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Obstetric Care for the Pregnant Person with Opioid Use Disorder

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Maryland Addiction Consultation Service (MACS) for Maternal Opioid Misuse (MOMs)

Provides support to maternal health providers and their practices in addressing the needs of their pregnant and postpartum patients with substance use disorders (SUD), particularly opioid use disorder (OUD).

All Services are FREE

- Phone consultation for clinical questions
- Education and training opportunities related to substance use disorders and pregnancy
- Assistance with addiction and behavioral health resources and referrals
- MACS for MOMs TeleECHO Clinics: collaborative medical education through didactic presentations and case-based learning

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Introduction

- Opioid use in pregnancy
- Treatment options
- Considerations during prenatal care
- Intrapartum management
- Postpartum management
- Breastfeeding
- Neonatal Opioid Withdrawal Syndrome (NOWS)

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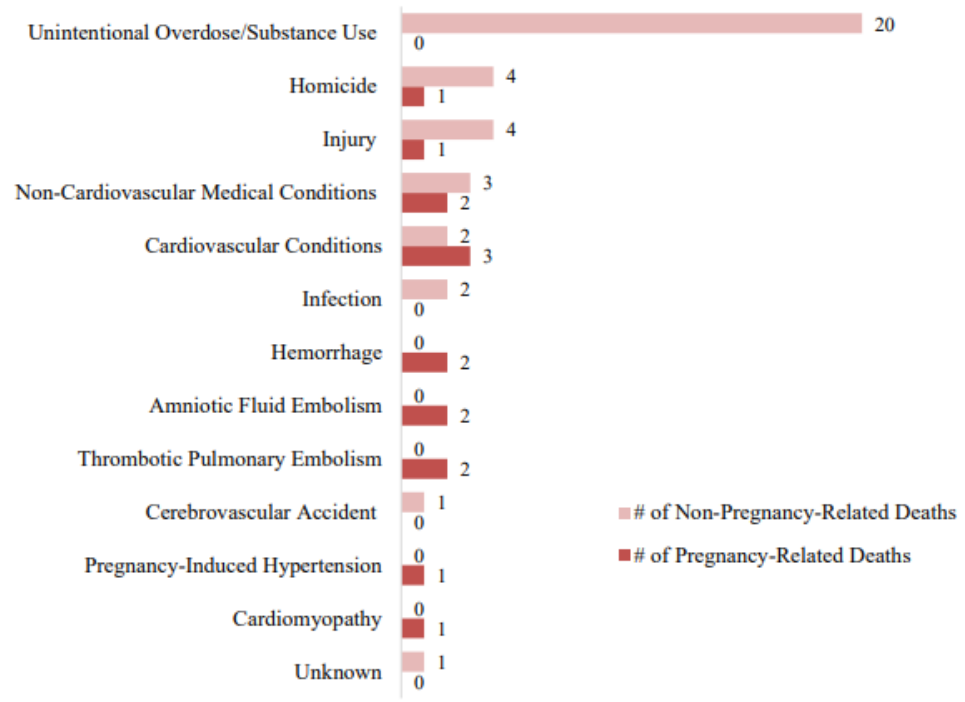
Figure 4. Number of Pregnancy-Related* and Non-Pregnancy-Related Deaths by Category of Cause of Death, Maryland, 2017 (Total Deaths = 52)**



* Deaths of women while pregnant or within 365 days of pregnancy from a cause related to or aggravated by pregnancy or its management.
** Deaths of women while pregnant or within 365 days of pregnancy from any cause not related to or aggravated by pregnancy or its management.
Data Source: MDH, VSA, and Maryland Maternal Mortality Review Program.

MMR MDH

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Medications for Opioid Use Disorder (MOUD)

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Goals of Treatment

- Prevent withdrawal
- Provide stable intrauterine environment
  - Most harm to fetus is from instability/increased cortisol
- Psychosocial improvements
- Risk reduction
  - Decreased risk of risky sexual behavior
  - Decreased risk of STIs (including HIV)
  - Decreased risk of overdose
  - Decrease all cause mortality

Gowing et al, J Gen Intern Med 2006
Hickman et al, Addiction 2018

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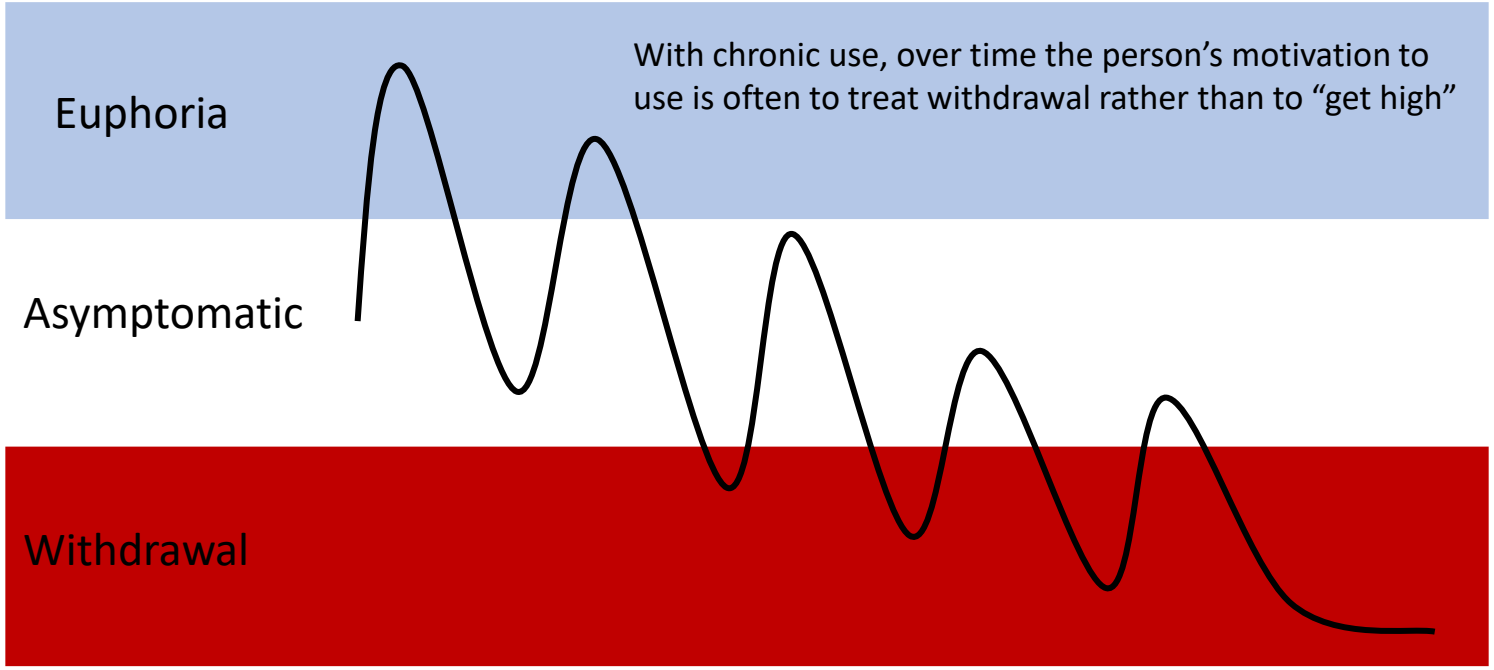
Chronic Opioid Use



