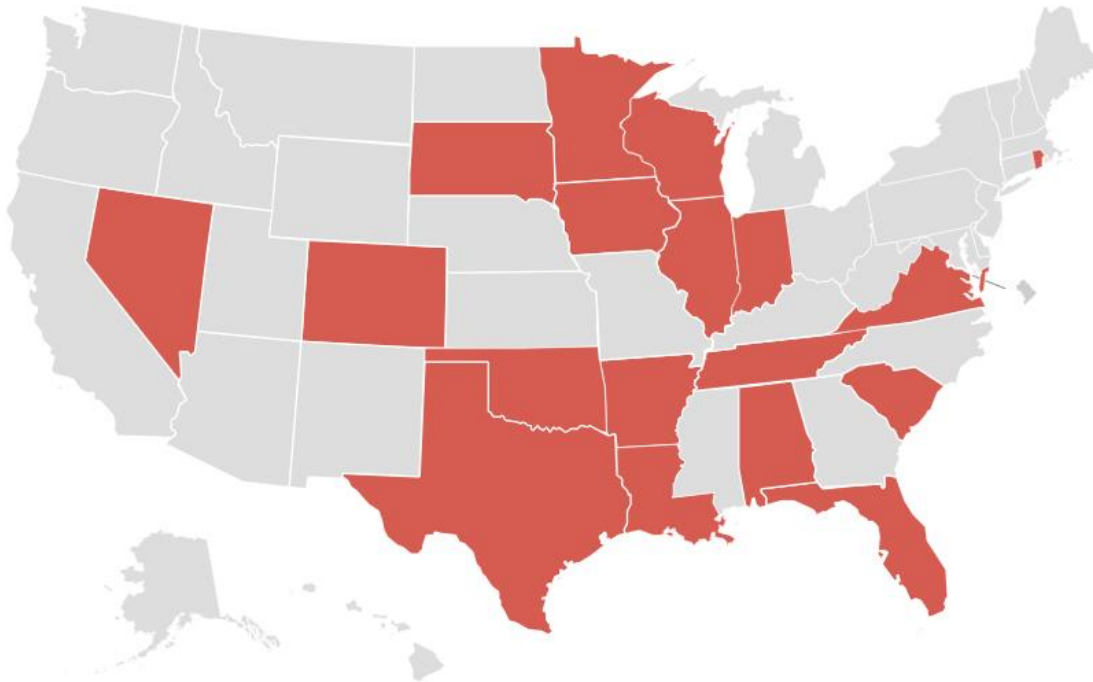
Crack cocaine epidemic of  
1980's  
and “crack babies”

Gender discrimination, ideas  
about “motherhood”

Trauma and SUD – a  
bidirectional  
relationship



# STATES WHERE SUBSTANCE USE DURING PREGNANCY IS CONSIDERED CHILD ABUSE





Original Investigation | Pediatrics

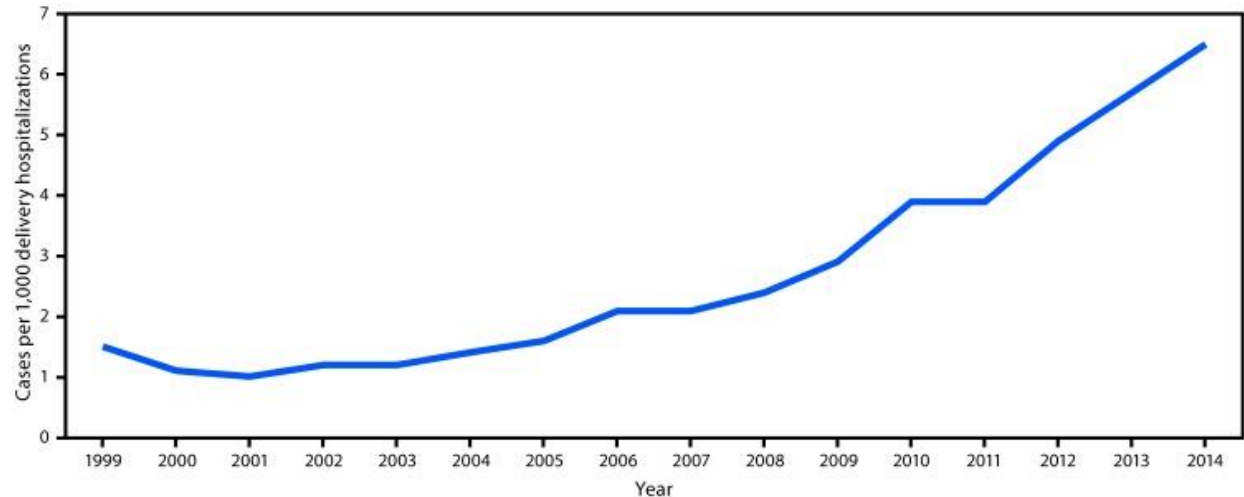
## Association of Punitive and Reporting State Policies Related to Substance Use in Pregnancy With Rates of Neonatal Abstinence Syndrome

