Opioid Use Disorders and Pregnancy

Marcela Smid, MD
Maternal-Fetal Medicine
OBJECTIVES

• Definitions
• Epidemiology
• Pharmacology
• Effects on pregnancy
• Screening
• Treatment
CARE FOR PREGNANT WOMEN WITH OUD

Opioid Use in Pregnancy, Neonatal Abstinence Syndrome, and Childhood Outcomes

Executive Summary of a Joint Workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, American College of Obstetricians and Gynecologists, American Academy of Pediatrics, Society for Maternal-Fetal Medicine, Centers for Disease Control and Prevention, and the March of Dimes Foundation

Uma M. Reddy, MD, MPH, Jonathan M. Davis, MD, Zhoxia Ren, MD, PhD, and Michael F. Greene, MD, for the Opioid Use in Pregnancy, Neonatal Abstinence Syndrome, and Childhood Outcomes Workshop Invited Speakers*
DEFINITIONS

- **Use** – Sporadic consumption without adverse consequences
- **Abuse** – Consumption with some adverse consequences
- **Physical Dependence** – State of adaptation manifested by a class-specific withdrawal syndrome produced by abrupt cessation or rapid dose reduction of the substance, or by administration of an antagonist
- **Psychological Dependence** – Subjective sense of a need for a specific psychoactive substance, either for its positive effects or to avoid negative effects associated with its abstinence
DEFINITIONS

- **Addiction** – A primary, chronic disease of brain reward, motivation, memory, and related circuitry.

- **Opioid use disorder** is a pattern of opioid use characterized by tolerance, craving, inability to control use and continued use despite adverse consequences.

- **Neonatal abstinence syndrome** – group of problems seen in neonates after prenatal drug exposure characterized by hyperactivity of central and autonomic nervous system.
BABIES CANNOT HAVE AN ADDICTION

ADDICTED AT BIRTH

sky NEWS Special Report
1996: OxyContin is marketed as “less abusive”

JCAHO pain as 5th vital sign

OxyContin formulation changed
Utah Drug Related Deaths

Estimated age-adjusted rates of drug poisoning deaths per 100,000 population

2002 2003 2004 2005 2006

2007 2008 2009 2010

2011 2012 2013 2014

ate of Drug Poisoning Deaths per 100,000 Population by County, Utah 2002-2014 (age-adjusted); (CDC and UTDH, 2016)
PREGNANCY AND OPIOID PRESCRIPTIONS

National 22%
Utah 42%
Idaho 36%
New Hampshire 34%
Wyoming 34%
Tennessee 34%

Fig. 1. Regional variation in the rates of prescription opioid dispensing during pregnancy, Medicaid 2000–2007. Arizona, Michigan, Montana, Connecticut, and Puerto Rico (white) are not represented in the cohort because of incomplete claims information.

Complicated Pregnancies or Births due to a Mother’s Drug Dependence

Figure 1. Number of hospital discharges as a result of complicated pregnancies or births due to a mother’s drug dependence, Utah, 2002–2011

Source: Utah Hospital Discharge Data
Newborns with Neonatal Abstinence Syndrome

Figure 2. Number of newborns (birth to 28 days) with NAS, Utah, 2002–2011

Source: Utah Hospital Discharge Data
NEONATAL ABSTINENCE SYNDROME IN UTAH

Charges for Newborns with Neonatal Abstinence Syndrome

Figure 3. Charges for newborns (birth to 28 days) with NAS, Utah, 2002–2011

Source: Utah Hospital Discharge Data
PREGNANCY AND OUD IN UTAH

- 2010 National Survey on Drug Use and Health: 4.4% of pregnant women reported illicit drug use in last 4 days
- Utah: 5% of neonates are positive for drugs, most are opioids
- One cause of maternal mortality in Utah is drug-related
EFFECTS ON PREGNANCY

- **Birth defects**
  - Heart defects
  - Spina bifida
  - Gastroschisis
- **Intrauterine growth restriction**
- **Abruption**
- **Preterm delivery**
- **Sexually transmitted infections**
- **Stillbirth**
  - Fluctuating opioid concentrations in maternal blood may lead to fetal withdrawal or death
  - Narcotic withdrawal in pregnancy: Stillbirth incidence with a case report
    - Jose Luis Rementeria, MD
    - Am J Ob Gyn, 1973
SBIRT – SCREENING, BRIEF INTERVENTION, REFERRAL TO TREATMENT

• EVERY pregnant woman prenatally and throughout pregnancy

• Utah HB 175 – REQUIRED training of physicians within nine years

SBIRT: Core Clinical Components

• **Screening:** Very brief screening that identifies substance related problems

• **Brief Intervention:** Raises awareness of risks and motivates patients to acknowledge & address problem. 1-2 sessions of 5-8 minutes.

