Opioid Use and Opioid Use Disorder in Pregnancy

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The Florida Alliance for Healthy Communities, Inc.
and
The State of Florida
Department of Children and Families
Learning Objectives

• Define and Describe Opioid Use Disorder and Screening in Pregnancy
• Describe the Effects of Opioids on Pregnancy Outcomes
• Describe Role of Obstetrician – Gynecologist and other Obstetric Care Providers
• Describe Opioid Treatment in Pregnancy Using Opioid Agonist Pharmacotherapy
• Describe the Antepartum, Intrapartum and Postpartum Care in Women with Opioid Use Disorder
• Review the Florida Statutes
Conflict of Interest Disclosure Statement

I have no financial relationships with any commercial interest related to the content of this activity.
The rate of overdose deaths among women has gone up more than 4 times among pregnant women. 4 times as many infants were born with neonatal abstinence syndrome (NAS) in 2014 than in 1999.
National Overdose Deaths
Number of Deaths from Prescription Drugs

Source: National Center for Health Statistics, CDC Wonder

Understanding the Epidemic

3 Waves of the Rise in Opioid Overdose Deaths

- Wave 1: Rise in Prescription Opioid Overdose Deaths
- Wave 2: Rise in Heroin Overdose Deaths
- Wave 3: Rise in Synthetic Opioid Overdose Deaths

Other Synthetic Opioids: e.g., Tramadol and Fentanyl, prescribed or illicitly manufactured
Commonly Prescribed Opioids: Natural & Semi-Synthetic Opioids and Methadone
Heroin

The Opioid Epidemic by the Numbers

The Opioid Epidemic in the U.S.

In 2015...

- **12.5 million** people used prescription opioids
- **2.1 million** people used opioids for the first time
- **135,000** people used heroin for the first time
- **33,091** people died from overdose on opioids
- **12,989** deaths due to overdose on heroin
- **9,580** deaths due to overdose on synthetic opioids
- **828,000** people used heroin
- **2 million** people had prescription opioid use disorder
- **$78.5 billion** in economic costs

Updated January 2018. For more information, visit: http://www.hhs.gov/opioids/

IN 2016...

- **116** people died every day from opioid-related drug overdoses
- **11.5 m** people misused prescription opioids
- **42,249** people died from overdosing on opioids
- **17,087** deaths due to overdose on commonly prescribed opioids
- **19,413** deaths due to overdose on synthetic opioids other than methadone
- **948,000** people used heroin
- **2.1 million** people had an opioid use disorder
- **170,000** people used heroin for the first time
- **15,469** deaths due to overdose on heroin
- **504 billion** in economic costs
THE OPIOID EPIDEMIC BY THE NUMBERS

130+ People died every day from opioid-related drug overdoses\(^3\) (estimated)

11.4 m People misused prescription opioids\(^1\)

47,600 People died from overdosing on opioids\(^2\)

2.1 million People had an opioid use disorder\(^1\)

81,000 People used heroin for the first time\(^1\)

2 million People misused prescription opioids for the first time\(^1\)

15,482 Deaths attributed to overdosing on heroin\(^2\)

28,466 Deaths attributed to overdosing on synthetic opioids other than methadone\(^3\)

SOURCES
2. NCHS Data Brief No. 293, December 2017
Women in the Epidemic

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

Elizabeth C. Atlee, PhD1, April L. Dawson, MPH1, Jennifer N. Lind, PharmD1, Suzanne M. Gilboa, PhD1, Meghan T. Frey, MPH1, Cheryl S. Broussard, PhD1, Margaret A. Heslin, PhD1 (Author affiliations at end of text)

Women aged 15-44 years who filled a prescription for an opioid medication, 2008-2012
Up to 22% of women have filled a prescription for an opioid while pregnant.
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.
Physiology and Pharmacology of Opioids
Your Brain on Opioids

sublocade.com
Definitions

Opioid:

- Natural or synthetic chemicals that interact with opioid receptors on nerve cells in the body and brain, and reduce the intensity of pain signals and feelings of pain. This class of drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and pain medications available legally by prescription, such as oxycodone, hydrocodone, codeine, morphine, and many others. Opioid pain medications are generally safe when taken for a short time and as prescribed by a health care professional, but because they produce euphoria in addition to pain relief, they can be misused.
Definitions

**Dependence:** A state in which an individual only functions normally in the presence of a substance, experiencing physical disturbance when the substance is removed. A person can be dependent on a substance without being addicted, but dependence sometimes leads to addiction.