Laura J. Faherty, MD, MPH, MS; Ashley M. Kranz, PhD; Joshua Russell-Fritch, MS; Stephen W. Patrick, MD, MPH, MS; Jonathan Cantor, PhD; Bradley D. Stein, MD, PhD

“In adjusted analyses among neonates in states with punitive policies, odds of NAS were significantly greater during the first full calendar year after enactment (adjusted odds ratio, 1.25; 95% CI, 1.06-1.46;  $P = .007$ ) and more than 1 full year after enactment (adjusted odds ratio, 1.33; 95% CI, 1.17-1.51;  $P < .001$ )”

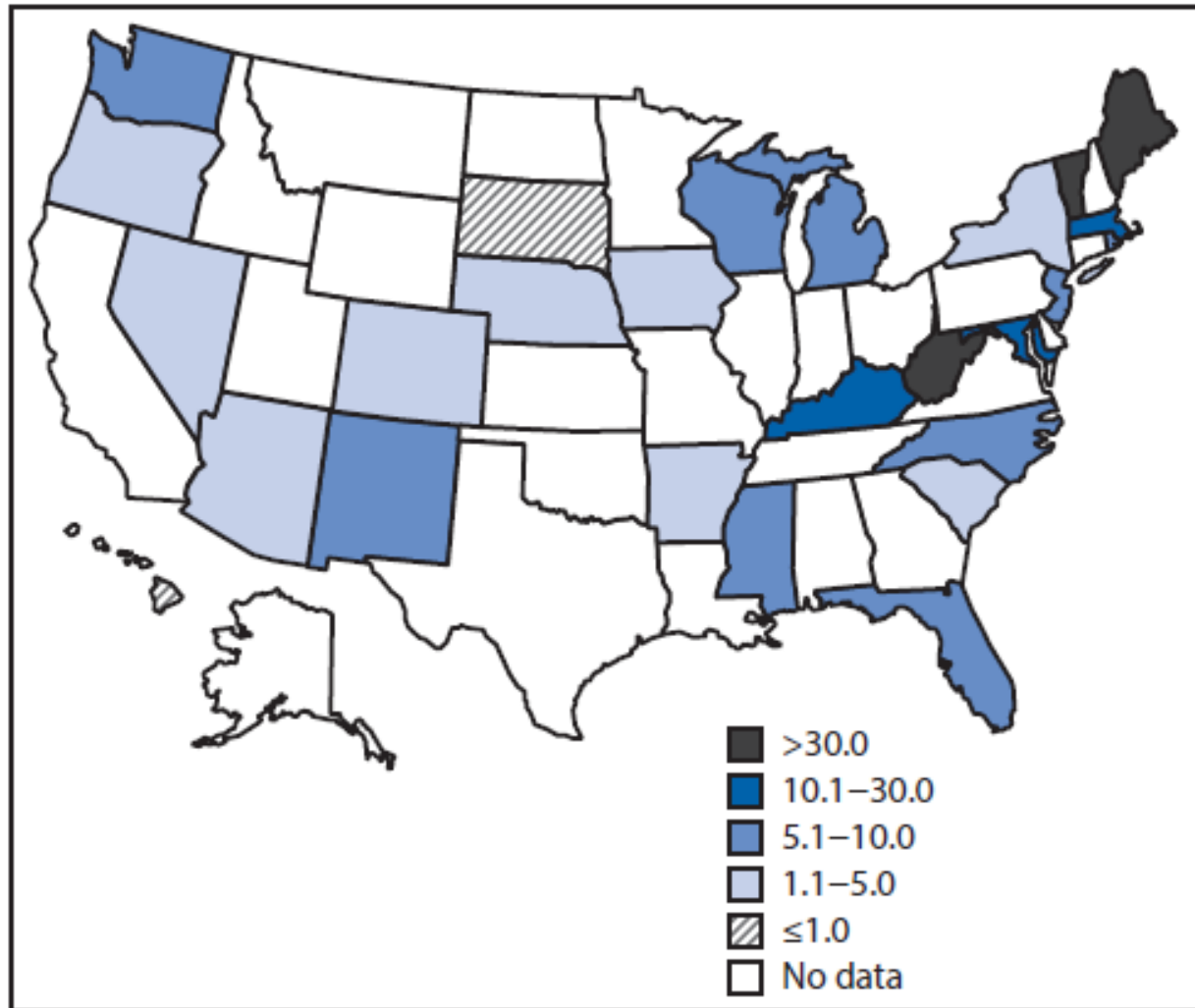
# SCOPE OF THE PROBLEM

- Prevalence of OUD in pregnancy is increasing
  - OUD diagnosis at delivery hospitalization increased from 1.5 per 1,000 in 1999 to 6.5 per 1,000 in 2014
  - NAS incidence increased from 1.5 per 1,000 in 1999 to 6 per 1,000 in 2013 (hospital births)
- In line with national trend



Ko et al 2016  
Haight et al 2018

FIGURE. Neonatal abstinence syndrome (NAS) incidence rate\* — 25 states, 2012–2013<sup>†</sup>



# RISKS OF OPIOID USE IN PREGNANCY

## To Birthing Person

- Overdose
- Less likely to receive appropriate prenatal care
- Infection (esp if injecting)
- Mood and psychotic symptoms (substance-induced or worsening of comorbid underlying illness)
- Unintended pregnancies
- Abuse/other trauma
- Legal consequences

## To Baby

- Intrauterine fetal demise/stillbirth
- Preterm labor
- Low birth weight
- Birth defects
