

Treating Opioid Use Disorder in the Perinatal Period



Alexis Hammond, MD, PhD

Psychiatrist, Headspace Health

Assistant Professor, JHU Dept. of Psychiatry & Behavioral Sciences

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Objectives

- Understand the risks associated with opioid use during pregnancy
- Learn best practices for prescribing medications for opioid use disorder in pregnancy
- Understand the importance of retention strategies
- Increase comfort level in management of dually diagnosed pregnant women

The Problem

The Problem

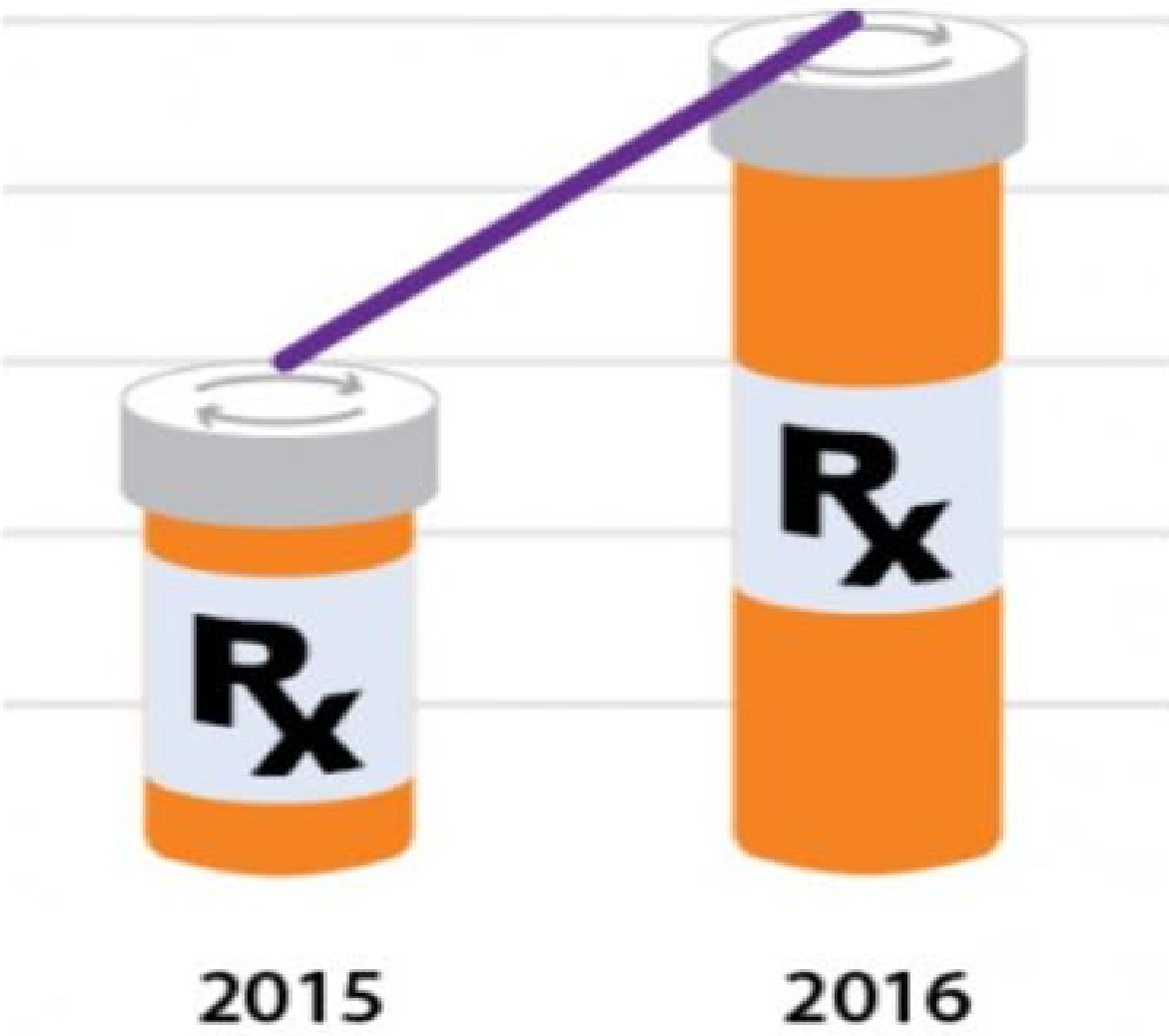
40.3M people had a substance use disorder (SUD) in 2020

