

Welcome

Thank you for joining us today. The webinar will begin in a few moments.

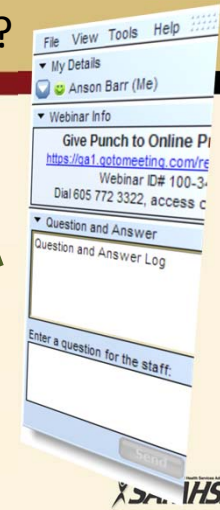
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2











Opioid Use Disorders and Treatment in Pregnancy


Wednesday, May 13, 2015

Anne Johnston, MD
 Hendree Jones, PhD
 Carl Seashore, MD





Behavioral Health is Essential To Health



Prevention Works



Treatment is Effective

People Recover

Agenda

- Introduction/Opening Remarks
Sharon Amatetti, MPA
- Opioid Use, Dependency and Treatment in Pregnancy
Hendree Jones, PhD
- Working with Mothers and Infants: Post-Delivery
Carl Seashore, MD
- Working with Mothers and Infants: Post-Discharge
Anne Johnston, MD
- Discussion

Sponsored by the SAMHSA Women's Coordinating Committee in observance of National Women's Health Week



National Women's Health Week: Opioid Use Disorders and Treatment in Pregnancy • May 13, 2015

Opioid Use, Dependency, and Treatment in Pregnancy



Hendrée E. Jones, PhD

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Acknowledgements

- Study patients and infants
- National Institute on Drug Abuse
 - R01 DAs: 015764, 015738, 017513, 015778, 018410, 018417, 015741, 15832
- Maternal Opioid Treatment: Human Experimental Research (MOTHER) Site PIs and investigative teams



Slide 1 Credits: "Husband And Pregnant Wife" by David Castillo Dominici; "Side View Of Pregnant Woman" by Imagerymajestic; "Mother Is Reading A Book For Her Baby" by Jomphong

Disclosures

- Discussing methadone and buprenorphine, labeled by the US Food and Drug Administration (FDA) as Category C for use in pregnancy for the treatment of maternal opioid dependence: "Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks."
- Pregnant women with opioid use disorders can be effectively treated with methadone or buprenorphine. Both these medications should not be considered "off-label" use in the treatment of pregnant patients with opioid use disorder [Jones et al., *Am J Obstet Gynecol.* 2014]
- Reckitt-Benckiser Pharmaceuticals for donated active placebo tablets and reimbursement for time and travel in 2011.

Objectives

1. Participants will review the historical and current contexts of opioid use by pregnant women
2. Participants will compare and contrast the risks and benefits of methadone and buprenorphine given during pregnancy for the fetus, child, and mother
3. Participants will identify treatment components for comprehensive treatment programs that provide medication-assisted treatment

Outline



- ♦ Context of Opioid Use during Pregnancy
 - Historical
 - Current
- ♦ Pharmacotherapy for Pregnant Women with Opioid Use Disorders
 - Methadone
 - Buprenorphine
- ♦ Treatment Components for Medication-assisted Treatment
- ♦ UNC Horizons: Women-centered comprehensive care focusing on mother and child

Credit: Public domain image domain by Greyerbaby

Historical Context of Opioid Use during Pregnancy

Substance use during pregnancy in the USA has been a long-standing important health issue. In the 1800s:

- 66–75% of individuals with opium use disorders were women
- Women's most common opium source was medical prescriptions to treat pain
- Physicians recognized neonatal opioid withdrawal and the need to treat in utero opium exposure with morphine in order to prevent morbidity and mortality
- ♦ Following the 1914 Harrison Narcotic Act, the treatment of substance use disorders was segregated from mainstream medical practice

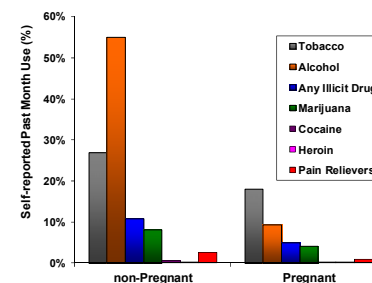


Credit: Still from *The Dividend*, 1916. public domain.