  - Data is limited/difficult to interpret
  - Oral clefts and ASD/VSD most common
- Longer hospital stay after birth
- Higher chance of rehospitalization within 30 days of birth
- NOWS

# NAS/NOWS

- Usually onset within 72 hours of birth
- More likely in male infants
- Tremors
- Irritability, including excessive or high-pitched crying
- Sleep problems
- Hyperactive reflexes
- Seizures
- Yawning, stuffy nose, or sneezing
- Poor feeding and sucking
- Vomiting
- Loose stools and dehydration
- Increased sweating

# DETOX DURING PREGNANCY?

- Data on risks of opioid detox in pregnancy is mixed
  - Prior concerns about PTL and IUFD but risk is small in more recent studies in controlled environment
  - Very few people complete detox protocols
- Rates of relapse are higher than with MOUD
- No decrease in risk of NAS compared to those maintained on MOUD
- Detox not generally recommended in pregnancy
  - *“Because of superior outcomes associated with MAT compared with withdrawal, ACOG continues to recommend use of MAT as the standard of care during pregnancy for women with opioid use disorders.” - ACOG*



# MOUD IN PREGNANCY

Stable serum levels → More stable birthing parent →  
Healthier pregnancy

Engagement in MAT:

- Increases engagement in prenatal care
- Decreases rates of HIV and blood borne pathogen transmission
- More stable social environment
- Decreases overdose risk
- Decreases NOWS risk and severity