**Addiction:** Common name for a severe substance use disorder, associated with compulsive or uncontrolled use of one or more substances. Addiction is a chronic brain disease that has the potential for both recurrence (relapse) and recovery.

**Tolerance:** Alteration of the body’s responsiveness to alcohol or a drug such that higher doses are required to produce the same effect achieved during initial use.

**Withdrawal:** A set of symptoms and signs that are experienced when discontinuing use of a substance to which a person has become dependent or addicted, which can include negative emotions such as stress, anxiety, or depression, as well as physical effects such as nausea, vomiting, muscle aches, and cramping, among others. Withdrawal symptoms often lead a person to use the substance again.
Definitions

Substance Misuse:
• The use of any substance in a manner, situation, amount, or frequency that can cause harm to users or to those around them.

Substance Use Disorder:
• Occurs when the recurrent use of alcohol and/or drugs causes clinically and functionally significant impairment, such as health problems, disability, and failure to meet major responsibilities at work, school, or home. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5, a diagnosis of substance use disorder is based on evidence of impaired control, social impairment, risky use, and pharmacological criteria.

Prescription opioid (or opioid pain reliever) misuse:
• Use of an opioid pain reliever in any way not directed by a health care professional.

Opioid Use Disorder:
• A disorder characterized by loss of control of opioid use, risky opioid use, impaired social functioning, tolerance, and withdrawal.
Addiction

- Compulsive behavior despite negative consequences
- Behavior is reinforcing, or rewarding
- Loss of control in limiting intake
Well-supported evidence suggests that the addiction process involves a three-stage cycle:

(1) **Binge/Intoxication**, the stage at which an individual consumes an intoxicating substance and experiences its rewarding or pleasurable effects;

(2) **Withdrawal/ Negative Affect**, the stage at which an individual experiences a negative physical and emotional state in the absence of the substance; and

(3) **Preoccupation/Anticipation**, the stage at which one seeks substances again after a period of abstinence. This cycle becomes more severe as a person continues substance use and as it produces dramatic changes in brain function that reduce a person’s ability to control his or her substance use. The three stages are linked to and feed on each other, but they also involve different brain regions: (1) the basal ganglia (binge/intoxication), (2) the extended amygdala (withdrawal/negative affect), and (3) the prefrontal cortex (preoccupation/anticipation).
Neurobiology of Addiction

The Brain and Addiction

Opioids and the medications used to treat addiction affect the limbic system, the brain’s pleasure and reward center. The obsessive behavior and cravings that characterize opioid addiction result from dysfunctional circuits in the limbic system that can disconnect it from the reasoning power of the cerebral cortex.

- **Limbic system**
  - Fear
  - Pleasure
  - Anger

- **Cerebral cortex**
  - Judgment
  - Awareness
  - Decision making

- **Brain stem**
  - Controls heart, lung and other essential bodily functions

- **Spinal cord**
  - Delivers messages to and from the body

- **prefrontal cortex**
- **nucleus accumbens**
- **VTA**
The Effect of Opioid Addiction on The Brain

• Before discussing different methods for treating opioid addiction, it’s important to understand how drugs like heroin, OxyContin, Percocet and other prescription pain medications actually affect the brain.

• They work on opioid receptors in the brain, which ordinarily are activated by a class of neurotransmitters called endorphins. Heroin and other opioid drugs flood the brain’s opioid receptors, creating a high or euphoric feeling.
The Effect of Opioid Addiction on The Brain

• When a person uses these kinds of drugs regularly, the number of opioid receptors in his or her brain increases to the point where natural endorphins are no longer capable of stimulating them. The more opioid receptors a person has, the more opioid drugs are needed to get high and, eventually, to simply feel normal. This is called building a tolerance.
The Effect of Opioid Addiction on The Brain

• When not all opioid receptors are activated, it can create feelings of anxiety, depression and physical pain or illness — what’s called withdrawal. Once someone has developed a tolerance for opioids, he or she requires an increasing amount of drugs to avoid the sensation of withdrawal.

