UCLA

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

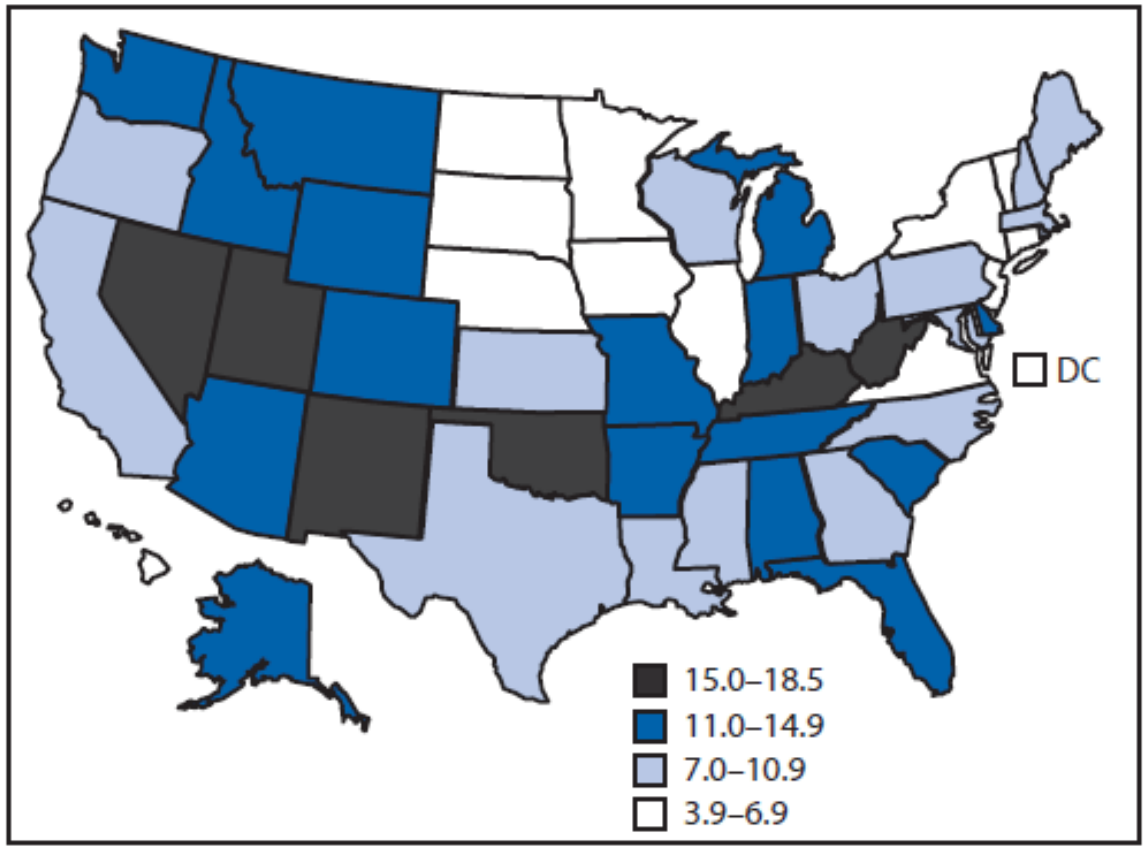
There are no relevant financial relationships with ACCME-defined commercial interests for anyone who was in control of the content of this activity.