More women are being diagnosed

SUD prevalence rate is 15% among pregnant women

(SAMHSA, 2021; Vesga-Lopez, 2008; Jones, 2013)

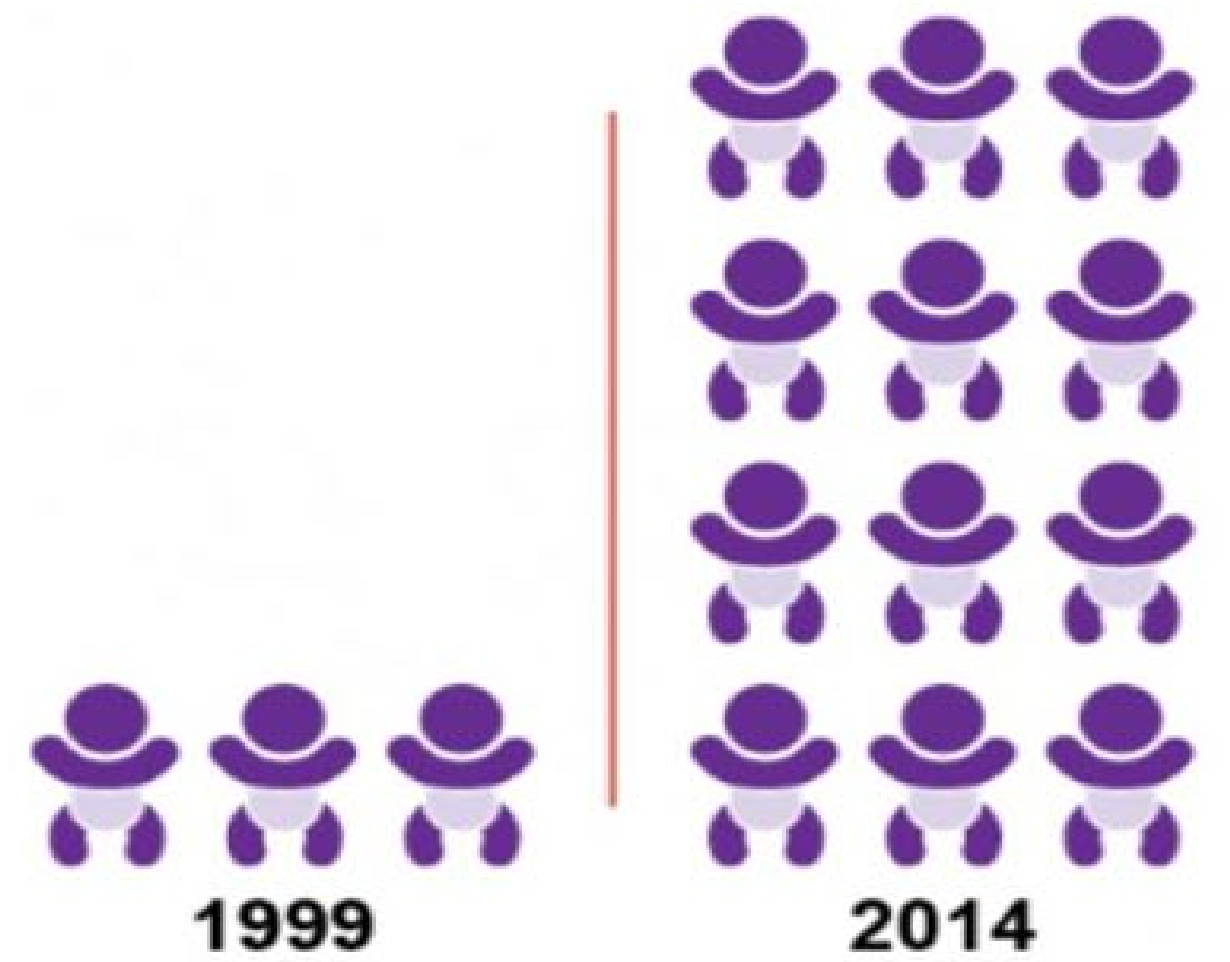
The Toll



The rate of overdose deaths among women



Opioid use disorder 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.

(CDC, 2018)

Health Outcomes

Opioid use disorder during pregnancy has been linked to:



**Preterm
Birth**



**Low
Birthweight**



**Breathing
Problems**



**Feeding
Problems**

(CDC, 2018)

General Management Principles

Specialized services and optimized treatment are essential

Combo of pharmacologic & psychosocial treatments are effective

Specialty referral may be indicated

Strategies for Addressing OUD among Pregnant Women

Ensure appropriate prescribing.