Illustration by Danny Miller, Animation by Paul A. Rosales / Yahoo News
Opioid use disorder is defined as two or more of the following within a 12-month period:

• Using larger amounts of opioids or over a longer period than was intended
• Persistent desire to cut down or unsuccessful efforts to control use
• Great deal of time spent obtaining, using, or recovering from use
• Craving, or a strong desire or urge to use substance
• Failure to fulfill major role obligations at work, school, or home due to recurrent opioid use
• Continued use despite recurrent or persistent social or interpersonal problems caused or exacerbated by opioid use
Giving up or reducing social, occupational, or recreational activities due to opioid use
• Recurrent opioid use in physically hazardous situations
• Continued opioid use despite physical or psychological problems caused or exacerbated by its use
• Tolerance (marked increase in amount; marked decrease in effect)
• Withdrawal syndrome as manifested by cessation of opioids or use of opioids (or a closely related substance) to relieve or avoid withdrawal symptoms.
• Tolerance and withdrawal criteria are not considered to be met for those taking opioids solely under appropriate medical supervision.

Severity of opioid use disorder is categorized as mild (presence of 2-3 symptoms), moderate (4-5 symptoms), or severe (6 or more symptoms).
Opioids Use and Opioids Use Disorder (OUD) in Pregnancy

Opioid use in pregnancy has escalated dramatically in recent years, paralleling the epidemic observed in the general population.
Drugs of Use or Abuse During Pregnancy

Major Drugs of Abuse:

- Opioids
- CNS stimulants
- CNS depressants
- Other sedative hypnotics
- Hallucinogens
- Inhalants
Opioid use disorder (OUD) rose more than 4x among pregnant women from 1999 to 2014.
OPIOID USE IS INCREASING AMONG PREGNANT WOMEN

Percentage of Women With an Opioid Pain Reliever in the 2nd or 3rd Trimester

Recent trends in treatment admissions for prescription opioid abuse during pregnancy

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[Graph showing trends over time]

Martin et al JSAT 2014
Role of the Healthcare Provider
• Ensure that opioids are appropriately indicated
• Discuss the risks and benefits of opioid use and review treatment goals with the patient at the outset
• Take a thorough history of substance use and access the Prescription Drug Monitoring Program (PDMR)
• Before initiating opioid therapy for chronic pain in reproductive age women discuss family planning and how long-term opioid use might affect care during a future pregnancy
• Access appropriate expertise in tapering opioids
• Offer Medically Assisted Treatment (MAT) with buprenorphine or methadone
• Arrange for delivery at facility equipped to monitor, evaluate for, and treat NAS
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

• Substance use disorders affect women across all racial and ethnic groups and all socioeconomic groups, and affect women in rural, urban, and suburban populations therefore universal screening (for licit and illicit substance use) is recommended.

• Selective screening based on “risk factors” perpetuates discrimination and misses most women with problematic use
How do we know?
We have to ask!

• ACOG Committee Opinion 422:
  • At first prenatal visit -and-
  • At least once per trimester (alcohol in 3rd tri)
• WHO Guidelines: every visit
ACOG Screening Guidelines

- Screening for substance use should be part of comprehensive obstetric care and should be done at the first prenatal visit in partnership with pregnant woman. Screening based only on factors, such as poor adherence to prenatal care or prior adverse pregnancy outcome, can lead to missed cases, and may add to stereotyping and stigma.

- Early universal screening, brief intervention (such as engaging the patient in a short conversation, providing feedback and advice), and referral for treatment (SBIRT) of pregnant women with opioid use disorder improve maternal and infant outcomes.

Who can perform SBIRT? Physicians, nurse practitioners, physician assistants, nurses, health or substance use counselors, prevention specialists, and other health or behavioral health staff.

SBIRT

Screening, Brief Intervention, and Referral to Treatment

• Screening- a health care professional assesses a patient for risky substance use behaviors using standardized screening tools. Screening can occur in any health care setting.

• Brief Intervention- a health care professional engages a patient showing risky substance use behaviors in short conversation, providing feedback and advice.

• Referral to Treatment- a health care professional provides a referral to brief therapy or additional treatment to patients who screen in need of additional services.

