

Opioid Use Disorder in Women: Focus on Pregnant Women and Women of Childbearing Age

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DISCLOSURES

Dr. Ramsey has no disclosures



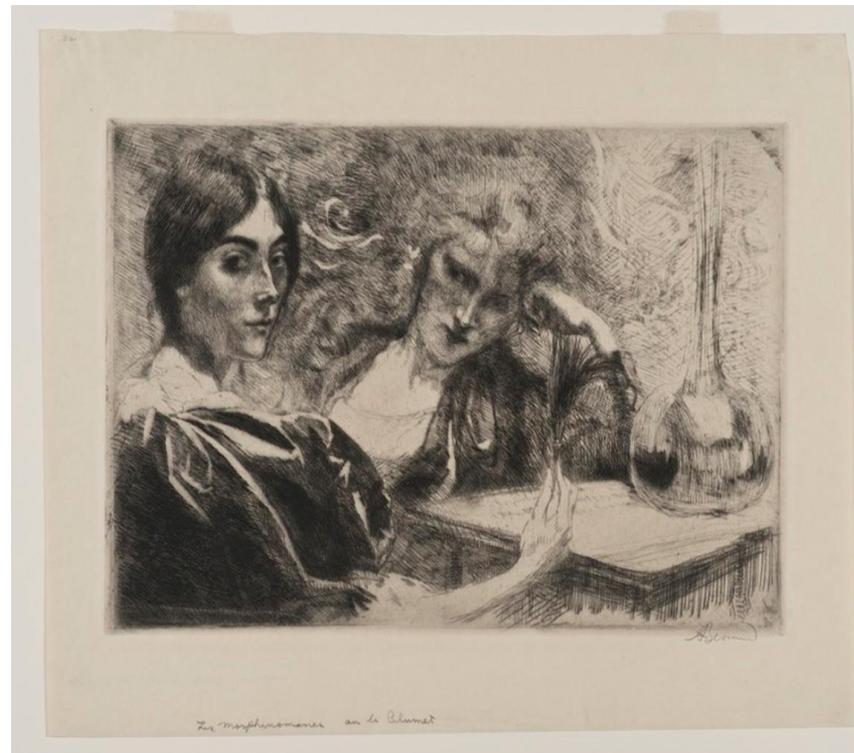
Epidemiology of OUD in women

Historically and currently

Historical Images of Women Under the Influence of Opioids



LES MORPHINÉES
(Tableau de M. Moreau de Tours)



Les morphinomane au lit de chambre

Historical Images of Women Under the Influence of Opioids



The First Opioid Epidemic Among Women in the US

- First surviving records of OUD (“opium addiction”) date from the end of the 18th century
- Morphine was isolated in 1804, heroin was synthesized in 1874, and dependence to these opioids became more common after their commercial production
- Throughout the early 1900s, opioid and coca (cocaine) based products were marketed as (unregulated) “medicinal tonics” for use with women and children for common maladies (cough and fatigue, respectively); doctors commonly prescribed opiates for middle and upper class white women for “nervousness” and “female problems”
- An increase in the incidence of OUD among women was noted as early as the 19th century; however, infants were not thought to be affected because it was believed that morphine use among women was associated with sterility and loss of sexual desire
- This fallacy was corrected with the first reported case of an affected neonate with opioid withdrawal at birth in 1875, labeled “congenital morphinism”; in 1903, the first infant with congenital morphinism survived after being treated with morphine

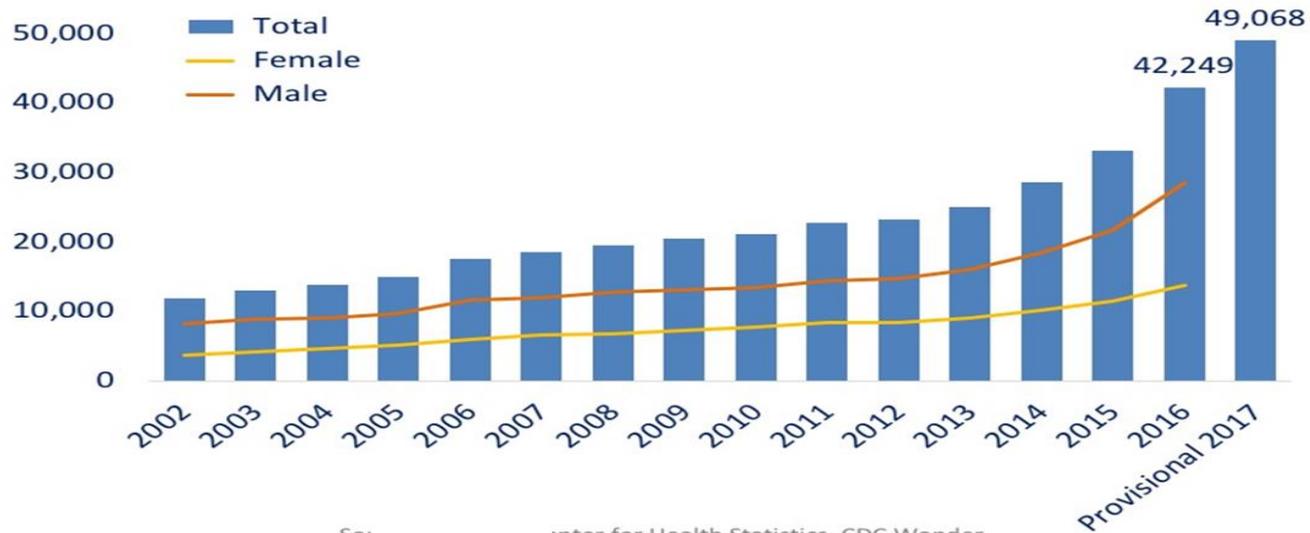
Historical View of SUD

- 1785: Dr. Benjamin Rush published his book entitled, *Inquiry in the Effects of Ardent Spirits Upon the Human Body and Mind*; he viewed alcoholism as a disease that required treatment and recommended setting up special hospitals (“sober houses”) to do so
- Of AUD, Dr. Rush said, “The use of strong drink is at first due to free agency. From habit it takes place and from necessity.”
- In the early 1900s, heroin was seen as a potential solution to the increasing problem of morphine addiction and the philanthropic St. James Society mounted a campaign to mail free heroin samples to morphine addicts
- During the time of Prohibition, SUD was recategorized as a “moral depravity” rather than as a medical illness or disease; we have yet to undo the damage that framework did for the understanding of and treatment for SUD

The Current Opioid Epidemic: 49,068 deaths in 2017



National Overdose Deaths Number of Deaths Involving Opioids

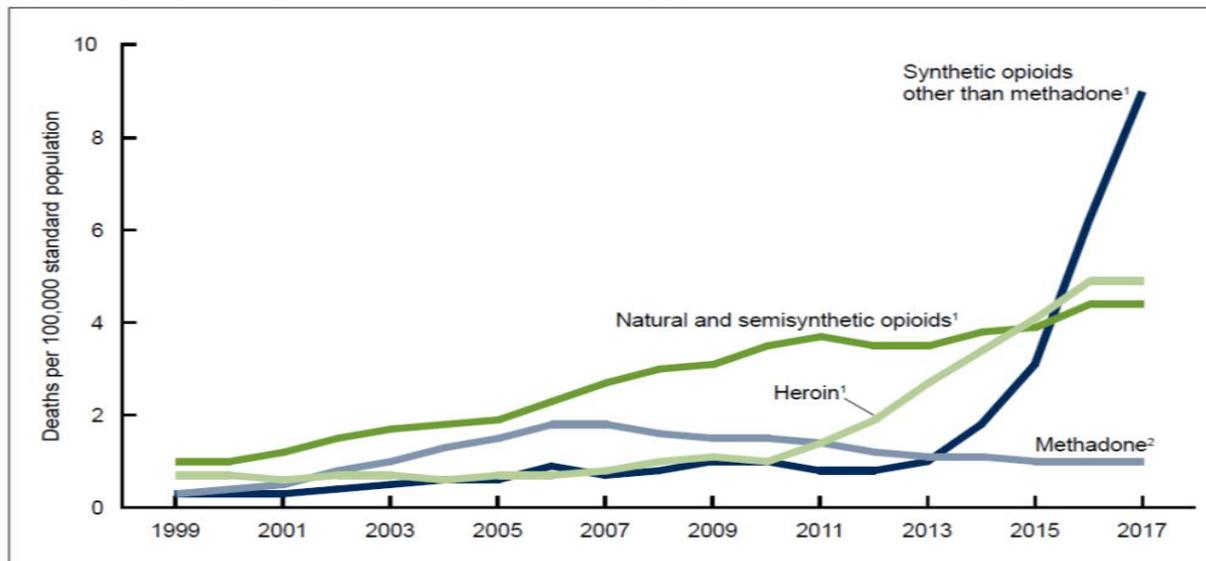


Source:

Center for Health Statistics, CDC Wonder

The Current Opioid Epidemic

Figure 4. Age-adjusted drug overdose death rates, by opioid category: United States, 1999–2017



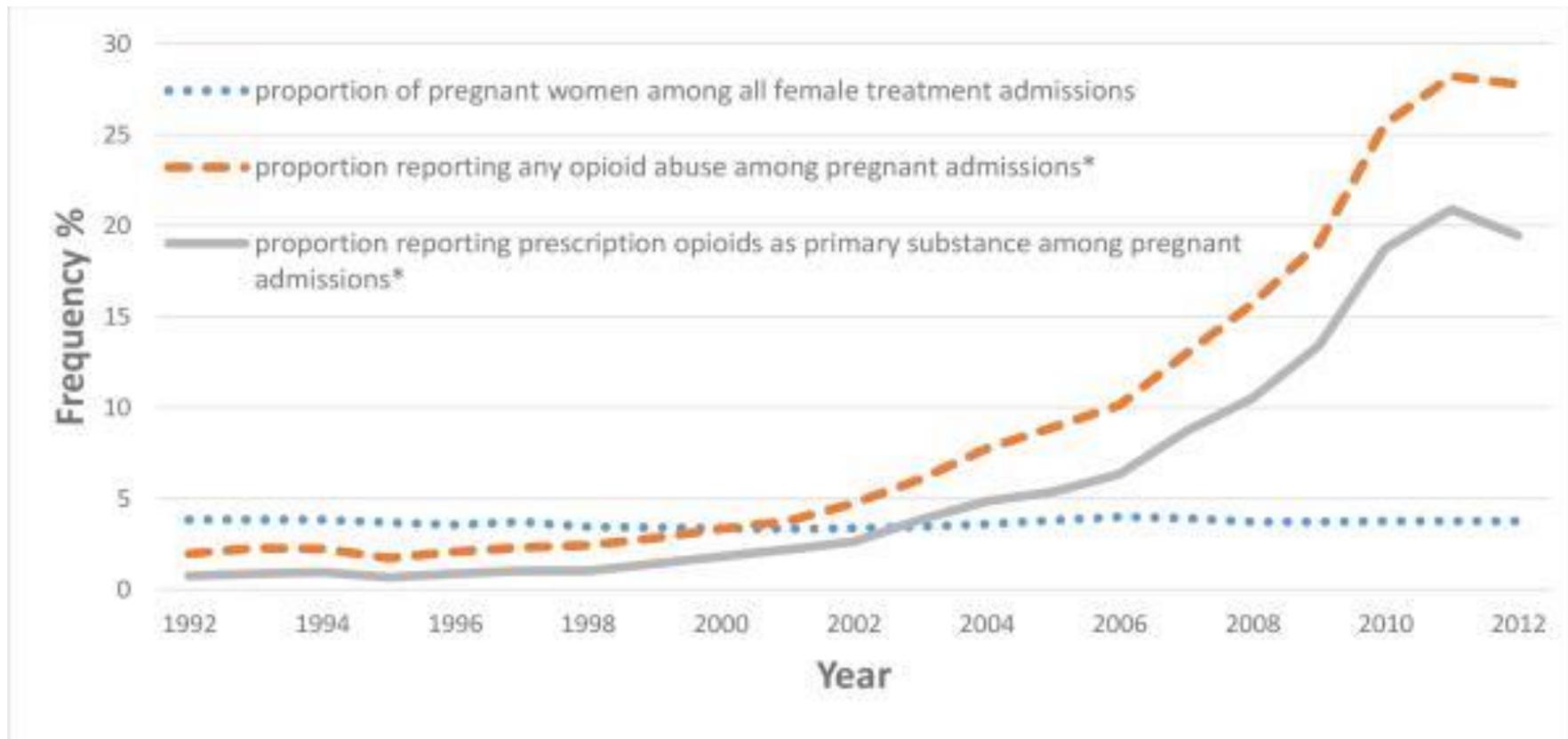
¹Significant increasing trend from 1999 through 2017 with different rates of change over time, $p < 0.05$.

²Significant increasing trend from 1999 through 2006, then decreasing trend from 2006 through 2017, $p < 0.05$.

NOTES: Deaths are classified using the *International Classification of Diseases, 10th Revision*. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug overdose deaths involving selected drug categories are identified by specific multiple-cause-of-death codes: heroin, T40.1; natural and semisynthetic opioids, T40.2; methadone, T40.3; and synthetic opioids other than methadone, T40.4. Deaths involving more than one opioid category (e.g., a death involving both methadone and a natural and semisynthetic opioid) are counted in both categories. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, with ranges of 75%–79% from 1999 through 2013 and 81%–88% from 2014 through 2017. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db329_tables-508.pdf#4.

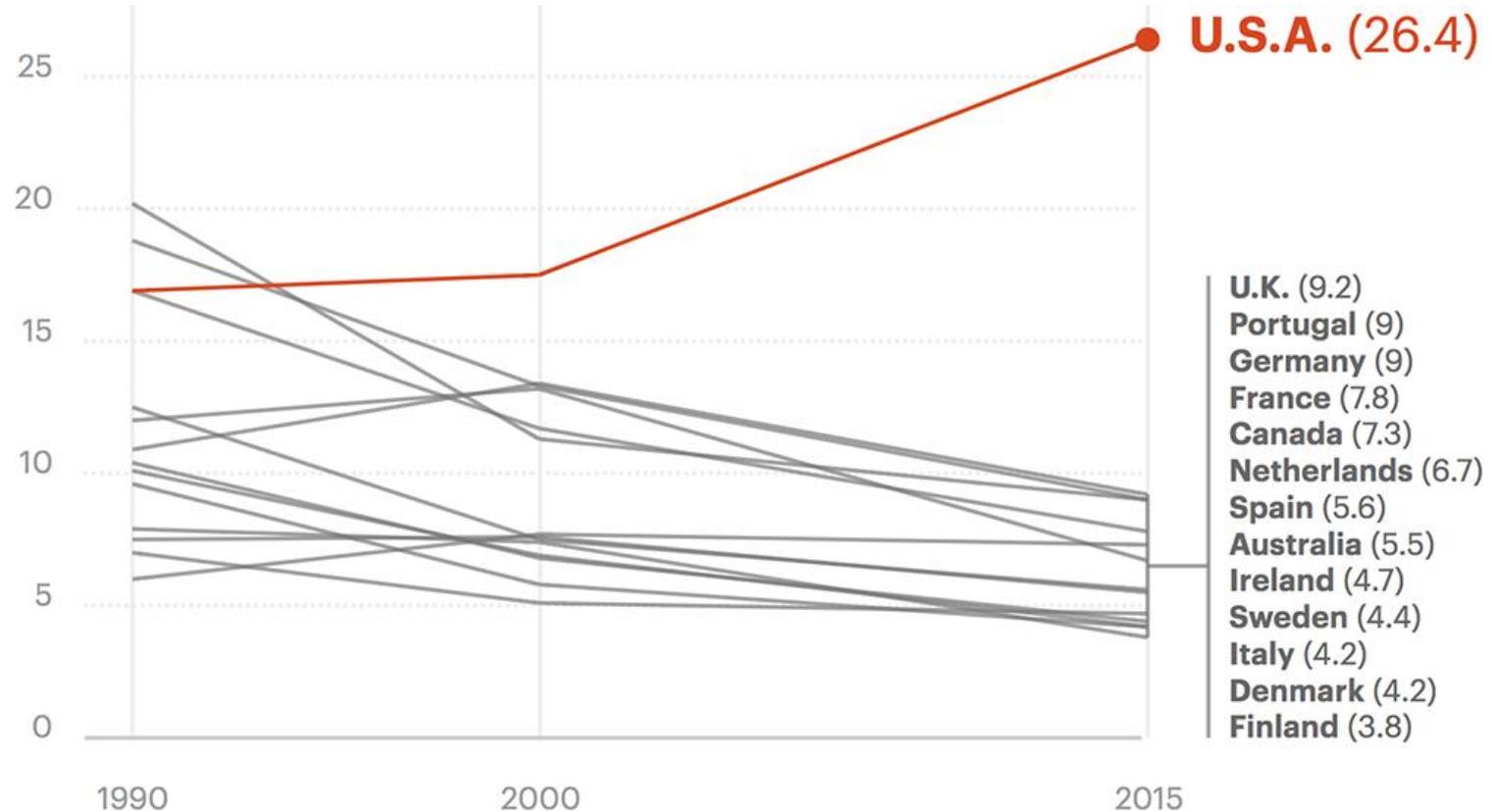
SOURCE: NCHS, National Vital Statistics System, Mortality.