(Kandall, *Substance and shadow*, 1996. Earle, *Medical Standards*, 1888.)

Current Context of Opioid Use during Pregnancy

National Survey on Drug Use and Health 2011-2012
Past Month Use



- ♦ The two most common drugs used by non-pregnant women have been alcohol and tobacco
- ♦ This same statement is true for pregnant women
- ♦ Among pregnant women in the United States, approximately 18% smoked cigarettes, 9.4% drank alcohol, and 5% used illicit drugs in the past month
- ↳ Among pregnant women, approximately .2% used heroin, and .9% used pain relievers non-medically in the past month

(SAMHSA Office of Applied Statistics, 2011-2012)

13 Current Context of Opioid Use during Pregnancy

◆ Neonatal Abstinence Syndrome (NAS) often results when a pregnant woman uses opioids (e.g., heroin, oxycodone) during pregnancy.

◆ Defined by alterations in the:

- **Central nervous system**
 - high-pitched crying, irritability
 - exaggerated reflexes, tremors and tight muscles
 - sleep disturbances
- **Autonomic nervous system**
 - sweating, fever, yawning, and sneezing
- **Gastrointestinal distress**
 - poor feeding, vomiting and loose stools
- **Signs of respiratory distress**
 - nasal stuffiness and rapid breathing

➤ NAS is not Fetal Alcohol Syndrome (FAS)

➤ NAS is treatable

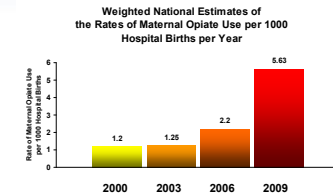
➤ There are no known long-term consequences from having NAS or being treated for NAS

(Finnegan et al., *Addict Dis.* 1975; Desmond & Wilson, *Addict Dis.* 1975)

14 Current Context of Opioid Use during Pregnancy

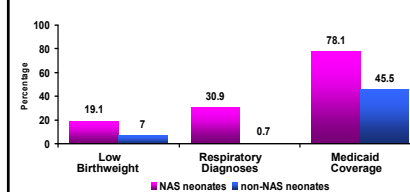
Neonatal Abstinence Syndrome and Associated Health Care Expenditures United States, 2000-2009

- A retrospective, serial, cross-sectional analysis of a nationally representative sample of newborns with NAS.
- Clinical conditions were identified using ICD-9-CM diagnosis codes.
- NAS and maternal opiate use were described as an annual frequency per 1000 hospital births.

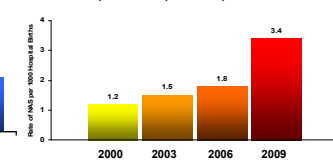


in the United States – one infant every hour – suffers from neonatal abstinence syndrome (NAS)

Low Birthweight, Respiratory Diagnoses, and Medicaid Coverage in 2009



Weighted National Estimates of the Rates of NAS per 1000 Hospital Births per Year



15 Current Context of Opioid Use during Pregnancy

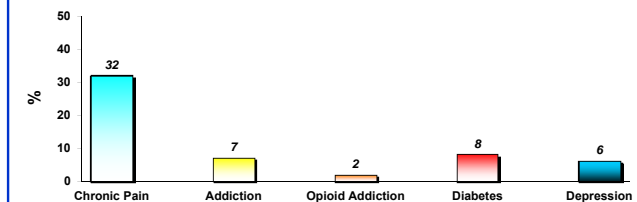
In the US, it is estimated that:

- 100 million people have chronic pain
- 22 million are living with addiction, and of those individuals

↳ 7 million misuse prescription medications

16 Current Context of Opioid Use during Pregnancy


Percentage of US Population Estimated to Have the Disorder



17 Current Context of Opioid Use during Pregnancy

Why are more individuals, including pregnant women, using opioids?