• This approach improves maternal and infant outcomes.

http://www.integration.samhsa.gov/clinical-practice/SBIRT
Screening Instruments

• No single best screening instrument to identify pregnant women with opioid substance problems.
• Self-administered or part of the patient interview
• Developed for or validated in pregnant women:
  4P’s Plus (Chasnoff 1999)
  NIDA Quick Screen
  CRAFFT (Chang 2011) (women 26 years or younger)
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?
4. Do you consider one of your Parents to be an addict or alcoholic?

• Remember to ask direct questions tactfully and respectfully!
• Any “yes” should trigger further questions
NIDA Quick Screen

Screen Your Patients
- Step 1. Ask patient about past year drug use—the NIDA Quick Screen
- Step 2. Begin the NIDA- Modified ASSIST
- Step 3. Determine risk level

Conduct a Brief Intervention
- Step 4. Advise, Assess, Assist and Arrange
National Institute of Drug Abuse (NIDA)

High Risk Score >27
- Provide feedback on screening results
- Advise, Assess, Assist
- Arrange referral
- Offer continuing support

Moderate Risk Score 4-26
- Provide feedback
- Advise, Assess, Assist
- Consider referral based on clinical judgment
- Offer continuing support

Lower Risk Score 0-3
- Provide feedback
- Reinforce abstinence
- Offer continuing support

Advise — Provide medical advice related to patient’s drug use
Assess — Determine patient’s readiness to change
Assist — Offer help based on patient’s readiness level
Arrange — Refer patient for specialty assessment and/or drug treatment, if necessary
<table>
<thead>
<tr>
<th>C</th>
<th>Have you ever ridden in a car driven by someone (including yourself) who was “high” or had been using alcohol or drugs?</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>Do you ever use alcohol or drugs to relax, feel better about yourself, or fit in?</td>
</tr>
<tr>
<td>A</td>
<td>Do you ever use alcohol or drugs while you are by yourself, alone?</td>
</tr>
<tr>
<td>F</td>
<td>Do you ever forget things you did while using alcohol or drugs?</td>
</tr>
<tr>
<td>F</td>
<td>Do your family or friends ever tell you that you should cut down on your drinking or drug use?</td>
</tr>
<tr>
<td>T</td>
<td>Have you ever gotten into trouble while you were using alcohol or drugs?</td>
</tr>
</tbody>
</table>
Tox Tests?

What about urine?

- Urine toxicology is not a screen, it’s a test
- More important to start with a conversation than an “accusation”
- ACOG (2012) “Not to be used as sole assessment of substance problems”
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
Effects of Opioids on Pregnancy and Pregnancy Outcomes

Opioid use disorder during pregnancy has been linked to:

- Preterm Birth
- Low Birthweight
- Breathing Problems
- Feeding Problems
- Maternal Mortality

Effects of Opioids on Pregnancy and Pregnancy Outcomes

Teratogenic effects of maternal opioid use:

• Congenital heart defects
• Neural tube defects
• Gastrochisis
• Respiratory malformations
• Diaphragmatic hernias

Maternal Use of Opioids During Pregnancy and Congenital Malformations: A Systematic Review.

Lind JN1,2, Interrante JD3,4, Ailes EC3, Gilboa SM3, Khan S3,5,6, Frey MT3, Dawson AL3, Honein MA3, Dowling NF3, Razzaghi H3,2, Creanga AA7,8, Broussard CS3.

Neonatal Abstinence Syndrome (NAS)
Rates of NAS are growing faster in rural areas

Newborns in Opioid Withdrawal

As more women use opioid painkillers, heroin, and addiction treatment medications such as methadone during pregnancy, the number of infants born with severe withdrawal symptoms is rising. New England and south central states have the highest rates of newborns in withdrawal.
EVERY 25 MINUTES, A BABY IS BORN SUFFERING FROM OPIOID WITHDRAWAL.