The Current Opioid Epidemic: Pregnancy and Prescription Opioid Misuse Among SUD Tx Admissions



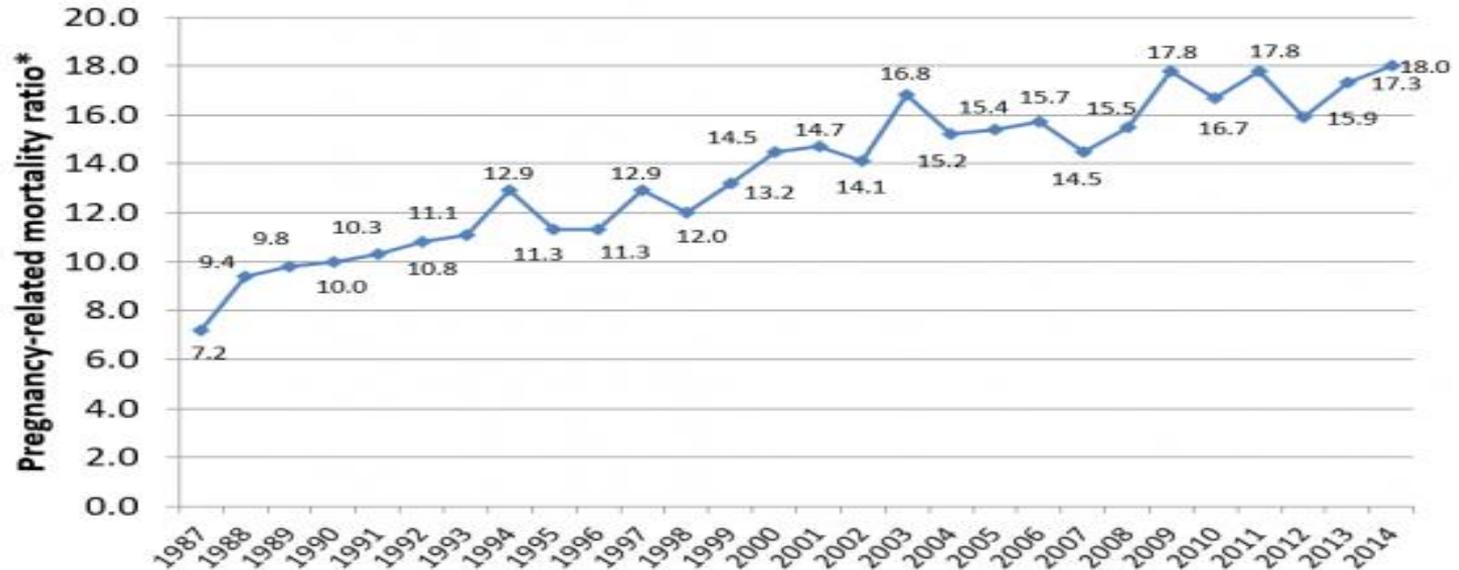
*Cochran-Armitage Trend Test $p < 0.01$

Maternal Mortality Rising in the US As It Declines Elsewhere, Deaths per 100,000 Live Births



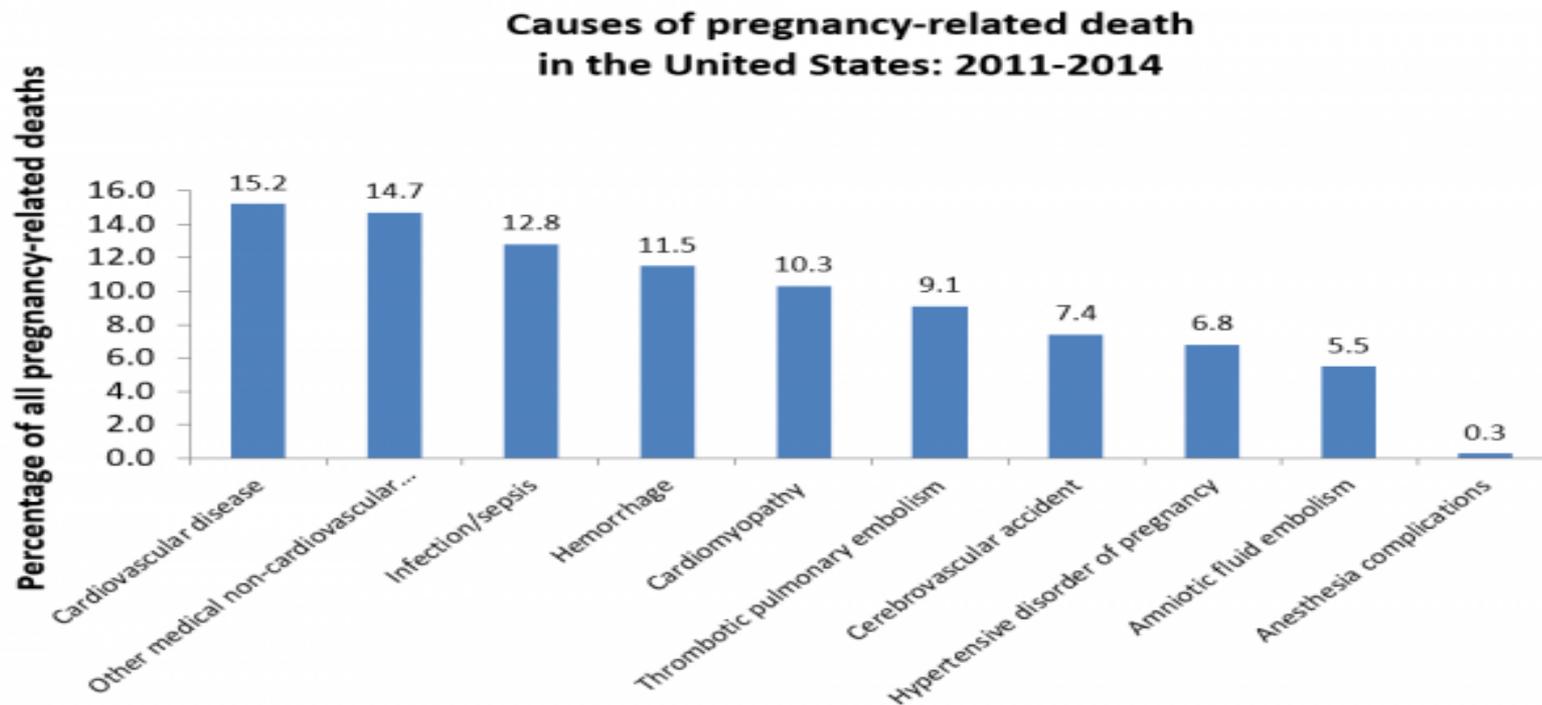
The Current Opioid Epidemic

**Trends in pregnancy-related mortality
in the United States: 1987–2014**



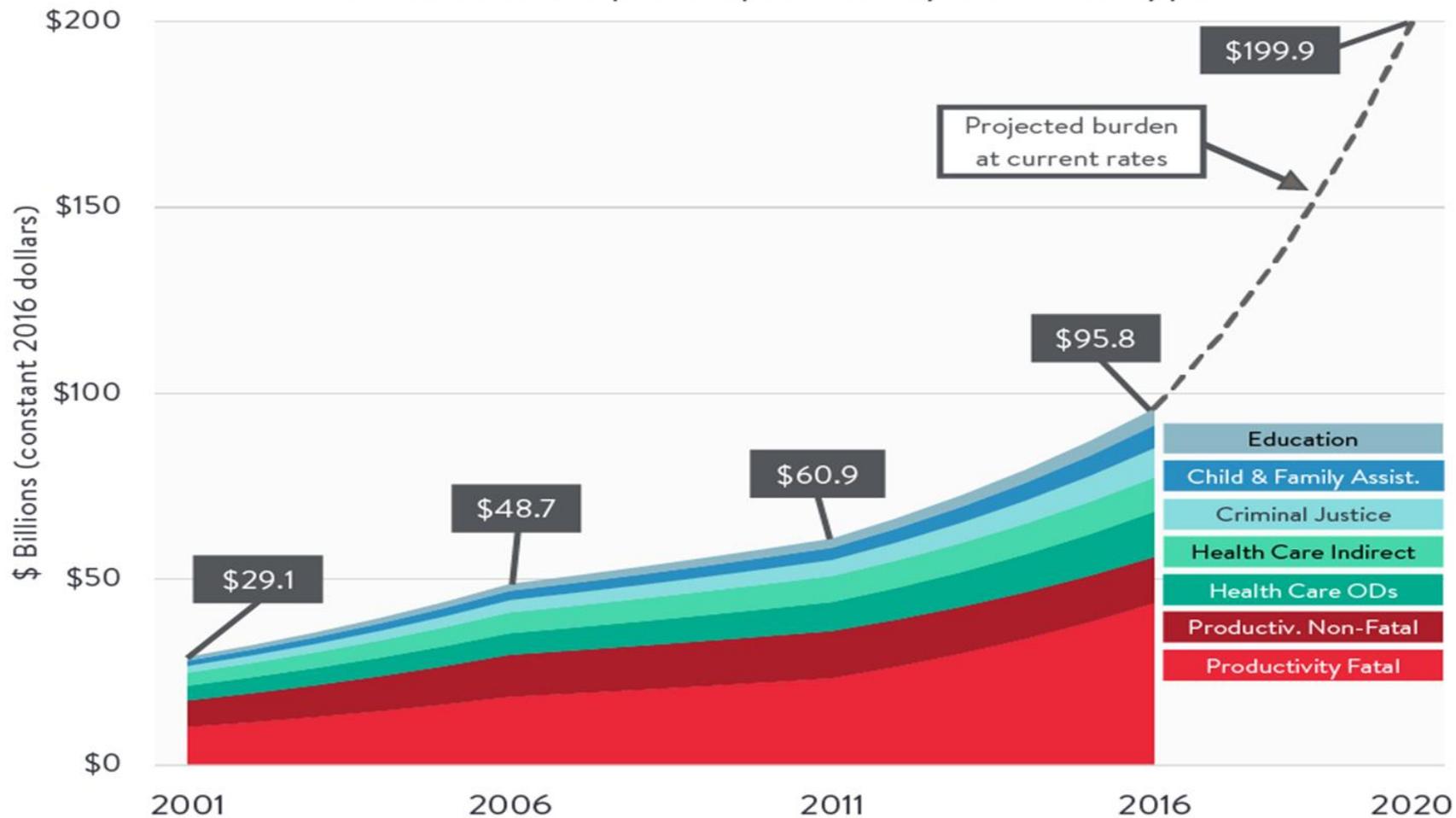
*Note: Number of pregnancy-related deaths per 100,000 live births per year.