Maximize & enhance prescription drug monitoring programs.

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 treatment and related services.



(CDC, 2018)

**Center for Addiction and
Pregnancy, Est. 1991**

Mental Health/Substance use
treatment

Individual/group therapy
Psychiatric care
Parenting

Obstetrics

Prenatal care
Postpartum visits
Contraception

Case
management

Housing
Legal
Financial

Comprehensive
treatment for
mother/baby dyad

Pharmacological

Methadone/buprenorphine
Psychiatric medication
For Infections or other medical
conditions (i.e. HIV,
hypertension)

Pediatrics

Well and sick child care
Developmental
assessment
Considering the mother
& environment



(Adapted from Velez & Jansson, 2015)

Being in Treatment Improves Outcomes

D.S. Svikis et al. / Drug and Alcohol Dependence 45 (1997) 105–113

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Table 3
Maternal and infant clinical outcomes

	Treatment (N = 100)	Controls (N = 46)	Adjusted P-value*
Maternal			
Positive drug screen at delivery	36.8%	63.2%	<0.001
Neonate			
EGA (mean wk)	38.6	35.4	<0.001
Birthweight (mean gm)	2934	2539	<0.001
Low birthweight (<2500 g)	15%	39%	<0.001
Very low birthweight (<1500 g)	0%	17.4%	<0.001
Apgar (mean 1 min)	7.7	6.8	0.004
Apgar (mean 5 min)	8.8	8.5	0.004
NICU hospitalization	10%	26%	0.01
Mean NICU length of stay			
NICU admissions only	6.6 days	38.9 days	0.01
All infants	0.8 days	10.2 days	0.01

* Controlling for initial group differences in age, education, and cocaine use.

Treatment retention is suboptimal

Dropout rates prior to delivery ~33%

Up to ½ of postpartum women leave AMA after 3-6 months

Fatal overdose risk is high during 1st year postpartum

>25% of women who initiate MOUD report low adherence or early discontinuation

High rates of methadone discontinuation in 1st month postpartum



CAP-specific treatment retention data

A pregnant woman with her hair in a ponytail, wearing a white long-sleeved shirt, is shown in profile from the waist up. She is looking out a window with her hands resting on her belly. The background is a blurred view of a residential neighborhood with houses and trees under a bright sky.

Overall 62% left prior to securing treatment elsewhere

42% left treatment prior to delivery

86% of these left AMA without interest in referral

37% of postpartum women left without follow-up treatment

General factors Driving Poor Retention

Co-occurring substance use

Presenting later in pregnancy

Financial pressures

Co-occurring medical & psychiatric
illness

Chronic social stress

Insufficient methadone doses



CAP Patient Opinions on Barriers to Treatment Retention

- 1) Financial worries (68%)
- 2) Taking medication for too long (50%)
- 3) Interferes with responsibilities (45%)
- 4) Lack of transportation (40%)
- 5) Criticism for taking MOUD (28%)



(Hammond et al, in preparation)

Medications for OUD Benefit Perinatal Women

Standard of care includes methadone or buprenorphine

Similar effectiveness

Reduces opioid use & risk behaviors

Reduces obstetric complications

Reduces maternal mortality and severe maternal morbidity

No increases in birth defects or neurodevelopmental deficits



(Minozzi et al., 2008; SAMHSA, 2018; Ecker et al., 2019; Zedler et al., 2016; SAMHSA, 2014; Johnson, 2016; Lefebvre et al., 2010, SAMHSA, 2016)

