The Science of Treating Pregnant Women with Opioid Use Disorder
Speakers by Date

- Thomas E. Freese, PhD - San Diego, April 23rd, 2019
- Douglas McMullin, MD - Redding, April 29th, 2019
- Hannah Snyder, MD - San Jose, April 30th, 2019
- Aimee Moulin, MD - Truckee, May 13th, 2019
- Sky Lee, MD - Sacramento, May 14th, 2019
- Candy Stockton, MD - All
Disclosures

There are no relevant financial relationships with ACCME-defined commercial interests for anyone who was in control of the content of this activity.
Substance Use Disorder and Pregnancy

- Women, opioid use disorder and pregnancy
- Treatment options in Pregnancy
  - Methadone
  - Buprenorphine (Bup)
  - Naltrexone
  - Detoxification
- Intra-partum care
- Postpartum care
  - Post-operative pain control
  - Breastfeeding
  - Contraception
Between 2004 and 2010: opioid-related overdose deaths increased more rapidly among Women (400%), then Men (276%)(1)
First time heroin use by gender

Opioid Use by Women

- In 2015 there were more past-year initiates of prescription opioid misuse among women (1.2 million - 0.9%) than men (0.9 million - 0.7%)(2)

- There are still more male than female adults who use heroin, heroin use is increasing twice as fast among women than men(2)
Pregnancy and Opioid Use Disorder (OUD)

- Nearly 50% of pregnant substance use disorder treatment admissions are for opioids(1)

- Overdose mortality has surpassed hemorrhage, pre-eclampsia and sepsis as a cause of pregnancy-associated death(2)
Gender, Pregnancy and OUD

- 86% of pregnant opioid-abusing women reported pregnancy was unintended (1)
  - In general population: 31%-47% are unintended
- Pregnancy can be a powerful catalyst for women to engage in treatment

During Pregnancy
- Adolescents report the highest illicit substance use in the prior month
  - Reported substance use decreases with increasing maternal age (NSDUH 2012-2013)
- Trend toward reduction of use over gestation
  - Reported substance use decreases with increasing gestational age (SAMHSA TEDS 2014)
ACOG Backs Buprenorphine and Methadone

- Only FDA approved treatments in pregnancy
- Reduce opioid use (cravings, withdrawal, euphoria)
- Increase birth at term, higher birth weights
- Prevent overdose deaths
- Prevent HIV transmission
- Support family function and appropriate parenting
Non MAT Opioids: full agonist heroin, oxycodone, Percocet, etc
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Methadone: full agonist
Activates receptor, prevents binding
Risk of sedation
Only at special clinics
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Naloxone (Narcan), Naltrexone (Vivitrol):
Full antagonist, high affinity
Non MAT Opioids: full agonist
heroin, oxycodone, Percocet, etc

Methadone: full agonist
Activates receptor, prevents binding, risk of sedation

Buprenorphine (Suboxone, Subutex): partial agonist
High affinity, ceiling effect
Risk of precipitated withdrawal
Any prescriber with X waiver

Naloxone (Narcan), Naltrexone (Vivitrol):
Full antagonist, high affinity
Staying well

Euphoria

Normal

Withdrawal

Tolerance & Physical Dependence

Opioid Agonist Therapy
No longer in the cycle

Euphoria

Normal

Withdrawal

Tolerance & Physical Dependence

Opioid Agonist Therapy
Medically Assisted Withdrawal in Pregnancy (Detoxification)

- Not recommended in pregnancy (1)(2)(3)
- 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 rate of relapse with associated overdose mortality following detoxification
- Increased access to opioid agonist treatment was associated with a reduction in heroin overdose deaths(4)
- Offering pharmacotherapy for OUD in pregnancy increases*
  - Treatment retention
  - Number of obstetrical visits attended
  - In-hospital deliveries
Medically Assisted Withdrawal in Pregnancy is NOT Recommended

- High risk of relapse (59-90%)
- Not standard of care
TREATMENT OPTIONS FOR OUD IN PREGNANCY

METHADONE
- Has been the *Gold Standard* for opioid use disorder in pregnancy
- Pregnancy category C
  - Limited dosing flexibility
    - Split dosing in pregnancy is preferred due to increased clearance in later gestation
  - Prolonged QT syndrome
    - Baseline EKG recommended
    - Repeat EKG for dosing changes above 100mg
  - May contribute to lower birth weights when compared to Bup-exposed newborns

BUPRENORPHINE
- Gaining First-line recognition for treatment of opioid use disorder in pregnancy
- Pregnancy category C
- When compared to methadone:
  - Lower preterm delivery rate*
  - Higher birth weight*
  - Larger head circumference*
- Allows for adjustable dosing (split dosing)
- Treatment retention for pregnant women may favor buprenorphine over methadone(2).
Neonatal Abstinence Syndrome: Methadone and Buprenorphine