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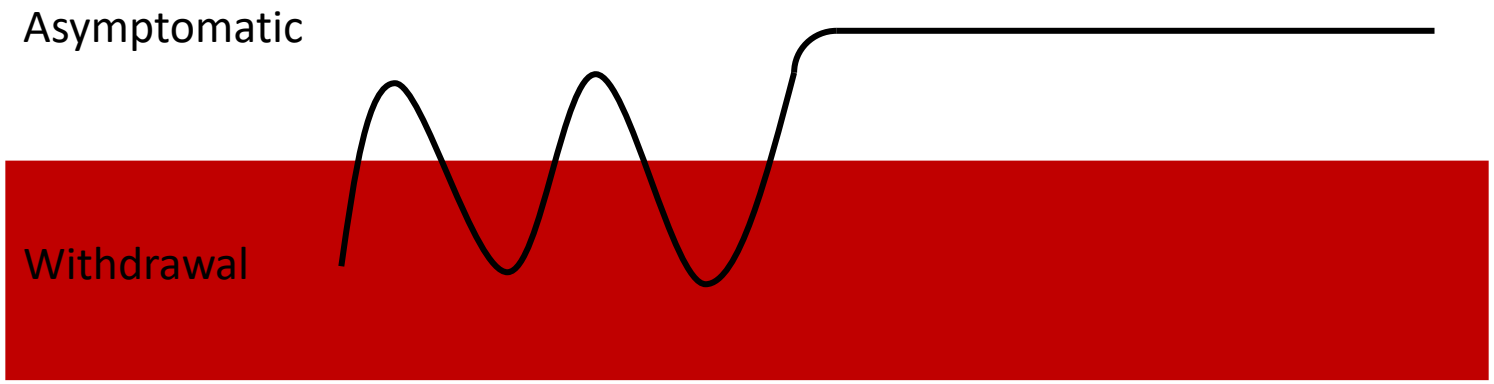
Medication for Opioid Use Disorder (MOUD)

Euphoria

The goal of medication for opioid use disorder is to keep people out of withdrawal and feeling “normal”



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Stigma of MOUD

- Addiction is a brain disease whose visible symptoms are behaviors
- Dependence ≠ Addiction
- Many medications can cause physical dependence
- Taking medication for opioid use disorder is like taking medication to control heart disease or diabetes.

MOUD is <u>NOT</u> substituting one addiction for another.

HHS.gov

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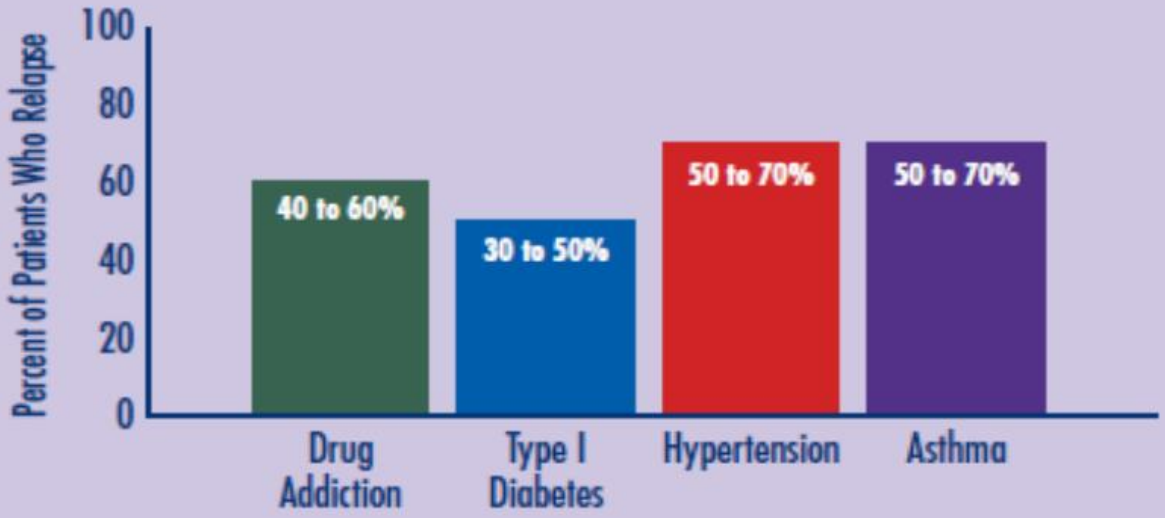
COMPARISON OF RELAPSE RATES BETWEEN DRUG ADDICTION AND OTHER CHRONIC ILLNESSES



Relapse in this chart refers to patients who experience recurrence of symptoms that requires additional medical care. The recurrence rates are similar across these chronic illnesses, underscoring that drug use disorders should be treated like other chronic conditions; symptom recurrence serves as a trigger for renewed intervention.

Source: JAMA, 284:1689-1695, 2000

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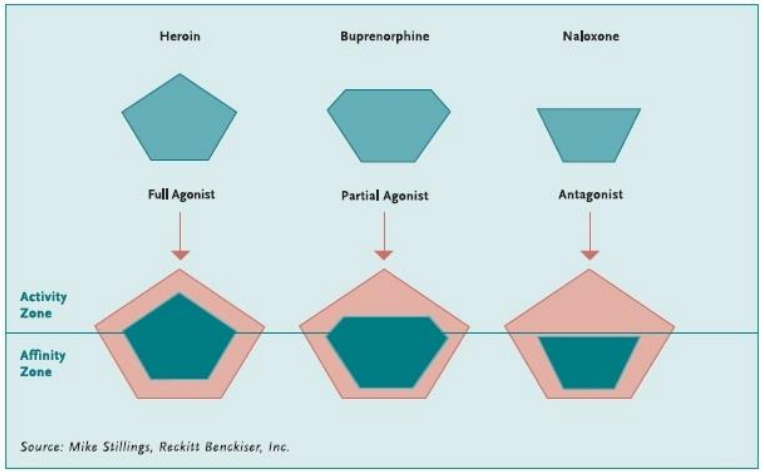
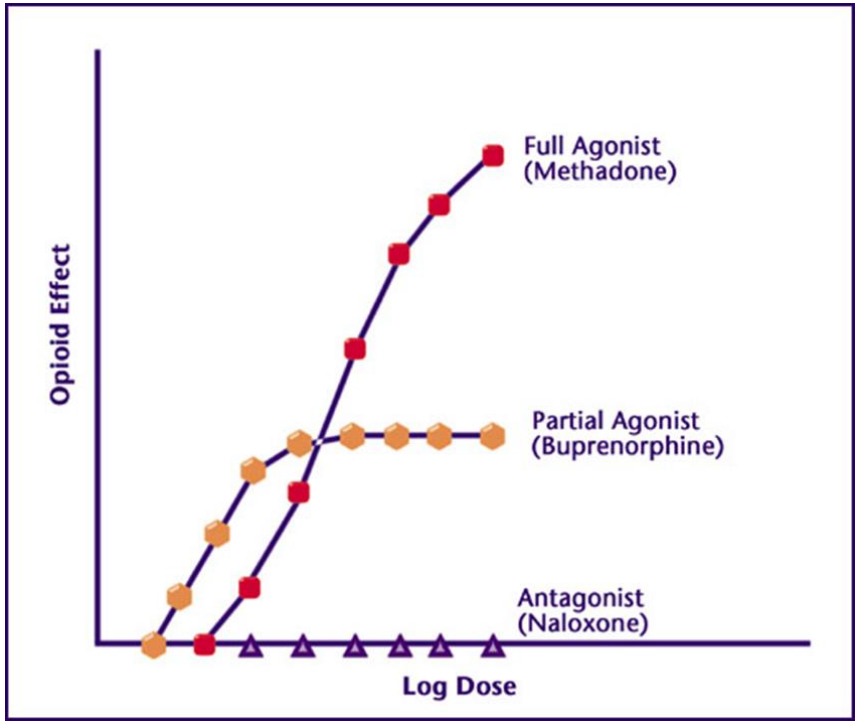
OPIOID RECEPTOR ACTIVATION