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

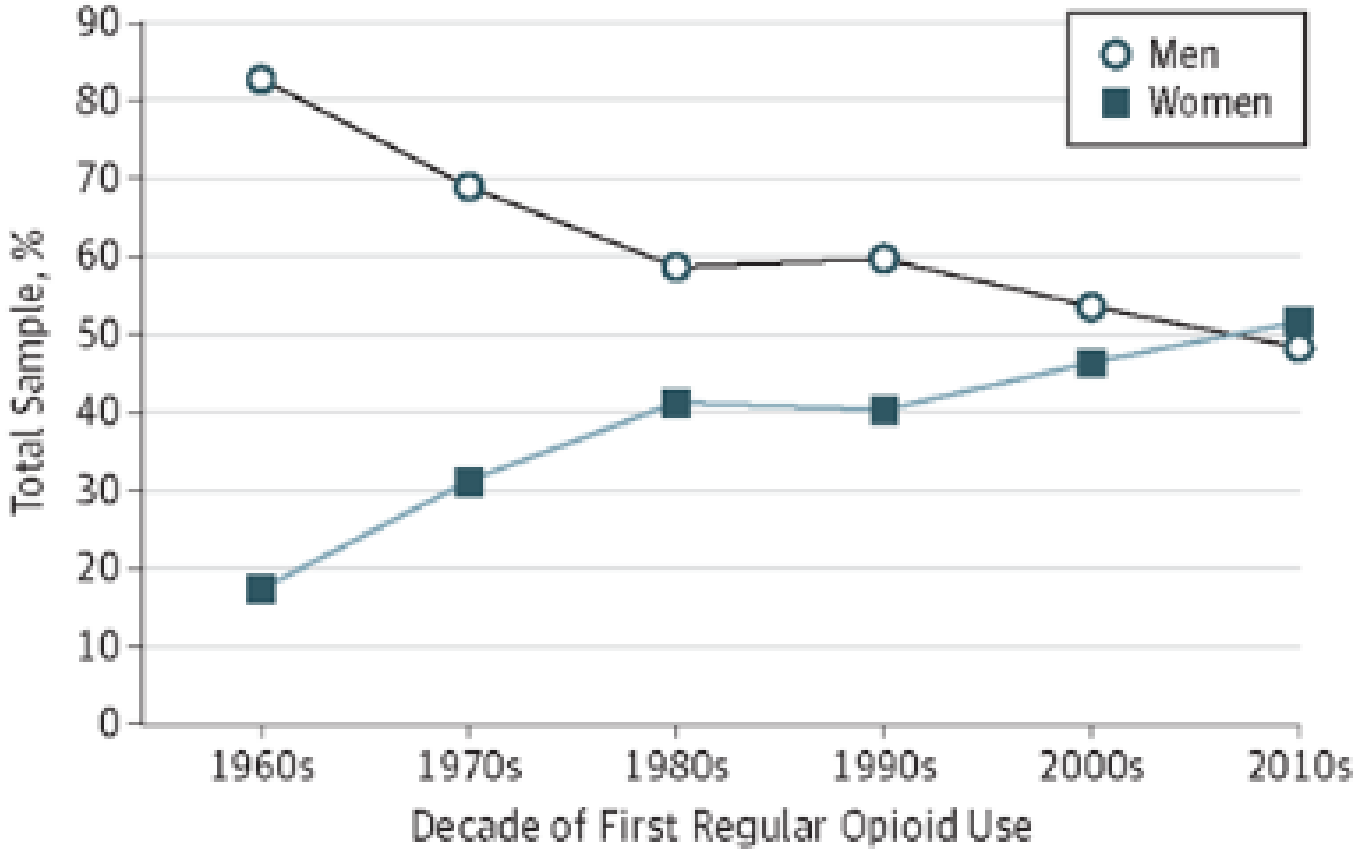
Opioid overdose deaths in women

- Between 2004 and 2010: opioid-related **overdose deaths increased** more rapidly among Women (400%), then Men (276%)(1)



Female deaths /100,000 due to opiate overdose 2009-10

First time heroin use by gender



(3) Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. JAMA Psychiatry. 2014 Jul 1;71(7):821–6.

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)

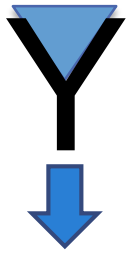
- **Overdose** mortality has surpassed **hemorrhage, pre-eclampsia and sepsis** as a cause of pregnancy-associated death(2)

Gender, Pregnancy and OUD

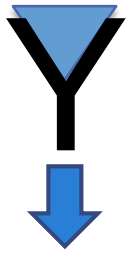
- **86%** of pregnant opioid-abusing women reported pregnancy was unintended (1)
  - In general population: 31%–47% are unintended
- Pregnancy can be a powerful catalyst for women to engage in treatment
- During Pregnancy
  - Adolescents report the highest illicit substance use in the prior month
    - 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

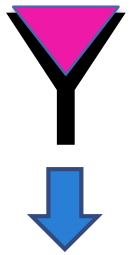
- Only FDA approved treatments in pregnancy
- Reduce opioid use (cravings, withdrawal, euphoria)
- Increase birth at term, higher birth weights
- Prevent overdose deaths
- Prevent HIV transmission
- Support family function and appropriate parenting



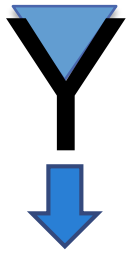
Non MAT Opioids: full agonist heroin, oxycodone, Percocet, etc



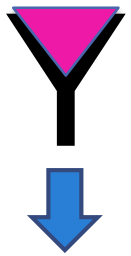
Non MAT Opioids: full agonist
heroin, oxycodone, Percocet, etc



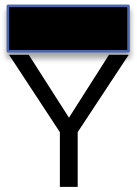
Methadone: full agonist
Activates receptor, prevents binding
Risk of sedation
Only at special clinics



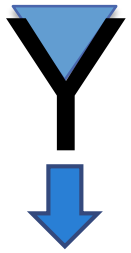
Non MAT Opioids: full agonist
heroin, oxycodone, Percocet, etc



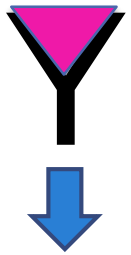
Methadone: full agonist
Activates receptor, prevents binding
Risk of sedation
Only at special clinics



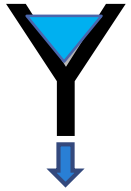
Naloxone (Narcan), Naltrexone (Vivitrol):
Full antagonist, high affinity



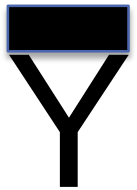
Non MAT Opioids: full agonist
heroin, oxycodone, Percocet, etc