The Current Opioid Epidemic



Note: The cause of death is unknown for 6.5% of all pregnancy-related deaths.

Costs of the Opioid Epidemic by Year and Type



* Data between labeled estimates interpolated using constant growth rates



Understanding Stigma Towards Women Who Use Drugs

Particularly Pregnant Women and Mothers

Stigma Then: Washington Post, 1989



Crack Babies: The Worst Threat Is Mom Herself

By Douglas J. Besharov

LAST WEEK in this city, Greater Southeast Community Hospital released a 7-week-old baby to her homeless, drug-addicted mother even though the child was at severe risk of pulmonary arrest. The hospital's explanation: "Because [the mother] demanded that the baby be released."

The hospital provided the mother with an apnea monitor to warn her if the baby stopped breathing while asleep, and trained her in CPR. But on the very first night, the mother went out drinking and left the child at a friend's house—without the monitor. Within seven hours, the baby was dead. Like Dooney Waters, the 6-year-old living in his mother's drug den, whose shocking story was reported in The Washington Post last week, this child was all but abandoned by the authorities.

Stigma Now



NBC NEWS HOME TOP VIDEOS ONGOING: ROBERT DURST EBOLA VIRUS OUTBREAK

U.S. WORLD LOCAL POLITICS HEALTH TECH SCIENCE POP CULTURE BUSINESS INVESTIGATIONS SPORTS MORE NIGHTLY NEWS TODAY MEET THE PRESS DATELINE

Pill-Popping Mommas: 'Many' Pregnant Women Take Opioids, CDC Finds

BY BILL BRIGGS

AMSTERDAM COORNE MEDIA PICTUREFILE

NEWS VIDEO WEATHER SPORTS PERFECT HEALTH PERFECT HOME COMMUNITY

Number of mothers using opioids while pregnant is rising in Tennessee

By Jessica Jaglois

Published: February 2, 2017, 4:45 pm | Updated: February 3, 2017, 3:38 pm



More women using opioids while pregnant

TENNESSEE'S OPIOID CRISIS

A MOTHER'S ADDICTION

Stigma Now

- Misrepresentation of NAS: “newborn’s death sentence”, “addicted baby”
- Pitting mother VERSUS child, rather than seeing mother and child as a dyad

A parent's heroin addiction, a newborn's death sentence



Mike De Sisti

Nicole Beltrame with her 18-month-old daughter, Nevaeh, with whom she was recently reunited. Beltrame became addicted to painkillers after a bad car accident, but she's off the drugs now and pregnant again, with her baby due this month.

By Crocker Stephenson of the Journal Sentinel

Nov. 14, 2014

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Photo Gallery



No bystander could be more innocent. No damage so helplessly collateral.

Trysten Jacob Powell, delivered by C-section at Wheaton Franciscan-St. Joseph hospital on March 28, 2013, lived three months.

f of his life was spent in St. Joe's neonatal intensive care unit,

NYS DOH AIDS Institute Recommendations for Improving Language and Establishing Stigma-Free, Supportive, Service Delivery Environments

- Use person-first language: examples: “person who uses drugs”, “woman who uses drugs”; NOT “drug addict” or “drug abuser” or “dope fiend”
- Use Identity-affirming language: encourage positive talk instead of negative talk
- Establish a welcoming environment: create a “safe space”
- Recognize the value of staff being representative of the communities served
- Build staff skills to dialogue with clients/patients about language
- Be on the alert for judgmental language: examples: “clean”, “dirty”, “infectious”
- Use quality improvement to dismantle stigma
- Promote ongoing discussions regarding stigma
- Document agency policies, practices, and progress toward eliminating stigma

How Stigma Leads to Punishment of Women of Childbearing Age

- *Stigma*: a mark of disgrace associated with a particular circumstance, quality, or person
- *Dehumanization*: the process of depriving a person or group of positive human qualities
- *Discrimination*: the unjust or prejudicial treatment of different categories of people or things, especially on the grounds of race, age, or sex
- *Prejudice*: preconceived opinion that is not based on reason or actual experience
- *Punishment*: the infliction or imposition of a penalty as retribution for an offense
- *Stigma -> Dehumanization -> Discrimination/Prejudice -> Punishment*

Prosecution of Pregnant Women for Drug Use: Substance Use in Pregnancy Is a Crime: AL, SC, TN

Compare states by

- Substance abuse during pregnancy is a crime
- Women have been prosecuted for drug use during pregnancy
- Substance abuse during pregnancy is child abuse
- Substance abuse during pregnancy is grounds for civil commitment
- Health care workers must report drug abuse during pregnancy
- Testing is required if drug use during pregnancy is suspected



State	Substance abuse during pregnancy is a crime	Women have been prosecuted for drug use during pregnancy	Substance abuse during pregnancy is child abuse	Substance abuse during pregnancy is grounds for civil commitment	Health care workers must report drug abuse during pregnancy	Testing is required if drug use during pregnancy is suspected	What courts have said
Alabama	Yes	Yes	Yes	No	No specific law	No	Under Alabama Supreme Court rulings in 2013 and 2014, prosecutors can charge a woman who uses drugs during pregnancy with chemical endangerment of a child.

State Policies on Substance Use During Pregnancy

- 23 states and the District of Columbia consider substance use during pregnancy to be child abuse under civil child-welfare statutes, and 3 consider it grounds for civil commitment.
- 24 states and the District of Columbia require health care professionals to report suspected prenatal drug use, and 8 states require them to test for prenatal drug exposure if they suspect drug use.
- 19 states have either created or funded drug treatment programs specifically targeted to pregnant women, and 17 states and the District of Columbia provide pregnant women with priority access to state-funded drug treatment programs.
- 10 states prohibit publicly funded drug treatment programs from discriminating against pregnant women.

Punishment of Pregnant Women: Is This Utilizing Best Practices?

- ***Discriminatory***: women of color and poor women are more likely to be prosecuted, despite white women being more likely to use during pregnancy
- ***Not evidence-based***: risks of illicit substances are often exaggerated in comparison to the risks of legal substances
- ***Unintended consequences***: punitive policies drive pregnant women away from SUD treatment and prenatal care
- ***Engagement***: in prenatal care counteracts the adverse effects of substance use during pregnancy

Women with SUD in Pregnancy

Consequences of SUD in pregnancy

Substance	Consequence
Alcohol	Preterm birth, low birth weight Teratogen: FAS/FASD Leading preventable cause of intellectual and developmental disorders in US Cognitive and behavioral deficits
Nicotine	Reduced fertility, Miscarriage Preterm delivery (premature rupture of membranes, placental abruption, previa) Low birth weight (reduced fetal growth), Stillbirth SIDS, respiratory infections
Opioids	NAS
Stimulants	? Low birth weight ? Stillbirth Placental abruption (rare)
Cannabis	? Low birth weight ? Stillbirth