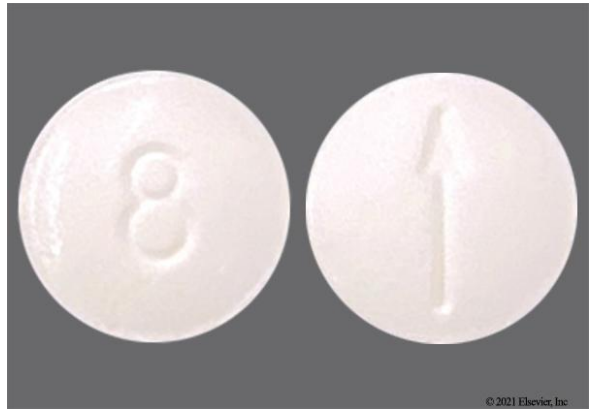
SAMHSA

Methadone (Full agonist)

- Pill and liquid form
- Can be started immediately
- Needs slow up titration due to long half-life
- Can only be prescribed/dispensed by licensed/regulated facilities

Buprenorphine mono product (Partial agonist)

- Brand name: Subutex
- Partial opioid receptor agonist
- Buccal tablets
- Bitter taste
- Infrequently used outside of pregnancy



Buprenorphine + Naloxone (Partial agonist)

SubOXONE

- Sublingual films
- Citrus taste

8mg suboxone = 5.7mg zubsolv

Zubsolv

- Suglingual tablet
- Mint-taste

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Buprenorphine + Naloxone

- Naloxone has no oral bioavailability
- If crushed and injected or snorted, will precipitate withdrawal
- Added **only to prevent diversion/misuse**

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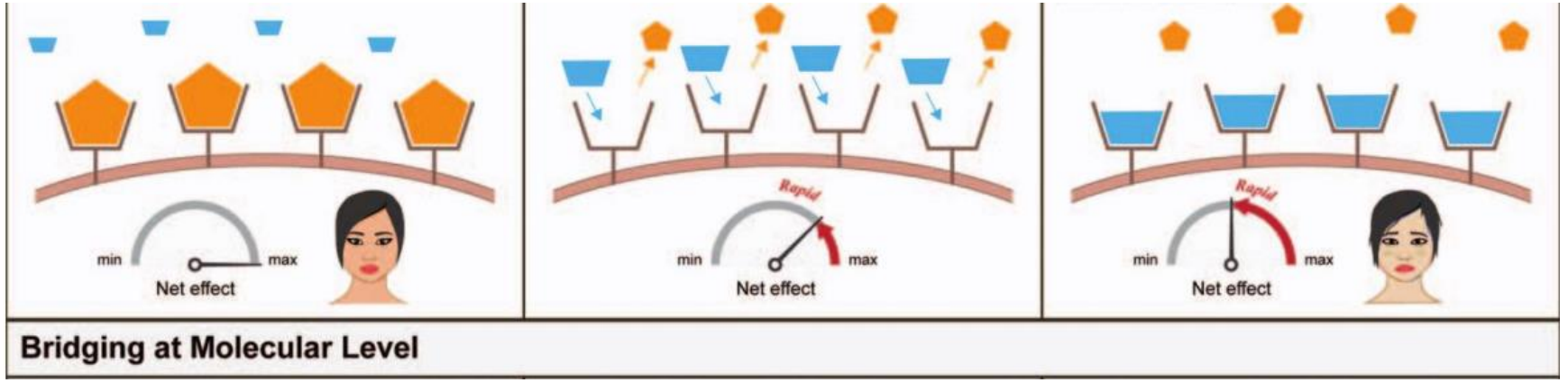
Myth Buster

- Myth: Suboxone should not be used in pregnancy
- Truth: There is no evidence to support this
  - Initial trials were done using buprenorphine mono product (Subutex)
  - Subsequent studies have shown safety of combined product (buprenorphine + naloxone)
  - **Naloxone is not orally bioavailable, so no biological plausibility that it should cause issues in pregnancy**

Myth Buster

- Myth: Buprenorphine product (Subutex) will not precipitate withdrawal
- Truth: Any buprenorphine product can precipitate withdrawal if given when someone is actively using a full opioid agonist



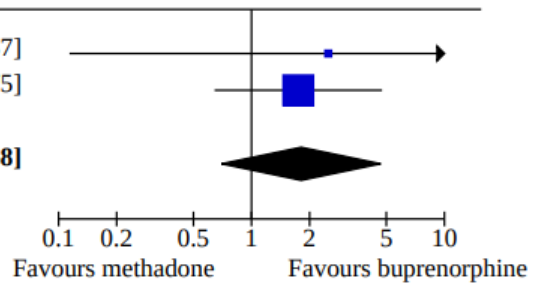
Analysis 1.2. Comparison 1: Methadone versus buprenorphine, Outcome 2: Use of primary substance

Study or Subgroup	Methadone Events	Methadone Total	Buprenorphine Events	Buprenorphine Total	Weight	Risk Ratio M-H, Random, 95% CI
Jones 2005	1	11	0	9	9.5%	2.50 [0.11 , 54.87]
MOTHER Study	11	73	5	58	90.5%	1.75 [0.64 , 4.75]
Total (95% CI)		**84**		**67**	**100.0%**	**1.81 [0.70 , 4.68]**
Total events:	12		5			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.05$, df = 1 (P = 0.83); $I^2 = 0\%$

Test for overall effect: Z = 1.22 (P = 0.22)

Test for subgroup differences: Not applicable



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Discriminatory History of MOUD

- Methadone is the country's most regulated medication
- Methadone approved for OUD treatment in 1972
- Limit person's control over daily routine
- Methadone clinics were placed in Black communities with the expressed goal of reducing crime
- Buprenorphine was approved for OUD treatment in 2002
  - Approved as the epidemic spread to suburban/white areas
- Buprenorphine remains more accessible in white communities

Goedel, JAMA Network Open 2020
Schuler, DAD 2021

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Full Antagonist

	Naloxone	Naltrexone
Indication	Reversal (overdose)	Maintenance of abstinence
Route	IM, IV, subcutaneous, intranasal	PO, Extended release IM

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Medically Supervised Withdrawal

- Addiction is a chronic disease
- Withdrawal is an acute treatment
- Relapse rates are as high as 90%
- Overdose deaths increase dramatically after period of abstinence
- In utero withdrawal is more harmful than NOWS

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Considerations in Prenatal Care

Buprenorphine dosing

- Factors contributing to dose change
  - CYP3A increase by 50%
  - Increased body fat/distribution
  - Absorption decreases due to salivary pH changes
- Increased frequency of dosing is often needed

