

Treating Women for Opioid Use Disorder during Pregnancy: Clinical Challenges

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Hendrée Jones Disclosures

- No conflicts of interest or disclosures relevant to the content of this presentation.

The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.

Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

Educational Objectives

- At the conclusion of this activity participants should be able to:
 - Compare and contrast the risks and benefits of medication assisted treatment vs. medication assisted withdrawal for the effective treatment of women with OUD during pregnancy and the post-partum period
 - Compare and contrast the risks and benefits of methadone and buprenorphine treatment during pregnancy for mother, fetus and child
 - Identify at least three factors that are associated with reducing neonatal abstinence syndrome (NAS) severity among babies that are prenatally exposed to methadone or buprenorphine

Outline to Meet Objectives

- Historical context of opioid use among women of childbearing age
- Current scope of the problem
- Define NAS
- Treatment options
- Opioid Agonist Treatment vs. Medication-assisted Withdrawal: Risks and Benefits
- Opioid agonist treatment options
 - Methadone
 - Buprenorphine alone
 - Buprenorphine+naloxone
- Opioid Antagonist Treatment Options
 - Naltrexone (not enough data to support it and review known safety and efficacy data for mother, fetus and child)
- Summary

History of FDA Labeling For Methadone and Buprenorphine: Part 1

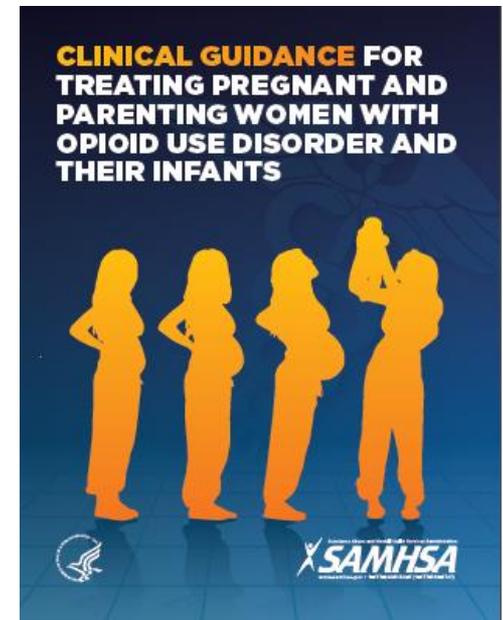
- Methadone and buprenorphine have historically been labeled by the US Food and Drug Administration (FDA) as Category C for use in pregnancy for the treatment of maternal opioid dependence: *“Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks”*
- As of May 2016, the FDA requires methadone and buprenorphine safety labeling to include information regarding the risk of neonatal opioid withdrawal syndrome (NOWS; also known as Neonatal Abstinence Syndrome - NAS)

History of FDA Labeling For Methadone and Buprenorphine: Part 2

- Pregnant women with opioid use disorder (OUD) can be effectively treated with methadone or buprenorphine. However, labeling states it should be used only if the potential benefit justifies the potential risk to the fetus.
- Pregnant women with opioid use disorder can be effectively treated with methadone or buprenorphine. Both these medications should not be considered “off-label” use in the treatment of pregnant patients with opioid use disorder (Jones et al., *Am J Obstet Gynecol*, 2014).

SAMHSA Clinical Guide Recommendations

- Medication assisted withdrawal is not recommended during pregnancy.
- Buprenorphine and methadone are the safest medications for managing OUD during pregnancy.
- Transitioning from methadone to buprenorphine or from buprenorphine to methadone during pregnancy is not recommended.
- Breastfeeding is recommended for women on buprenorphine and methadone.
- Neonatal abstinence syndrome (NAS) should not be treated with dilute tincture of opium.



The *Clinical Guide* consists of 16 factsheets that are organized into 3 sections: Prenatal Care (Factsheets #1–8); Infant Care (Factsheets #9–13); and Maternal Postnatal Care (Factsheets #14–16).

Historical Context of Opioid Use and Women

Opioid use during pregnancy in the 1800s:

- 66–75% of people using opioids were women
- Opium prescriptions to treat pain and uniquely female “issues”
- The southern United States had a larger per capita number of people using opioids
- Early drug control legislation focused on immigrants and minorities and focus on white women being “lured into opium dens and corrupted”
- Media began to link and sensationalize drug use, women and sexuality in an effort to stimulate public outrage at drug use



<http://usslave.blogspot.com.br/2012/02/opiate-addiction-and-cocaine-use-in.html> <https://pixabay.com/en/vintage-fashion-dress-tag-cutout-2874377/>

Courtwright D. *J Southern History* 1983; Kandall S *Substance and shadow*, 1996. Earle, *Medical Standards*, 1888

History: Opioids, Pregnancy, and Neonatal Withdrawal

1875: 1st documented NAS case in Western culture first appeared in Germany

1892: 1st NAS cases reported in the USA by Happel

1934: 1st review of NAS cases in Germany and USA (N=50)

1965: Goodfriend et al. report neonatal withdrawal signs

1971: Zelson et al. reported frequency of signs on neonatal withdrawal in 259 of 384 infants born to mothers using drugs

1975: Desmond and Wilson publish Neonatal Abstinence Syndrome: Recognition and Diagnosis

1975: Finnegan et al. publish a neonatal abstinence syndrome tool



<https://www.flickr.com/photos/nlireland/> See Jones H, Fielder A. *Preventive Medicine*, 2015 for a review

Menninger-Lerchenthal, E., *Monatschr f Kinderh* 1934; Happel, *Med. Surg. Rep.* 1892; Desmond and Wilson, *Addict. Dis.* 1975; Goodfriend et al. *Am. J. Obstet. Gynecol* 1956; Finnegan et al. *Addict. Dis.* 1975; Zelson C, Rubio E, Wasserman E. *Addict. Dis.* 1971; <https://pixabay.com/en/family-anno-anno-family-19-year-1318682/>

History: Defining Neonatal Abstinence Syndrome (NAS)

Neonatal Abstinence Syndrome (NAS) often results when a pregnant woman regularly uses opioids (e.g., heroin, oxycodone) during pregnancy

NAS defined by alterations in the:

- *Central nervous system*
 - High-pitched crying, irritability
 - Exaggerated reflexes, tremors and tight muscles
 - Sleep disturbances
- *Autonomic nervous system*
 - Sweating, fever, yawning, and sneezing
- *Gastrointestinal distress*
 - Poor feeding, vomiting and loose stools
- *Signs of respiratory distress*
 - Nasal congestion and rapid breathing

- NAS is not Fetal Alcohol Syndrome (FAS)
- NAS is treatable
- NAS and treatment are not known to have long-term effects; interactions between the caregiver and child can impact resiliency/risk with potential long-term effects in some cases.

Historical Context: Opioid Use and Women

Main Eras of Opioid Use in the USA

- **1800s:** 66-75% of people using opioids were women
- **1940s-50s:** New York saw large increases in teenage opioid use
- **1969-70s:** Opioid use by Vietnam veterans
- **1996-now:** Pain as the 5th vital sign and pain medication access

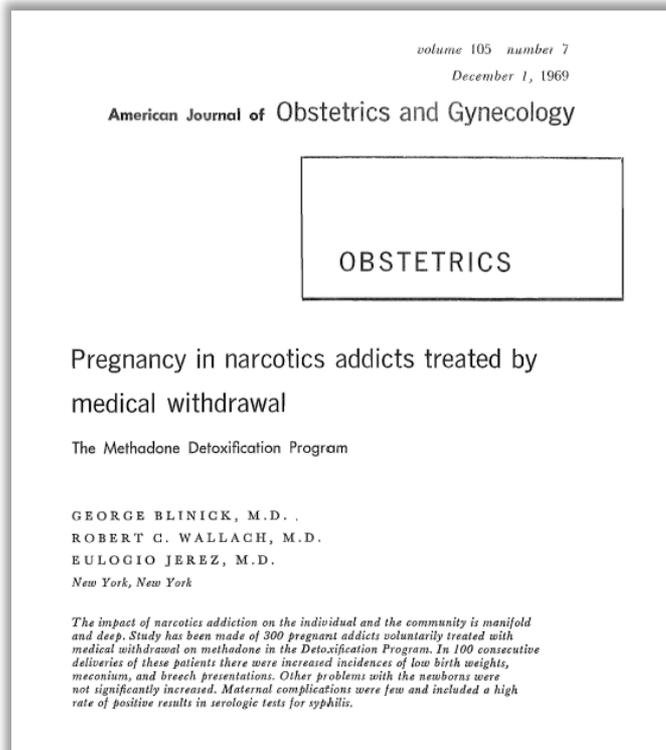


<http://usslave.blogspot.com.br/2012/02/opiate-addiction-and-cocaine-use-in.html>; <https://pixabay.com/en/vintage-retro-ladies-photo-paper-1303815/>

Courtwright D. *J Southern History* 1983; Kandall S *Substance and shadow*, 1996. Earle, *Medical Standards*, 1888

The Incidental Economist 2014 <https://pointsadhsblog.files.wordpress.com/2012/03/08-0620hair20salon20loc20nywt202226b.jpg>

History: Methadone and Pregnancy



1973 FDA said all pregnant women on methadone should undergo a 21-day detoxification

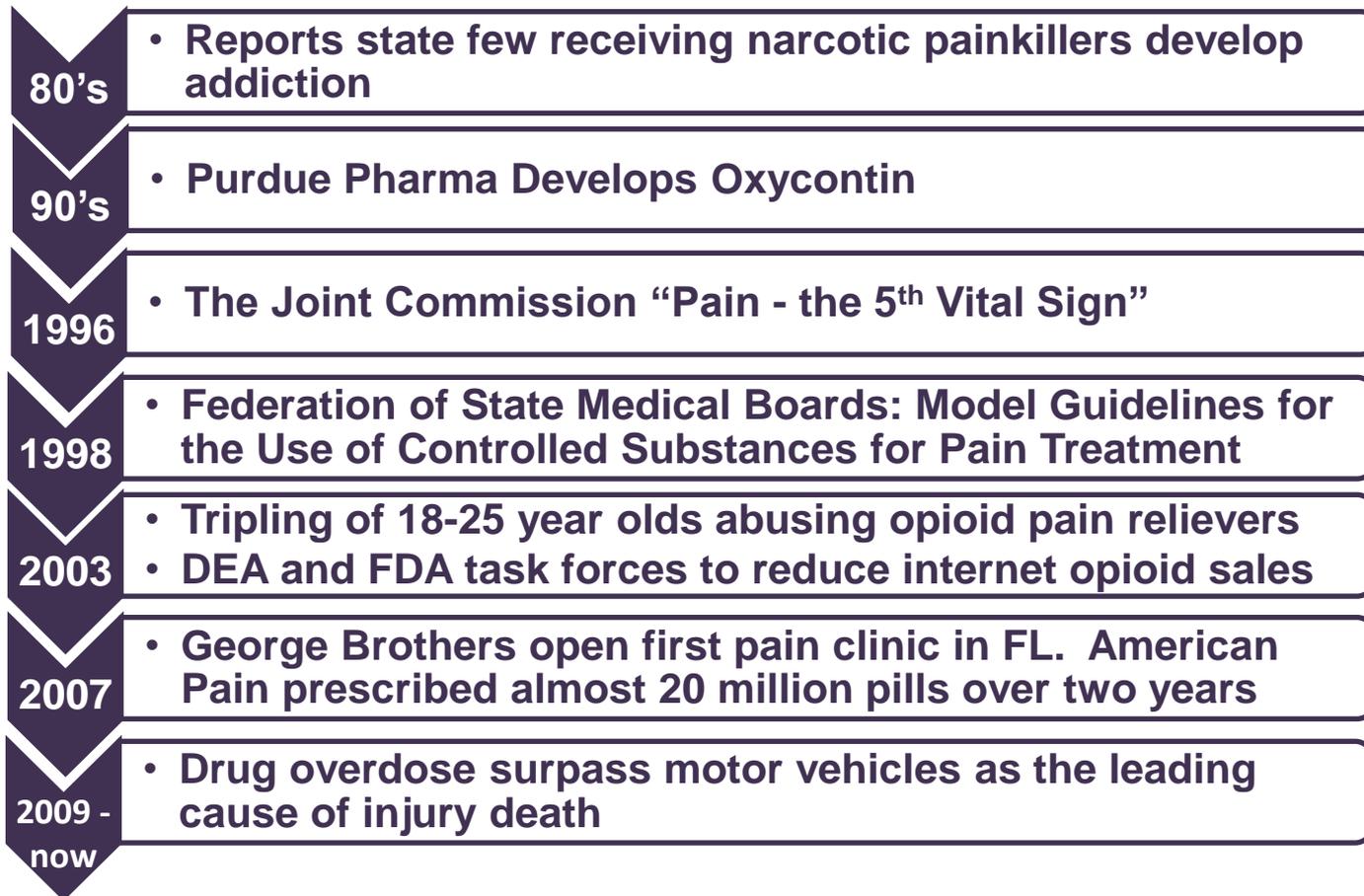
Research shows that methadone:

- Reduces maternal craving and repetitive episodes of fetal withdrawal
- When provided in the context of a comprehensive program, allows other behavior changes which decrease health risks to both mother and fetus
- Reduces the likelihood of complications with fetal development, labor, and delivery

Blinick G, et al., *Am J Obstet Gynecol.* 1969.