Substance Use in the Past Month by Pregnant Women

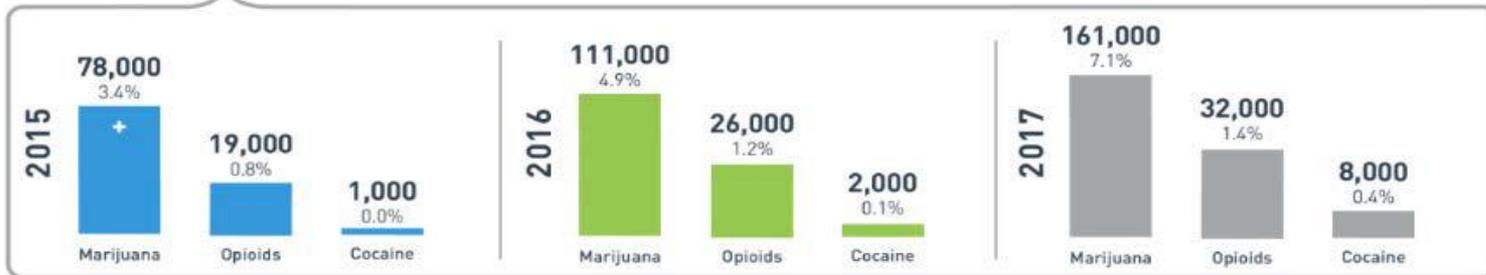
ILLICIT DRUGS



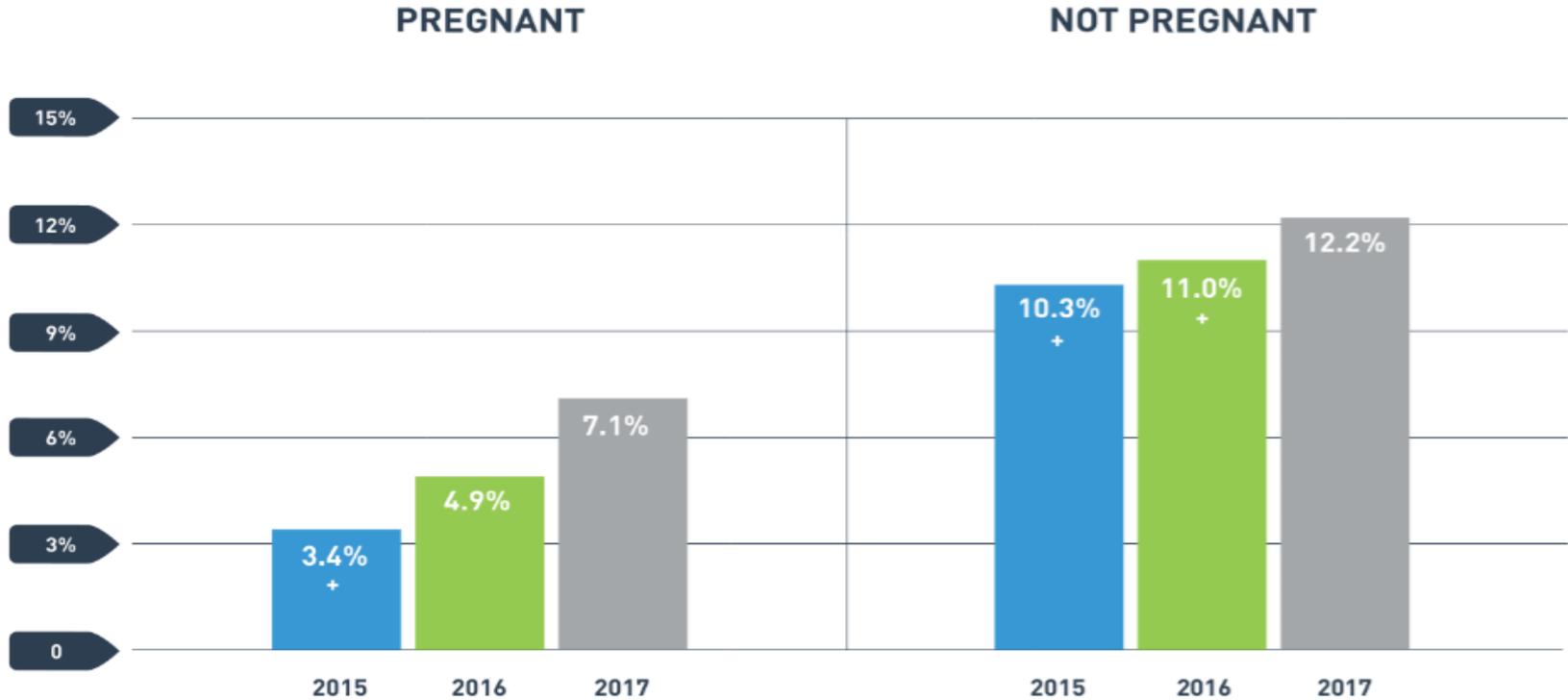
TOBACCO PRODUCTS



ALCOHOL

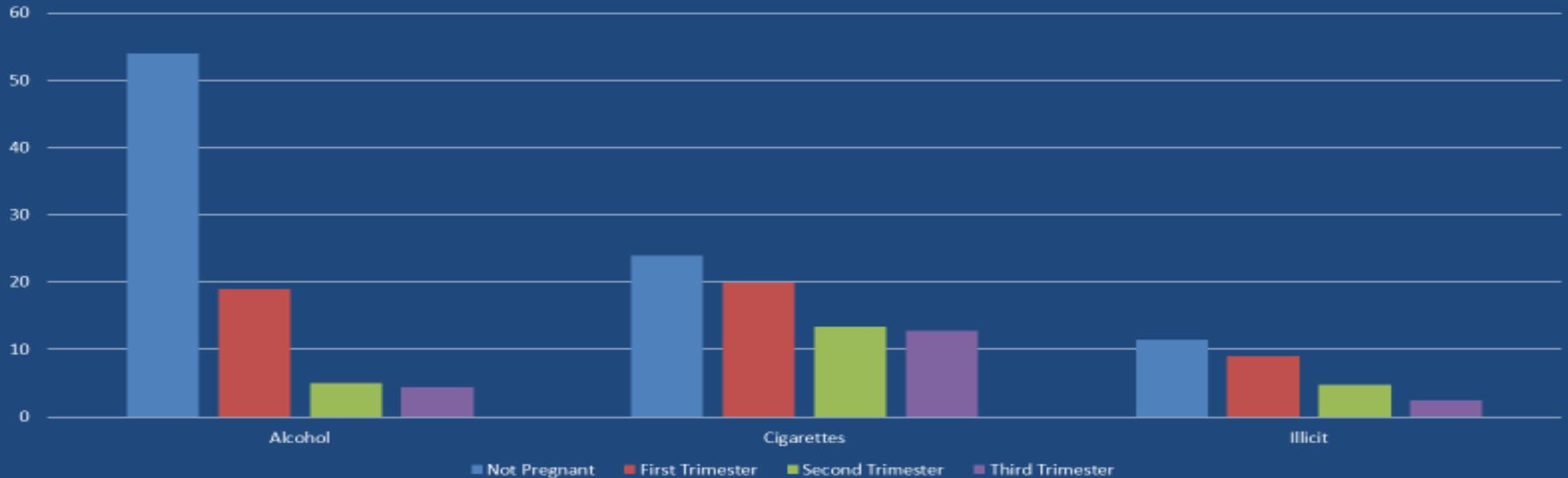


Marijuana Use Among Women, by Pregnancy Status



Substance Use During Pregnancy

What happens when women who use drugs get pregnant?



Teasing out use versus a use disorder in pregnant women...

- The *vast majority* of pregnant women are motivated to maximize their own health and the health of their developing fetus
- Those pregnant women who can't cut back or quit using, *likely* have a substance use disorder
- Continued use in pregnancy is *pathognomonic* for a substance use disorder

Women with SUD in Pregnancy

Mental Health:

- 2/3 with co-occurring mental health diagnoses (MDD, GAD, PTSD)
- Majority with childhood trauma (pre-adolescent sexual or physical trauma)
- High level of IPV (intimate partner violence) in the last year

Reproductive Health:

- Unplanned pregnancy (80%); low rates of contraception use

Other Substance Use:

- Tobacco use: >90%

Social Functioning:

- Inadequate social supports; social isolation; exposure to poor parenting models

Women with SUD in Pregnancy

- Pregnant women with SUD have a unique set of needs across multiple domains; domains that affect both obstetric health and outcomes and SUD treatment
- Care needs to address all those complex needs, ideally, with co-located, integrated services

Women with SUD in Pregnancy

LOW BIRTH WEIGHT	PNC	No PNC
No drug use	14%	19%
Drug Use	19%	48%

Identifying SUD During Pregnancy

Universal screening (not risk-based screening): identify at risk women early; utilize motivational interviewing; normalize questions and embed in EMR; use validated screening tools (DAST, MAST, 4 P's Plus, CRAFFT: for adolescents)

Urine toxicology NOT recommended for screening: for myriad reasons (short detection window, confirmation testing needed, may not capture intermittent or binge use, ethical issues)

Patient/Provider Barriers to Screening: patient fear of discrimination/mistreatment/CPS; provider lack of training/time/knowledge regarding how to address positive results

Prevalence of Screening During Prenatal Care

Prenatal Care Screening

Condition	Prevalence
Cystic Fibrosis (Caucasians)	1/2500 = 0.0004%
HIV	1/500 = 0.002%
Birth Defects	2%
Anemia	2-4%
Pre-eclampsia	2-8%
Gestational diabetes	2-10%
Post partum depression	10-15%