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

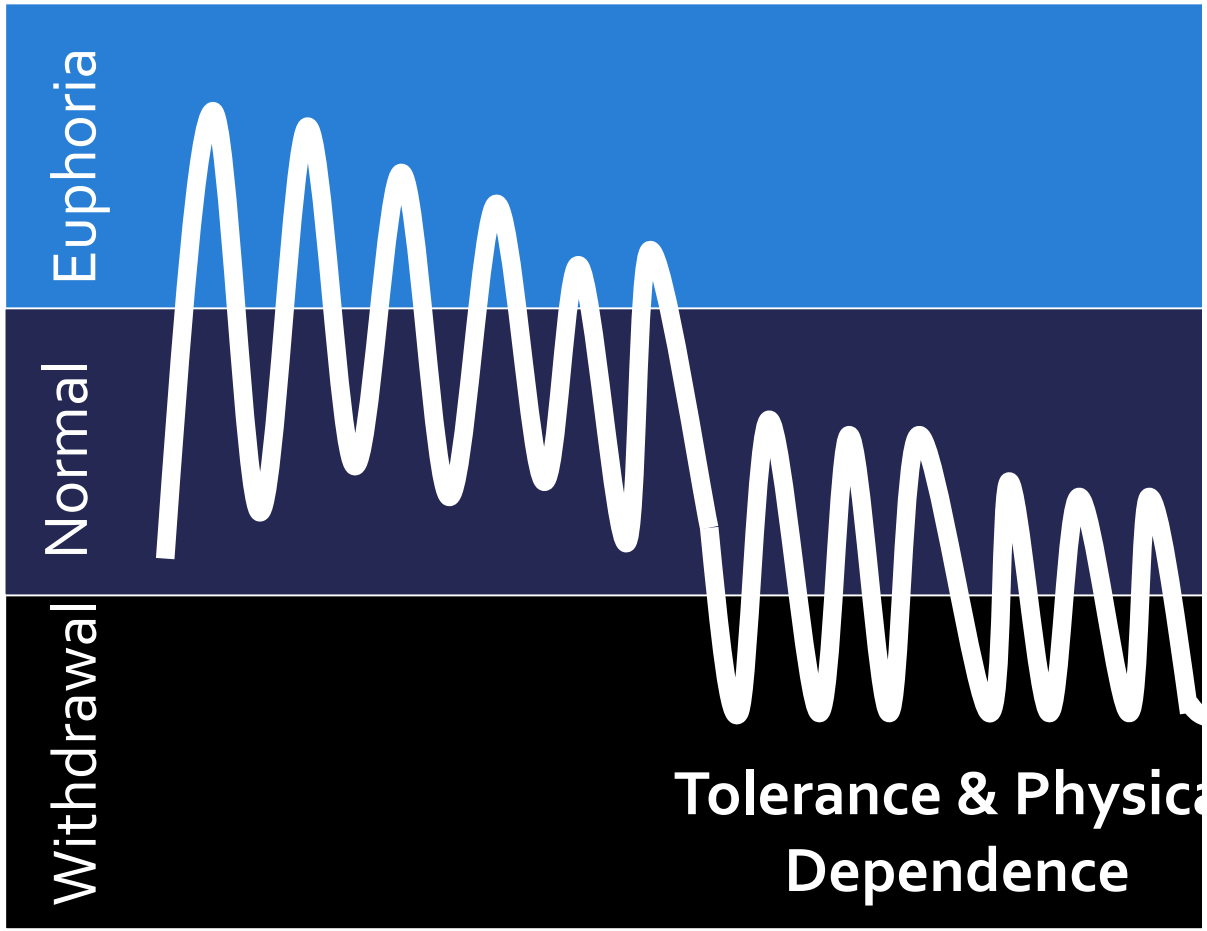


Buprenorphine (Suboxone, Subutex):
partial agonist
High affinity, ceiling effect
Risk of precipitated withdrawal
Any prescriber with X waiver