AVERAGE LENGTH OR COST OF HOSPITAL STAY

<table>
<thead>
<tr>
<th>Newborns</th>
<th>Days</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>With NAS</td>
<td>16.9</td>
<td>$66,700</td>
</tr>
<tr>
<td>W/O NAS</td>
<td>2.1</td>
<td>$3,500</td>
</tr>
</tbody>
</table>

NAS AND MATERNAL OPIOID USE ON THE RISE

- Newborns suffering from opioid withdrawal
- Maternal opioid use

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)

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 Narcotic Withdrawal Syndrome

Variable onset of manifestations depending on:

- Drug used during pregnancy
- Single drug versus polydrug use
- Dosage
- Timing of use before delivery
- Anesthesia/analgesia (labor and delivery)
- Fetal accumulation
- Delayed excretion due to tissue binding
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

When drug history is unavailable, test urine, meconium, or umbilical cord tissue.
Treatment
Opioid Use in Pregnancy
Acute Pain

• Vaginal Delivery

Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for patients undergoing normal spontaneous vaginal delivery. If opioids are used:
- lowest effective dose
- immediate-release opioids
- avoid prescribing benzodiazepines concurrently
- review patient’s history of controlled substance use
- follow state guidelines
Opioid Use in Pregnancy
Acute Pain

• Cesarean Delivery

Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for patients undergoing cesarean delivery.

Neuraxial opioids - epidurals

The standard of care for pain management after cesarean delivery includes opioids, NSAID’s such as ibuprofen or ketorolac, and acetaminophen.

If opioids are used:
- lowest effective dose
- immediate-release opioids
- avoid prescribing benzodiazepines concurrently
- review patient’s history of controlled substance use
- follow state guidelines
Centers for Disease Control and Prevention (CDC) Guidelines

When to Initiate or Continue Opioids for Chronic Pain:

• Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.
• Consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.
• Combine with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
• Establish treatment goals with patients, including realistic goals for pain and function, how to discontinue therapy if benefits do not outweigh risks.
When to Initiate or Continue Opioids for Chronic Pain (Cont’d):

• Continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
• Discuss with patients
  • known risks and realistic benefits of opioid therapy and
  • patient and clinician responsibilities for managing therapy
Chronic Pain Management

• For chronic pain, practice goals include strategies to avoid or minimize the use of opioids for pain management, using alternative pain therapies:

• Nonpharmacologic:

  - Acupuncture
  - Exercise
  - Physical Therapy
  - Behavioral Approaches- cognitive behavioral therapy
  - Nerve Blocks
  - TENS- transcutaneous electrical nerve stimulation
Chronic Pain Management (cont.)

• Nonopioid Pharmacologic Analgesic Therapy:
  
  Acetaminophen
  NSAID’s – non-steroidal anti-inflammatory drugs
  Skeletal Muscle Relaxants
  Antidepressants
  Anticonvulsants
  Topical Medications
Options for opioid dependence during pregnancy

• Detoxification
• Methadone
• Buprenorphine
Opioid Use Disorder Treatment in Pregnancy

Maintenance Therapy with an Opioid Agonist Remains the Standard of Care

• Methadone and buprenorphine (both category C) are safe and effective treatment options in pregnancy
• The decision of which therapy to start is complex and should be individualized for each woman
  • Based on available options, patient preference, patients’ previous treatment experiences, disease severity, social supports, and intensity of treatment needed

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
Treatment modalities for opioid use disorder: **Medically Assisted Treatment (MAT)** or Opioid agonist pharmacotherapy:

- Opioid agonist therapy, also known as medication-assisted treatment, with methadone or buprenorphine is the standard for pregnant women with opioid use disorder.
- Safe and effective in pregnancy
- Associated with improved maternal and infant outcomes

**Medically Supervised Withdrawal:**

- Abrupt discontinuation of opioids in pregnancy not recommended
  - Preterm labor
  - Fetal distress
  - Fetal demise
  - Withdrawal
  - High relapse rates
• 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.
Medication Assisted Treatment (MAT) Options

Methadone:
• Gold standard since 1960s for maintenance as well as to avoid withdrawal during detox Category C by FDA
• Babies may be born with opioid acute withdrawal otherwise known as Neonatal Abstinence Syndrome (NAS)

Buprenorphine: (Subutex)
• Babies born average weight and between 38-40 weeks
• Less traces of opioid in system therefore NAS usually less severe

Suboxone: (Naloxone and Buprenorphine)
**FDA-Approved Medications**

**Methadone**
In use since the 1960s, the slow-acting synthetic opioid agonist effectively treats moderate to severe heroin addiction. It is only available in heavily regulated clinics.