Zuspan. *Am J Obstet Gynecol.* 1975. et al., Kaltenbach K et al., *Obstet Gynecol Clin North Am.* 1998.

Recent History: Opioid Use in the USA



Current Scope of the Problem: Opioid Epidemic in the United States

In 2015...  **12.5 million**
People misused prescription opioids¹

 **2.1 million**
People misused prescription opioids for the first time¹

 **33,091**
People died from overdosing on opioids²

 **2 million**
People had prescription opioid use disorder¹

 **15,281**
Deaths attributed to overdosing on commonly prescribed opioids^{2,3}

 **828,000**
People used heroin¹

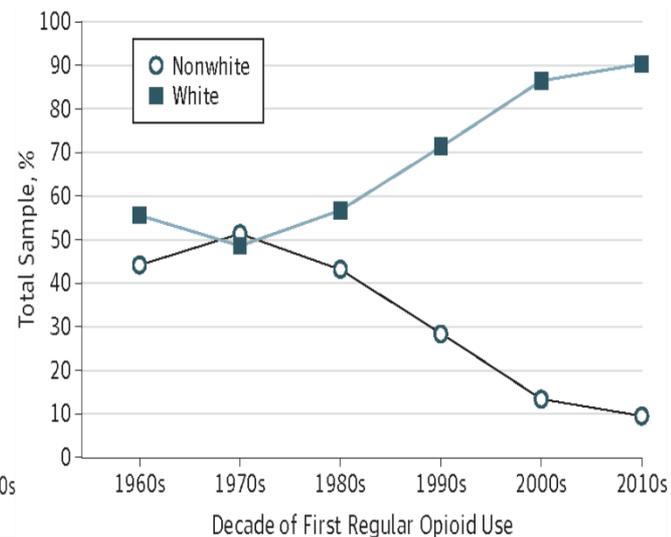
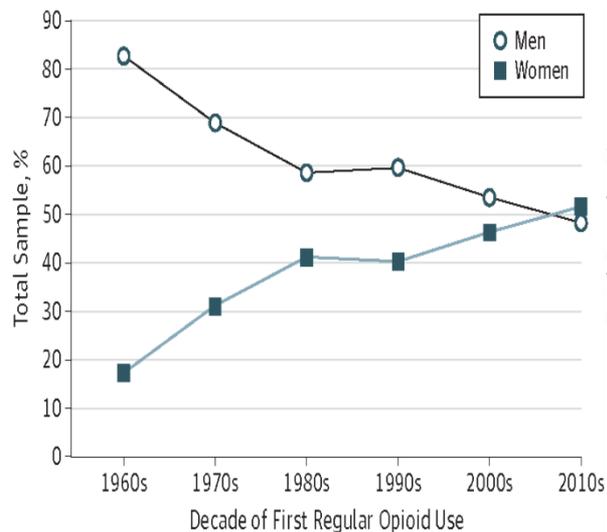
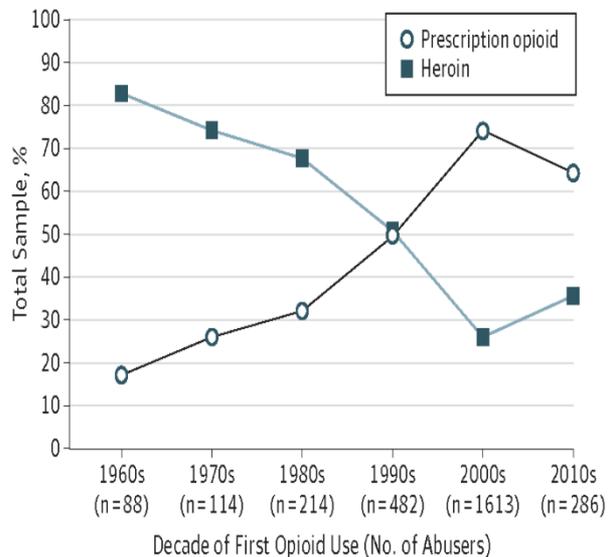
 **9,580**
Deaths attributed to overdosing on synthetic opioids^{2,3}

 **135,000**
People used heroin for the first time¹

 **12,989**
Deaths attributed to overdosing on heroin^{2,4}

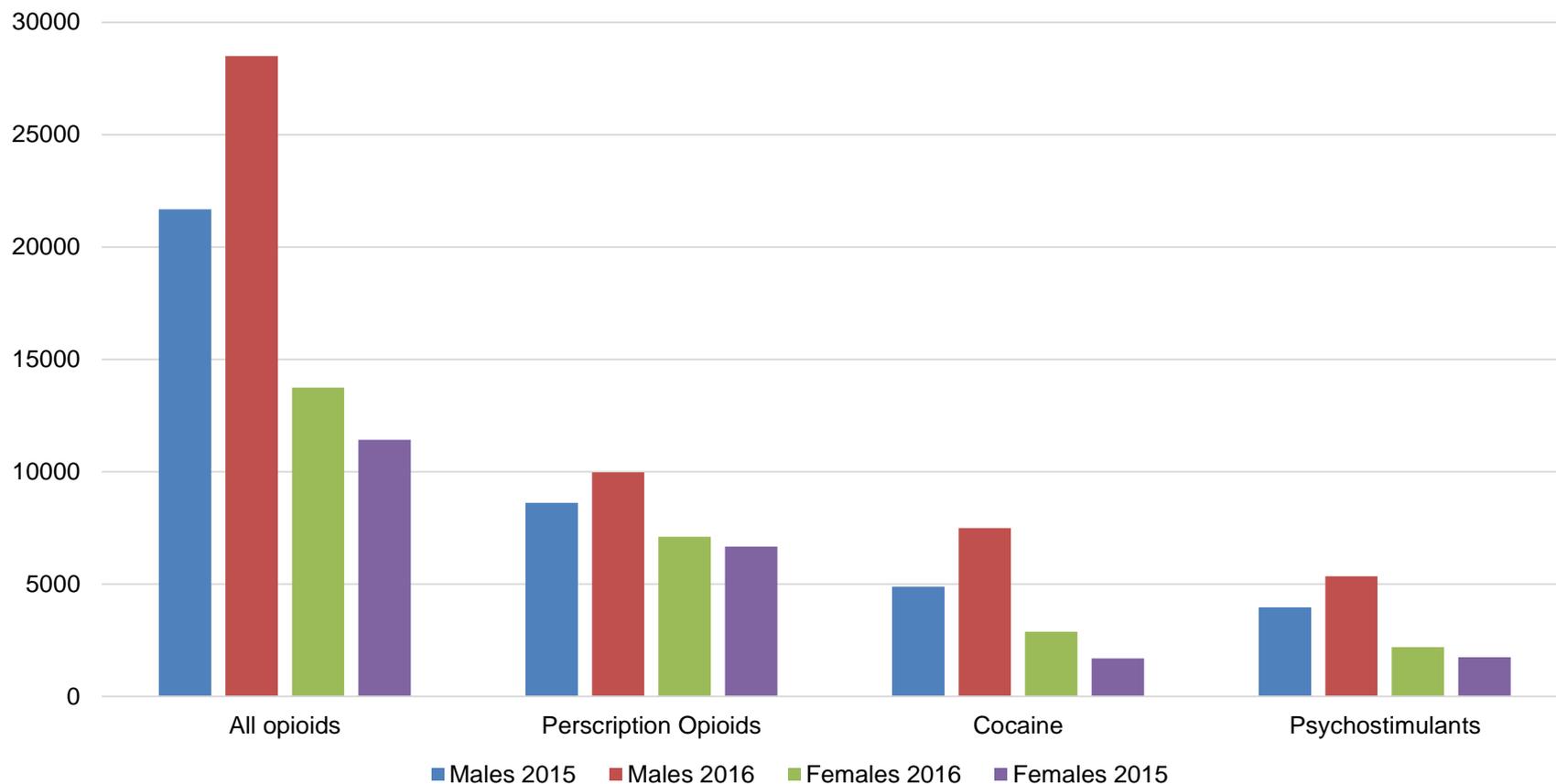
 **\$78.5 billion**
In economic costs (2013 data)⁶

Current Context: The Changing Face of Those Taking Opioids



Current Context of Opioid Misuse in the USA for Women

2015-2016 Annual number and age-adjusted rate of drug overdose deaths



Current Context: Opioid Use and Women

Compared to men, women are more likely to:

- Report chronic pain
- Be prescribed prescription pain relievers
- Be given higher doses
- Use them for longer time periods than men
- Have a shorter duration between opioid use initiation and seeking help for an opioid use disorder
- Less likely to receive naloxone for an overdose



Specific risks for the misuse of prescription opioid medication among women include: experience of violence and trauma, being a native minority, adolescent, young, older, pregnant, a sexual minority, and being a transwoman

Current Issues in the Opioid Problem: Women Compared to Men

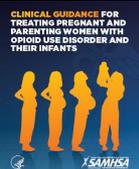
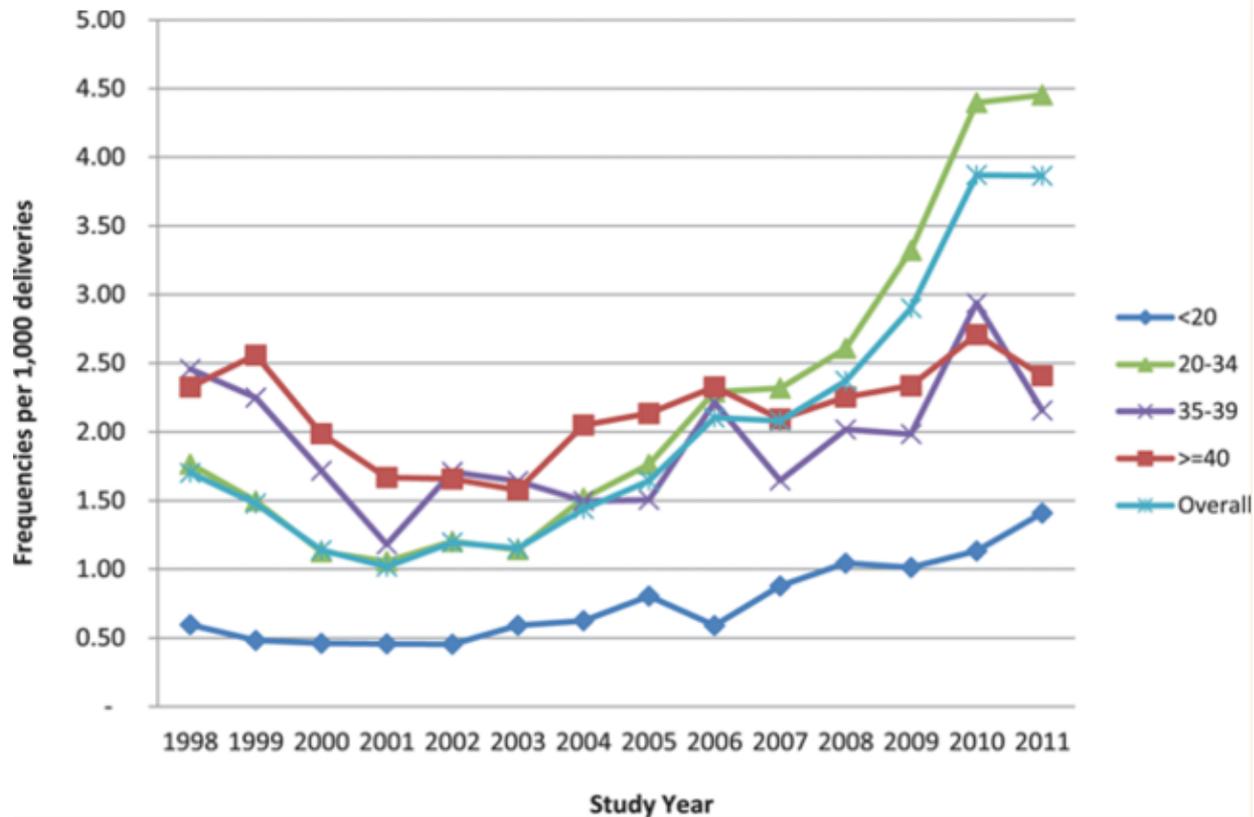
- Women experience greater impairments in employment, social, psychiatric and medical domains compared with men
- Women are more susceptible to risky sex and injection practices compared with men
- Less than 20% of women who need treatment receive it in a given year