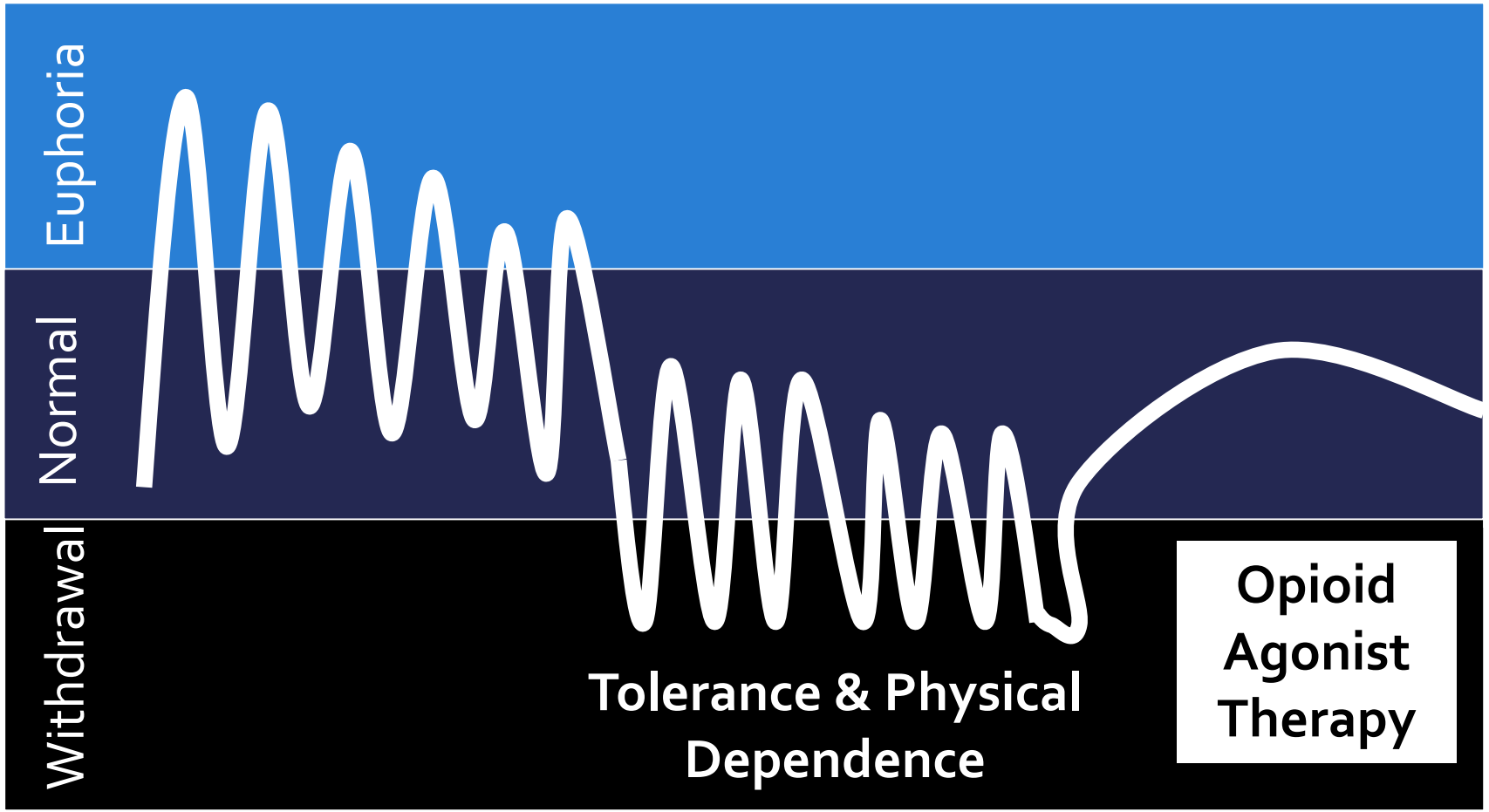
Naloxone (Narcan), Naltrexone (Vivitrol):
Full antagonist, high affinity

Staying well



ASAM American Society of Addiction Medicine

No longer in the cycle



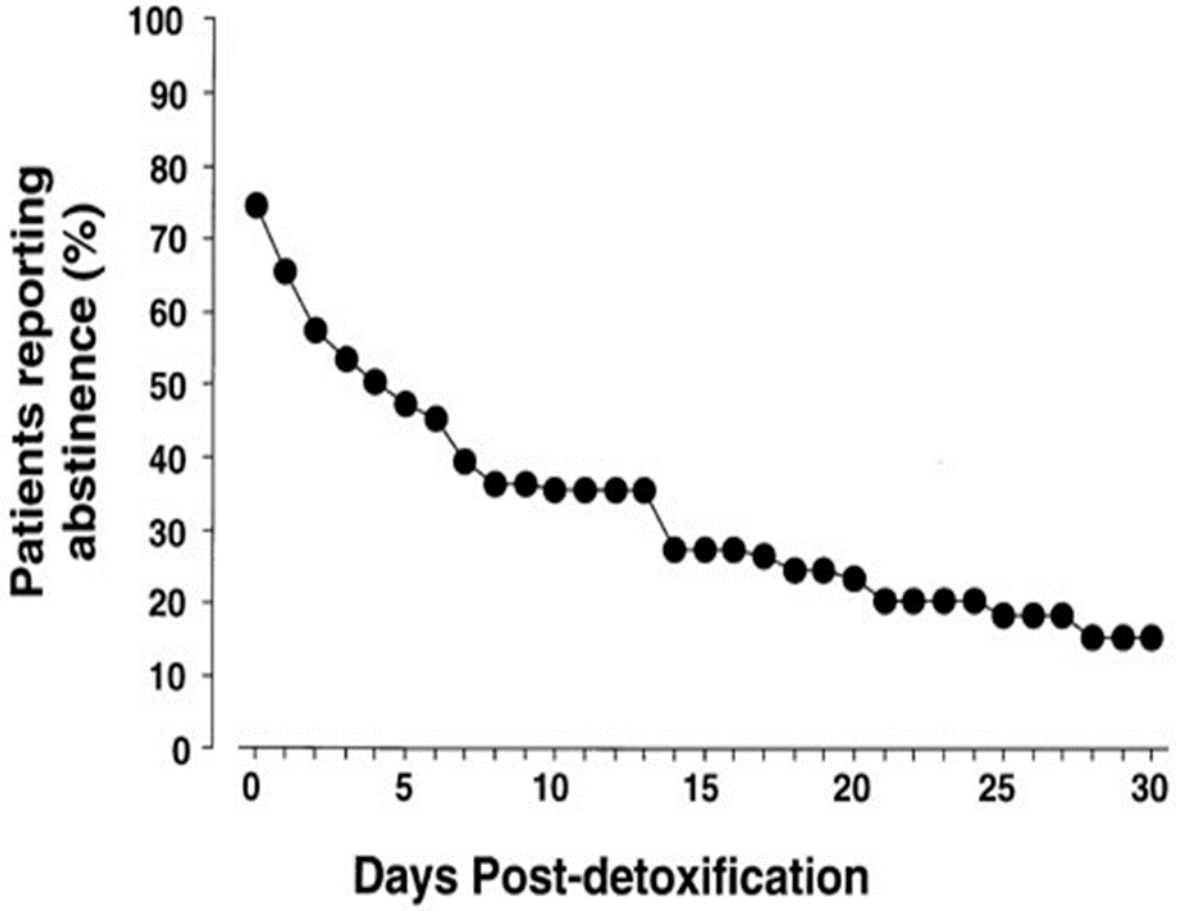
ASAM American Society of Addiction Medicine