# MOUD IN PREGNANCY

## Options for OUD in Pregnancy

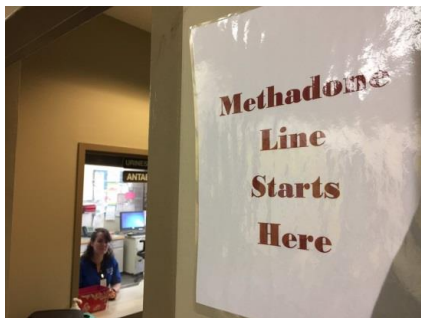
- Methadone – improved treatment retention
- Buprenorphine – decreased NOWS severity
- Naltrexone (Vivitrol®) – increasingly reassuring data but medically supervised detox **NOT** recommended for initiation
- MOST EFFECTIVE MEDICATION IS THE ONE PATIENT IS WILLING TO TAKE

# MOTHER STUDY – COMPARING METHADONE TO BUPRENORPHINE

- Double-blind, flexible dosing RCT at 8 sites (6 in US, 1 in Canada, 1 in Austria), 175 women
- Results
  - percentage of neonates requiring treatment for NOWS – no difference
  - peak NOWS score – no difference
  - neonatal head circumference – no difference
  - total amount of morphine needed to treat NOWS – less in buprenorphine group
  - length of hospital stay for neonates –less in buprenorphine group
- Methadone arm had significantly better retention

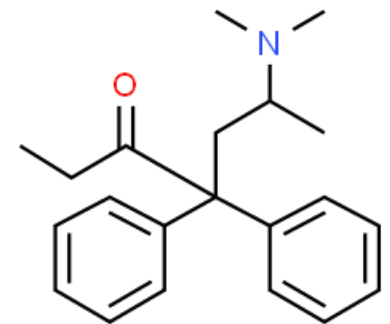
# METHADONE VS BUPRENORPHINE META-ANALYSIS

- Infants exposed to buprenorphine
  - Lower overall risk of NOWS requiring treatment, shorter hospital stays, lower total morphine dose
  - Higher mean gestational age and greater weight, length, and head circumference at birth
- Participants treated with buprenorphine had less illicit opioid use near delivery
  - Confounding?? Who gets prescribed buprenorphine and who gets methadone



# METHADONE

- Full agonist at  $\mu$ -opioid receptor
- Beware QT prolongation/Torsades risk
- Fetus “see’s” ~ half the serum dose
- Not uncommon to need several dose increases during pregnancy
- Oral dose  $\neq$  risk for NOWS
- Adequate dose decreases relapse risk



# METHADONE METABOLISM

- Methadone is primarily metabolized by CYP 3A4, 2B6 – induced by pregnancy
  - Inactive metabolite (EDDP)
  - Usual half life of methadone is ~24 hours, in pregnancy ~12 hours or as short as 4-6
  - Split dosing often needed! Possible but can be difficult
    - Split dosing may decrease risk of NOWS



# OUTCOMES WITH METHADONE

- No data indicating increased risk of miscarriage
- Some studies show increased risk of IUGR, PTL, others do not
- Data on birth defects is mixed, some studies showed increased overall risk but no specific pattern
- Overall risk of NAS varies widely in studies
  - 30%-80%
  - Illicit opioid use and polysubstance use increase risk
  - importance of therapeutic dose

# OUTCOMES WITH METHADONE

- Long term effects
  - Data is all over the place – some studies with worse developmental outcomes
  - Many women relapse/drop out of care after delivery
  - Participants of MOTHER study up to age 3 had no differences in development



# BUPRENORPHINE BASICS

- May be titrated quickly over several days-weeks
- Usual dose 16mg-24mg/day but varies
- 3 active metabolites
  - Less need for dose adjustments
- No constraints around splitting dose
- Main risk is precipitated withdrawal at initiation
- Less overdose risk than Methadone
- Lower risk of major med interactions, QT prolongation risk