Sumner SA et al., *Prehosp Emerg Care*. 2016; Hernandez-Avila CA et al., *Drug Alcohol Depend* 2004; McHugh RK et al. *J Subst Abuse Treat* 2013; Brooks A et al. *Subst Use Misuse* 2010; Frajzyngier V et al. *Drug Alcohol Depend* 2007; Terplan M et al., *Journal of Addictive Diseases* 2012
Hemsing N, et al. *Pain Res Manag*. 2016

<http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/>

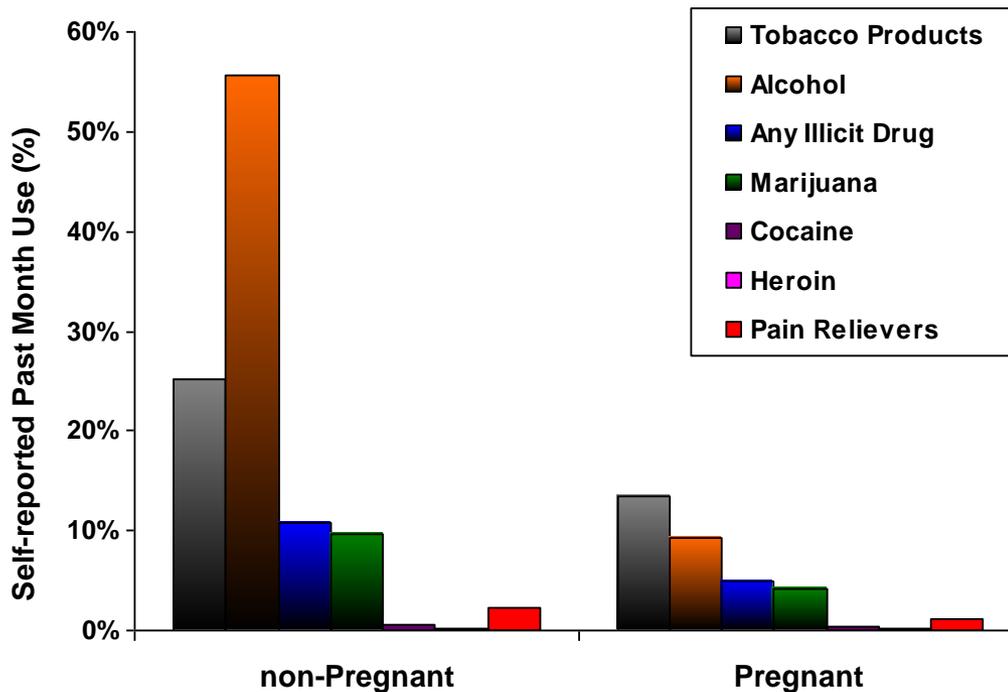
Prevalence of OUD During Delivery

Opioid abuse or dependence per 1,000 deliveries, overall and by age: United States, 1998–2011.



Current Context of Substance Use during Pregnancy

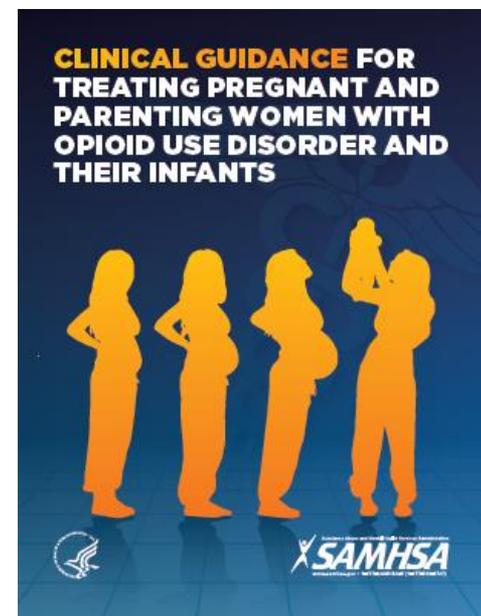
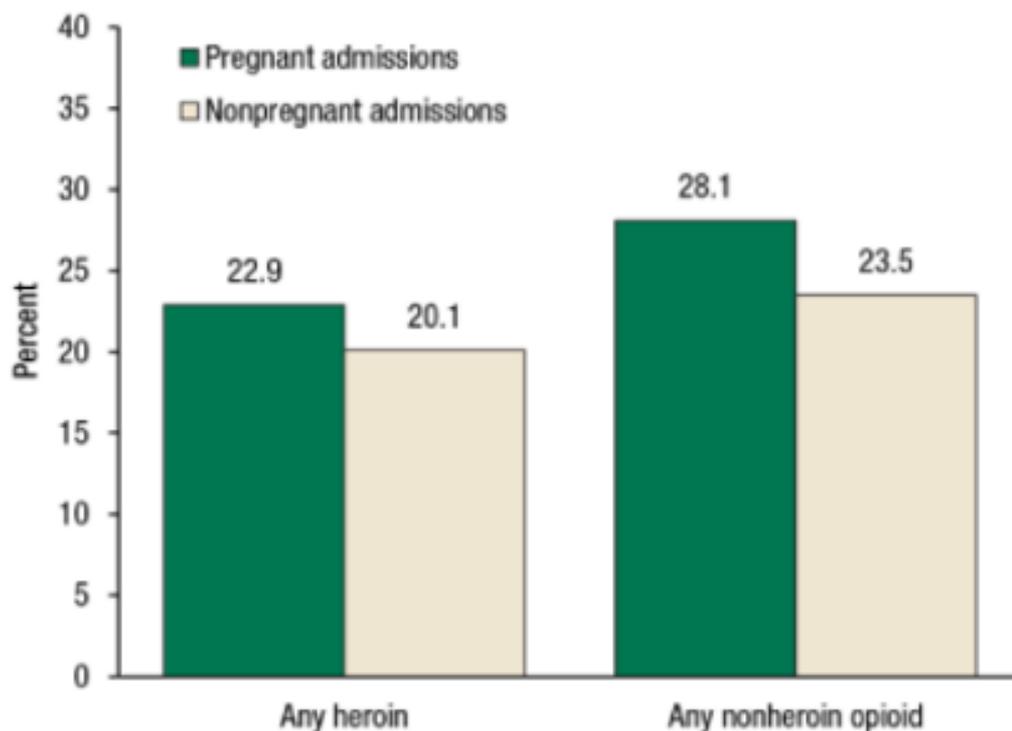
National Survey on Drug Use and Health, 2015
Past Month Use



- The two most common drugs used by non-pregnant women have been alcohol and tobacco
- This same statement is true for pregnant women
- Among pregnant women, approximately .2% used heroin, and 1.1% used pain relievers non-medically in the past month

Past-Month Opioid Misuse Among Women Admitted for Substance Use

Reported opioid misuse among female admissions aged 15 to 44, by pregnancy status: 2012



Source: SAMHSA, CBHSQ. (2012). Retrieved from https://www.samhsa.gov/data/sites/default/files/report_2724/ShortReport-2724.html

Pregnancy: A Unique Treatment Opportunity

- Mothers with substance use disorders have a mortality rate 8.4 times that of US women of similar age
- Pregnant women who use illicit substances may delay prenatal care and miss more healthcare visits than women who do not use substances
- Prenatal care may help to reduce the negative impact of illicit drug use on birth outcomes
- Lower prenatal care utilization may be due to a diverse set of barriers to seeking and obtaining care, including fear of child custody issues
- After childbirth, ongoing substance use disorders by caregivers and the dysfunctional home environment may create detrimental effects on children's psychological growth and development
- Maternal well-being has been recognized as a key determinant of the health of the next generation

Tipping Point Data

Neonatal Abstinence Syndrome and Associated Health Care Expenditures United States, 2000-2009

Stephen W. Patrick, MD, MPH, MS

Robert E. Schumacher, MD

Brian D. Benneyworth, MD, MS

Elizabeth E. Krans, MD, MS

Jennifer M. McAllister, MD

Matthew M. Davis, MD, MAPP

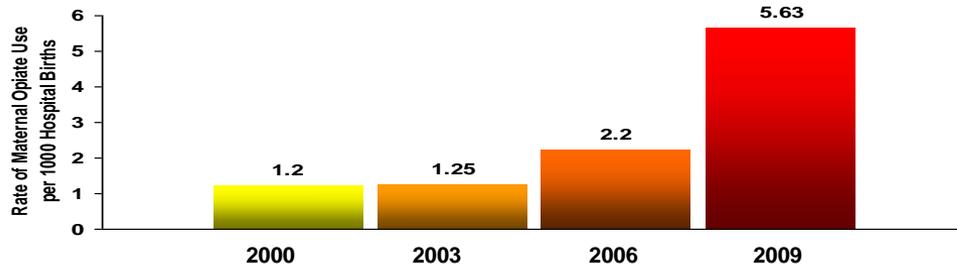
Context Neonatal abstinence syndrome (NAS) is a postnatal drug withdrawal syndrome primarily caused by maternal opiate use. No national estimates are available for the incidence of maternal opiate use at the time of delivery or NAS.

Objectives To determine the national incidence of NAS and antepartum opiate use and to characterize trends in national health care expenditures with NAS between 2000 and 2009.

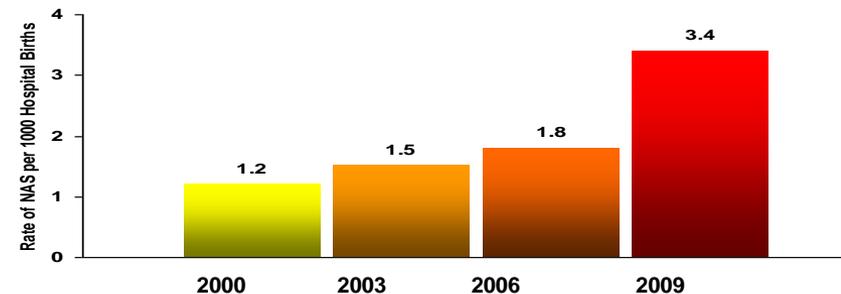
Design, Setting, and Patients A retrospective, serial, cross-sectional analysis of a nationally representative sample of newborns with NAS. The Kids' Inpatient Data was used to identify newborns with NAS by *International Classification of Diseases*

- A retrospective, serial, cross-sectional analysis of a nationally representative sample of newborns with NAS.
- Clinical conditions were identified using ICD-9-CM diagnosis codes.
- NAS and maternal opiate use were described as an annual frequency per 1000 hospital births.