• **Brief Treatment:** Cognitive Behavioral Therapy/MET with patients with higher risk or early dependence. 2-6 sessions of 30 minutes.

• **Referral:** Referral of those with more serious addictions to specialized treatment services.
SCREENING IN PREGNANCY

• 4 Ps
• NIDA Quick Screen
• CRAFFT

4 P’s for Substance Abuse
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?
4. Do you consider one of your Parents to be an addict or alcoholic?

TABLE 5 The CRAFFT questions

Two or more “Yes” answers suggest high risk of a serious substance-use problem or a substance-use disorder.

<table>
<thead>
<tr>
<th>NIDA Quick Screen Question:</th>
<th>Never</th>
<th>Once or Twice</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily or Almost Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• For men, 5 or more drinks a day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• For women, 4 or more drinks a day</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tobacco Products</td>
<td></td>
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</tr>
<tr>
<td>Prescription Drugs for Non-Medical Reasons</td>
<td></td>
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<tr>
<td>Illegal Drugs</td>
<td></td>
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</tr>
</tbody>
</table>

Abbreviation: CRAFFT, Car, Relax, Alone, Forget, Friends, Trouble.
Knight JR, et al.21
OUD TREATMENT IN PREGNANCY

• **Standard of care is opioid substitution** therapy with behavioral therapy
• Methadone or buprenorphine
  – Prevent complications of illicit opioid use and narcotic withdrawal
  – Encourage prenatal care
  – Reduce criminal activity
  – Harm reduction
OUD TREATMENT IN PREGNANCY

- Detoxification is controversial and NOT well studied

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>108</td>
<td>23</td>
<td>77</td>
<td>93</td>
<td>301</td>
</tr>
<tr>
<td>Mean maternal age, y</td>
<td>26.9 ± 3.7</td>
<td>26.4 ± 3.5</td>
<td>26.6 ± 3.6</td>
<td>27.2 ± 3.9</td>
<td>26.8 ± 3.7</td>
</tr>
<tr>
<td>Maternal age range, y</td>
<td>18–43</td>
<td>17–38</td>
<td>18–39</td>
<td>17–39</td>
<td>17–43</td>
</tr>
<tr>
<td>Maternal age &lt;30 y</td>
<td>82 (76%)</td>
<td>18 (78%)</td>
<td>55 (71%)</td>
<td>67 (72%)</td>
<td>222 (74%)</td>
</tr>
<tr>
<td>Multiparity</td>
<td>94 (87%)</td>
<td>14 (61%)</td>
<td>54 (70%)</td>
<td>73 (78%)</td>
<td>235 (78%)</td>
</tr>
<tr>
<td>White</td>
<td>85 (79%)</td>
<td>22 (96%)</td>
<td>74 (96%)</td>
<td>84 (90%)</td>
<td>265 (88%)</td>
</tr>
<tr>
<td>African-American</td>
<td>22 (20%)</td>
<td>1 (4%)</td>
<td>3 (4%)</td>
<td>8 (9%)</td>
<td>34 (11%)</td>
</tr>
<tr>
<td>Gestational age at detoxification and NICU admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detoxification first trimester, 5–13 wks gestation</td>
<td>10 (9%)</td>
<td>4 (17%)</td>
<td>12 (15%)</td>
<td>2 (2%)</td>
<td>28 (9%)</td>
</tr>
<tr>
<td>Detoxification second trimester, 14–27 wks gestation</td>
<td>65 (60%)</td>
<td>10 (43%)</td>
<td>36 (47%)</td>
<td>37 (40%)</td>
<td>148 (49%)</td>
</tr>
<tr>
<td>Detoxification third trimester, ≥28 wks gestation</td>
<td>33 (31%)</td>
<td>9 (30%)</td>
<td>20 (38%)</td>
<td>54 (58%)</td>
<td>125 (42%)</td>
</tr>
<tr>
<td>Preterm deliveries prior to 37 wks gestation</td>
<td>21 (19%)</td>
<td>3 (13%)</td>
<td>13 (17%)</td>
<td>16 (17%)</td>
<td>53 (17.6%)</td>
</tr>
<tr>
<td>Neonatal intensive care unit admission</td>
<td>32 (30%)</td>
<td>5 (22%)</td>
<td>60 (78%)</td>
<td>22 (24%)</td>
<td>119 (40%)</td>
</tr>
<tr>
<td>Pregnancy outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of NAS</td>
<td>20 (18.5%)</td>
<td>4 (17.4%)</td>
<td>54 (70.1%)</td>
<td>16 (17.2%)</td>
<td>94 (31%)</td>
</tr>
<tr>
<td>Rate of relapse</td>
<td>25 (23.1%)</td>
<td>4 (17.4%)</td>
<td>57 (74.0%)</td>
<td>21 (22.5%)</td>
<td>107 (36%)</td>
</tr>
</tbody>
</table>
ADDICTION AS CHRONIC MEDICAL CONDITION
– Similar to diabetes management
METHADONE VERSUS BUPRENOORPHINE

Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, Ph.D., Kevin E. O'Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D.