**Buprenorphine/Suboxone**
Approved in 2002, the long-acting opioid agonist relieves drug cravings with fewer side effects than other opioids and is available by prescription from certain doctors. Suboxone is designed to deter illicit use.

**Naltrexone/Vivitrol**
Approved in pill form in 1984, it has been available since 2010 as a 30-day time-release injectable medication called Vivitrol. Patients must be completely off all opioids for seven to 10 days. Both block the effect of opioids, do not activate the opioid receptor system, and do not cause physical dependence.

**Naloxone**
Approved in 1971, the short-acting medication, also known as Narcan and Evzio, reverses opioid overdoses but does not treat opioid addiction.
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)
Buprenorphone Formulations

Buprenorphone 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
Benefits of Opioid Agonist Therapy

Maternal Benefits:
- Reduction in overdose related deaths
- Decrease in risk of HIV, HBV, HCV
- Increased engagement in prenatal care and recovery treatment

Fetal Benefits:
- Reduces fluctuations in maternal opioid levels; reducing fetal stress
- Decrease in intrauterine fetal demise
- Decrease in intrauterine growth restriction
- Decrease in preterm delivery
Opioids During Pregnancy

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 Use Disorder (OUD)
Antepartum Care

• Testing for STI’s
• Screening for depression and behavioral health conditions
• Screen for use of other substances (alcohol, tobacco)
• Consultations with anesthesia, addiction specialists, maternal-fetal-medicine, pediatrics
• Anticipatory breastfeeding guidance
• US 1st T for accurate dating
  2nd T for fetal anatomy
  3rd T for fetal growth abnormalities
OUD
Intrapartum Care

• Continue maintenance opioid agonist dose
• Patients will require higher doses of opioids to achieve analgesia because of their increased drug tolerance and hypersensitivity to pain
• Epidural or spinal anesthesia should be offered, when appropriate for management of pain in labor and for delivery
• A multimodal pain control approach with neuraxial analgesia and nonsteroidal anti-inflammatory drugs and acetaminophen typically is needed to provide effective intrapartum and postpartum pain relief
OUD
Postpartum Care

- Nonpharmacologic and pharmacologic therapies
- Parenteral or oral opioids
  - Reserve for breakthrough pain when analgesia from combination neuraxial opioids and nonopioid adjuncts becomes inadequate
- Review risks/benefits/signs of toxicity of codeine-containing medication
- Counsel patients prescribed opioid analgesics on risk of CNS depression in mother/breastfed infant
- Limit opiate prescriptions to the shortest reasonable course
  - A shared decision-making approach to postpartum discharge opioid prescription can optimize pain control while reducing the number of unused opioid tablets
• Sleep deprivation, dramatic hormonal shifts and the day-to-day realities of caring for an infant create enormous stress for all women, but especially for those who are struggling to stay in recovery from drug use.

• Most medical protocols and social safety net programs are set up to shift attention away from the mother after delivery and focus exclusively on the new baby.

• For many women, access to medical care and social supports evaporates after a baby is born.

• Growing evidence suggests that women should receive continuous medical attention during what is now called the “fourth trimester” — a period lasting at least a year after childbirth. Even for women without an opioid addiction, the likelihood of severe depression soars. Research indicates that nearly 15 percent of all mothers suffer postpartum depression. For minority women and those living in poverty, the rate can more than double.

• In May, the American College of Obstetricians and Gynecologists issued new medical guidelines for postpartum care, saying that ongoing attention rather than a single encounter with a medical professional is urgently needed to “reduce severe maternal morbidity and mortality.”
Treatment Options for NAS
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

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
NAS Pharmacologic Treatment

- The incidence of neonatal abstinence syndrome (NAS) in the U.S. has increased more than 5-fold since 2004, to 8.0 per 1000 live births, but the choice of first-line treatment remains variable. An estimated 53% of neonates with NAS receive morphine, 36% receive phenobarbital, and the rest receive methadone or other treatments.

- Buprenorphine might be the best pharmacological treatment for neonatal abstinence syndrome, based on limited evidence, according to a systematic review and network meta-analysis.