Weighted National Estimates of the Rates of Maternal Opiate Use per 1000 Hospital Births per Year



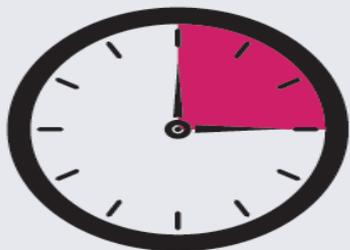
Weighted National Estimates of the Rates of NAS per 1000 Hospital Births per Year



Current Data



Neonatal abstinence syndrome (NAS) is a withdrawal syndrome in infants born to mothers who used opioids during pregnancy.



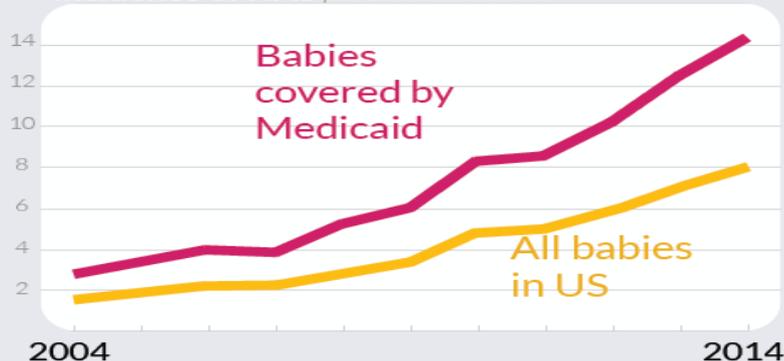
Every 15 minutes a baby is born with NAS



Hospital costs for NAS have grown more than **6x** since 2004

Infants with Medicaid are disproportionately affected

Incidence of NAS per 1000 live births



NAS resulted in approximately **\$2 billion** in excess costs among Medicaid-financed deliveries



Moms need resources & compassionate care



Prevention and treatment of substance use disorders are vital for women **before, during, and after pregnancy**



NAS is Not Addiction

- Newborns can't be “born addicted”
- NAS is withdrawal – due to physical dependence
- Physical dependence is not addiction
- Addiction is brain illness whose visible signs are behaviors
- Newborn do not have the life duration or experience to meet the addiction definition

Issues of Neonatal Withdrawal Diagnosis

Neonatal withdrawal symptoms from maternal use psychoactive substances

- A constellation of signs and symptoms observable in a neonate that are consistent with “maternal substance abuse or withdrawal while pregnant”
- “Fetal and neonatal addiction and withdrawal as a result of the mother's dependence on drugs during pregnancy.” Withdrawal or abstinence symptoms develop shortly after birth. Symptoms exhibited are loud, high-pitched crying, sweating, yawning and gastrointestinal disturbances

Applicable to

- Drug withdrawal syndrome in infant of dependent mother
- Neonatal abstinence syndrome

Approximate synonyms

- “Neonatal drug withdrawal syndrome, maternal drug abuse”
- “Neonatal drug withdrawal syndrome, maternal drugs of abuse”

NAS is not a diagnosis
of an Opioid Use
Disorder

NAS: Various Substances

STATE-OF-THE-ART REVIEW ARTICLE

Neonatal Abstinence Syndrome

TABLE 1 Onset, Duration, and Frequency of NAS Caused by Various Substances

Drug	Onset, h	Frequency, %	Duration, d
Opioids			
Heroin	24–48	40–80 ²⁷	8–10
Methadone	48–72	13–94 ³⁷	Up to 30 or more
Buprenorphine	36–60	22–67 ^{46,48}	Up to 28 or more
Prescription opioid medications	36–72	5–20 ^{56,60}	10–30
Nonopioids			
SSRIs	24–48	20–30 ⁶⁴	2–6
TCAs	24–48	20–50 ⁶⁴	2–6
Methamphetamines	24	2–49 ¹⁰¹	7–10
Inhalants	24–48	48 ⁷⁰	2–7

NAS: Factors

Other factors that contribute to the severity of NAS in neonates exposed to opioid agonists in utero:

- Genetics
- Other Substances
 - Tobacco use
 - Benzodiazepines
 - SSRIs
- Birth weight
- Hospital Protocols
 - NICU setting
 - The NAS assessment choice
 - NAS medication choice
 - Initiation and weaning protocols
 - Not breastfeeding
 - Separating mother and baby

MOTHER NAS Predictors

- Receipt of NAS treatment for infants was predicted by:
 - Higher infant birthweight
 - Greater maternal nicotine use
- Total medication dose needed to treat NAS was predicted by:
 - Maternal use of SSRIs
 - Greater nicotine use
 - Fewer days of study medication received

Methadone or buprenorphine dose is not consistently related to NAS severity

Limits of Urine Testing

- It is not a parenting test
- Toxicology tests for drugs are not sufficient for a diagnosis of a substance use disorder
- Having a substance use disorder is only one of many other factors in determining child safety



- Urine toxicology testing and confirmatory testing
- Patient consent required before specimen collection

Toxicology tests are not a substitute for verbal, interactive questioning and screening of patients about their drug and alcohol use.

Federal Policy: Plan of Safe Care



States receiving CAPTA funding are required to assure the federal government that they have a law or statewide program in effect and under operation that:

*“Addresses the needs of infants born and identified as being affected by **illegal** substance abuse or withdrawal symptoms resulting from prenatal drug exposure, or a Fetal Alcohol Spectrum Disorder (FASD) with*

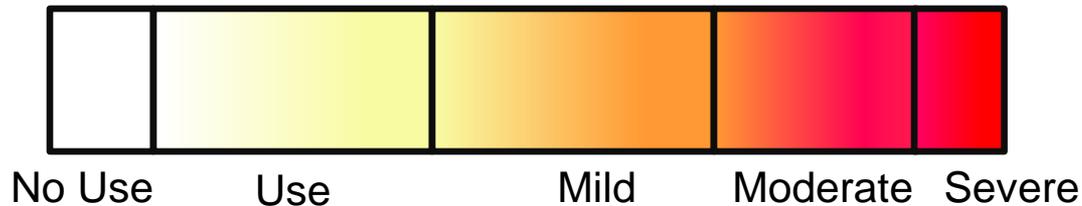
A requirement that health care providers involved in the delivery or care of such infants notify the child protective services system of the occurrence of such condition of such infants

*The development of a plan of safe care for the **infant...to ensure the safety and well-being of such infant following release from the care of healthcare providers, including through –***

Addressing the health and substance use disorder treatment needs of the infant and affected family or caregiver; and

Development and implementation by the State of monitoring systems regarding the implementation of such plans to determine whether and in what manner local entities are providing, in accordance with State requirements, referrals to and delivery of appropriate services for the infant and affected family or caregiver.”

Treatment Response Needs to Match the Severity of the Problems



Substance Use Disorder

American Society of Addiction Medicine Placement Criteria

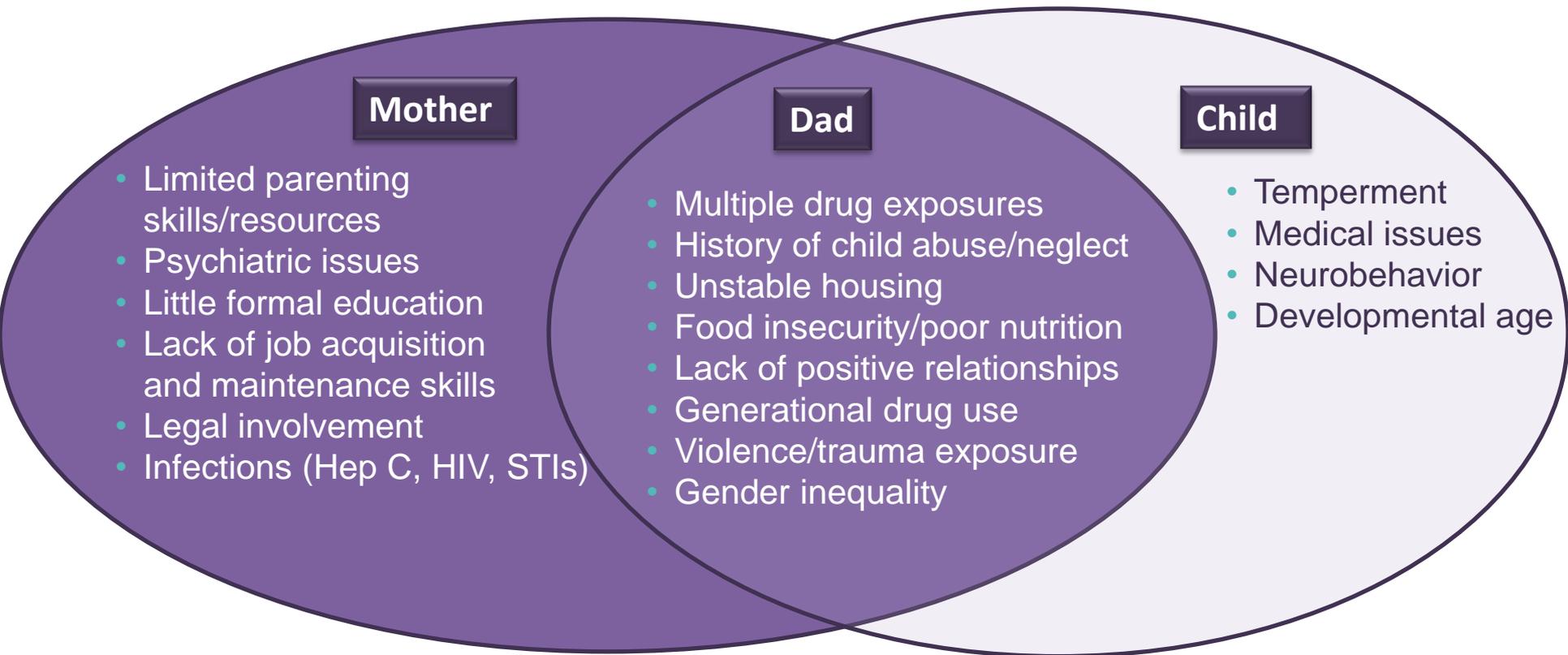
LEVEL 0.5	→	Early Intervention
LEVEL I	→	Outpatient Treatment
LEVEL II	→	Intensive Outpatient/ Partial Hospitalization
LEVEL III	→	Residential/ Inpatient Treatment
LEVEL IV	→	Medically Managed Intensive Hospital/Inpatient Treatment

Case Study: What Would You Do?

- A 24-year-old woman comes to you for OUD treatment
- She is 13 weeks pregnant
- It is her first pregnancy
- She has been using opioids for 7 years- just started injecting heroin a few months ago
- ***How would you manage this patient?***

Potential Complex Issues: Opioid Use during Pregnancy

Possible Issues facing pregnant women who use substances and their children



These factors with or without drug use can influence mother and child outcomes

Not All Opioid Exposure is the Same

IMPORTANT NOTE

Common Patient Situations:

Untreated
Opioid Use
Disorder

- Heroin crosses the placenta; pregnant women using heroin (untreated) have a 6-fold increase in risk of obstetrical complications and a 74-fold increase in risk of sudden infant death syndrome
- Much of this risk is attributed to repeated cycles of withdrawal experienced by the pregnant women and fetus

Opioids to Treat
OUD

- Buprenorphine and methadone carry risks (see later slides), risks are minor relative to *ongoing untreated* heroin or other non-medical opioid use

Opioids for Pain
(Without OUD)

- Both methadone and buprenorphine allow for more steady blood levels of opioids that prevents exposure to repeated fetal/maternal withdrawal events.
- Know these relative risks/benefits when discussing treatment options

Fear, Discrimination, and Barriers to Care

- Fear of being incarcerated for illicit drug use or for exposing their fetus to illicit drugs
- Fear of losing custody of their children
- Shame and fear of being judged
- Limited resources
- Lack of funds to pay for:
 - Services
 - Transportation
 - Daycare

Clinical Question:

- A 32 year old woman
- 4 months pregnant
- lost custody of her 3 year old
- she has endocarditis, a STI and smokes cigarettes
- she denies drug use

What do you do?