Maternal Opioid Treatment: Human Experiential Research

Double blind, double dummy multi-site
RCT

Comprehensive care- 8 sites

175 women with OUD

Primary outcomes were related to NAS

The NEW ENGLAND JOURNAL of MEDICINE

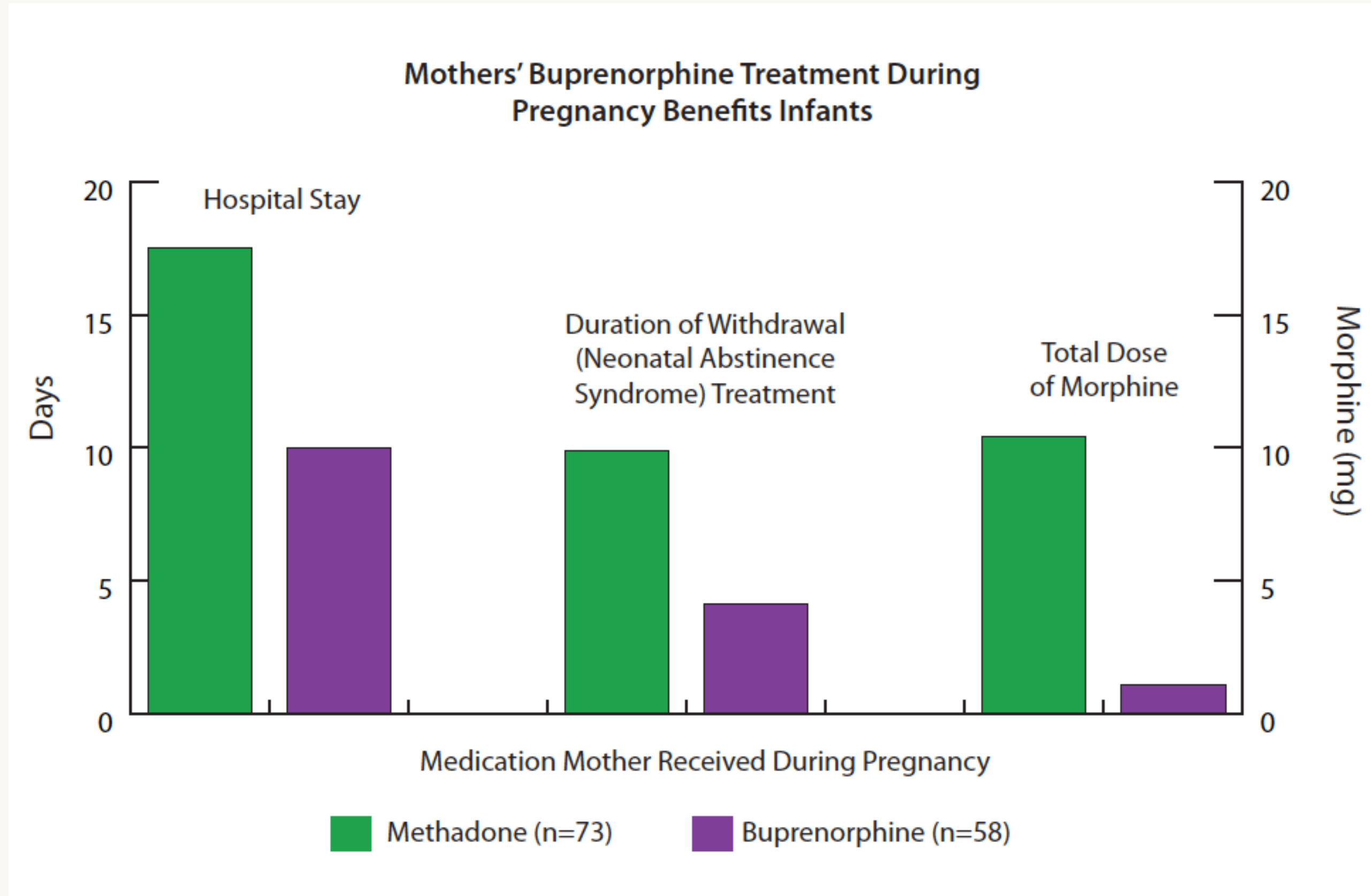
ORIGINAL ARTICLE

Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

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

ABSTRACT

Neonatal outcomes for prenatal exposure to methadone vs. buprenorphine



Lessons from the MOTHER study

Higher drop out rate
with buprenorphine
(33% vs 18%)

Higher dissatisfaction
rates with
buprenorphine (71% vs
13%)

Buprenorphine vs. Methadone

- Lower risk of overdose
- Fewer drug interactions
- Ability to be treated in a private office setting without the need for daily visits to a licensed treatment program
- Dosing of buprenorphine is similar to that in nonpregnant women
- Insurance in the United States may cover buprenorphine prescribed by a private physician in an office setting, while not covering methadone dispensed in a licensed opioid treatment program
- Fewer side effects
- Low risk of adverse cardiovascular side effects (by contrast, methadone is associated with small increase in risk of arrhythmia)
- For the newborn, in utero exposure to buprenorphine rather than methadone may result in a lower risk of preterm birth, higher birth weight, larger head circumference, and a lower rate and severity of neonatal withdrawal