# WHICH PRODUCT?

- Mono-product (Subutex) previously recommended due to concern about naloxone crossing placenta
  - Data on combo product (Suboxone) increasingly reassuring, likely safe, can be considered per SAMHSA guidelines
  - No need to continue mono-product after delivery
  - Mono-product usually requires prior auth

# OUTCOMES WITH BUPRENORPHINE

- No data indicating increased miscarriage risk
- No data clearly suggesting increased birth defect risk
- Infants smaller on average than unexposed
- Risk of NOWS
  - Also varies between studies, ~20-60% require treatment
  - No clear association with dose
  - Increases greatly with polysubstance use

# EXTENDED-RELEASE BUPRENORPHINE IN PREGNANCY

- Little data
- Excipient used (N-methyl-2-pyrrolidone) has produced teratogenic effects in animal studies
  - manufacturer recommends against use
  - Trials in progress for alternative extended-release bup w/o this
- Couple of case reports w/ no NOWS or adverse neonatal outcomes

# FINAL CONSIDERATIONS

## Methadone

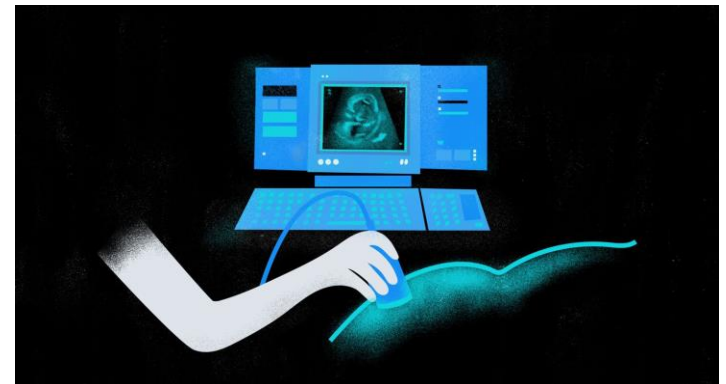
- Methadone clinic barriers for dosing but more case management
- Switching to buprenorphine is difficult
- Titration/stabilization is slow
- More drug interactions
- Higher overdose risk
- No risk of precipitated withdrawal, do not need to be in withdrawal to start
- Better treatment retention?

## Buprenorphine

- Office-based treatment, fewer barriers
- Switching to methadone is easy
- Titration/stabilization is rapid
- Few drug interactions
- Overdose risk exceedingly low if used properly
- Risk of precipitated withdrawal, must be in withdrawal to start
- Lower risk of NOWS

# ANTENATAL MONITORING

- No clear guidelines
- Discuss with ObGyn/MFM
- Overall stability will likely determine monitoring needs
- Possible additional monitoring
  - More frequent prenatal visits
  - Hep B/C and HIV every trimester
  - Growth US q2-4weeks after 20 week anatomy scan
  - BPP and/or NST in third trimester



# POSTPARTUM CARE

- Support rooming in
  - Minimizes stimulation
  - Maximizes contact with mother/skin to skin
  - Reduces NAS severity/total morphine need
  - Reduces likelihood of NICU admission and LOS
- Encourage and support breastfeeding
- Eat, Sleep, Console Model
- Continue MOUD

# BREASTFEEDING

- Safe to breastfeed for women on MOUD
- Breastmilk excretion is minimal
- Infants who are breastfed generally have
  - Shorter hospital LOS
  - Less need for pharmacotherapy for NOWS
  - Lower withdrawal scores
- Mechanism unclear – exposed to small amounts of medication vs act itself





# INFANT CARE

- NAS or NOWS – normal result of MAT not failure
  - Implications of NAS?
    - Fill et al found children with NAS were more likely to be referred for a disability evaluation, meet criteria for a disability, and require classroom therapies or services
      - Did not separate out whether NAS was in context of MAT, illicit use, use for pain, etc
    - Back to MOTHER study...no differences in development between children who had NAS and those who did not