*Figure 2. Mean Neonatal Morphine Dose, Length of Neonatal Hospital Stay, and Duration of Treatment for Neonatal Abstinence Syndrome.*
# Neonatal Abstinence Syndrome (NAS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset, hours</th>
<th>Incidence</th>
<th>Duration, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>24-48</td>
<td>40-80%</td>
<td>8-10</td>
</tr>
<tr>
<td>Methadone</td>
<td>48-72</td>
<td>13-94%</td>
<td>Up to 30 or more</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>36-60</td>
<td>22-67%</td>
<td>Up to 28 or more</td>
</tr>
<tr>
<td>Prescription opioids</td>
<td>36-72</td>
<td>5-20%</td>
<td>10-30</td>
</tr>
</tbody>
</table>

Adapted from Kocherlakota, P *Pediatrics* 2014; 134(2):e547-561.
**Buprenorphine and Naloxone Compared With Methadone Treatment in Pregnancy**

*Samantha L. Wiegand, MD, Elizabeth M. Stringer, MD, Alison M. Stuebe, MD, Hendree Jones, PhD, Carl Seashore, MD, and John Thorp, MD*

**Table 2. Neonatal Outcomes**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Methadone (n=31)</th>
<th>Buprenorphine and Naloxone (n=31)</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated for NAS</td>
<td>16 (51.6)</td>
<td>8 (25.1)</td>
<td>2.55 (1.31–4.98)</td>
</tr>
<tr>
<td>Morphine used (mg)</td>
<td>5.0±3.3†</td>
<td>3.4±1.2</td>
<td></td>
</tr>
<tr>
<td>Duration of NAS treatment (d)</td>
<td>11.4±3.4§</td>
<td>10.6±3.1</td>
<td></td>
</tr>
<tr>
<td>Peak NAS score†</td>
<td>10.7±3.7</td>
<td>9.0±4.4</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>32.9±2.5</td>
<td>34.4±1.4</td>
<td></td>
</tr>
<tr>
<td>Birth weight (gm)</td>
<td>2,885.9±691.2</td>
<td>3,174.6±532.8</td>
<td></td>
</tr>
<tr>
<td>Length (cm)</td>
<td>47.9±4.0</td>
<td>50.1±2.5</td>
<td></td>
</tr>
<tr>
<td>Preterm</td>
<td>5 (16.1)</td>
<td>1 (3.2)</td>
<td>5.00 (0.62–40.36)†</td>
</tr>
<tr>
<td>NICU admission</td>
<td>11 (35.5)</td>
<td>6 (19.4)</td>
<td>1.06 (0.75–1.50)</td>
</tr>
<tr>
<td>Length of hospitalization (d)</td>
<td>9.8±7.4</td>
<td>5.6±5.0</td>
<td></td>
</tr>
<tr>
<td>Apgar score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min</td>
<td>8 (3–9)</td>
<td>8 (2–9)</td>
<td></td>
</tr>
<tr>
<td>5 min</td>
<td>9 (7–10)</td>
<td>9 (7–9)</td>
<td></td>
</tr>
</tbody>
</table>
## POLYPHARMACY AND NAS

Risk of neonatal drug withdrawal after intrauterine co-exposure to opioids and psychotropic medications: cohort study

Krista F Huybrechts,¹ Brian T Bateman,¹,² Rishi J Desai,¹ Sonia Hernandez-Diaz,³ Kathryn Rough,¹,³ Helen Mogun,¹ Leslie S Kerzner,⁴ Jonathan M Davis,⁵ Megan Stover,⁶ Devan Bartels,⁷ Jennifer Cottral,⁷ Elisabetta Patorno¹