Maternal Opioid Treatment Human Experimental Research (MOTHER): NEJM 12/2010

- Double-blind, double-dummy, flexible-dosing, parallel-group clinical trial
- Neonatal Outcomes: Comparing MMT (n=73) and Buprenorphine (n=58)
Neonatal Abstinence Syndrome: Methadone and Buprenorphine
Naltrexone: Emerging Data in Pregnancy

- 25 published human cases: all with normal birth outcomes(1)(2)(3)
- Animal literature without evidence for teratogenicity, although behavioral changes in animal offspring have been noted(4)
- No human long-term outcomes or developmental studies available
- May be appropriate for select patients
- High maternal interest in treatment without NAS sequelae(5)
Eat/Sleep/Console Assessment

Can infant eat ≥1 ounce per feed or breastfeed well?
- Yes
  - Can infant sleep ≥1 hour?
    - Yes
      - Can infant be consoled within 10 minutes?
        - Yes
          - Infant is considered to be well managed and no further interventions are necessary
        - No
          - Nonpharmacologic interventions increased if possible:
            - Feeding on demand
            - Swaddling and holding
            - Low-stimulation environment
            - Parental presence
      - No
        - Not improved
          - Start morphine at 0.05 mg/kg per dose every 3 hours or increase dosing by 0.01 mg/kg per dose
Infants were treated with morphine significantly less frequently than they would have been using the traditional Finnegan Neonatal Abstinence Scoring System (12% vs 60%).

An effective approach that limits pharmacologic treatment (morphine increase on 3% of days vs 25% of days).

May lead to substantial decrease in length of stay (5.9 days vs 22.5 days) (Grossman, et al)
Intrapartum Care

- Pharmacotherapy should be continued through labor (and postpartum) at same prenatal dose
- Labor pain should be managed with regional anesthesia (epidural)
- Do not use mixed opioid agonist-antagonist (butorphanol (Stadol)/ nalbuphine (Nubain))
  - Will precipitate a withdrawal syndrome for women on opioid pharmacotherapy
- Spinal anesthesia provides adequate pain control for C-sections
Postpartum

(patient’s wishes regarding opioids postpartum should be established)

- Pharmacotherapy should be continued at same dose postpartum
  - Some women will require/request a dose decrease after delivery due to sedation; but any decrease should be individualized and carefully monitored
  - For MMT, Postpartum fatigue and potential peak dose sedation should be anticipated; and precautions taken

- NSAIDS and non-opioid pain medications should be maximized (scheduled orders; not PRN) (ketorolac, acetaminophen)

- Full opioid agonists should be used for post-operative pain
  - Bup and MMT patients have higher opioid requirements than general population (1)
  - Bup does not appear to prevent/block efficacy of full-opioids (Vilkins 2017)
Postpartum Monitoring and Counseling

- Frequent maternal follow up is needed
- Postpartum women are at high risk of a return to opioid use
- The first year postpartum marks the highest risk of overdose death, with the highest rates 7-12 months after delivery
Postpartum overdose death rates

A

B
Naltrexone: Intrapartum and Postpartum

- Between 35-38 weeks gestation: women should be transitioned from IM Naltrexone to oral (Naltrexone 50mg po qd)
- With the onset of labor, women should hold oral dosing
  - Precautions allow for postoperative full opioid agonists pain control prn
- IM Naltrexone can be resumed postpartum
Breastfeeding

Methadone and buprenorphine are safe for breastfeeding <1% of maternal opioid intake transmitted to breastmilk (1)

*Published guidelines from the American Academy of Pediatrics (AAP), the American College of Obstetricians and Gynecologists (ACOG), and the Academy of Breastfeeding Medicine (ABM) all support breastfeeding for women on opioid pharmacotherapy

- **Maternal benefits**: increased oxytocin levels are linked to lower stress, increased maternal-infant bonding both lower the risk of postpartum relapse (2)

- **Newborn benefits**: reduction in pharmacologic treatment for NAS, shorter hospital stays (2)
Contraception

- All postpartum women should be offered reliable contraception
- Contraception options should be reviewed/disclosed during prenatal care with a set plan prior hospital discharge
- Access to long acting reversible contraceptive (LARC) options should be readily available
Important Links & References (1)


Important Links & References (2)

- [https://elearning.asam.org/buprenorphine-waiver-course](https://elearning.asam.org/buprenorphine-waiver-course) The ASAM Treatment of Opioid Use Disorder Course: Includes Waiver Qualifying Requirements

- ASAM National Practice Guideline | May 27, 2015

- WHO. Guidelines for the identification and management of substance use and substance use disorders in pregnancy. 2014


Important Links & References (3)


Contact Us

- Hub & Spoke Website: [http://www.uclaisap.org/ca-hubandspoke/](http://www.uclaisap.org/ca-hubandspoke/)
- Contact Christian Frable, Hub & Spoke Training Coordinator, for questions about future trainings
  - cfrable@mednet.ucla.edu