"I was one of the people that was scared to seek treatment. That's why I stopped going to my OB appointments."

– Veronica Robinson, UNC Horizons Patient

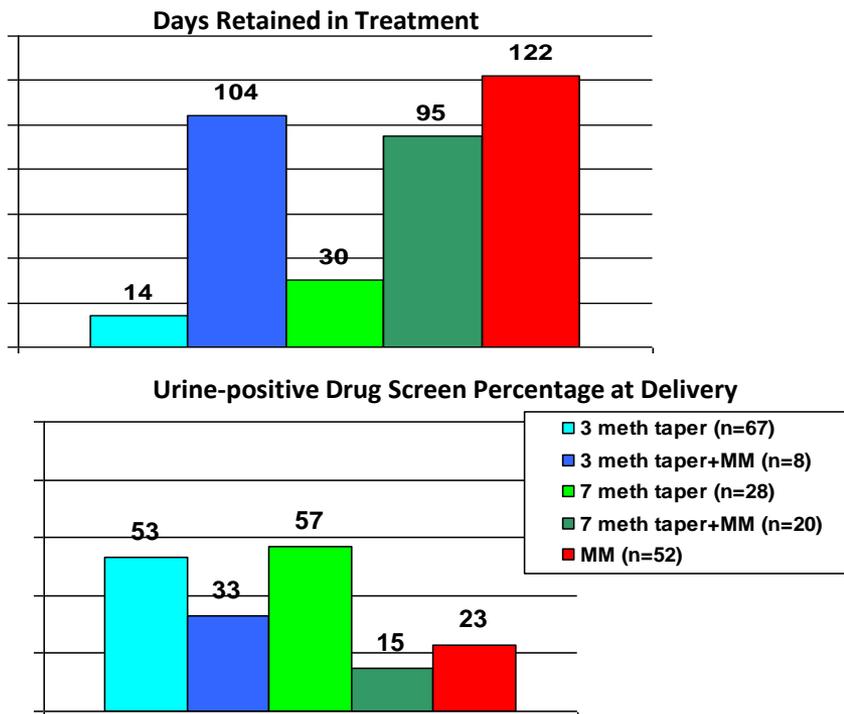
Medication Assisted Treatment vs. Medication-Assisted Withdrawal

- WHO 2014 Guidelines: “Pregnant women dependent on opioids should be encouraged to use opioid maintenance treatment whenever available rather than to attempt opioid detoxification. Opioid maintenance treatment in this context refers to either methadone maintenance treatment or buprenorphine maintenance treatment.”
- Medication followed by no medication treatment has frequently been found to be unsuccessful, with relatively high attrition and a rapid return to illicit opioid use
- Maintenance medication facilitates retention of patients and reduces substance use compared to no medication
- Biggest concern with opioid agonist medication during pregnancy is the potential for occurrence of neonatal abstinence syndrome (NAS) – a treatable condition

Maintenance vs. Medication-assisted Withdrawal (MAW)

Chart review of 5 groups of patients:

- 3-day methadone-assisted withdrawal (MAW) alone ($n=67$)
- 3-day MAW followed by methadone maintenance (MM) ($n=8$)
- 7-day MAW alone ($n=28$)
- 7-day MAW followed by MM ($n=20$)
- continuous MM ($n=52$)



Patients in the three MM groups:

- remained in treatment longer
- had few drug positive urine drug screening test results
- attended more obstetrical visits
- more often delivered at the program hospital than patients in the two MAW alone groups

Most Recent Medication-Assisted Withdrawal Study

	Group 1	Group 2	Group 3	Group 4	Total
Number	108	23	77	93	301
White	85 (79%) ^a	22 (96%)	74 (96%)	84 (90%) ^a	265 (88%)
African-American	22 (20%) [^]	1 (4%)	3 (4%)	8 (9%)	34 (11%)
Gestational age at detoxification and NICU admission					
Detoxification first trimester, 5–13 weeks' gestation	10 (9%)	4 (17%)	12 (15%)	2 (2%)	28 (9%)
Detoxification second trimester, 14–27 weeks' gestation	65 (60%)	10 (43%)	36 (47%)	37 (40%)	148 (49%)
Detoxification third trimester, ≥28 weeks' gestation	33 (31%)	9 (39%)	29 (38%)	54 (58%)	125 (42%)
Preterm deliveries prior to 37 weeks' gestation	21 (19%)	3 (13%)	13 (17%)	16 (17%)	53 (17.6%)
Neonatal intensive care unit admission	32 (30%)	5 (22%)	60 (78%)	22 (24%)	119 (40%)
Pregnancy outcome					
Rate of NAS	20 (18.5%)	4 (17.4%)	54 (70.1%)	16 (17.2%)	94 (31%)
Rate of relapse	25 (23.1%)	4 (17.4%)	57 (74.0%)*	57 (22.5%)	107 (36%)

- Consistent with past literature in the ability to withdraw without obstetric complication
- Lower relapse rates than most other studies
- Lack of fetal or maternal monitoring during withdrawal
- Diagnosis of opioid dependence or use disorder was not an eligibility criterion
- Only included patients who were “fully detoxified”
- No mention of women lost to follow-up

^a One Hispanic in group 1 and one Asian in group 4

[^] P<.01 African American women were more likely to be Group 1 (incarcerated) than Groups 2-4

* P<.001 Group 3 had a higher rate of relapse compared to Groups 2 and 4

Bell J, et al., *Am J Obstet Gynecol.* 2016

Medically Assisted Withdrawal (Detoxification): Consider the Mother-Infant Dyad

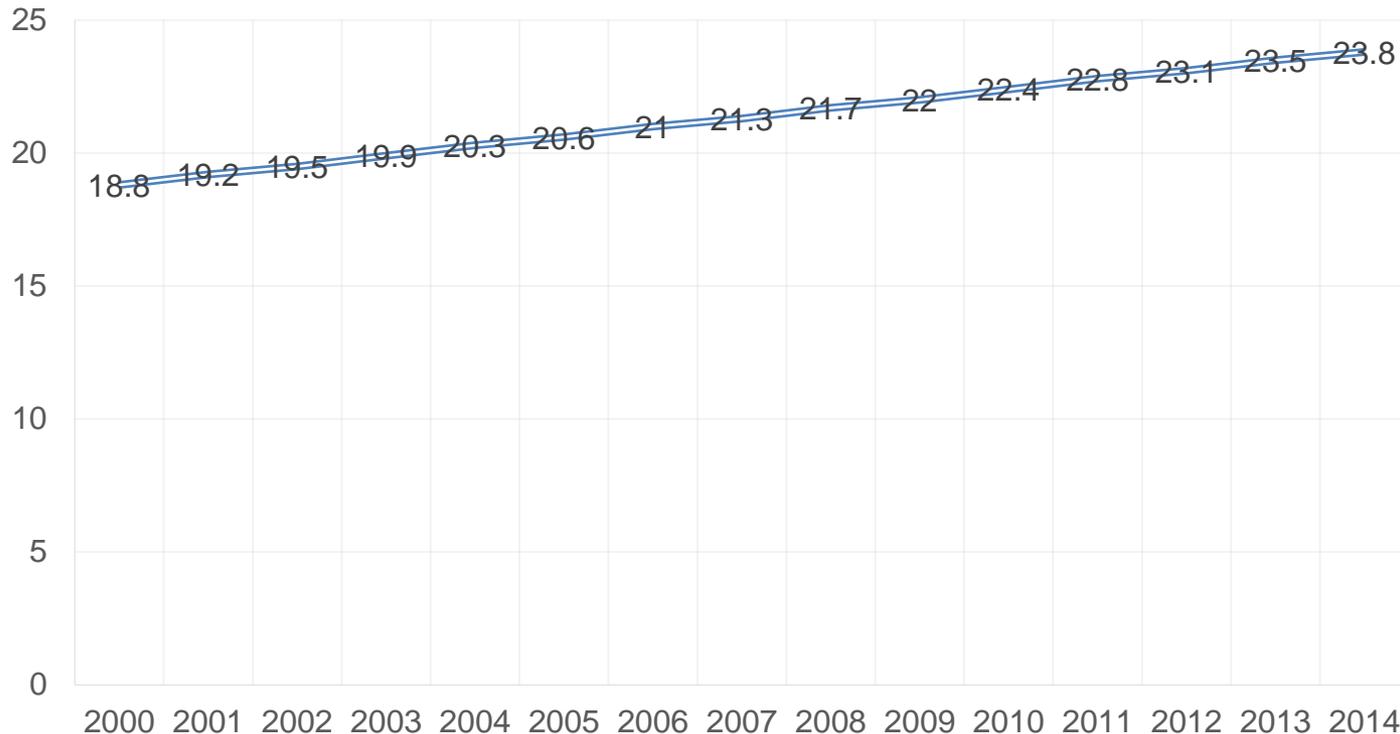
- Early reports associated withdrawal with maternal relapse and fetal demise
- Recent case series data do not support this association
- Relapse remains a significant clinical concern - rates ranging from 17% to 96% (average 48%)
- Current data do not support a reduction in NAS with medically assisted withdrawal relative to opioid agonist treatment
- Medically assisted withdrawal increases the risk of maternal relapse and poor treatment engagement and does not improve newborn health
- Treatment of chronic maternal disease, including opioid use disorder, should be directed toward optimal long-term outcome

SAMHSA's Guidance: Medication Assisted Withdrawal is *Not* Recommended

- Opioid agonist treatment is the recommended standard of care.
- Opioid agonist treatment helps pregnant women with OUD avoid a return to substance use, which has the potential for overdose or death.
- A decision to withdraw from opioid agonist treatment should be made with great care on a case-by-case basis.
- A pregnant woman receiving treatment for OUD may decide to move forward with medication assisted withdrawal if it can be conducted in a controlled setting. The benefits to her outweigh the risks.

Pregnant patients should be advised that withdrawal during pregnancy increases the risk of relapse without fetal or maternal benefit.

Maternal Mortality is Increasing



Possible Factors:

- Drug use with homicide/suicide
- Overdose
- Medicaid coverage loss at 6 weeks postpartum
- “Detox” during pregnancy to prevent NAS
- Inadequate Access to drug treatment/MAT

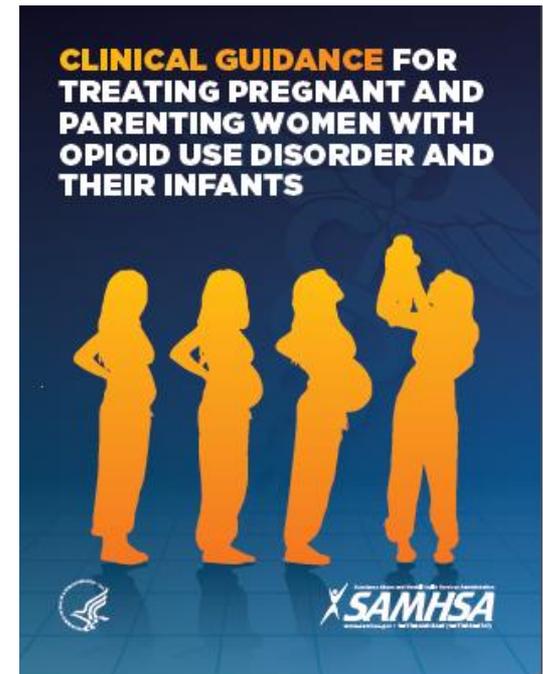
*Excludes California and Texas California showed a declining trend, whereas Texas had a sudden increase in 2011-2012.