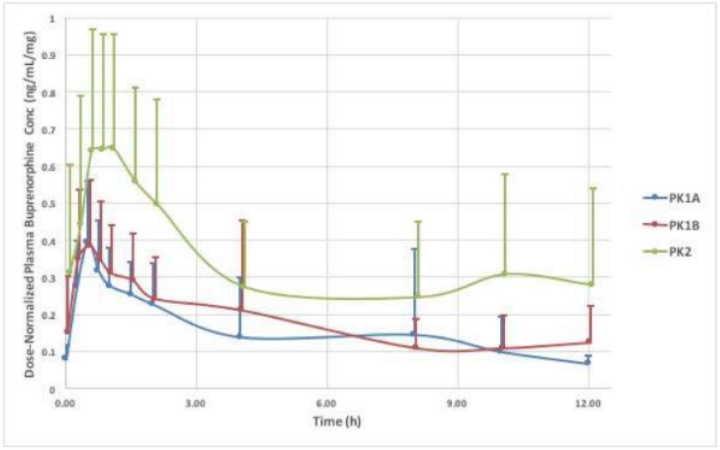


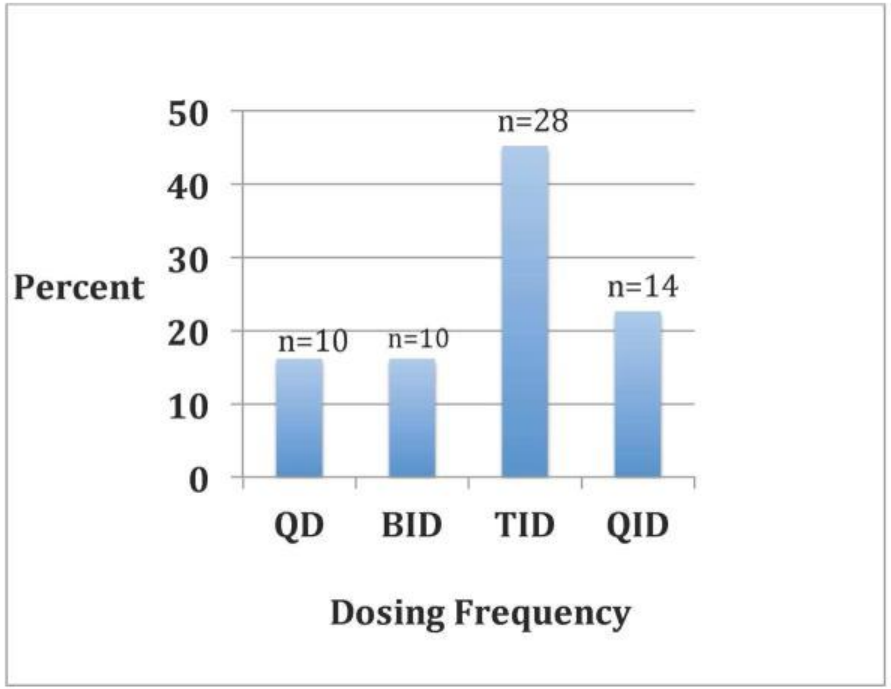
Figure 1. Dose-Normalized Buprenorphine Plasma Concentrations during Pregnancy and Postpartum

The mean dose-normalized buprenorphine plasma concentration-time curves (±SD) during the 12h pharmacokinetic study visits: PK1a (n=7), PK1b (n=11) and PK2 (n=10). X axis = time in hours; Y axis = mean dosenormalized buprenorphine plasma concentrations in ng/mL per mg of buprenorphine.

Bastian, AJOG 2017

- Gave patients their ideal daily dose and let them chose when to take the medication in order to decrease cravings and withdrawal symptoms

- Most chose 3-4 times daily



Caritis, AJOG 2017

Methadone in pregnancy

Table 2 Methadone dose by trimester of pregnancy and postpartum

Methadone dose	*N*	Mean	Median	Range
Women who converted during or before the first trimester[a]				
Peak dose 1st trimester	14	70.4	57.5	30–145
Peak dose 2nd trimester	14	93.4	89	50–155
Peak dose 3rd trimester/delivery	14	111.7	114	50–180
Women who converted during the second trimester[b]				
Peak dose 2nd trimester	7	90	80	60–135
Peak dose 3rd trimester/delivery	7	111.4	100	75–200
Women who converted during the third trimester				
Peak dose 3rd trimester/delivery	4	46.3	45	20–75
Dose 3 to 6 months postpartum[c]	22	106	97.5	26–190

- Clearance increases in pregnancy, so dose **often needs to be increased**
- Half life is 50% shorter during pregnancy, so many pregnant people need to **split doses**
- Medication changes should be based on patient reported symptoms

Bogen, Psychopharm 2013

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Women with SUD in pregnancy

- Mental Health
  - Two thirds co-occurring mental health disorders (Benningfield 2010)
    - Past 30 days: Mood disorder (50%), Anxiety (40%), PTSD (16%)
  - Childhood trauma: 50-90% physical or sexual abuse (Cormier 2000)
  - 60-80% past year intimate partner violence (Engstrom 2012, Tuten 2004)

80-95% smoke cigarettes

Metz, Obstet Gynecol 2016

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Intrapartum management

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Intrapartum Management

- Continue MOUD
- Neuraxial analgesia can be used
- IV pain medication can be given with full agonists (morphine, dilaudid)
- AVOID PARTIAL AGONISTS SUCH AS BUTORPHANOL (STADOL)

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MOUD and Baseline FHR

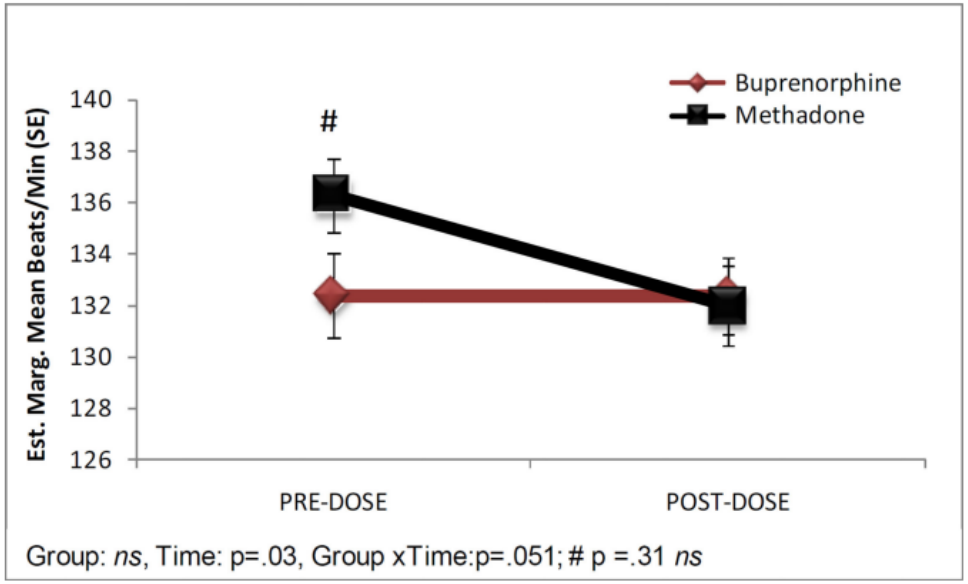

Figure 1.
Fetal heart rate estimated marginal means in beats per minute in the pre and post-dose assessments. #Pairwise comparison with a Bonferonni correction, $P > 0.05$, not significant (ns).

Salisbury, Addiction 2012

MOUD and FHR accelerations

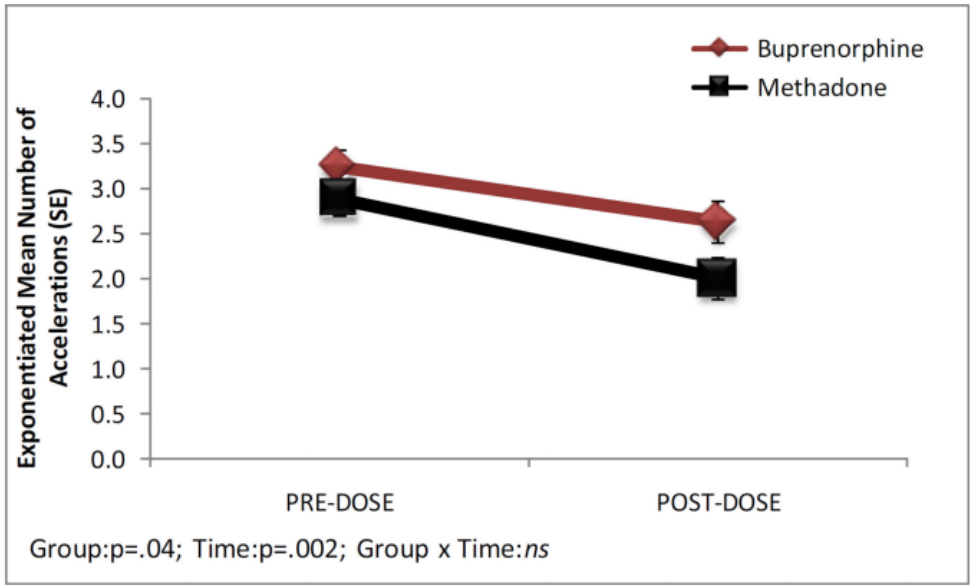

Figure 2.
Exponentiated mean number of Fetal Heart Rate (FHR) Accelerations in the pre- and post-dose assessments.