# RECOVERY ENVIRONMENT

- Addiction is a chronic disease
  - Recommend continuing MOUD
  - Relapse risk in the first year postpartum is high and care drops off significantly
- Help reduce stigma
- Reinforce successes
- Discuss help/supports for new parents



# RESOURCES

- Chemical Using Pregnant Women (CUPW)s Programs
  - 26 day inpatient programs for Medicaid eligible women
  - Stabilization on MAT
  - Great option for high risk pregnancies
  - Several in Washington, one at Swedish Ballard
  - <https://www.hca.wa.gov/health-care-services-supports/apple-health-medicaid-coverage/chemical-using-pregnant-women>
- Pregnant and Parenting Women Programs
  - 6 month residential programs
- Parent Child Assistance Program (PCAP)
- Many more options through the Washington Pregnant Women Substance Use Disorder Resource Guide

# UW PERINATAL PSYCHIATRY CONSULTATION LINE (PAL FOR MOMS)

— WEEKDAYS 9:00 – 5:00PM | ☎ 877-725-4666 (PAL4MOM) | ✉ PPCL@UW.EDU

- Who can call? Any provider who cares for pregnant/postpartum patients
- What kind of questions? Any behavioral health-related questions for patients who are pregnant, in the first year postpartum, or who have pregnancy-related complications (e.g. pregnancy loss, infertility). Topics may include:
  - Depression, anxiety, other psychiatric disorders (e.g., bipolar disorder, post-traumatic stress disorder), substance use disorders, or co-occurring disorders
  - Pregnancy loss, complications, or difficult life events
  - Weighing risks and benefits of psychiatric medication, non-medication treatments
  - Local resources & referrals
- Staffed by UW perinatal psychiatrists
- Learn more <https://www.mcmh.uw.edu/ppcl>

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# RETURN TO CASE

# REFERENCES

- Ries, R., Miller, S., Saitz, R., Fiellin, D. (2014). The ASAM principles of addiction medicine.
- Tipu Khan MD, Mother-Infant Dyad in *Pregnancy and Women's SUD*, CSAM Review Course Sept 7<sup>th</sup> 2019, Anaheim CA.
- Okie, S. (2009). Crack Babies: The Epidemic That Wasn't. N.Y. Times. Retrieved from <https://www.nytimes.com/2009/01/27/health/27coca.html>
- How States Handle Drug Use During Pregnancy. (2019, December 25). Retrieved from <https://projects.propublica.org/graphics/maternity-drug-policies-by-state>
- Faherty LJ, Kranz AM, Russell-Fritch J, Patrick SW, Cantor J, Stein BD. Association of Punitive and Reporting State Policies Related to Substance Use in Pregnancy With Rates of Neonatal Abstinence Syndrome. *JAMA Netw Open*. 2019;2(11):e1914078. doi:10.1001/jamanetworkopen.2019.14078
- Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD. Incidence of Neonatal Abstinence Syndrome — 28 States, 1999–2013. *MMWR Morbidity and Mortality Weekly Report* [Internet]. 2016 Aug 12;65(31):799–802. Available from: <http://dx.doi.org/10.15585/mmwr.mm6531a2>
- Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. Opioid Use Disorder Documented at Delivery Hospitalization — United States, 1999–2014. *MMWR Morb Mortal Wkly Rep* 2018;67:845–849.
- Lind JN, Interrante JD, Ailes EC, et al. Maternal Use of Opioids During Pregnancy and Congenital Malformations: A Systematic Review. *Pediatrics*. 2017;139(6): e20164131; DOI: <https://doi.org/10.1542/peds.2016-4131>
- Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE, et al. Opioid Detoxification During Pregnancy. *Obstetrics & Gynecology* [Internet]. 2018 May;131(5):803–14. Available from: <http://dx.doi.org/10.1097/aog.0000000000002562>