<table>
<thead>
<tr>
<th></th>
<th>Opioids + psychotropic medications</th>
<th>Opioids alone</th>
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<tbody>
<tr>
<td></td>
<td>Cases/total: 495/14 183</td>
<td>1743/173 841</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>3.49 (3.19 to 3.79)</td>
<td>1.00 (0.96 to 1.05)</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>67/993</td>
<td>2481/199 151</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>413/5361</td>
<td>1989/191 863</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>57/501</td>
<td>2509/200 204</td>
</tr>
<tr>
<td>Z drugs</td>
<td>229/10 105</td>
<td>2286/188 216</td>
</tr>
<tr>
<td>1 psychotropic*</td>
<td>612/16 524</td>
<td>1423/168 086</td>
</tr>
<tr>
<td>≥2 psychotropics*</td>
<td>172/17 37</td>
<td>1423/168 086</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Risk (/100) (95% CI)</th>
<th>Risk (/100) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.49 (3.19 to 3.79)</td>
<td>1.00 (0.96 to 1.05)</td>
</tr>
<tr>
<td></td>
<td>6.75 (5.19 to 8.31)</td>
<td>1.25 (1.20 to 1.29)</td>
</tr>
<tr>
<td></td>
<td>7.70 (6.99 to 8.42)</td>
<td>1.04 (0.99 to 1.08)</td>
</tr>
<tr>
<td></td>
<td>11.38 (8.60 to 14.16)</td>
<td>1.25 (1.20 to 1.30)</td>
</tr>
<tr>
<td></td>
<td>2.27 (1.98 to 2.56)</td>
<td>1.21 (1.17 to 1.26)</td>
</tr>
<tr>
<td></td>
<td>3.70 (3.42 to 4.00)</td>
<td>0.85 (0.80 to 0.89)</td>
</tr>
<tr>
<td></td>
<td>9.90 (8.56 to 11.37)</td>
<td>0.85 (0.80 to 0.89)</td>
</tr>
</tbody>
</table>

*Antidepressants, benzodiazepines, gabapentin.
INTRAPARTUM MANAGEMENT

• Treat women with OUD in labor on just like others
  – Continue ethadone or buprenorphine

• Avoid opioid antagonists (butorphanol, nalbuphine, pentazocine) which can precipitate withdrawal

• Pediatric staff should be available

• Awareness
  – More analgesia during labor than non opioid-dependent patients
  – Neuraxial anesthesia is appropriate as needed
POSTPARTUM MANAGEMENT

• Increased pain
  – increased opioid treatment whether on methadone or buprenorphine

• Breastfeeding can be encouraged with methadone or buprenorphine
  – NOT if continuing to use heroin or HIV
  – Hepatitis B and C NOT a contraindication

• Contraception
• Naloxone counseling
• Drug treatment
# Substance Use During Pregnancy

## State Policies On Substance Use During Pregnancy

<table>
<thead>
<tr>
<th>State</th>
<th>Substance Use During Pregnancy Considered:</th>
<th>When Drug Use Suspected, State Requires:</th>
<th>Drug Treatment For Pregnant Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utah</td>
<td>Child Abuse</td>
<td>Reporting</td>
<td>Targeted Program Created</td>
</tr>
<tr>
<td></td>
<td>Grounds For Civil Commitment</td>
<td>Testing</td>
<td>Pregnant Women Given Priority Access In General Programs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pregnant Women Protected From Discrimination In Publicly Funded Programs</td>
</tr>
</tbody>
</table>

Utah Code > Title 76 > Chapter 5 > Part 1 > § 76-5-112.5

Utah Code 76-5-112.5. Endangerment of a child or vulnerable adult
NALOXONE

If you are not sure, any use is okay. Call 9-1-1 or get medical help immediately.

Utah Naloxone Rescue Kits
(385) 495-9050
www.UtahNaloxone.org
UtahNaloxone@gmail.com

You can save a life.
SUPERAD CLINIC – (SUBSTANCE USE IN PREGNANCY RECOVERY, ADDITION AND DEPENDENCE)

- South Jordan Health Center
- Monday afternoons
- Appointments (801) 581-8425
QUESTIONS

QUESTIONS, HAVE YOU?

ANSWERS, HAVE I.

Well I might just have opinions... lots of opinions.
1. American Society of Addiction Medicine: www.asam.com
5. ACOG Committee Opinion: Opioid Abuse, Dependence, and Addiction in Pregnancy, Number 524, May 2012
7. Ewing H. A practical guide to intervention in health and social services with pregnant and postpartum addicts and alcoholics: theoretical framework, brief screening tool, key interview questions, and strategies for referral to recovery resources. (copyrighted)
8. Center for Adolescent Substance Abuse Research, Children’s Hospital, Boston. The CRAFFT screening interview. Boston (MA): CeSAR; 2009.
12. Methadone Maintenance During Pregnancy: UpToDate, July 2012
13. DOLE VP, NYSWANDER M. A MEDICAL TREATMENT FOR DIACETYLMORPHINE (HEROIN) ADDICTION. A CLINICAL TRIAL WITH METHADONE HYDROCHLORIDE. JAMA. 1965;193:646.
• Broussard, et al., Maternal treatment with opioid analgesics and risk for birth defects. AJOG. Volume 204 issue 4, 314.e1-314.e11, April 2011
• Volkow, et al., Curtailing Diversion and Abuse of Opioid Analgesics Without Jeopardizing Pain Treatment. JAMA. 2011; 305(13):1346-1347
• Liu, et al., Growth restriction in pregnancies of opioid-dependent mothers. Arch Dis Child Fetal Neonatal Ed 2010; 95: F258-F262