Opioid Use Disorder in Pregnancy:
Care and Context of Mother and Newborn

PRESENTED BY:
Mishka Terplan MD MPH FACOG FASAM
Kelley Saia MD FACOG DABAM
Elizabeth Krans MD MSc FACOG

September, 22 2016
Participating speakers in “Opioid Use Disorder in Pregnancy: Care and Context of Mother and Newborn” have the following conflict of interest to disclose relative to the content of the presentation:

Mishka Terplan, MD: Provides consultant services to the National Center on Substance Abuse and Child Welfare – technical assistance and knowledge expertise
Overview

• The opioid epidemic: historical and current context
• Screening for opioid use and use disorder in pregnancy
• Maternal treatment
• Newborn care - Neonatal abstinence syndrome
• Substance exposed newborn reporting
History and Context
Turn of the century treatment: Addiction is a disease

• Addiction – seen as a medical condition and treated like one
  • Short acting opioids
  • Specialty clinics – detoxification and maintenance

• Neonatal abstinence syndrome (NAS) – described and treated

Dr Benjamin Rush
The current opioid epidemic

- Iatrogenic
  - 2012 259,000,000 opioid prescriptions for pain
  - Enough for every adult in US to have month supply
- Women in the epidemic
  - Overdose death (2004-2010) increased:
    - 237% for men
    - 400% for women

MMWR 11/4/11
Pill-Popping Mommas: 'Many' Pregnant Women Take Opioids, CDC Finds

BY BILL BRIGGS
Opioid Prescription Claims Among Women of Reproductive Age — United States, 2008–2012

Elizabeth C. Allen, PhD1, April L. Dawson, MPH1, Jennifer N. Lived, PharmD3, Suzanne M. Gilboa, PhD1, Meghan T. Frey, MPH1, Cheryl S. Benussi, PharmD3, Margaret A. Houle, PhD3 (Author affiliations at end of text)

**FIGURE 1.** Percentage of women aged 15–44 years who filled a prescription for an opioid from an outpatient pharmacy, by health care coverage type and year — United States, 2008–2012
Patterns of Opioid Utilization in Pregnancy in a Large Cohort of Commercial Insurance Beneficiaries in the United States

Brian T. Bateson, M.D., M.Sc., Sonia Hernandez-Diez, M.D., Dr.P.H., James P. Rethmeier, M.D., John D. Seeger, Pharm.D., Dr.P.H., Michael Doherty, M.S., Michael A. Fischer, M.D., M.S., Krista F. Huybrechts, M.S., Ph.D.

Anesthesiology, V 120 • No 5
May 2014
Recent trends in treatment admissions for prescription opioid abuse during pregnancy

Caitlin E. Martin, M.D., M.P.H. a, Nyaradzo Longinaker, M.S. a,b, Mishka Terplan, M.D., M.P.H. c

a Department of obstetrics and gynecology, University of North Carolina Hospitals
b Graduate Program in Life Sciences – Epidemiology and Ilana Gitlin Program, University of Maryland, Baltimore
c Department of Epidemiology & Public Health, University of Maryland School of Medicine, Baltimore, MD
• 2014 Maryland Maternal Mortality Review
• 30% Overdose (opioid)
  • 70% had documented comorbid mental health conditions or intimate partner violence
• 20% Homicide/Suicide
• Overall: 50% Maternal Deaths Behavioral Health Related
Heroin Increasing, Especially among Women