Medication Options

- Methadone
- Buprenorphine alone
- Buprenorphine + naloxone
- *Naltrexone*

Methadone and Buprenorphine: Advantages

	Methadone	Buprenorphine
Advantages		
Reduces/eliminates cravings for opioid drugs	●	●
Prevents onset of withdrawal for 24 hours	●	●
Blocks the effects of other opioids	●	●
Promotes increased physical and emotional health	●	●
Higher treatment retention than other treatments	●	
Lower risk of overdose Fewer drug interactions Office-based treatment delivery Shorter NAS course		●



Methadone and Buprenorphine: Disadvantages

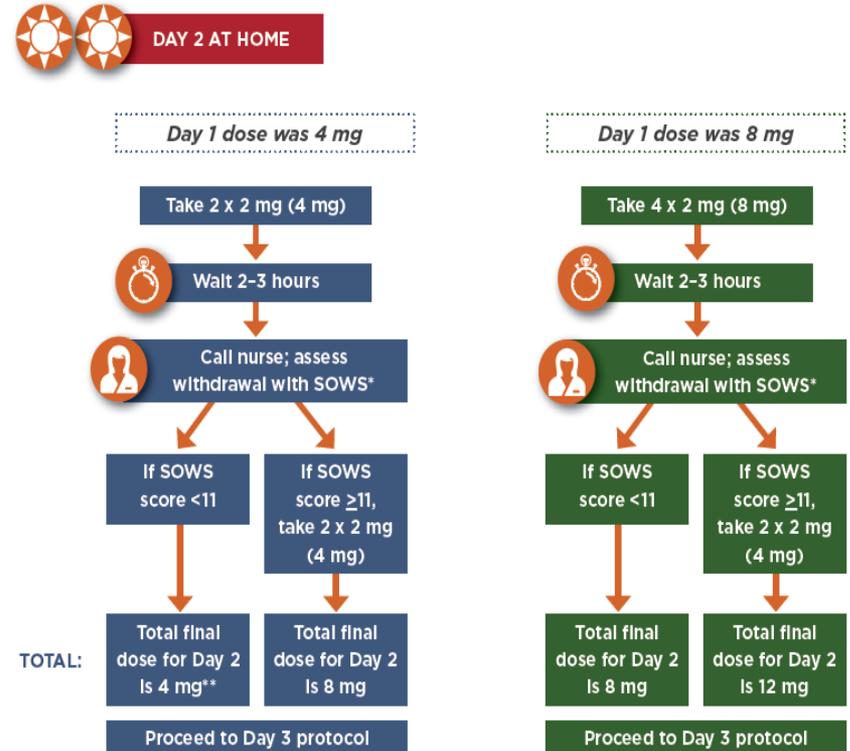
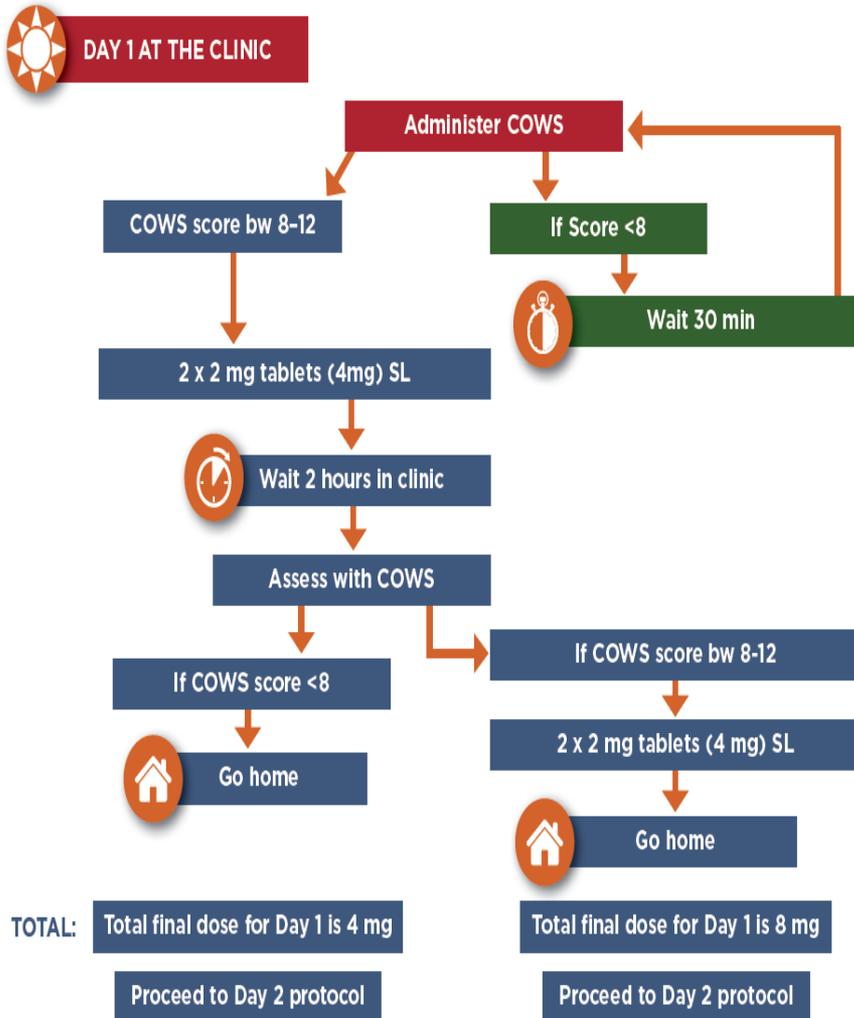
Methadone Disadvantages:

- Achieving stable dose could take days to weeks
- Increased risk of overdose compared to no treatment
- Usually requires daily visits to federally certified opioid treatment programs
- Longer neonatal abstinence syndrome (NAS) duration and more medication to treat NAS than other treatments

Buprenorphine Disadvantages:

- Demonstrated clinical withdrawal symptoms
- Possible increased risk of diversion due to more access from prescribers

Buprenorphine: Outpatient Induction



*On Days 2-4, when the patient calls the nurse to discuss possible withdrawal signs, the nurse will use the Subjective Opioid Withdrawal Scale (SOWS) and walk the patient through the items in the instrument.

**Although rare, it is possible a pregnant woman would have all withdrawal symptoms relieved at this low dose. If this happens she should continue to apply 4 mg buprenorphine each morning until her next in-person follow up appointment.

Buprenorphine: Outpatient Induction (continued)

DAY 3 AT HOME

DAY 4 AT HOME

Day 2 dose was 8 mg

Day 2 dose was 12 mg

Day 3 dose was 8 mg

Day 3 dose was 12 mg

Day 3 dose was 16 mg

Take 4 x 2 mg (8 mg)

Take 6 x 2 mg (12 mg) In AM. Do not divide dose.

Take 4 x 2 mg (8 mg)

Take 6 x 2 mg (12 mg) In AM. Do not divide dose.

Take 8 x 2 mg (16 mg) In AM. Do not divide dose unless advised to do so by the nurse on Day 3.

Wait 2-3 hours

Wait 2-3 hours

Wait 2-3 hours

Wait 2-3 hours

Maintain this dose until next in-person appointment.

Call nurse; assess withdrawal with SOWS

Call nurse; assess withdrawal with SOWS*

Call nurse; assess withdrawal with SOWS

Call nurse; assess withdrawal with SOWS

If SOWS score <11

If SOWS score ≥11, take 2 x 2 mg (4 mg)

If SOWS score <11

If SOWS score ≥11, take 2 x 2 mg (4 mg)

If SOWS score <11

If SOWS score ≥11, take 2 x 2 mg (4 mg)

If SOWS score <11

If SOWS score ≥11, take 2 x 2 mg (4 mg)

TOTAL: Total final dose for Day 3 is 8 mg

TOTAL: Total final dose for Day 3 is 12 mg

TOTAL: Total final dose for Day 3 is 12 mg

TOTAL: Total final dose for Day 3 is 16 mg

TOTAL: Total final dose for Day 4 is 8 mg

TOTAL: Total final dose for Day 4 is 12 mg

TOTAL: Total final dose for Day 4 is 12 mg

TOTAL: Total final dose for Day 4 is 16 mg

TOTAL: Total final dose for Day 4 is 16 mg

Proceed to Day 4 protocol

Proceed to Day 4 protocol

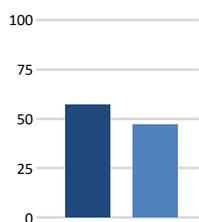
Maintain this dose until the scheduled in-person visit.

*If the patient reports excessive daytime sleepiness, consider separating the next day's dose into 2 equal doses approximately 8 hours apart.

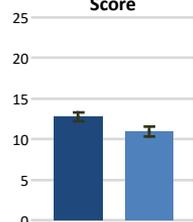
MOTHER: Buprenorphine vs. Methadone

Primary Outcomes

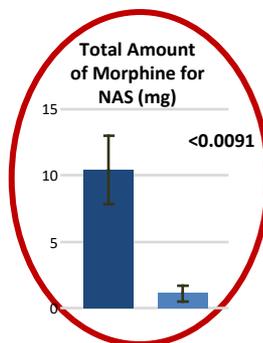
% Treated for NAS [Yes]



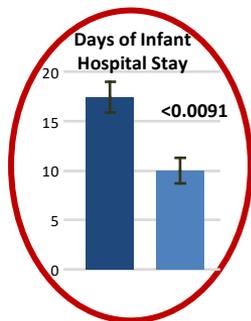
NAS Peak Score



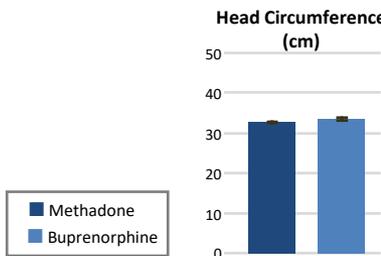
Total Amount of Morphine for NAS (mg)



Days of Infant Hospital Stay



Head Circumference (cm)



■ Methadone
■ Buprenorphine

- Compared with methadone-exposed neonates, buprenorphine-exposed neonates
 - Required 89% less morphine to treat NAS
 - Spent 43% less time in the hospital
 - Spent 58% less time in the hospital being medicated for NAS

- **Both medications in the context of comprehensive care produced similar maternal treatment and delivery outcomes**

Notes: Significant results are encircled. Site was a blocking factor in all analyses. The O'Brien-Fleming α spending function resulted in $\alpha=0.0091$ for the inferential tests of the Medication Condition effect for the 5 primary outcome measures at the conclusion of the trial.

Methadone vs. Buprenorphine: 12 study Meta-analysis

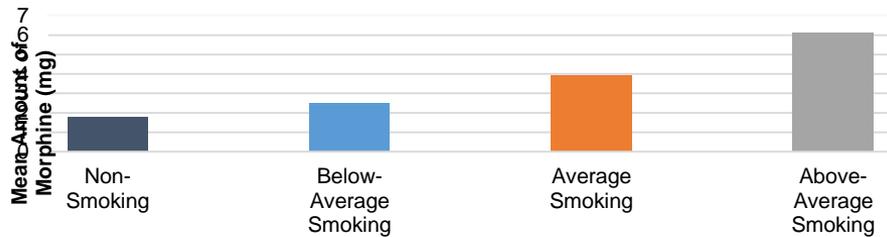
- N=515 neonates born to mothers receiving methadone and N=855 neonates born to mothers receiving buprenorphine in 12 studies
- In buprenorphine compared with methadone-exposed neonates:
 - The unadjusted NAS treatment risk was lower
 - The mean length of hospital stay shorter
- In treated neonates, NAS treatment duration was shorter and total morphine dose was lower
- Buprenorphine-exposed neonates also had:
 - Higher mean gestational age
 - Greater weight
 - Length
 - Head circumference at birth.
- Fewer women treated with buprenorphine used illicit opioids near delivery

Buprenorphine+Naloxone vs. Buprenorphine or Methadone

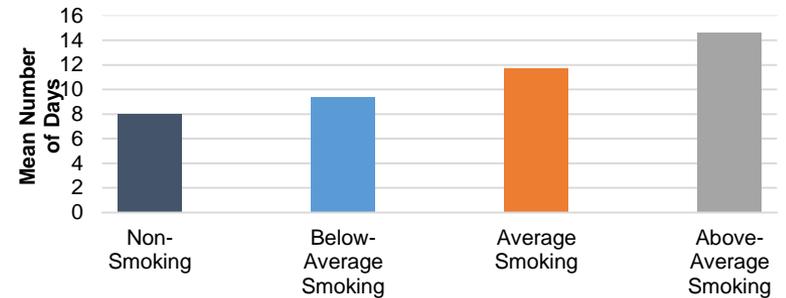
- Collective data comparing buprenorphine+naloxone to methadone show:
 - Similar maternal outcomes as those seen with buprenorphine alone
 - Similar reductions in NAS severity
- Collective data comparing buprenorphine+naloxone to buprenorphine alone show:
 - Similar maternal outcomes
 - Similar birth outcomes including NAS severity