Salisbury, Addiction 2012

MOUD and likelihood of non-reactive NST

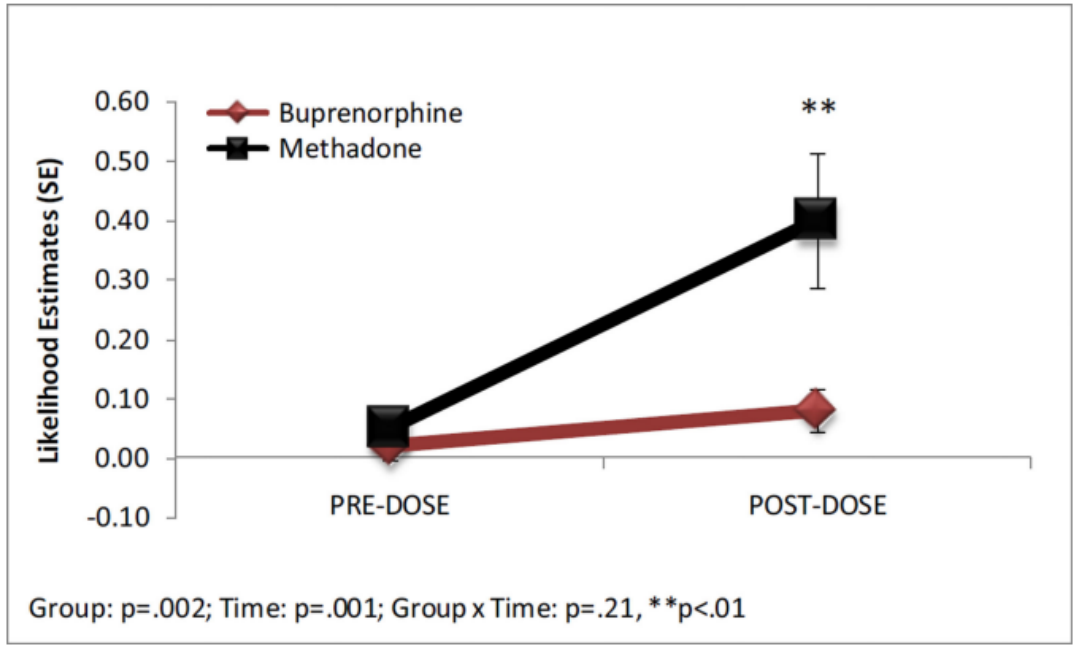

Figure 3.
Likelihood estimates for a non-reactive fetal non-stress test in the pre- and post-dose assessments. ** Pairwise comparison with a Bonferonni correction, $P < 0.01$.

Salisbury, Addiction 2012

MOUD and BPP

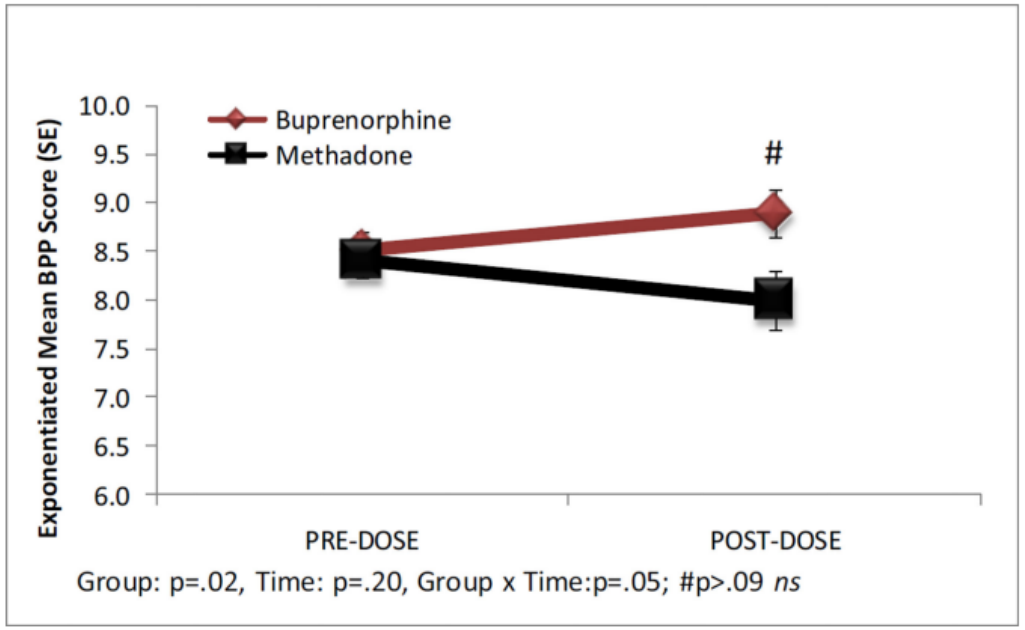

Figure 4.
Exponentiated mean Biophysical Profile Score (BPP) in the pre- and post-dose assessments. #Pairwise comparison with a Bonferonni correction, $P > 0.05$, not significant (ns).

Salisbury, Addiction 2012

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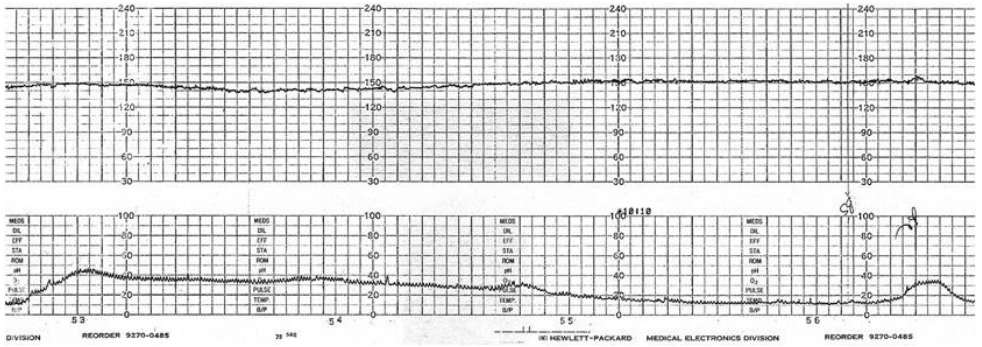
Intrapartum FHR monitoring

- No major differences with buprenorphine administration
- Methadone lower baseline and variability, fewer accels
- **<u>Any change in FHR should be investigated</u>**