The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years

Heroin Use Has INCREASED Among Most Demographic Groups

<table>
<thead>
<tr>
<th></th>
<th>2002-2004*</th>
<th>2011-2013*</th>
<th>% CHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.4</td>
<td>3.6</td>
<td>50%</td>
</tr>
<tr>
<td>Female</td>
<td>0.8</td>
<td>1.6</td>
<td>100%</td>
</tr>
<tr>
<td><strong>AGE, YEARS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td>1.8</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>18-25</td>
<td>3.5</td>
<td>7.3</td>
<td>109%</td>
</tr>
<tr>
<td>26 or older</td>
<td>1.2</td>
<td>1.9</td>
<td>58%</td>
</tr>
<tr>
<td><strong>RACE/ETHNICITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1.4</td>
<td>3</td>
<td>114%</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1.7</td>
<td>--</td>
</tr>
<tr>
<td><strong>ANNUAL HOUSEHOLD INCOME</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>3.4</td>
<td>5.5</td>
<td>62%</td>
</tr>
<tr>
<td>$20,000-$49,999</td>
<td>1.3</td>
<td>2.3</td>
<td>77%</td>
</tr>
<tr>
<td>$50,000 or more</td>
<td>1</td>
<td>1.6</td>
<td>60%</td>
</tr>
<tr>
<td><strong>HEALTH INSURANCE COVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4.2</td>
<td>6.7</td>
<td>60%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>4.3</td>
<td>4.7</td>
<td>--</td>
</tr>
<tr>
<td>Private or other</td>
<td>0.8</td>
<td>1.3</td>
<td>63%</td>
</tr>
</tbody>
</table>

Data are plotted as a function of decade in which respondents initiated their opioid abuse.
2002-2009:
• Rate of NAS increased

Cost of care 2009
• NAS = $53,400
• All other births = $9500

Proportion of NAS paid for from Medicaid
• 2002 = 69%
• 2009 = 78%
Substance Exposed Newborn Reporting

• The Child Abuse and Prevention Treatment Act (CAPTA) Reauthorization Act of 2010 requires States to have policies and procedures for hospitals to notify child protective services (CPS) of all children born who are affected by illegal substance abuse or withdrawal symptoms resulting from prenatal drug exposure or indications of fetal alcohol spectrum disorder.
Estimated Number of Infants* Affected by Prenatal Exposure, by Type of Substance and Infant Disorder

<table>
<thead>
<tr>
<th>Substance</th>
<th>Estimated Number</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>640,000</td>
<td>15.9%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>340,000</td>
<td>8.5%</td>
</tr>
<tr>
<td>Illicit Drugs</td>
<td>240,000</td>
<td>5.9%</td>
</tr>
<tr>
<td>Binge Drinking</td>
<td>108,000</td>
<td>2.7%</td>
</tr>
<tr>
<td>Heavy Drinking</td>
<td>12,000</td>
<td>0.3%</td>
</tr>
<tr>
<td>FAS/ARND/ARBD</td>
<td>30,000</td>
<td></td>
</tr>
<tr>
<td>NAS</td>
<td>22,000</td>
<td></td>
</tr>
</tbody>
</table>

*Approximately 4 million (3,952,841) live births in 2012


Includes nine categories of illicit drugs, including heroin and the nonmedical use of prescription medications.

Parental AOD as Reason for Removal in the United States, 1999-2014

Note: Estimates based on all children in out of home care at some point during Fiscal Year

Source: AFCARS Data, 2014
<table>
<thead>
<tr>
<th>Reason for Removal</th>
<th>Percent of Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent Alcohol or Drug Abuse</td>
<td>37.6%</td>
</tr>
<tr>
<td>Parent Unable to Cope</td>
<td>20.0%</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>15.6%</td>
</tr>
<tr>
<td>Inadequate Housing</td>
<td>13.4%</td>
</tr>
<tr>
<td>Parent Incarceration</td>
<td>7.1%</td>
</tr>
<tr>
<td>Abandonment</td>
<td>6.1%</td>
</tr>
<tr>
<td>Child Behavior</td>
<td>5.3%</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>5.0%</td>
</tr>
<tr>
<td>Child Disability</td>
<td>3.7%</td>
</tr>
<tr>
<td>Child Alcohol or Drug Abuse</td>
<td>2.8%</td>
</tr>
<tr>
<td>Relinquishment</td>
<td>1.6%</td>
</tr>
<tr>
<td>Parent Death</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

Note: Estimates based on all children in out of home care at some point during Fiscal Year

Source: AFCARS Data, 2014
Age of Children who Entered Foster Care by Age, 2014 (N=264,746)
Maternal-Fetal Unit
A structurally and functionally interconnected metabolic unit shared by a mother and fetus through the placenta

Maternal-Infant Dyad
“There is no such thing as a baby … If you set out to describe a baby, you will find you are describing a baby and someone. A baby can not exist alone, but is essentially part of a relationship” (D.W. Winnicott 1966)
Screening and Treatment
How do we identify women with substance use in pregnancy?