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

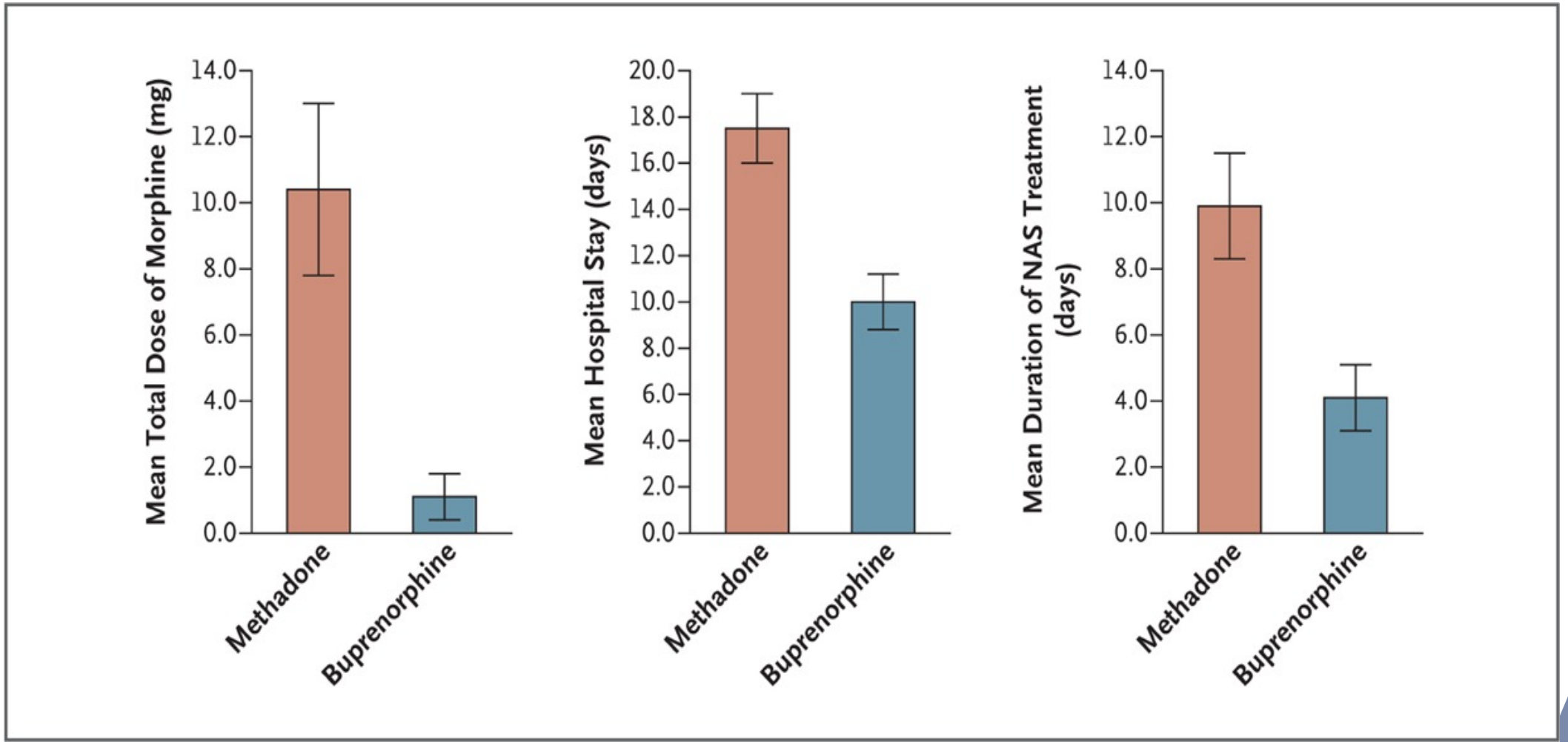
- Gaining First-line recognition for treatment of opioid use disorder in pregnancy
- Pregnancy category C
- When compared to methadone:
  - Lower preterm delivery rate*
  - Higher birth weight*
  - Larger head circumference*
- Allows for adjustable dosing (split dosing)
- Treatment retention for pregnant 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)