- For the primary outcome, the network meta-analysis estimated that with buprenorphine, treatment was 2.19 days shorter than with clonidine and 12.75 days shorter than with morphine, according to the January 22nd JAMA Pediatrics online report.

NAS Pharmacological Interventions

MOTHER Study

Randomized trial of methadone versus buprenorphine

Primary outcome: NAS

• Similar prevalence of treatment for NAS

• Less neonatal abstinence severity and treatment (buprenorphine)

• Shorter neonatal LOS (buprenorphine)

• Bigger HC

Jones HE, NEJM, 2010

Table 2. Primary and Secondary Outcomes in the Methadone and Buprenorphine Groups.6

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Methadone (N=73)</th>
<th>Buprenorphine (N=58)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated for NAS—no. (%)</td>
<td>41 (57)</td>
<td>27 (47)</td>
<td>0.7 (0.2−1.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>NAS peak score</td>
<td>12.8±0.6</td>
<td>11.0±0.6</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Total amount of morphine for NAS—mg</td>
<td>10.4±2.6</td>
<td>11.1±0.7</td>
<td>&lt;0.009†</td>
<td></td>
</tr>
<tr>
<td>Duration of infant’s hospital stay—days</td>
<td>17.5±1.5</td>
<td>10.0±1.2</td>
<td>&lt;0.009†</td>
<td></td>
</tr>
<tr>
<td>Infant’s head circumference—cm</td>
<td>33.0±0.3</td>
<td>33.8±0.3</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Secondary neonatal outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of treatment for NAS—days</td>
<td>9.9±1.6</td>
<td>4.1±1.0</td>
<td>&lt;0.003125†</td>
<td></td>
</tr>
<tr>
<td>Weight at birth—g</td>
<td>2873.5±663</td>
<td>3093.7±726</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Length at birth—cm</td>
<td>47.8±0.5</td>
<td>49.8±0.5</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Preterm, &lt;37 wk—as no. (%)</td>
<td>14 (19)</td>
<td>4 (7)</td>
<td>0.3 (0.1−2.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>Gestational age at delivery—wk</td>
<td>37.9±0.3</td>
<td>39.1±0.3</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Apgar score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min</td>
<td>8.0±0.2</td>
<td>8.1±0.2</td>
<td>0.87</td>
<td></td>
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<tr>
<td>5 min</td>
<td>9.0±0.1</td>
<td>9.0±0.1</td>
<td>0.69</td>
<td></td>
</tr>
</tbody>
</table>

Addressing Opioid Use Disorder (OUD) among Pregnant Women

Ensure appropriate prescribing.

Maximize & enhance prescription drug monitoring programs (PDMPs).

Ensure mothers with OUD receive adequate post-birth care, including substance use treatment and relapse-prevention programs.

Ensure pregnant women with OUD have access to medication assisted therapy and related services.
Multi-disciplinary long-term follow up:

Service Barriers for Women
- Social stigma of SUD during pregnancy
- Social Supports
- Child welfare (DCF) implications
- Childcare and transportation needs
- Health Insurance
- MAT access

General Health Care
- Obstetric-gynecological care
- Co-occurring medical and psychiatric conditions
- HIV prevention
- Nutritional counseling
- Family planning
- Screening for IPV/DV

Medication Assisted Treatment
- Determining best MAT options for individualized treatment
- Buprenorphine
- Methadone

Social Functioning Supports
- Parenting Skills
- Family and Friends Involvement
- Communication and Conflict resolution
- Family Planning

Multi-disciplinary long-term follow up:
- Medicine
- Obstetric
- Pediatric
- Family
- Addiction medicine

Social Work
Complementary Medicine Approaches

http://www.healthrecovery.org/maternal-opioid-use/
Florida Legislation

On March 19, 2018, Florida Governor Rick Scott signed HB 21, a comprehensive opioid bill, into law (effective July 1, 2018). It addresses opioid abuse by increasing the regulation of prescriptions for controlled substances and expanding the use of the Prescription Drug Monitoring Program (PDMP). In summary, the law:

- Requires all practitioners who have a DEA number and are authorized to prescribe controlled substances to complete a board approved 2-hour CME course offered by a statewide professional association of physicians in Florida accredited to provide AMA Category 1 (or American Osteopathic Category 1-A) CME credit as part of their biennial license renewal. This course must be completed at each subsequent renewal.