Substance Use	Prevalence
Alcohol	9.4%
Cigarettes	15.4%
Illicit drugs	5.4%



Treatment Options for Women with OUD

MAT for Pregnant/Breastfeeding Women

Standard of Care for the Treatment of OUD During Pregnancy

- Medication Assisted Treatment (MAT) with either methadone or buprenorphine: pregnant women do not need to meet DSM V criteria for OUD to receive MAT
- MAT endorsed by: CDC, WHO, SAMHSA, ACOG, ASAM, AAFP, AAP
- Access to behavioral counseling, as an adjunctive treatment, if needed
 - Either with the MAT provider/staff or by referral to mental health or a dual diagnosis program (outpatient)

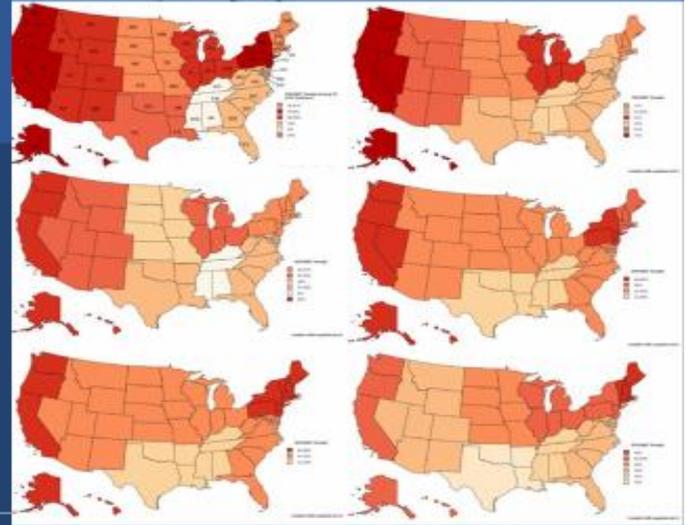
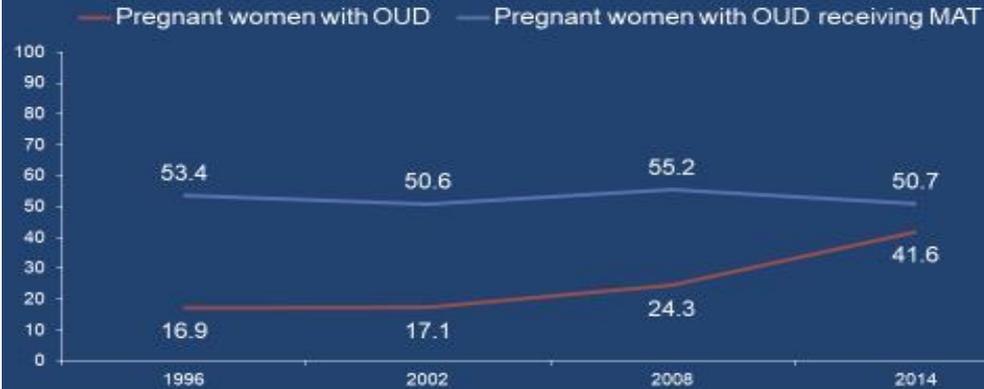
Off-label Use???

- 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 use disorder: "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 January 2018, the FDA requires methadone and buprenorphine safety labeling to include information regarding the risk of neonatal opioid withdrawal syndrome (NOWS)
- Pregnant women with opioid use disorder can be treated effectively with methadone or buprenorphine; however, labeling states it should be used only if the potential benefit justifies the potential risk to the fetus
- Both 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)

OUD Treatment During Pregnancy: Most Pregnant Women Receive No Pharmacotherapy

Trends and disparities in receipt of pharmacotherapy among pregnant women in publicly funded treatment programs for opioid use disorder in the United States
Journal of Substance Abuse Treatment 89 (2018) 67-74

Vanessa L. Short^{a,*}, Dennis J. Hand^{a,b}, Lauren MacAfee^c, Diane J. Abatemarco^a, Mishka Terplan^d



Only half of pregnant women in treatment receive pharmacotherapy

*SUD Treatment During Pregnancy:
Most Pregnant Women Receive No Treatment*

NSDUH 2007-2014	Pregnant	Not pregnant
Need Treatment	744,361 30.2%	43,239,606 15.7%
Received Treatment	87,388 11.7%	2,938,403 6.8%

Benefits of MAT in Pregnancy

Maternal:

- 70% reduction in maternal overdose deaths
- Decrease in acquisition/transmission of HIV, HCV, HBV
- Increased engagement in prenatal care and SUD treatment
- Improved maternal outcomes

Fetal:

- Decrease in fetal stress due to stable opioid levels
- Decrease in intrauterine fetal demise
- Decrease in intrauterine growth restriction
- Decrease in preterm delivery

MAT for OUD

Medication Options

- ◆ **Methadone**
- ◆ **Buprenorphine alone**
- ◆ **Buprenorphine and naloxone**
- ◆ **Naltrexone**

SAMHSA. Treatment Improvement Protocol (TIP) Series 43. HHS PubNo. (SMA) 12-4214. Rockville, MD: 2012.; World Health Organization (WHO). *Guidelines for the identification and management of substance use and substance use disorders in pregnancy*. Geneva, Switzerland: World Health Organization, 2014. American Society of Addiction Medicine (ASAM). *The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use*. Chevy Chase, MD: American Society of Addiction Medicine, 2015. Saia KA et al. *Curr Obstet Gynecol Rep*. 2016;5(3):257-263. Jones HE, et al., *Addiction*. 2013;108:233-247.

MAT: Methadone v. Buprenorphine

Methadone:

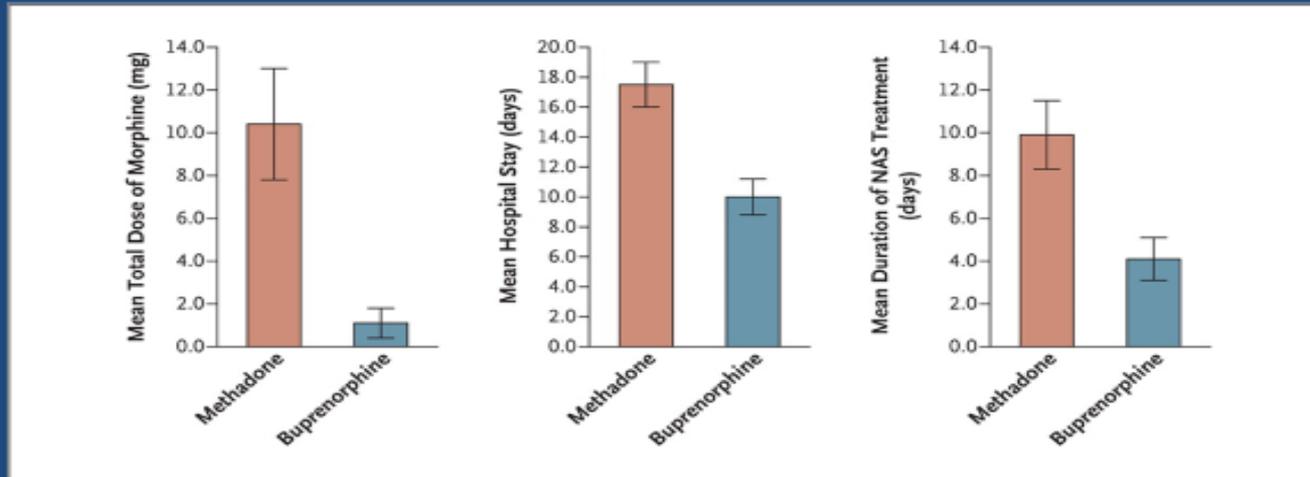
- Pregnancy Category C
- No risk of precipitating opioid withdrawal
- Historically, has been the gold standard treatment in pregnancy
- Potential for prolonged QT
- May require split dosing
- May contribute to low birth weight compared with buprenorphine

Buprenorphine:

- Pregnancy Category C
- Gaining first-line recognition for OUD treatment in pregnant women
 - _Retention in care for pregnant women may now favor buprenorphine over methadone
- More flexible dosing (more times per day)
- Less severe NAS
 - _Some neonatal outcomes better
- Reduced risk of overdose during induction and in children exposed to buprenorphine

MAT: Methadone v. Buprenorphine: NAS

Mean Neonatal Morphine Dose, Length of Neonatal Hospital Stay, and Duration of Treatment for Neonatal Abstinence Syndrome



MAT: Methadone v. Buprenorphine

MOTHER Study: Secondary Outcomes:

- maternal outcomes similar in both groups (n=131): low rates of illicit substance use during pregnancy and at delivery
- neonates who were exposed to buprenorphine spent 58% less time in the hospital receiving medication (4.1 v. 9.9 days)
- clinically meaningful attrition rate in the buprenorphine group* (33%) compared with the methadone group (18%)