Salisbury, Addiction 2012
Jannson, Neurotox Teratol 2011

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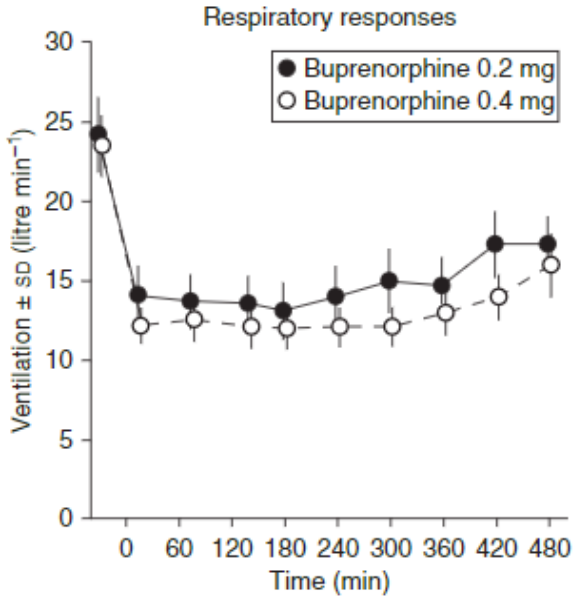
Postpartum management

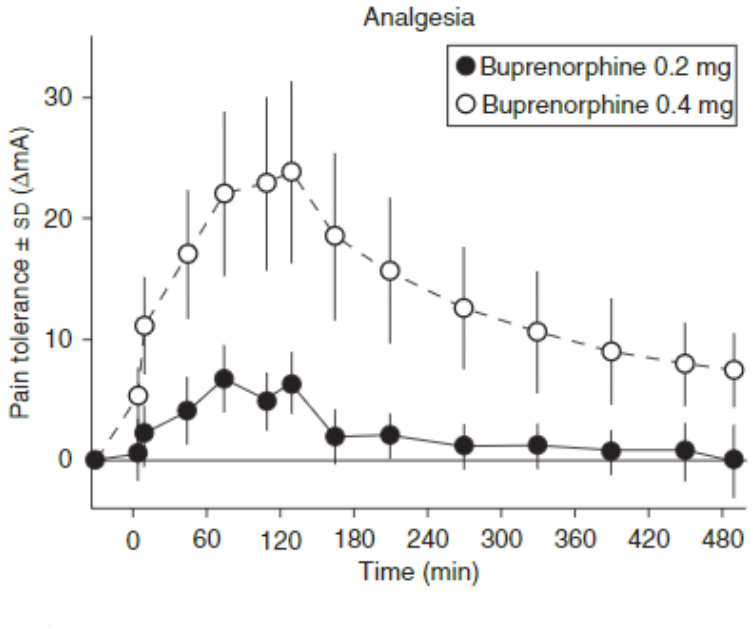
PAIN MANAGEMENT

Postpartum pain management

- **Continue MOUD and**….
  - Add full opioid agonist (oxycodone, morphine, dilaudid, ect)
  - Add additional doses of buprenorphine QID
- Stopping buprenorphine to give full agonist for pain is unnecessary and can lead to destabilization of the patient and increase risk of return to use
- Appropriate discharge planning
  - Discuss in advance what medications patient is comfortable with
  - Consider having a support person to monitor medications

Buprenorphine for pain





Dahan, British J of Anest, 2006

Myth: buprenorphine products will block full opioid agonist pain medications (oxycodone, morphine, ect)

Truth: People whose MOUD was discontinued required higher doses of morphine PCA postoperatively

Recommendation: Continue MOUD and add appropriate pain medications

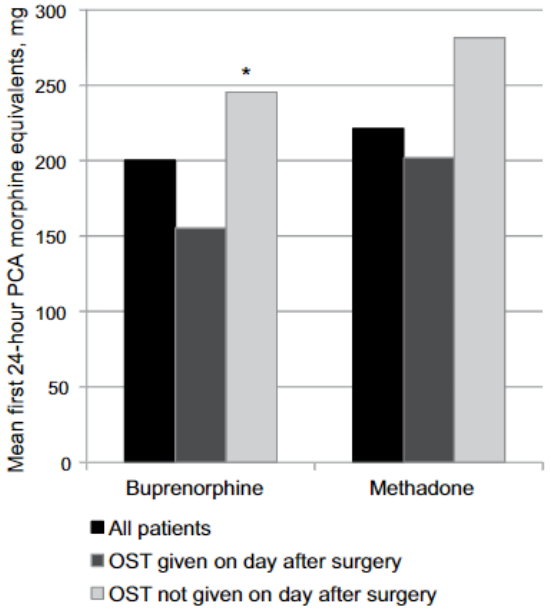


Figure 1: Comparison of PCA opioid requirements in buprenorphine and methadone opioid substitution therapy patients. * The mean PCA morphine equivalent dose was significantly higher (P=0.02) in patients who did not receive buprenorphine the first day after surgery compared with those who did. PCA=patient-controlled analgesia, OST=opiod substitution therapy.

Macintyre, Anaesth Intensive Care 2013

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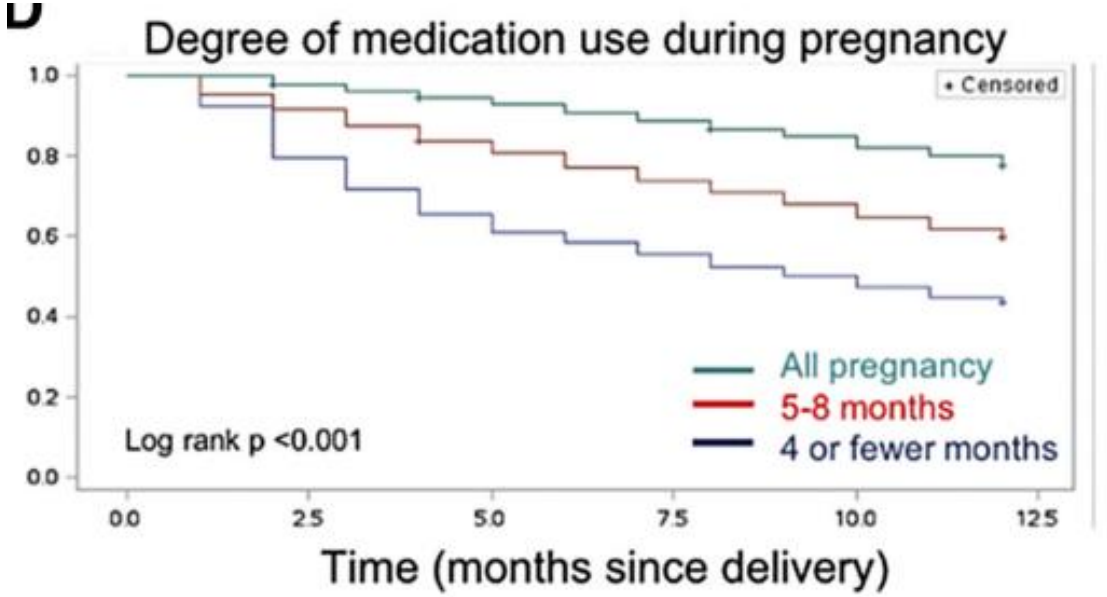
Hyperalgesia

- "A state of nociceptive sensitization caused by exposure to opioids"
- Presents as an exaggerated response to painful stimuli
  - Due to changes in receptor activity due to chronic stimuli from opioids
- Is reproducible in laboratory animals
- Is NOT "drug seeking"