MOTHER: Smoking and NAS

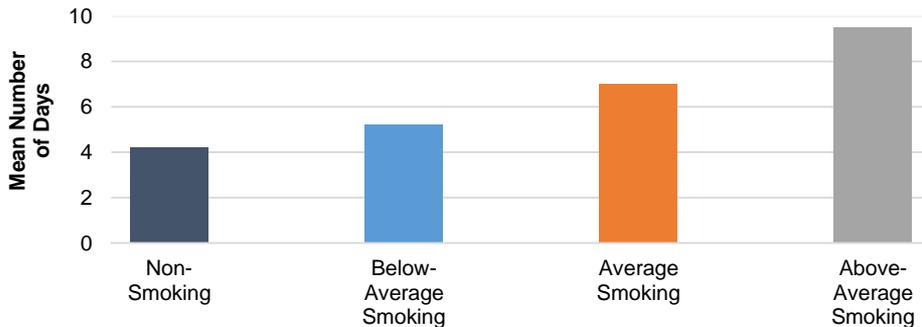
Total Amount of Morphine Needed to Treat NAS



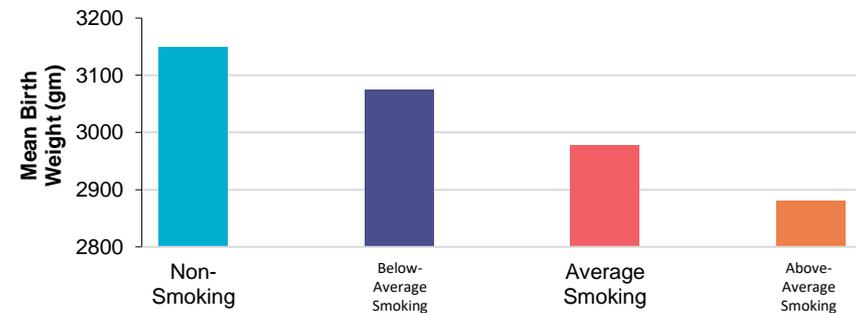
Total Length of Hospital Stay¹



Number of Days Medicated for NAS



Neonatal Weight at Birth



Providers need to support women in reducing and ceasing tobacco use to increase chances of healthier birth outcomes

MOTHER Child Outcomes up to 36 months

N=96 children

- No pattern of differences in physical or behavioral development to support medication superiority
- No pattern of differences for infants treated for NAS v. infants who did not receive treatment for NAS
- Compared to standardized testing norms, results indicate children born in the MOTHER study are following a path of normal development in terms of growth, cognitive and psychological development

Pain Management: Labor and Delivery

- Medications that are full agonist opioids can effectively treat pain in patients stabilized on either methadone or buprenorphine.
- These results are consistent with data from non-pregnant surgery patients.
- The importance of uninterrupted methadone or buprenorphine treatment in these patients is critical.
- Each patient needs a pain management plan before delivery.

Pain Relief Medications for Perinatal Patients With OUD

- Providing pain relief to pregnant women on opioid agonist treatment for OUD is essential (e.g., epidural, short-acting opioids).
 - Acute pain management
 - Morphine sulfate
 - Fentanyl
 - Hydromorphone
- Effective dose should be used for 3 or fewer days and rarely more than 7 days
- Partial opioid agonists should be avoided because they have antagonist properties and will precipitate acute opioid withdrawal.
 - Butorphanol
 - Nalbuphine
 - Pentazocine

Breastfeeding: Methadone and Mono-Buprenorphine

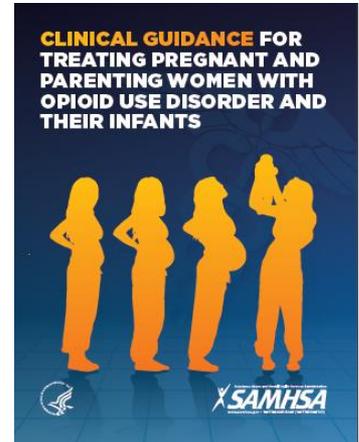
- Breast feeding has advantages to mother and child
- Both methadone and buprenorphine are compatible with breastfeeding
- Concentration of either medication in breast milk is low
 - Little buprenorphine is bioavailable to infant, owing in part to the need for sublingual absorption
- Most recent guidelines: “the amounts of buprenorphine in human milk are small and unlikely to have negative effects on the developing infant”
- “The advantages of breast feeding prevail despite the risks of an infant opiate intoxication caused by methadone or buprenorphine.”

Breastfeeding: Buprenorphine+Naloxone

- There are no data on the combination product buprenorphine/naloxone in breastfeeding, however oral absorption of naloxone is minimal.
- Caution should be exercised when buprenorphine+naloxone is administered to a nursing woman.
- The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for the medication and any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition.
- Advise the nursing mother taking buprenorphine+naloxone to monitor the infant for increased drowsiness and breathing difficulties.

Naltrexone

- Is an antagonist
- Binds and blocks opioid receptors
- Reduces opioid cravings
- Has no misuse and diversion potential



The expert panel did not agree on whether women on naltrexone should continue to use it during pregnancy. They did agree that methadone and buprenorphine should be used to treat women with OUD during pregnancy

Naltrexone: Issues During and After Pregnancy

1. Induction of women new to the medication will be a challenge
2. Stress of withdrawal on mother and fetus
3. Naltrexone precludes use of opioids for pain relief – may make women more sensitive to pain
4. Concerns about ability to breastfeed due to reduced milk production and effects of medication consumed via breast milk on the neonate

What We Need to Know

What is the relative safety and efficacy of naltrexone for the mother, fetus and child?

Need an initial safety and efficacy study in pregnancy to examine maternal, fetal and child outcomes

Documentation

- Document any antepartum discussion or guidance regarding:
 - Risks and benefits of medication
 - Pain relief during labor, delivery, and postpartum in the antepartum or intrapartum record
 - Breastfeeding recommendations
 - Advice regarding NAS and infant care
- Make information accessible to all members of the treatment team. These practices improve communication among team members.
 - For example: The healthcare professional responsible for prescribing opioid agonist treatment for pain can instruct the team regarding the management of the opioid agonist treatment for OUD and provide guidance for acute pain management to support the treatment team in achieving adequate pain control.

Screening Versus Urine Testing

- Screening for substance use: Verbal, written, or computer-assisted questioning about patient history and current drug use is the gold standard for substance-use screening.
- Urine drug testing can also identify women who use drugs, but it should never replace written or verbal screening because biologic tests cannot diagnose a drug-use disorder or its severity, nor can it determine use quantity, frequency, or route of administration of a given drug.
- Before urine drug testing, providers should obtain the patient's consent and explain the reasons for and limitations of any such test.

High Risk?

- Although patients with opioid use disorders or patients who misuse opioids may benefit from more frequent prenatal visits, in the absence of other indications, they do not necessarily require more intense medical care than other pregnant patients.

Discontinuation of Opioid Agonist Treatment?

- Discontinuation of opioid agonist treatment for OUD should generally be avoided in the immediate postpartum period.
- It may be considered later if the mother is stable and the mother and child are well bonded and have a safe, stable social environment and home.
- Plans to stop taking a medication should be made by the mother in conjunction with her treatment team.

The longer the patient continues on opioid agonist treatment for OUD, the lower her risk of return to substance use when she eventually chooses to taper.

Discontinuation of Opioid Agonist Treatment

- Opioid agonist treatment for OUD should be discontinued only when it is in the best interest of the mother and infant.
- A safety plan for the mother and family needs to be in place before the tapering starts; the mother must know what to do if she returns to substance use.
- Once a decision has been made to discontinue opioid agonist treatment with methadone or buprenorphine, the medication must be tapered gradually to mitigate withdrawal.
- Discontinuation of opioid agonist treatment should, at the very least, be delayed until after the infant is consistently sleeping through the night and has completed breastfeeding.
- Ensure naloxone is at home and that caregivers know how to use it.

Case Study: What Would You Do?

- A 24-year-old woman comes to you for OUD treatment
- She is 13 weeks pregnant
- It is her first pregnancy
- She has been using opioids for 7 years- just started injecting heroin a few months ago
- ***How would you manage this patient?***
- ***How have your answers changed since the start of the presentation?***

Summary I

- OUD is growing among women and pregnancy is not a protective factor against it
- Untreated opioid use disorders present a host of risks to pregnant woman, the fetus and child
- NAS is a serious and treatable condition
- There are many factors that health care providers can do to reduce NAS severity
- Medication assisted withdrawal is not recommended during pregnancy.

Summary II

- Both methadone and buprenorphine FDA approved product inserts include a discussion of pregnancy and its related issues
- Buprenorphine and methadone are the safest medications for managing OUD during pregnancy.
- Induction onto methadone or buprenorphine does not have to be more complicated during pregnancy
- Breastfeeding is recommended for women being treated with buprenorphine and methadone.

Summary III

- Methadone and buprenorphine have several advantages and disadvantages relative to one another, and ultimately a conversation about these aspects with a pregnant woman who is considering these medications is indicated.
- Less is known about naltrexone during the perinatal period
- Naltrexone, buprenorphine, and methadone are all found in breast milk, and decisions regarding their use should be made with the patient in the context of the relative risks/benefits of each of these approaches.

References

- Bell J, Towers C V., Hennessy MD, Heitzman C, Smith B, Chattin K. Detoxification from opiate drugs during pregnancy. *Am J Obs Gynecol*. 2016;215(3):374.e1-374.e6. doi:10.1016/j.ajog.2016.03.015.
- Blinick G, Wallach RC, Jerez E. Pregnancy in narcotics addicts treated by medical withdrawal. The methadone detoxification program. *Am J Obs Gynecol*. 1969;105(7):997-1003. <http://www.ncbi.nlm.nih.gov/pubmed/5352597>.
- 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(7):673-686. doi:10.1093/aje/kwu190.
- Brooks A, Meade CS, Potter JS, Lokhnygina Y, Calsyn DA, Greenfield SF. Gender differences in the rates and correlates of HIV risk behaviors among drug abusers. *Subst Use Misuse*. 2010;45(14):2444-2469. doi:10.3109/10826084.2010.490928.
- CDC. No Title. <https://www.cdc.gov/drugoverdose/data/fentanyl.html>. Published 2017.
- CDC. No Title. <http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/>. Published 2017.
- CDC. No Title. <https://www.cdc.gov/drugoverdose/data/overdose.html>. Published 2017.
- CDC. No Title. <https://www.cdc.gov/mmwr/volumes/65/wr/mm655051e1.htm>. Published 2016.
- CDC. No Title. <https://www.cdc.gov/drugoverdose/data/heroin.html>. Published 2017.
- Chatterji P, Markowitz S. The impact of maternal alcohol and illicit drug use on children's behavior problems: Evidence from the children of the national longitudinal survey of youth. *J Health Econ*. 2001;20(5):703-731. doi:10.1016/S0167-6296(01)00090-X.