*this data is changing of late

MOTHER Study: Child Outcomes at 36 Months

- n=96
- 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
- Results indicate children born in the MOTHER study are following a path of normal development in terms of growth, cognitive and psychological development

Methadone v. Buprenorphine/Naloxone

Methadone v. Buprenorphine + Naloxone

<u>Neonatal Outcomes</u> <i>Primary outcomes</i>	Methadone (n=31)	Buprenorphine + Naloxone (n=31)	p-Value
Number Treated for NAS	16 (51.6 %)	8 (25.1%)	0.01
Amount of Morphine (mg)	5.0 (3.3)	3.4 (1.2)	0.18
Duration of NAS treatment (days)	11.4 (3.4)	10.6 (3.1)	0.88
Peak NAS Score (range 1–25)	10.7 (3.7)	9.0 (4.4)	0.02

Results are given as number (%) or mean (SD)

Methadone v. Buprenorphine/Naloxone

Methadone v. Buprenorphine + Naloxone

Neonatal Outcomes	Methadone	Buprenorphine + Naloxone	p-Value
Number of infants	92	58	
Required NAS treatment, n (%)	74 (80)	37 (64)	0.03
Time to NAS onset (days) median (range)	2 (1–9)	2 (1–6)	ns
Cumulative methadone dose (mg) ^a	7 ± 5	5 ± 3	ns
Oral morphine equivalent (mg) ^{a,b}	28 ± 21	21 ± 14	ns
Total NAS treatment duration (days) ^a	38 ± 21	32 ± 21	ns
Required adjunctive phenobarbital, n (%)	5 (5)	4 (7)	ns
NAS-related hospital readmission, n (%)	0 (0)	1 (1)	ns

SD, standard deviation

^aMean ± SD

^b1 mg methadone = 4 mg morphine sulfate

Gawronski KM, Prasad MR, Backes CR, Lehman KJ, Gardner DK, Cordero L. *SAGE Open Med.* 2014

Evidence: Comparison Opioids v. Buprenorphine/Naloxone

Setting: Rural: Northwestern Ontario, Canada

Design: A retrospective cohort study

Participants: 855 mother infant dyads:

- the majority from indigenous communities
- buprenorphine/naloxone during pregnancy (n=62)
- no opioid exposure in pregnancy (n=618)
- opioid exposure other than buprenorphine/naloxone (n=159)

Results: Compared to women taking other opioids, women taking buprenorphine/naloxone had higher birthweight babies (p=0.001) and less exposure to marijuana (p<0.001) during pregnancy.

Conclusions: No harm from taking buprenorphine/naloxone opioid agonist treatment during pregnancy. “Larger, prospective studies are needed to further assess safety.”

Evidence: Buprenorphine/Naloxone During Pregnancy

Retrospective Chart Review: n=10; opioid dependent women on buprenorphine/naloxone during pregnancy; 7 maternal outcome measures: weight gain, fetal presentation at delivery, Cesarean delivery, analgesia during delivery, UDS results at delivery, # of days of maternal hospital stay, and began breastfeeding at delivery, and 11 neonatal measures; extracted from medical records

Results: Maternal findings were unremarkable, and comparable with what might be found following treatment with the buprenorphine-mono product. Neonates were full-term with normal birth parameters. Four neonates were treated for NAS, and number of days treated for NAS and number of hospital days were in line with values reported for the buprenorphine-mono product.

Conclusions: Findings suggest no obvious significant adverse maternal or neonatal outcomes related to the use of buprenorphine + naloxone for the treatment of opioid dependence during pregnancy.

Evidence: Buprenorphine/Naloxone During Pregnancy

A comparison of buprenorphine to buprenorphine/naloxone to methadone for the treatment of OUD during pregnancy

Maternal outcomes: There were no significant differences in maternal outcomes for women exposed to buprenorphine + naloxone compared to women exposed to buprenorphine, methadone, or methadone-assisted withdrawal.

Neonatal outcomes: Head circumference was significantly higher on average among neonates exposed in utero to buprenorphine + naloxone compared to neonates exposed to methadone-assisted withdrawal; $M_s = 32.8$ (SE = 0.60) versus 31.2 (SE = 0.36), $F(1, 307) = 5.24$, $P < 0.03$, while neonates exposed in utero to buprenorphine + naloxone were shorter on average than neonates exposed to buprenorphine alone; $M_s = 46.3$ (SE = 1.08) versus 50.56 (SE = 0.51), $F(1, 307) = 12.74$, $P < 0.001$, although both groups were within the normal range according to the World Health Organization (WHO) international standards of child growth.²⁶ Mean Apgar scores at 5 minutes were significantly lower in the buprenorphine + naloxone group compared to the buprenorphine alone group; $M_s = 8.6$ (SE = 0.29) versus 9.6 (SE = 0.12), $F(1, 499) = 4.88$, $P < 0.03$.

Conclusions: Findings from the present study suggest no obvious significant adverse maternal outcomes related to the use of buprenorphine + naloxone for the treatment of opioid dependence in pregnancy. The birth parameters for the neonates in the buprenorphine + naloxone group were within the normal range. However, the potential for lower physical birth parameters in this group compared to neonates exposed to buprenorphine alone merit further research on neonatal physical development, and suggests caution in the use of buprenorphine + naloxone. Larger samples, in controlled clinical trials, and in prospective studies that control for confounding factors, are necessary to further examine the relative neonatal safety of buprenorphine + naloxone for the treatment of opioid-dependent pregnant women.

From ACOG Committee Opinion: Opioid Use and OUD in Pregnancy

“The buprenorphine mono product has been recommended during pregnancy to avoid any potential prenatal exposure to naloxone, especially when injected.

However, recent studies that evaluated the use of the combination product buprenorphine with naloxone found no adverse effects, and outcomes were similar when compared with buprenorphine alone.”

OUD Treatment During Pregnancy, Intrapartum Care, Postpartum Care: Dosing

Pregnancy: dose to comfort level of the pregnant women (no withdrawal symptoms, no opioid cravings); dose will likely increase during the pregnancy due to increased metabolism and increased circulating blood volume; educate pregnant women that neither a higher methadone dose nor a higher buprenorphine dose is associated with an increased risk of NAS

Intrapartum Care: *continue methadone or buprenorphine dose through labor and postpartum at the prenatal dose*; most labor pain and c-section pain can be managed with regional anesthesia, non-opioids, an increased dose of methadone or buprenorphine, or, if necessary, by using opioids IN ADDITION TO the prenatal methadone or buprenorphine dose

Postpartum Care: continue prenatal dose of MAT: individualize dose decreases; if opioid pain management is needed, requirements will be higher

Buprenorphine Induction During Pregnancy

- I recommend the pregnant patient initiating home induction with a small dose of buprenorphine/naloxone (2-4 mg of buprenorphine; for example, one quarter to one half of a 8/2 mg film or tablet) when in she is in mild withdrawal (show the COWS to the patient); if she feels better with this small dose, then she can take more; if she doesn't feel better or feels worse, then she should wait longer
- The timing of the induction will depend on the half life of the opioid used by the pregnant woman; for example: if she is using a long acting opioid, like methadone (the wait time would be 48+ hours), v. using a short acting opioid, like heroin or oxycodone (the wait time may be 4-6 hours)
- She should not wait until she is in moderate withdrawal, as this can put the fetus at risk for potential harm (miscarriage in the first trimester, premature delivery in the third trimester); the second trimester is the safest time for the fetus to experience OWS

MAT: Naltrexone in Pregnancy

Naltrexone

- There are advantages to using naltrexone
- Little information currently available about the use of naltrexone by pregnant women
- The increased use of long-acting naltrexone formulations will increase the likelihood of women becoming pregnant while in treatment with naltrexone
- Preliminary clinical studies have not revealed adverse fetal events with prenatal exposure to naltrexone
- Preclinical studies have been mixed
- Questions still exist, including the potential for precipitated withdrawal and the exacerbation of opioid-related neuroendocrine dysregulation

Jones HE, Chisolm MS, Jansson LM, Terplan M. *Addiction*. 2013;108:233-247.

From ACOG Committee Opinion: Opioid Use and OUD in Pregnancy

“To date, information regarding its use [injectable naltrexone] in pregnancy is limited to small case series and case reports, with normal birth outcomes reported.

However, significant concerns exist regarding unknown fetal effects, as well as risk of relapse and treatment dropout with subsequent return to opioid use and risk of overdose...The decision whether or not to continue naltrexone treatment for a woman already using naltrexone before pregnancy should involve a careful discussion with the patient that compares the limited safety data versus the potential risk of relapse with treatment discontinuation.”