• Early identification is key
  • Allows for early intervention and treatment that minimizes potential harms to the mother and her pregnancy
  • Maximizes motivation for change during pregnancy

• 2 types of screening
  • Pregnant women in prenatal care for substance use
  • Reproductive-aged women in SUD treatment for pregnancy – pregnancy intention
Screening Pregnant Women for Substance Use

• Universal screening (for licit and illicit substance use) is recommended
  - Alcohol (ACOG 2011)
  - Prescription opioids (ACOG 2012)

• Selective screening based on “risk factors” perpetuates discrimination and misses most women with problematic use
Screening Instruments

• No single best screening instrument to identify pregnant women with substance problems
• Self-administered or part of the patient interview
• Developed for or validated in pregnant women (partial list)
  • Alcohol: T-ACE (Sokol 1989); TWEAK (Chang 1999)
  • Alcohol and other drugs: DAST and MAST (Kemper 1993); 4P’s Plus (Chasnoff 1999); CRAFFT (Chang 2011) for pregnant adolescents
The 4 P’S

1. Have you ever used drugs or alcohol during Pregnancy?
2. Have you had a problem with drugs or alcohol in the Past?
3. Does your Partner have a problem with drugs or alcohol?
3. Do you consider one of your Parents to be an addict or alcoholic?

• Remember to ask direct questions tactfully and respectfully!
• Parents: Did either of your parents ever have a problem with alcohol or drugs?
• Partner: Does your partner have a problem with alcohol or drugs?
• Past: Have you ever drunk beer, wine, or liquor?
• Pregnancy: In the month before you knew you were pregnant, How many cigarettes did you smoke? How much (beer/wine/liquor) did you drink?
Screening: Urine toxicology?

- Do not use as sole assessment of substance use/use disorder (ACOG 2012)
  - Short detection window (substance dependent)
  - Might not capture binge or intermittent use
  - Rarely detects alcohol
  - Doesn’t capture prescription opioids (without confirmation testing)
- Useful adjunct primarily for individuals in treatment
- Ethical issues – patient needs to give consent prior to specimen collection
Importance of Consistency

• Intra-Institutional and Intra-Departmental Consistency:
  • Obstetrics, Pediatric and Social Work Departments within institutions must work collaboratively to develop consistent care protocols

• Inter-Institutional Consistency:
  • Regional treatment programs, obstetric practices and Family Services must communicate and collaborate to ensure consistent care and treatment
  • Family legal services (DCF) and the State Legislation must collaborate with local medical and recovery services (avoid contradiction, conflict and disservice to the patient)
Treatment:
*treatment works*

Opioid agonist treatment + Behavioral therapy
Heroin overdose deaths and opioid agonist treatment: Baltimore, MD, 1995–2009

Schwartz RP, et al. 2013
Opioid Agonist Treatment: Improved Pregnancy Outcomes

• Maternal:
  • reduction in overdose mortality
  • Relapse prevention
  • Reduces polysubstance use
  • HBV, HCV, HIV
  • Increases engagement with prenatal care/ health care

• Neonatal:
  • Decreases preterm delivery and IUGR
  • Decreases NICU admissions
  • Decreases morbidity/ mortality
• Pregnant women who are physically dependent on opioids should receive treatment using agonist medications rather than withdrawal management or abstinence as these approaches may pose a risk to the fetus.