References

- Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826. doi:10.1001/jamapsychiatry.2014.366.
- Courtwright DT. The hidden epidemic: Opiate addiction and cocaine use in the South, 1860-1920. *J South Hist*. 1983;49(1):57-72. doi:10.2307/2209306.
- Dattel BJ. Substance abuse in pregnancy. *Semin Perinatol*. 1990;14(2):179-187. <http://www.ncbi.nlm.nih.gov/pubmed/2187251>.
- Desmond MM, Wilson GS. Neonatal abstinence syndrome: Recognition and diagnosis. *Addict Dis*. 1975;2(1-2):113-121. <http://www.ncbi.nlm.nih.gov/pubmed/1163356>.
- Drugs website. <https://www.drugs.com/pro/suboxone.html#s46>
- Earle FB. Maternal opium habit and infant mortality. *Med Standard* 1888;III:2-4.
- El-Mohandes A, Herman AA, El-Khorazaty MN, Katta PS, White D, Grylack L. Prenatal care reduces the impact of illicit drug use on perinatal outcomes. *J Perinatol*. 2003;23(5):354-360. Fajemirokun-Odudeyi O, Sinha C, Tutty S, et al. Pregnancy outcome in women who use opiates. *EurJ Obs Gynecol Reprod Bio*. 2006;126(2):170-175. doi:10.1016/j.ejogrb.2005.08.010.
- Finnegan LP, Connaughton JF, Kron RE, Emich JP. Neonatal abstinence syndrome: assessment and management. *Addict Dis*. 1975;2(1-2):141-158. <http://www.ncbi.nlm.nih.gov/pubmed/1163358>.
- Florence CS, Zhou C, Luo F, Xu L. The economic burden of prescription opioid overdose, abuse, and dependence in the United States, 2013. *Med Care*. 2016;54(10):901-906.

References

- Fitzsimmons J, Tunis S, Webster D, Izes J, Wapner R, Finnegan L. Pregnancy in a drug-abusing population. *Am J Drug Alcohol Abuse* 1986;12:247-55
- Frajzyngier V, Neaigus A, Gyarmathy VA, Miller M, Friedman SR. Gender differences in injection risk behaviors at the first injection episode. *Drug Alcohol Depend.* 2007;89(2-3):145-152.
- Frakt A, Carroll A. Painkiller Abuse, a Cyclical Challenge. *The New York Times*. December 22, 2014.
- Funai EF, White J, Lee MJ, Allen M, Kuczynski E. Compliance with prenatal care visits in substance abusers. *J Matern Fetal Neonatal Med.* 2003;14(5):329-332. Gawronski KM, Prasad MR, Backes CR, Lehman KJ, Gardner DK, Cordero L. Neonatal outcomes following in utero exposure to buprenorphine/naloxone or methadone. *SAGE Open Med.* 2014;2:205031211453028. Goodfriend MJ. The effects of maternal narcotic addiction on the newborn. *Am J Obs Gynecol.* 1956;71(1):29-36.
- Happel TJ. Morphinism in its relation to the sexual functions and appetite, and its effect on the offspring of the users of the drug. *Med Surg Report.* 1892;67:403-407.
- Hemsing N, Greaves L, Poole N, Schmidt R. Misuse of prescription opioid medication among women: A scoping review. *Pain Res Manag.* 2016;2016:1754195. Hernandez-Avila CA, Rounsaville BJ, Kranzler HR. Opioid-, cannabis- and alcohol-dependent women show more rapid progression to substance abuse treatment. *Drug Alcohol Depend.* 2004;74(3):265-272.
- Hser YI, Kagihara J, Huang D, Evans E, Messina N. Mortality among substance-using mothers in California: A 10-year prospective study. *Addiction.* 2012;107(1):215-222. doi:10.1111/j.1360-0443.2011.03613.x.
- Jansson LM, Velez M. Neonatal abstinence syndrome. *Curr Opin Pediatr.* 2012;24(2):252-258. doi:10.1097/MOP.0b013e32834fdc3a.

References

- Jarvis MA, Schnoll SH. Methadone treatment during pregnancy. *J Psychoact Drugs*. 26(2):155-161. doi:10.1080/02791072.1994.10472263.
- Johnson RE, Jones HE, Jasinski DR, et al. Buprenorphine treatment of pregnant opioid-dependent women: Maternal and neonatal outcomes. *Drug Alcohol Depend*. 2001;63(1):97-103. doi:10.1016/S0376-8716(00)00194-0.
- Jones HE, Johnson RE, Milio L. Post-cesarean pain management of patients maintained on methadone or buprenorphine. *Am J Addict*. 15(3):258-259. doi:10.1080/10550490600626721.
- Jones HE, O'Grady KE, Malfi D, Tuten M. Methadone maintenance vs. methadone taper during pregnancy: maternal and neonatal outcomes. *Am J Addict*. 2008;17:372-386. doi:10.1080/10550490802266276.
- Jones HE. Acceptance of naltrexone by pregnant women enrolled in comprehensive drug addiction treatment: An initial survey. *Am J Addict*. 2012;21(3):199-201. doi:10.1111/j.1521-0391.2012.00229.x.
- Jones HE, Deppen K, Hudak ML, et al. Clinical care for opioid-using pregnant and postpartum women: The role of obstetric providers. *Am J Obs Gynecol*. 2014;210(4):302-310. doi:10.1016/j.ajog.2013.10.010.
- Jones HE, Fielder A. Neonatal abstinence syndrome: Historical perspective, current focus, future directions. *Prev Med*. 2015;80(Nov):12-17. doi:10.1016/j.ypmed.2015.07.017.
- Jones HE, Heil SH, Tuten M, et al. Cigarette smoking in opioid-dependent pregnant women: neonatal and maternal outcomes. *Drug Alcohol Depend*. 2013;131(3):271-277. doi:10.1016/j.drugalcdep.2012.11.019.

References

- Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med*. 2010;363(24):2320-2331. doi:10.1056/NEJMoa1005359.
- Jones HE, Terplan M, Meyer M. Medically assisted withdrawal (Detoxification): Considering the mother-infant dyad. *J Addict Med*. 2017;11(2):90-92. doi:10.1097/ADM.0000000000000289.
- Kaltenbach K, Berghella V, Finnegan L. Opioid dependence during pregnancy. Effects and management. *Obs Gynecol Clin N Am*. 1998;25(1):139-151.
<http://www.ncbi.nlm.nih.gov/pubmed/9547764>.
- Kaltenbach K, Holbrook AM, Coyle MG, et al. Predicting treatment for neonatal abstinence syndrome in infants born to women maintained on opioid agonist medication. *Addiction*. 2012;107 Suppl(SUPPL.1):45-52. doi:10.1111/j.1360-0443.2012.04038.x.
- Kaltenbach K, O'Grady KE, Heil SH, et al. Prenatal exposure to methadone or buprenorphine: Early childhood developmental outcomes. *Drug Alcohol Depend*. 2018;185(July 2017):40-49. doi:10.1016/j.drugalcdep.2017.11.030.
- Kandall S. *Substance and Shadow: Women and Addiction in the United States*. Boston: Harvard University Press; 1996.
- Kocherlakota P. Neonatal Abstinence Syndrome. *Pediatrics*. 2014;134(2):e547-e561. doi:10.1542/peds.2013-3524.
- Lindemalm S, Nydert P, Svensson JO, Stahle L, Sarman I. Transfer of buprenorphine into breast milk and calculation of infant drug dose. *J Hum Lact*. 2009;25(2):199-205. doi:10.1177/0890334408328295.

References

- Ludlow JP, Evans SF, Hulse G. Obstetrics and perinatal outcomes in pregnancies associated with illicit substance abuse. *Aust N Z J Obs Gynaecol*. 2004;44(4):302-306. doi:10.1111/j.1479-828X.2004.00221.x.
- Lund IO, Fischer G, Welle-Strand GK, et al. A comparison of buprenorphine + naloxone to buprenorphine and methadone in the treatment of opioid dependence during pregnancy: Maternal and neonatal outcomes. *Subst Abus*. 2013;7:61-74. doi:10.4137/SART.S10955.
- Macdorman MF, Declercq E, Cabral H, Morton C. Recent Increases in the U.S. Maternal Mortality Rate: Disentangling Trends from Measurement Issues. *Obs Gynecol*. 2016;128(3):447-455. doi:10.1097/AOG.0000000000001556.
- Maeda A, Bateman BT, Clancy CR, Creanga AA, Leffert LR. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. *Anesthesiology*. 2014;121(6):1158-1165. doi:10.1097/ALN.0000000000000472.
- McHugh RK, Devito EE, Dodd D, et al. Gender differences in a clinical trial for prescription opioid dependence. *J Subst Abus Treat*. 2013;45(1):38-43. doi:10.1016/j.jsat.2012.12.007.
- Menninger-Lerchenthal, E., 1934. Die morphinkrankheit der neugeborenen morphinistischer mütter [The morphine disease of the newborn in morphine-using mothers]. *Monatschr f Kinderh* 60, 182–193.
- Nickerson JW, Attaran A, Westerberg BD, Curtis S, Overton S, Mayer P. Tuberculosis Contact Investigations--United States, 2003-2012. *MMWR Morb Mortal Wkly Rep*. 2016;64(50-51):1375-1377. doi:10.15585/mmwr.mm6450a1.

References

- Rayburn WF, Bogenschutz MP. Pharmacotherapy for pregnant women with addictions. *Am J Obs Gynecol*. 2004;191(6):1885-1897. doi:10.1016/j.ajog.2004.06.082.
- Reece-Stremtan S, Marinelli KA. ABM Clinical Protocol #21: Guidelines for Breastfeeding and Substance Use or Substance Use Disorder, Revised 2015. *Breastfeed Med*. 2015;10(3). <https://www-liebertpub-com.libproxy.lib.unc.edu/doi/10.1089/bfm.2015.9992>.
- Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths—United States, 2000-2014. *MMWR. Morbidity and Mortality Weekly Report*. <https://www.cdc.gov/mmwr/pdf/wk/mm6450.pdf>. Published 2016.
- SAMHSA, CBHSQ. No Title. 2012. https://www.samhsa.gov/data/sites/default/files/report_2724/ShortReport-2724.html.
- Schempf AH, Strobino DM. Drug use and limited prenatal care: an examination of responsible barriers. *Am J Obs Gynecol*. 2009;200(4):412.e1-412.e10. doi:10.1016/j.ajog.2008.10.055.
- Seth P, Scholl L, Rudd RA, Bacon S. Overdose Deaths Involving Opioids, Cocaine, and Psychostimulants - United States, 2015-2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(12):349-358. doi:10.15585/mmwr.mm6712a1.
- Staton M, Leukefeld C, Webster JM. Substance use, health, and mental health: problems and service utilization among incarcerated women. *Int J Offender Ther Comp Criminol*. 2003;47(2):224-239. doi:10.1177/0306624X03251120.
- 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.

References

- Sumner SA, Mercado-Crespo MC, Spelke MB, et al. Use of naloxone by emergency medical services during opioid drug overdose resuscitation efforts. *Prehosp Emerg Care*. 2016;20(2):220-225. doi:10.3109/10903127.2015.1076096.
- Terplan M, McNamara EJ, Chisolm MS. Pregnant and non-pregnant women with substance use disorders: the gap between treatment need and receipt. *J Addict Dis*. 2012;31(4):342-349. doi:10.1080/10550887.2012.735566.
- Tharner A, Luijk MP, Raat H, et al. Breastfeeding and its relation to maternal sensitivity and infant attachment. *J Dev Behav Pediatr*. 2012;33(5):396-404. doi:10.1097/DBP.0b013e318257fac3.
- Wagner CL, Katikaneni LD, Cox TH, Ryan RM. The impact of prenatal drug exposure on the neonate. *Obs Gynecol Clin North Am*. 1998;25(1):169-194. <http://www.ncbi.nlm.nih.gov/pubmed/9547766>.
- World Health Organization's "Guidelines for the identification and management of substance use and substance use disorders in pregnancy" Available at http://apps.who.int/iris/bitstream/10665/107130/1/9789241548731_eng.pdf.
- Zelson C, Rubio E, Wasserman E. Neonatal narcotic addiction: 10 year observation. *Pediatrics*. 1971;48(2):178-189. <http://www.ncbi.nlm.nih.gov/pubmed/1163356>.
- Zuspan FP, Gumpel JA, Mejia-Zelaya A, Madden J, Davis R. Fetal stress from methadone withdrawal. *Am J Obstet Gynecol*. 1975;122(1):43-46. <http://www.ncbi.nlm.nih.gov/pubmed/1130446>.
- The Incidental Economist. <https://pointsadhsblog.files.wordpress.com/2012/03/08-0620hair20salon20loc20nywt20226b.jpg>. Published 2014.

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