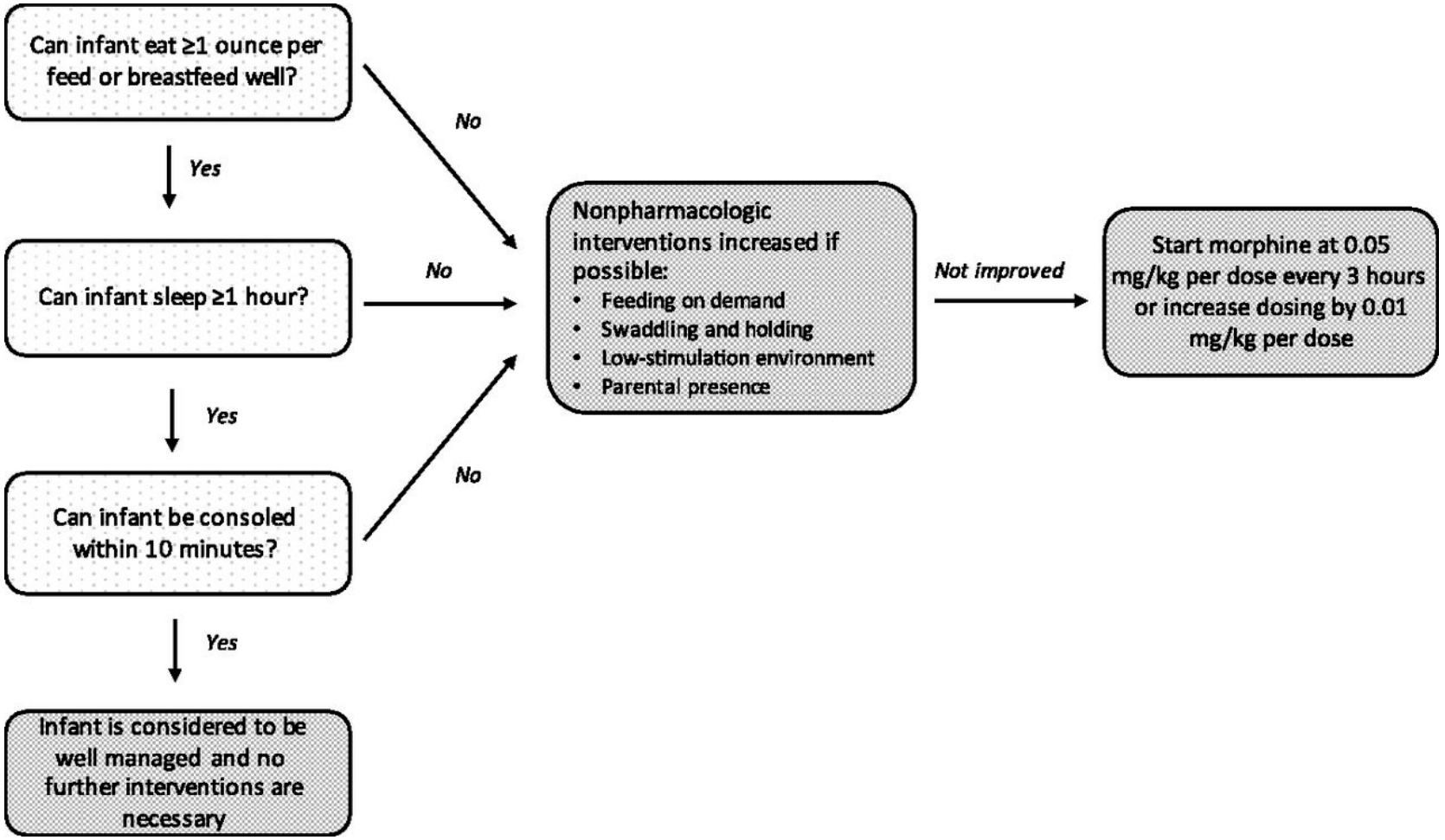
Neonatal Abstinence Syndrome: Methadone and Buprenorphine