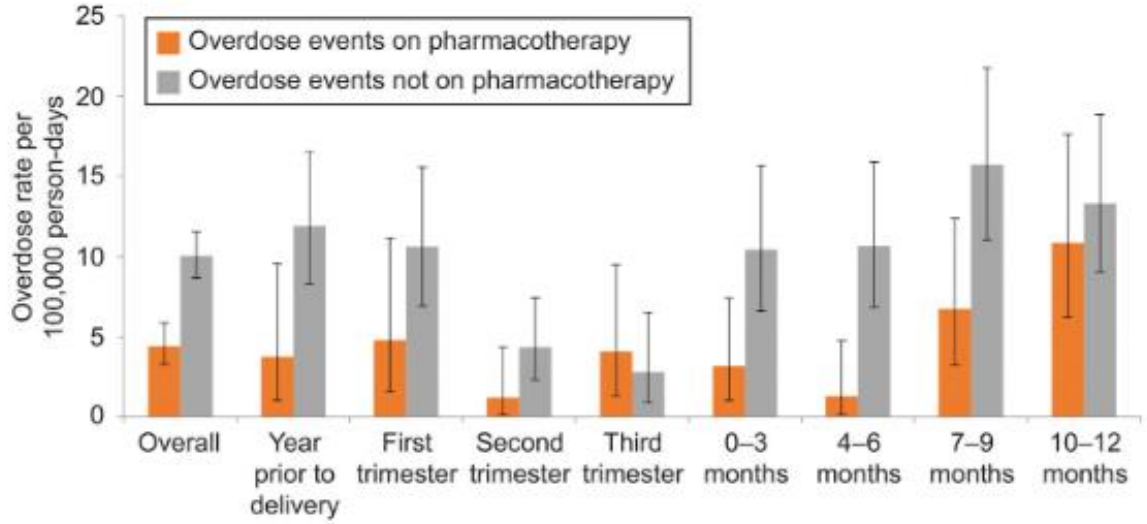
Lee, Pain Physician 2011

Continuation of MOUD



Schiff Am J Obstet Gynecol 2021

Postpartum MOUD



- Risk of overdose is the highest in the year postpartum
- Risk of overdose is significantly higher in those who do not continue MOUD

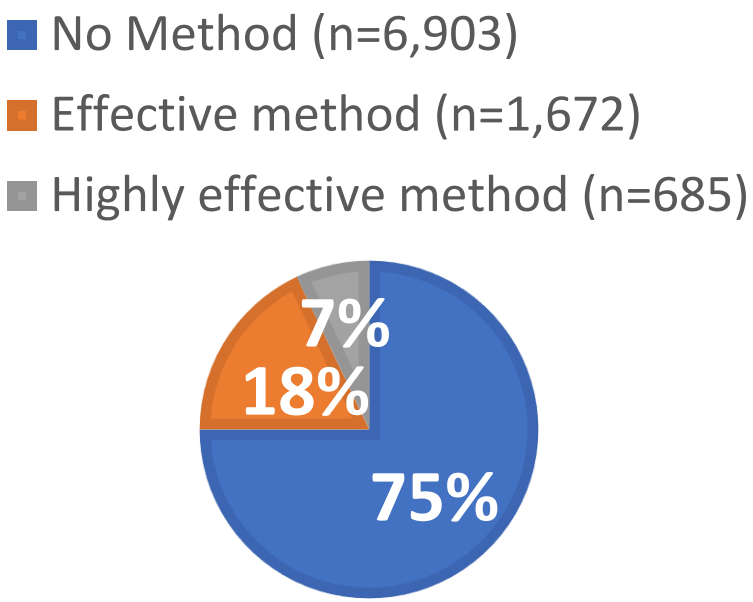
Schiff, Obstet Gynecol 2021

Postpartum MOUD

- **Recommendation is to continue MOUD postpartum**
- Addiction is a chronic illness that requires longterm treatment
- Doses typically do not need to be decreased postpartum
- For those who desire weaning
  - Evaluate motivating factors
    - External pressure
    - Desire to use
    - Cost/time required for treatment
  - Recommend waiting 12 months

Martin, Curr Treat Opt Psych 2020
Pace, J Subst Abus Treat 2014

Postpartum Contraception for People with OUD



Analysis of PA Medicaid recipients

Approximately 20% had short interval pregnancy

Krans, DAD 2018

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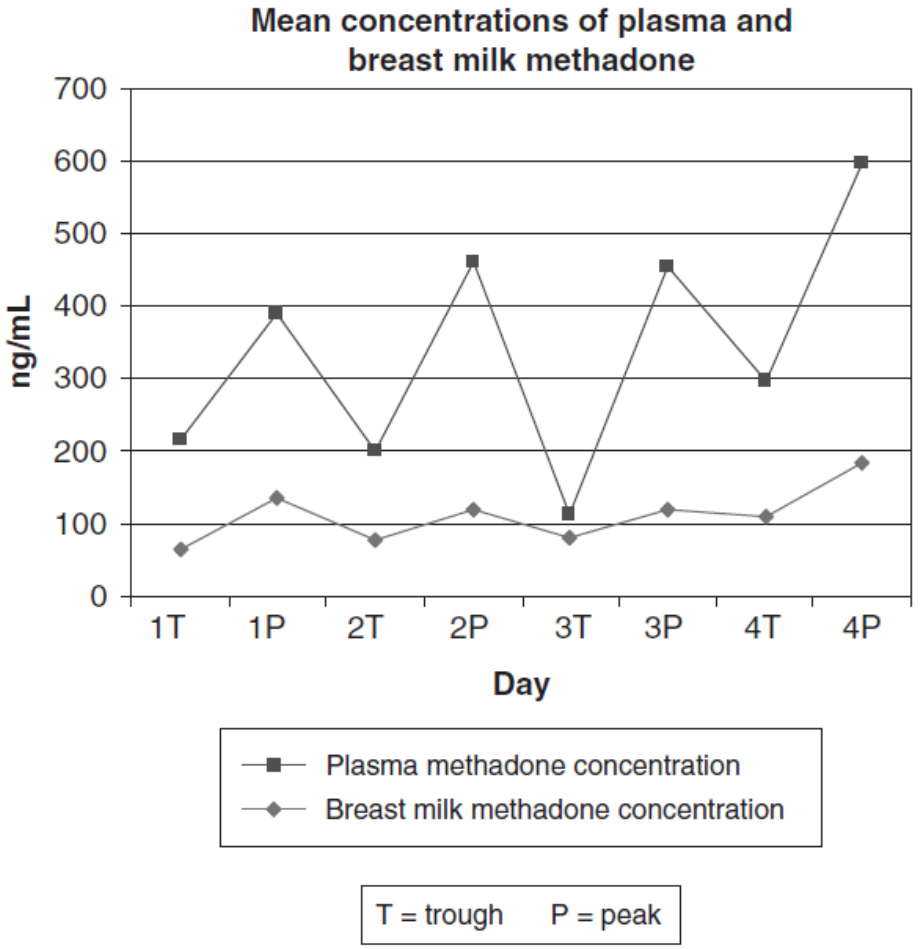
Breastfeeding



- Methadone concentrations were small
  - **Doses ingested ranged from 0.006mg to 0.084mg per day**
- Concentration was not related to maternal dose

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Breastfeeding

- Breastfeeding is recommended in people on MOUD with usual contraindications

- All pregnant/postpartum people should be encouraged to make lifestyle modifications to decrease stress and risk of relapse postpartum
  - Sleep schedule
  - Eating schedule
  - Identify support system

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Neonatal Opioid Withdrawal Syndrome (NOWS)

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Neonatal Opioid Withdrawal Syndrome (NOWS)

- **NOWS is an expected and treatable condition among infants exposed to opioids in utero.**
- When treated appropriately, there is no evidence that NOWS has negative long-term consequences
- Counseling regarding NOWS is necessary during the antenatal period
  - Know your hospital policies regarding monitoring

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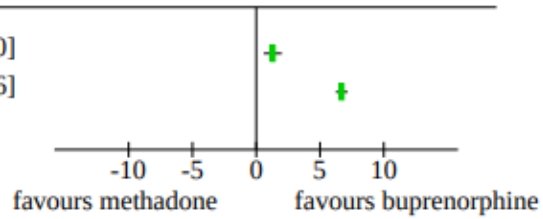
Neonatal Opioid Withdrawal Syndrome