- Limits the prescription for a Schedule II opioid for acute pain to a **3-day supply, or a 7-day supply if deemed medically necessary by the prescriber and with proper documentation.** The definition of acute pain excludes pain related to cancer, terminal illness, palliative care, and serious traumatic injury with an injury Severity Score (ISS) of 9 or greater.

- Requires a concurrent prescription for an emergency opioid antagonist with the prescription of Schedule II controlled substances for the treatment of pain related to a serious traumatic injury with an ISS of 9 or greater.
Florida Legislation Cont’d

• Requires regulatory boards within the Department of Health to establish guidelines for prescribing controlled substance for acute pain.

• Requires healthcare providers to review a patient’s PDMP history before prescribing or dispensing a controlled substance, with limited exemptions.

• Authorizes a dispensing practitioner to dispense Schedule II and III substances that have been approved by the FDA for treating opiate addictions to the practitioner’s own patients for the medication-assisted treatment of opiate addiction.

• Adds substances to the definitions of Schedule II, Schedule III, Schedule IV, and Schedule V and requires that Schedule V substances must be reported to the PDMP.

• Authorizes electronic prescriptions for controlled substances.

• Requires pharmacists and dispensing to verify a patient’s identity prior to dispensing controlled substances.

Florida Statutes 456.44  456.0301
WHAT CAN YOU DO TO PREVENT OPIOID MISUSE?

TALK ABOUT IT.
Opioids can be addictive and dangerous. We all should have a conversation about preventing drug misuse and overdose.

BE SAFE.
Only take opioid medications as prescribed. Always store in a secure place. Dispose of unused medication properly.

UNDERSTAND PAIN.
Treatments other than opioids are effective in managing pain and may have less risk for harm. Talk with your healthcare provider about an individualized plan that is right for your pain.

KNOW ADDICTION.
Addiction is a chronic disease that changes the brain and alters decision-making. With the right treatment and supports, people do recover. There is hope.

BE PREPARED.
Many opioid overdose deaths occur at home. Having naloxone, an opioid overdose reversing drug, could mean saving a life. Know where to get it and how to use it.

For help, resources, and information:
https://www.hhs.gov/opioids/
1-800-662-HELP (4357)
1-800-662-HELP

Substance Abuse and Mental Health Services Administration (SAMHSA) helpline, 800-662-HELP
Key Federal Resources

The Surgeon General’s Report
https://addiction.surgeongeneral.gov/

CDC Guideline for Prescribing Opioids for Chronic Pain
https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

MMWR Opioid Reports
https://www.cdc.gov/mmwr/opioid_reports.html

SGR Appendix B: Review Process for Prevention Programs
https://addiction.surgeongeneral.gov/sites/default/files/appendices.pdf

NIDA Opioid Risk Tool

NIDA Quick Screen

CDC general resources
https://www.cdc.gov/drugoverdose/prescribing/resources.html

CDC resources related to People Who Inject Drugs (PWID)
https://www.cdc.gov/pwid/index.html

CDC’s Rx Awareness Campaign
https://www.cdc.gov/rxawareness/index.html

CDC Adverse Childhood Experiences page
https://www.cdc.gov/violenceprevention/acesstudy/index.html

Preventing the Consequences of Opioid Overdose: Understanding the Naloxone Access Laws

The Surgeon General’s Advisory on Naloxone and Opioid Overdose

SAMHSA Opioid Overdose Prevention Toolkit
https://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA16-4742

SAMHSA Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants
References


• Opioid Use and Opioid Use Disorder in Pregnancy- ACOG [https://m.acog.org/Clinical.../Opioid-Use-and-Opioid-Use-Disorder-in-Pregnancy](https://m.acog.org/Clinical.../Opioid-Use-and-Opioid-Use-Disorder-in-Pregnancy)
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• Substance Abuse and Mental Health Services Administration, Advancing the Care of Pregnant and Parenting Women With Opioid Use Disorder and Their Infants: A Foundation for Clinical Guidance, Rockville, MD: Substance Abuse and Mental Health Services Administration, 2016.