- Relative to methadone, fewer data are available on pregnancy outcomes after first trimester exposure
- Lack of long-term neurodevelopmental outcome data
- Clinically important patient dropout rate due to dissatisfaction with the drug
- More difficult induction protocol with the potential risk of precipitated withdrawal
- Increased risk of diversion* (especially the buprenorphine monotherapy formulation)
- Less stringent structure of some office-based treatment programs
- Reports of maternal hepatic dysfunction and elevated transaminases
- Effects of buprenorphine are only partially reversible by naloxone
- The maximum daily dose of buprenorphine is 32 mg, due to a ceiling effect, which may not be sufficient in all women (usually those requiring more than 140 mg per day of methadone)
- More expensive than methadone
- Treatment with methadone may result in greater reduction in illicit opioid use

Considerations

Patient selection/preference

Dispensing

Treatment retention

Starting dose

Target dose

Interval at which dose may be increased

Buprenorphine

May be preferable for patients who are new to treatment because it is easier to transfer from buprenorphine to methadone (it can be very difficult to transfer from methadone to buprenorphine), who do not like or want methadone, or who have requested this medication

May be prescribed in an office setting with weekly or biweekly prescribing/dispensing or provided in an opioid treatment program

Some studies show treatment dropout is higher than that for methadone

2 to 8 mg sublingually

Daily, 16 mg sublingually or product equivalent to 16 mg sublingually, is the most common dose. The optimal dose will be determined by regular assessment of the individual and her response to treatment

Daily, but dose changes should not be made without patient assessment

Methadone

May be preferable for patients who do not like or want buprenorphine treatment or who have requested this medication

Requires daily visits to a federally certified opioid treatment program; take-home medication is provided for patients meeting specific requirements

Some studies show treatment retention is higher than that for buprenorphine

20 to 30 mg orally

Daily, 80 to 120 mg orally. The optimal dose will be determined by regular assessment of the individual and her response to treatment

Three days is a common interval in a clinical practice, but dose changes should not be made without patient assessment

(Adapted from Seligman, Rosenthal & Berghella., 2021)

Considerations

Risk of overdose and death

Risk of sedation

Risk of NAS

Time to NAS onset

Breastfeeding considerations

Neurodevelopmental outcomes of exposed children

Buprenorphine

Generally lower risk compared with full opioid agonists; overdose is possible when combined with other CNS depressants

Buprenorphine treatment reduces the risk of death in people dependent on opioids and drug-related mortality in the first four weeks of treatment, a high-risk period

Sedation is possible but typically milder than that with full mu opioid agonists.

Approximately 50% of exposed neonates are treated for NAS; NAS may be milder with buprenorphine compared with full mu opioid agonists such as most opioid analgesics and methadone.

The AAP recommends monitoring prenatally opioid-exposed neonates for a minimum of four to seven days after delivery

Generally safe if the mother is stable

Available research suggests there is not a linear cause and effect relationship between prenatal buprenorphine exposure and developmental problems when compared with other opioids; the research base is limited

Methadone

Generally greater risk of overdose compared with mixed agonist/antagonist opioids; overdose is possible when combined with other CNS depressants, but reduced risk compared to no treatment

Methadone treatment reduces the risk of death in people dependent on opioids and drug-related mortality in the first four weeks of treatment, a high-risk period

Sedation is possible and may be greater than that with partial agonist opioids

Approximately 50% of exposed neonates are treated for NA

The AAP recommends monitoring prenatally opioid-exposed neonates for a minimum of four to seven days after delivery

Generally safe if the mother is stable

Available research suggests there is not a linear cause and effect relationship between prenatal methadone exposure and developmental problems when compared with other opioids; the research base is limited.

(Adapted from Seligman, Rosenthal & Berghella., 2021)

Other considerations to optimize health and improve retention

Start with thoughtful discussion of risks and benefits to choose appropriate level of care and MOUD

Split dosing may be required

Use effective doses, which are often higher than for nonpregnant women

Work towards getting to an effective dose as quickly as safely possible

Strive to differentiate between pregnancy symptoms such as morning sickness with aversions, adverse effects and WD