• Furthermore, 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.
Opioid Use Disorder Treatment in Pregnancy

Opioid Agonist Treatment is the Standard of Care

Treatment options

- **Methadone**: gold-standard in obstetrics
- **Buprenorphine**: first line appreciation

Methadone and buprenorphine (both category C) are safe and effective treatment options in pregnancy

*(Fischer et al., 1998, 1999). (Jones et al 2010)*
Methadone

- Synthesized in Germany (1937) during opium shortage: painkiller for World War II troops
- Full opioid agonist: T1/2 7-60hrs
- Receptor blockade effect (>60mg)
- Regulated in US for opioid use disorder: daily clinic dosing
- Gold Standard for OUD in pregnancy
  
  *not FDA approved in pregnancy*
Buprenorphine

- Partial opioid agonist
- **1978**: (UK) IV/IM long acting pain medication
- **2000**: (US) Drug Addiction Treatment Act (DATA): permitting MDs to prescribe schedule II, III, IV opioids for opioid addiction and detoxification
- **2002**: (US) FDA approved Buprenorphine for treatment of opioid addiction
  - Schedule III drug (from IV)
Opioid Agonist Treatment

Methadone

Buprenorphine
Buprenorphine Formulations

Buprenorphine mono-therapy
• Subutex
• Original formulation
• Basis for initial safety studies in pregnancy

Buprenorphine + Naloxone
• Suboxone
• Formulation rationale
• Ratio: Bup/ Nal=0.25
• Tablet/ Film : 2/0.5 and 8/2
• Perception effect of initial formulations
Pregnant Physiology

- **Total blood volume**: 45% increase by 28wks
- **Cardiac Function**:
  - HR 10-15 bpm
  - CO 30-50% increase by 2nd
- **GFR increases**

Maintenance Dose

- **Terminal half-life decreases** in 2nd and 3rd trimesters
- **Lower trough levels**
- **Withdrawal symptoms**
Opioid Maintenance in Pregnancy

- Dosing changes
- Split dosing
Neonatal Abstinence Syndrome
Neonatal Abstinence Syndrome (NAS)

Definition

- Postnatal drug withdrawal syndrome among opioid-exposed infants
- 40-80% of opioid exposed newborns develop NAS
- Expected and treatable consequence of opioid exposure in utero
  - Illicit opioids, prescription opioids, medication assisted treatment (MAT)
Neonatal Abstinence Syndrome (NAS)

Clinical features of NAS

- Gastrointestinal
  - Poor feeding/vomiting/loose stools

- Central nervous system
  - Tremors, irritability/decreased sleep, exaggerated reflexes, seizures

- Autonomic activation
  - Tachypnea, yawning, dilated pupils

NAS scoring and treatment

- NAS scoring tools (i.e. Finnegan scale)

- Medication initiation
  - “Control” withdrawal to minimize complications
  - Slowly decreasing doses of opioids

- Scoring context
  - Lack of evaluation in preterm infants
  - Lack of validation in polysubstance exposed infants
  - Significant inter-rater reliability challenges

Neonatal Abstinence Syndrome (NAS)

NAS is withdrawal due to dependence vs. addiction

- NAS is a withdrawal syndrome due to physiologic dependence following chronic opioid exposure during pregnancy

- Addiction is a biologic process that results from chronic exposure to an addictive stimulus
  - Addiction is characterized by reinforcing behavior or compulsive engagement in rewarding stimuli
  - Babies do not exhibit addictive behavior
Neonatal Abstinence Syndrome (NAS)

NAS is withdrawal due to dependence vs. addiction

- NAS is a withdrawal syndrome due to physiologic dependence following chronic opioid exposure during pregnancy

- Addiction is a biologic process that results from chronic exposure to an addictive stimulus
  - Addiction is characterized by reinforcing behavior or compulsive engagement in rewarding stimuli
  - Babies do not exhibit addictive behavior
NAS can be caused by opioid and non-opioid medications

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset, h</th>
<th>Frequency, %</th>
<th>Duration, d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>24–48</td>
<td>40–80&lt;sup&gt;27&lt;/sup&gt;</td>
<td>8–10</td>
</tr>
<tr>
<td>Methadone</td>
<td>48–72</td>
<td>13–94&lt;sup&gt;37&lt;/sup&gt;</td>
<td>Up to 30 or more</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>36–60</td>
<td>22–67&lt;sup&gt;46,48&lt;/sup&gt;</td>
<td>Up to 28 or more</td>
</tr>
<tr>
<td>Prescription opioid medications</td>
<td>36–72</td>
<td>5–20&lt;sup&gt;56,60&lt;/sup&gt;</td>
<td>10–30</td>
</tr>
<tr>
<td><strong>Nonopioids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td>24–48</td>
<td>20–50&lt;sup&gt;64&lt;/sup&gt;</td>
<td>2–6</td>
</tr>
<tr>
<td>TCAs</td>
<td>24–48</td>
<td>20–50&lt;sup&gt;64&lt;/sup&gt;</td>
<td>2–6</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>24</td>
<td>2–49&lt;sup&gt;101&lt;/sup&gt;</td>
<td>7–10</td>
</tr>
<tr>
<td>Inhalants</td>
<td>24–48</td>
<td>48&lt;sup&gt;70&lt;/sup&gt;</td>
<td>2–7</td>
</tr>
</tbody>
</table>