No Role for Medically Assisted Withdrawal (“Detox”) During Pregnancy

-“Withdrawal management has been found to be inferior in effectiveness over pharmacotherapy with opioid agonists and ***increases the risk of relapse without fetal or maternal benefit.***” (ASAM); increased rates of NAS; increased rates of relapse

-Increased rate of relapse with associated overdose mortality following detox

-Increased access to MAT with opioid agonists is associated with a reduction in heroin overdose deaths

-Offering pharmacotherapy for OUD in pregnancy increases treatment retention, # of OB visits attended, and in-hospital deliveries

The 4th Trimester: Postpartum Care

Reality check:

- caring for a newborn, breastfeeding, bonding
- mood changes, sleep disturbance, physiologic changes
- cultural norms; pressure to be the “ideal mother”
- social isolation
- often CPS involved...

Less Focus on the Mother:

- shift of attention from the mother (prenatal care) to the baby (pediatric care)
- 40% of women miss their postpartum visit (ACOG, 5/2018)
- care often shifts to social service agencies (WIC, etc.)
- Often the MAT provider is the only continuity of care for the mother
- Remember contraception! (LARC)

Breastfeeding

- Methadone and buprenorphine are safe for breastfeeding: <1% maternal opioid intake transmitted to breast milk
- Published guidelines from ACOG, AAP, and the Academy of Breastfeeding Medicine (ABM) all support breastfeeding for women on opioid agonist therapy for OUD
- Maternal benefits of breastfeeding: increased oxytocin levels lead to decreased stress and increased bonding which lower relapse risk
- Newborn benefits of breastfeeding: reduction in the need for pharmacologic treatment of NAS and shorter hospital stays
- Breastfeeding more controversial with active use of EtOH and MJ

Defining NAS: A Brief Word...

Neonatal Abstinence Syndrome (NAS) often results when a pregnant woman uses opioids during pregnancy: “*an expected and treatable consequence of opioid exposure in utero*” (ACOG, 2012 and GAO, 2015)

NAS is defined by alterations in the:

- CNS (central nervous system): high-pitched crying, irritability, exaggerated reflexes, tremors, tight muscles, sleep disturbance
- Autonomic nervous system: sweating, fever, yawning, sneezing
- Gastrointestinal distress: poor feeding, vomiting loose stool
- Signs of respiratory distress: nasal congestion and rapid breathing

NAS is NOT fetal alcohol syndrome (FAS)

NAS is treatable: it is withdrawal only, not “addiction” (absence of compulsion/behaviors)

NAS and treatment for NAS are not known to have long-term effects; interactions between the caregiver and the child can impact resiliency/risk with potential long-term effects in some cases

NAS: Neonatal Abstinence Syndrome

Common Categories of Drugs

- Opioids
- Semi-synthetic Opioids
- Synthetic Narcotics
- CNS Depressants
- CNS Stimulants
- SSRI's
- Hallucinogens & Designer Drugs



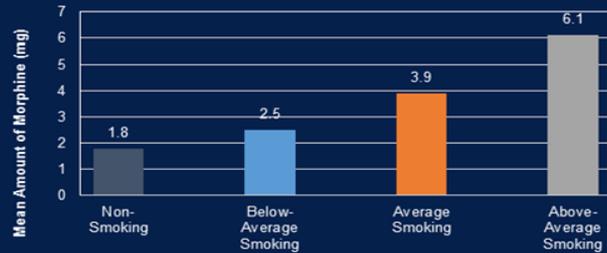
Other Factors Contributing to NAS:

- maternal smoking
- not breastfeeding, lack of skin-to-skin contact
- NAS assessments (subjective), NAS protocols (NICU v. rooming-in with parents), medication initiation, and weaning protocols
- non-modifiable genetic factors (OPRM1 receptor, placental transfer)

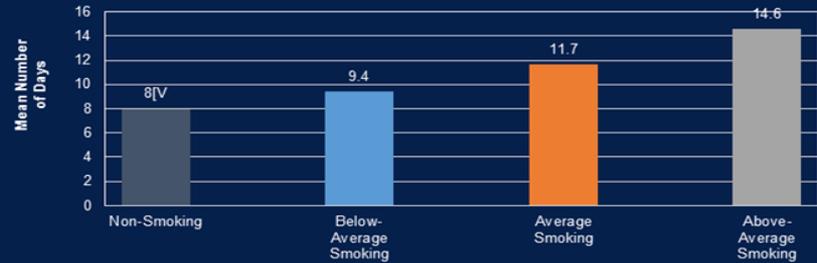
The MOTHER Study

MOTHER: Smoking and NAS

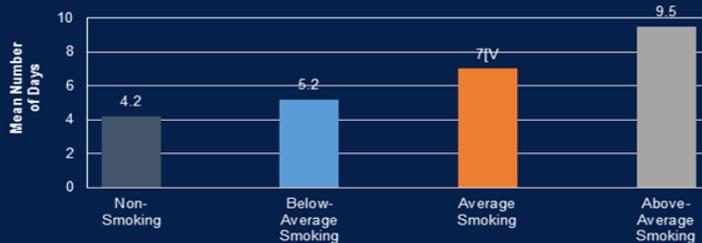
Total Amount of Morphine Needed to Treat NAS



Total Length of Hospital Stay



Number of Days Medicated for NAS



Jones HE, et al. *Drug Alcohol Depend.* 2013;131(3):271-277.

Ordinary least squares and Poisson regression analyses were used to test average daily number of cigarettes smoked in the past 30 days at $\alpha=0.05$, adjusting for both Medication Condition and Site.

Below-average cigarette smoking was defined as 6 cigarettes/day (-1 SD), average cigarette smoking as 14 cigarettes/day (Mean), and above-average cigarette smoking as 21 cigarettes/day (+1 SD).

NAS: Neonatal Abstinence Syndrome: Food for Thought...

Non-Pharmacologic Therapies

- “Skin to Skin’ at delivery
- Early breast feeding unless contra-indicated (HIV+ mothers 7 mothers using illicit substances)
- Rooming-in 24/7
- Quiet soothing environments
- Natural light
- Soothing voices
- Clustering Care
- Swaddling
- Rocking
- Use of pacifiers
- Frequent & smaller feedings – true demand feedings



A New Approach ...

- **PARENTS are the treatment/therapy**
- Non-pharmacologic focus – true family-centered care
- Dedicated team of experts in caring for all aspects of family and NAS care
- **In the PERFECT world – every healthcare facility would have a dedicated NAS unit**



From ACOG Committee Opinion: Opioid Use and OUD in Pregnancy

“...it is important to advocate for this often-marginalized group [pregnant women with OUD] of patients, particularly in terms of working to improve availability of treatment and to ensure that pregnant women with OUD who seek prenatal care are not criminalized.

Finally, obstetric care providers have an ethical responsibility to their pregnant and parenting patients with SUD to discourage the separation of parents from their children solely based on SUD, either suspected or confirmed.”

What Can You Do??

What You Can Do

Individual level

- ❖ Mothers and children need strength-based support
- ❖ Be careful in your language choice
- ❖ Pictures and visuals matter
- ❖ Consider mother and child not mother vs. child
- ❖ Be familiar with toolkits like ACOG's on state legislation regarding *Pregnant Women & Prescription Drug Abuse, Dependence and Addiction*
- ❖ Help tell stories of recovery and success

A More Comprehensive Health Approach for Women

Structural Level Changes

Supportive policies that provide:

- Reimbursement for comprehensive services
- Access to appropriate identification, assessment, and treatment for OUD across the lifespan
- Access to whole body/whole person health care (avoid compartmentalization)
- Responsible/safe prescribing by medical providers and training on SUD diagnosis and treatment for medical providers
- Tobacco cessation support
- NAS hospital policies and protocols that support the mother/child dyad staying together and avoid unnecessary or unnecessarily long NICU stays

Conclusions

- most pregnant women are motivated to maximize their own health and the health of their fetus during pregnancy
- most women are able to stop or decrease substance use during pregnancy; those who cannot, have a SUD
- engagement in care improves outcomes
- pregnant women with SUD experience discrimination and scrutiny on an unparalleled level
- care, ideally, is co-located, multidisciplinary, non-judgmental, and patient-centered
- preventing substance exposed pregnancies means decreasing unplanned pregnancies by increasing access to contraception

Resources

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- Front Line: PBS. *A Social History of America's Most Popular Drugs*, 2014
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- TWEAK: <https://www.unodc.org/ddt-training/treatment/VOLUME%20A/Volume%20A%20-%20Module%201/5.Screening%20and%20Assessment%20Tools,%20Assist/9.TWEAK.pdf>
- T-ACE: [https://www.mirecc.va.gov/visn22/T-ACE alcohol screen.pdf](https://www.mirecc.va.gov/visn22/T-ACE%20alcohol%20screen.pdf)
- DAST: <https://www.sbirttraining.com/node/527>
- MAST: <https://counsellingresource.com/quizzes/drug-testing/alcohol-mast/>
- 4 P's Plus: <http://www.ntiupstream.com/4psabout/>
- CRAFFT: [https://www.integration.samhsa.gov/clinical-practice/sbirt/CRAFFT Screening interview.pdf](https://www.integration.samhsa.gov/clinical-practice/sbirt/CRAFFT%20Screening%20interview.pdf)
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Thank you!

QUESTIONS?

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