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



Matthew R. Grossman et al. Hospital Pediatrics 2018;8:1-6

Eat/Sleep/Console

- 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

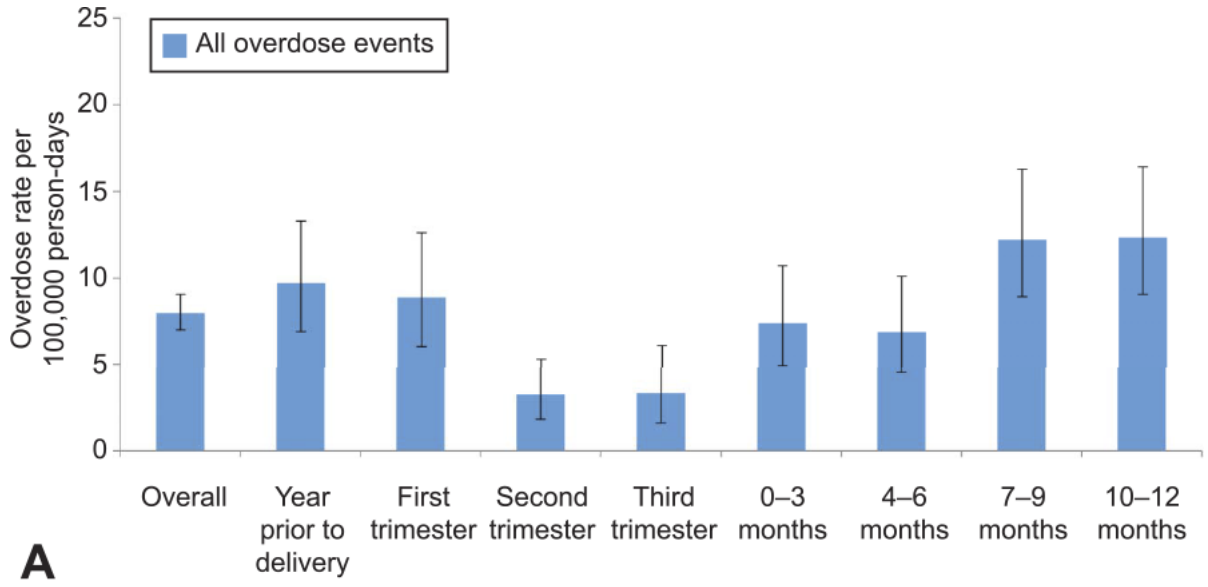
Postpartum
(patient's wishes regarding opioids postpartum should be established)

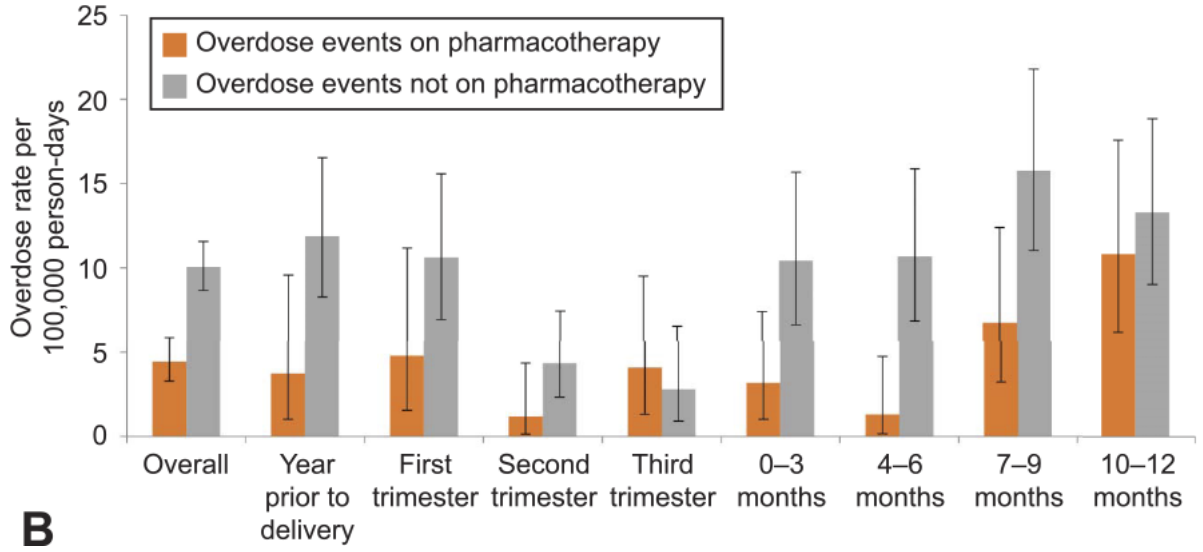
- Pharmacotherapy should be continued at same dose postpartum
  - Some women will require/request a dose decrease after delivery due to sedation; but any decrease should be individualized and carefully monitored
  - For MMT, Postpartum fatigue and potential peak dose sedation should be anticipated; and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





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/ discussed 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)