# REFERENCES

- Wang M, Kuper S, Sims B, Paddock C, Dantzer J, Muir S, et al. Opioid Detoxification in Pregnancy: Systematic Review and Meta-Analysis of Perinatal Outcomes. *American Journal of Perinatology* [Internet]. 2018 Sep 19;36(6):581–7. Available from: <http://dx.doi.org/10.1055/s-0038-1670680>
- ACOG Statement on Opioid Use During Pregnancy - ACOG. (2019, December 15). Retrieved from <https://www.acog.org/About-ACOG/News-Room/Statements/2016/ACOG-Statement-on-Opioid-Use-During-Pregnancy?IsMobileSet=false>
- Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM, et al. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. *New England Journal of Medicine* [Internet]. 2010 Dec 9;363(24):2320–31. Available from: <http://dx.doi.org/10.1056/NEJMoa1005359>
- Jones HE, Deppen K, Hudak ML, Leffert L, McClelland C, Sahin L, et al. Clinical care for opioid-using pregnant and postpartum women: the role of obstetric providers. *American Journal of Obstetrics and Gynecology* [Internet]. 2014 Apr;210(4):302–10.
- Brogly SB, Saia KA, Walley AY, Du HM, Sebastiani P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. *Am J Epidemiol* 2014;180:673-686
- Cleary BJ, Donnelly J, Strawbridge J, Gallagher PJ, Fahey T, Clarke M, Murphy DJ. Methadone dose and neonatal abstinence syndrome-systematic review and meta-analysis. *Addiction*. 2010;105:2071–84.
- McCarthy, J., Stephenson, D. (2019). California Society of Addiction Medicine Guidelines: Guidelines for Physicians Working in Opioid Treatment Programs 4(), 46-63.
- Substance Abuse and Mental Health Services Administration. Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. HHS Publication No. (SMA) 18-5054. Rockville MD: Substance Abuse and Mental Health Services Administration. 2018

# REFERENCES

- Kaltenbach K, et al. 2018. Prenatal exposure to methadone or buprenorphine: Early childhood developmental outcomes. *Drug Alcohol Depend* 185: 40–49.
- Johnson Q et al. BuprenorphineNaloxone vs. Buprenorphine for Medication Assisted Therapy of Opioid Use Disorder in Pregnancy 2019
- Jones HE, Heil SH, Baewert A, et al. Buprenorphine treatment of opioid-dependent pregnant women: a comprehensive review. *Addiction* 2012; 107 suppl 1:5–27.
- Towers CV, Deisher H. Subcutaneous Extended-Release Buprenorphine Use in Pregnancy. *Case Rep Obstet Gynecol*. 2020 Jul 17;2020:3127676. doi: 10.1155/2020/3127676. PMID: 32724686; PMCID: PMC7382717.
- Ryan G, Dooley J, Windrim R, Bollinger M, Gerber Finn L, Kelly L. Maternal-Fetal Monitoring of Opioid-Exposed Pregnancies: Analysis of a Pilot Community-Based Protocol and Review of the Literature. *Journal of Obstetrics and Gynaecology Canada [Internet]*. 2017 Jun;39(6):443–52.
- Klamon SL, Isaacs K, Leopold A, et al. Treating Women Who Are Pregnant and Parenting for Opioid Use Disorder and the Concurrent Care of Their Infants and Children: Literature Review to Support National Guidance. *J Addict Med*. 2017;11(3):178-190.
- Fill MA, Miller AM, Wilkinson RH, et al. Educational Disabilities Among Children Born With Neonatal Abstinence Syndrome. *Pediatrics*. 2018;142(3):e20180562. doi:10.1542/peds.2018-0562
- Pregnant Women Substance Abuse Resource Guide <https://www.hca.wa.gov%2Fassets%2Ffree-or-low-cost%2Fpregnant-women-sud-resource-guide.pdf&usg=AOvVaw0GucbHYGwvFnKunzhvClaW>
- Heil, S., Jones, H., Arria, A., Kaltenbach, K., Coyle, M., Fischer, G., Stine, S., Selby, P., Martin, P. (2011). Unintended pregnancy in opioid-abusing women *Journal of Substance Abuse Treatment* 40(2), 199-202. <https://dx.doi.org/10.1016/j.jsat.2010.08.011>



# THANK YOU!