Other considerations to optimize health and improve retention

Can switch from bup to meth but the opposite is not advised

Continue MOUD until at least 1 year postpartum

Adjust approach as needed in context of fentanyl use

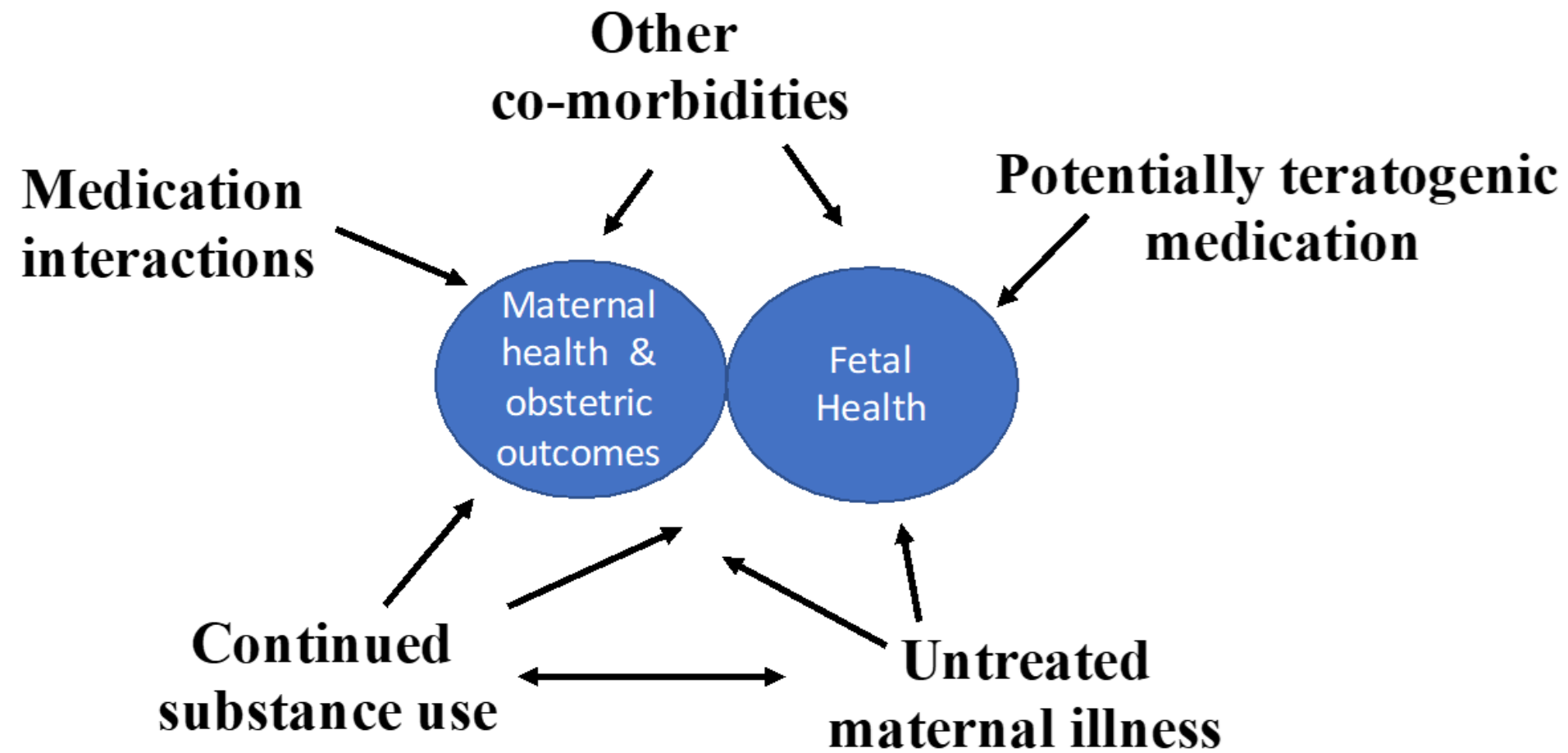
Consider induction in hospital for severe use

Utilize comfort meds as able during induction

Utilize contingency management, while keeping treatment demands manageable



Pregnant women with SUD have higher rates of co-occurring mental health conditions (1% vs. 10%)



(Vesga-López, 2008; Jones, 2013, Hammond and Chisholm; 2018)

Summary

Perinatal OUD treatment is safe and effective

Treatment retention is poor among pregnant women with OUD

Co-occurring SUDs & other mental health conditions further complicate the picture

Proper assessment, screening and referral to appropriate care is key

Treatment plans must be individualized and agreed upon

Include instillation of hope, and reduction of stigma

More rigorous and safe studies involving pregnant women are needed to expand treatment options



Thank you

CAP patients, past and present
CAP Faculty and Staff

Denis Antoine, II, MD

Michael Kidorf, PhD

Eric Strain, MD

Meg Chisolm, MD

Alexis Hammond, MD, PhD
ahammond04@gmail.com

443-228-8482

CAP Intake Line: 410-550-3066



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