- Vital Signs: Overdoses of Prescription Opioid Pain Relievers and Other Drugs Among Women — United States, 1999–2010 [Internet]. [cited 2016 Dec 27]. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6226a3.htm
- Key Substance Use and Mental Health Indicators in the United States: Results from the 2015 National Survey on Drug Use and Health - NSDUH-FFR1-2015.pdf [Internet]. [cited 2016 Dec 21]. Available from: https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2015/NSDUH-FFR1-2015/NSDUH-FFR1-2015.pdf
- TEDS 2004-2014 National Admissions to Substance Abuse Treatment Services - 2014_teds_rpt_natl.pdf [Internet]. [cited 2016 Dec 21]. Available from: https://wwwdasis.samhsa.gov/dasis2/teds_pubs/2014_teds_rpt_natl.pdf
- O'Malley M, Brown AG, Sharfstein JM. MARYLAND MATERNAL MORTALITY REVIEW. [cited 2016 Dec 19]; Available from: http://phpa.dhmh.maryland.gov/mch/documents/2011mmrrpt.pdf
- Heil SH, Jones HE, Arria A, Kaltenbach K, Coyle M, Fischer G, et al. Unintended pregnancy in opioid-abusing women. J Subst Abuse Treat. 2011 Mar;40(2):199–202.
- Opioid abuse, dependence, and addiction in pregnancy. Committee Opinion No. 524. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;119:1070–6.

Important Links & References (2)

- 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
- ACOG Statement on Opioid Use During Pregnancy - ACOG [Internet]. [cited 2016 Nov 21]. Available from: http://www.acog.org/About-ACOG/News-Room/Statements/2016/ACOG-Statement-on-Opioid-Use-During-Pregnancy
- Jones, H. E., O'Grady, K. E., Malfi, D. and Tuten, M. (2008), Methadone Maintenance vs. Methadone Taper During Pregnancy: Maternal and Neonatal Outcomes. The American Journal on Addictions, 17: 372–386. doi:10.1080/10550490802266276
- Zedler BK, Mann AL, Kim MM, Amick HR, Joyce AR, Murrelle EL, et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta-analysis of safety in the mother, fetus and child. Addict Abingdon Engl. 2016 May 25
- Meyer MC, Johnston AM, Crocker AM, Heil SH. Methadone and buprenorphine for opioid dependence during pregnancy: A retrospective cohort study. J Addict Med. 2015;9(2):81–6.

Important Links & References (3)

- Jones HE, Fischer G, Heil SH, et al. Maternal Opioid Treatment: Human Experimental Research (MOTHER) – Approach, Issues, and Lessons Learned. *Addiction (Abingdon, England)*. 2012;107(0 1):28-35. doi:10.1111/j.1360-0443.2012.04036.x.
- https://www.drugabuse.gov/news-events/nida-notes/2012/07/buprenorphine-during-pregnancy-reduces-neonate-distress Jones HE, Kaltenbach K, Heil S, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. N Engl J Med. 2010;363(24):2320-2331. doi:10.1056/NEJMoa1005359.
- Hulse G, O'Neil G. Using naltrexone implants in the management of the pregnant heroin user. Aust N Z J Obstet Gynaecol. 2002 Oct 1;42(5):569–73.
- Hulse GK, Arnold-Reed DE, O'Neil G, Hansson RC. Naltrexone implant and blood naltrexone levels over pregnancy. Aust N Z J Obstet Gynaecol. 2003 Oct 1;43(5):386–8.
- Hulse G, O'Neill G. A possible role for implantable naltrexone in the management of the high-risk pregnant heroin user. Aust N Z J Obstet Gynaecol. 2002 Feb 1;42(1):104–5.
- Farid WO, Lawrence AJ, Krstew EV, Tait RJ, Hulse GK, Dunlop SA. Maternally Administered Sustained-Release Naltrexone in Rats Affects Offspring Neurochemistry and Behaviour in Adulthood. PLoS ONE [Internet]. 2012 Dec 26 [cited 2016 Dec 19];7(12). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530485/
- Jones HE. Acceptance of naltrexone by pregnant women enrolled in comprehensive drug addiction treatment: an initial survey. Am J Addict 2012; 2(3): 199-201.

Important Links & References (4)

- Matthew R. Grossman, Matthew J. Lipshaw, Rachel R. Osborn, Adam K. Berkwitt. A Novel Approach to Assessing Infants With Neonatal Abstinence Syndrome. Hospital Pediatrics. January 2018, VOLUME 8 / ISSUE 1.
- Meyer M, Wagner K, Benvenuto A, Plante D, Howard D.Intrapartum and postpartum analgesia for women maintained on methadone during pregnancy. Obstet Gynecol2007;110:261–6.
- AU Schiff DM, Nielsen T, Terplan M, Hood M, Bernson D, Diop H, Bharel M, Wilens TE, LaRochelle M, Walley AY, Land T SO. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018;132(2):466.
- Glatstein MM, Garcia-Bournissen F, Finkelstein Y, Koren G. Methadone exposure during lactation. *Canadian Family Physician*. 2008;54(12):1689-1690.
- Saia KA, Schiff D, Wachman EM, Mehta P, Vilkins A, Sia M, et al. Caring for Pregnant Women with Opioid Use Disorder in the USA: Expanding and Improving Treatment. Curr Obstet Gynecol Rep. 2016;1–7.

Contact Us

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