NAS incidence in the United States, 2000-2009

Patrick et al., JAMA, 2014
NAS geographic distribution

Neonatal Abstinence Syndrome per 1000 Hospital Births by US Census Division, 2012

Patrick et al., J Perinatology, 2015
Hospital charges for NAS vs. other newborns, 2000-2009

Patrick et al., JAMA, 2014
<table>
<thead>
<tr>
<th>Year</th>
<th>Medicaid</th>
<th>Private Payer</th>
<th>Self-pay</th>
<th>Other Payer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>68.7%</td>
<td>18.2%</td>
<td>8.7%</td>
<td>4.4%</td>
</tr>
<tr>
<td>2003</td>
<td>69.9%</td>
<td>19.8%</td>
<td>6.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>2006</td>
<td>73.7%</td>
<td>19.0%</td>
<td>5.5%</td>
<td>1.9%</td>
</tr>
<tr>
<td>2009</td>
<td>77.6%</td>
<td>17.6%</td>
<td>2.9%</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

* Weighted percentages
<table>
<thead>
<tr>
<th>Year</th>
<th>Medicaid</th>
<th>Private Payer</th>
<th>Self-pay</th>
<th>Other Payer</th>
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</thead>
<tbody>
<tr>
<td>2009</td>
<td>$563</td>
<td>$133</td>
<td>$20</td>
<td>$14</td>
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<tr>
<td>2010</td>
<td>$865</td>
<td>$167</td>
<td>$35</td>
<td>$29</td>
</tr>
<tr>
<td>2011</td>
<td>$903</td>
<td>$208</td>
<td>$30</td>
<td>$30</td>
</tr>
<tr>
<td>2012</td>
<td>$1,170</td>
<td>$202</td>
<td>$40</td>
<td>$33</td>
</tr>
</tbody>
</table>

* Millions of dollars
Non-pharmacologic interventions for NAS

Importance of preserving the maternal-infant dyad

- Breastfeeding and breastmilk are strongly recommended
  - Stress reduction, increased maternal confidence
  - Enhanced mother-infant bonding
  - Motivation to avoid illicit drug use

- Breastfeeding and neonatal outcomes
  - Delayed onset of NAS
  - Less pharmacologic treatment for NAS

- Rooming-in of mother and infant
  - Holding, cuddling, swaddling and manual rocking
  - Kangaroo care and pacifiers
  - Minimal stimulation

Kocherlakota, Pediatrics, 2014
Caring for moms improves neonatal outcomes

• Family Planning support
  • Over 80% of pregnancies are unintended
  • Fewer than 10% of women use highly-effective contraception (i.e. LARC)

• Support for co-occurring psychiatric disorders
  • 65-73% of women suffer from anxiety and depression
  • 45% of women screen positive for postpartum depression

• Support for parenting
  • Many women lack knowledge about basic infant care
  • 64% believed they would spoil their newborn by holding them when they cried

Conclusions

• (Pregnant) women are one of the faces of the opioid epidemic
• Screening for substance use should be a universal and routine part of Prenatal Care
• Treatment in pregnancy begins from the primacy of the maternal-fetal/infant dyad
• Care needs to be compassionate and non-judgmental, comprehensive and coordinated with PNC provider
• Evidence-based treatment = MAT plus behavioral counseling plus PNC
• NAS is complex – not the same as opioid exposure
• Preventing substance exposed pregnancies means decreasing unplanned pregnancies, increasing access to reproductive health services, specifically contraception
Thank You
Questions?