- Infant withdrawal usually begins a few days after the baby is born but may begin as late as 2 to 4 weeks after birth.
- Reducing the dose of MOUD before delivery will NOT reduce NAS expression or severity.
- Smoking cessation and minimization of other substance use can reduce NAS expression and severity

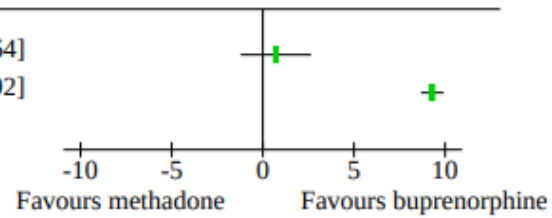
Analysis 1.7. Comparison 1: Methadone versus buprenorphine, Outcome 7: Length of hospital stay

Study or Subgroup	Methadone Mean	Methadone SD	Methadone Total	Buprenorphine Mean	Buprenorphine SD	Buprenorphine Total	Mean Difference IV, Random, 95% CI
Jones 2005	8.1	0.78	11	6.8	0.86	10	1.30 [0.60 , 2.00]
MOTHER Study	17.5	1.5	73	10.8	1.2	58	6.70 [6.24 , 7.16]



Analysis 1.8. Comparison 1: Methadone versus buprenorphine, Outcome 8: Total amount of morphine for NAS

Study or Subgroup	Methadone Mean	Methadone SD	Methadone Total	Buprenorphine Mean	Buprenorphine SD	Buprenorphine Total	Mean Difference IV, Random, 95% CI
Fischer 2006	2.71	1.68	6	2	2	8	0.71 [-1.22 , 2.64]
MOTHER Study	10.4	2.6	73	1.1	0.7	58	9.30 [8.68 , 9.92]



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NOWS and MOUD

- Length of stay and total dose of morphine needed for NOWS are slightly less with buprenorphine than with methadone
- Dose of buprenorphine and methadone are not related to severity or length of treatment for NOWS

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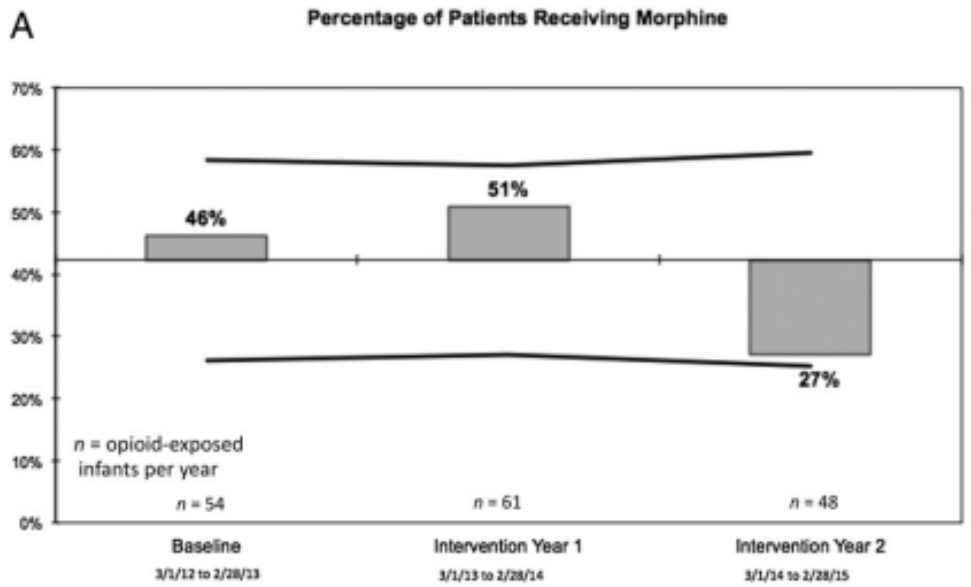
Rooming-In to Treat Neonatal Abstinence Syndrome: Improved Family-Centered Care at Lower Cost

Alison Volpe Holmes, MD, MPH,[a,b,c] Emily C. Atwood,[a] Bonny Whalen, MD,[a,b] Johanna Beliveau, RN, MBA,[b] J. Dean Jarvis, RN, MBA,[b] John C. Matulis, DO, MPH,[d] Shawn L. Ralston, MD[a,b]



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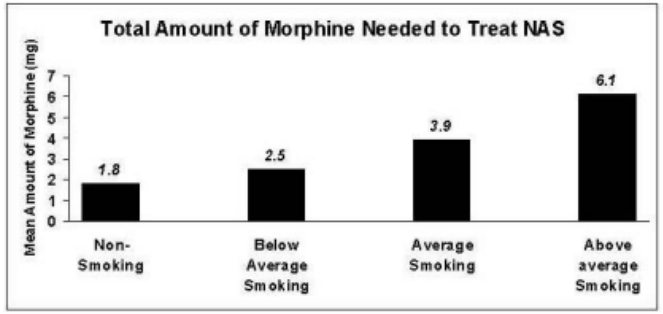
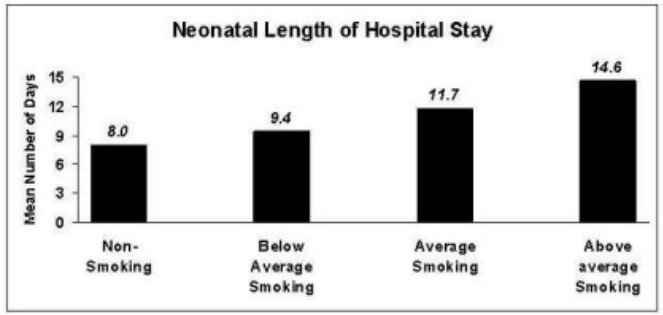
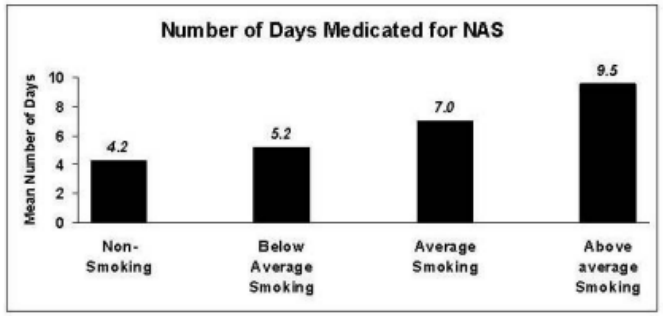
- Tobacco smoking and NOWS
  - Increased need for morphine
  - Increased length of hospital stay
  - Longer treatment course







Jones, DAD 2013

MACS
Maryland Addiction Consultation Service for MOMS

Summary

- Opioid use in pregnancy is common and treatable
- MOUD is standard of care in pregnancy
- Methadone and buprenorphine +/- naloxone are safe and effective
- MOUD should be continued postpartum and add appropriate pain medications
- Continued support in the postpartum period is critical

MACS
Maryland Addiction Consultation Service for MOMS

Summary (continued)

- Breastfeeding should be encouraged
- NOWS is an expected and treatable sequelae of opioid exposure
- Severity of NOWS is not related to dose of MOUD
- Nicotine use increases the severity/length of NOWS
- Rooming in should be considered part of treatment for NOWS
- **Anticipatory guidance should be provided to all pregnant people to improve likelihood of maintaining recovery and decreasing stress and stigma**

QUESTIONS OR WANT MORE INFORMATION?

Questions:

1-855-337-MACS (6227)
MACS@som.umaryland.edu

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Prescribers: Sign up for MACS for MOMs

https://j.mp/3hJZsO9

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