- There has been an increase in the access to these medications
- Pain became the 5th vital sign in the early 21st century
- Federal prosecutors allege in documents filed in U.S. District Court that Chris and Jeff George from Florida dramatically increased the numbers of pain clinics in Florida and routed opioid pain medications to Kentucky, Ohio and South Carolina

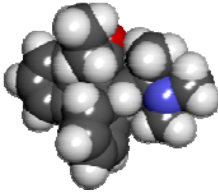


Credit: "Back Pain During Pregnancy" by Imagerymajestic

18 Summary of Historical and Current Context

- Although less frequent than alcohol and tobacco use, opioid misuse during pregnancy is nonetheless a serious and growing issue
- This increase in use of opioids by pregnant women appears to be driving an increase in the incidence of neonatal opioid withdrawal
- Opioid use by pregnant women is often complicated by polydrug use, and often occurs intertwined with complex personal, interpersonal, family, social, and environmental factors that can contribute to adverse consequences
- Women have unique needs for addiction treatment and multi-faceted interventions are needed to help prevent and treat opioid-dependence among women during pregnancy and their infants

19 Pharmacotherapy for Opioid Dependence




- Prevention of erratic maternal opioid levels lessens fetal exposure to repeated withdrawal episodes
- Reduces maternal craving and fetal exposure to illicit drugs
- With drug abstinence, other behavior changes can follow which decrease risks to mother fetus of infection from HIV, hepatitis and sexually transmitted infections
- Reduces the incidence of obstetrical and fetal complications and improves outcomes

Credit: Image in the public domain by SubDural12 (Review in Kaltenbach et al., *Obstet Gynecol Clin North Am*, 1998.)

20 Current Context of Opioid Use during Pregnancy

Issues facing drug-using pregnant women and their children

- Exposure to violence and trauma
- Generational drug use
- Lack of formal education
- Lack of job acquisition and maintenance skills
- Gender inequality/male-focused society
- Legal involvement
- Multiple drug exposures
- Limited parenting skills and resources
- History of child abuse and neglect
- Multiple psychiatric issues
- Unstable housing
- Lack of positive and supportive relationships
- Food insecurity and lack of nutrition



→ *These factors with or without drug use can influence mother and child outcomes*

Credit: "Stress Definition Indicates Explanation Pressures And Tension" by Stuart Miles

21 **Role of Medication-assisted Withdrawal**

NIDA's 13 Principles of Effective Treatment:

- 1) Addiction is a complex but treatable disease that affects brain function and behavior.
- 2) No single treatment is appropriate for everyone.
- 3) Treatment needs to be readily available.
- 4) Effective treatment attends to multiple needs of the individual, not just drug abuse.
- 5) Remaining in treatment for an adequate period of time is critical.
- 6) Behavioral therapies—including individual, family, or group counseling—are the most commonly used forms of drug use treatment.
- 7) Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies.
- 8) An individual's treatment and services plan must be assessed continually and modified as necessary to ensure that it meets his or her changing needs.
- 9) Many drug-addicted individuals also have other mental disorders.
- 10) Medically assisted detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug abuse.
- 11) Treatment does not need to be voluntary to be effective.
- 12) Drug use during treatment must be monitored continuously, as lapses occur.
- 13) Treatment programs should test patients for infectious diseases and provide targeted risk-reduction counseling, linking patients to treatment if necessary.

22 **Maintenance v. Medication-assisted Withdrawal**

- WHO 2014 Guidelines: "Pregnant women dependent on opioids should be encouraged to use opioid maintenance treatment whenever available rather than to attempt opioid detoxification. Opioid maintenance treatment in this context refers to either methadone maintenance treatment or buprenorphine maintenance treatment."
- Guidance regarding maintenance versus medication-assisted withdrawal has traditionally been based largely on good clinical judgment
- Medication followed by no medication treatment has frequently been found to be unsuccessful, with relatively high attrition and a rapid return to illicit opioid use
- Maintenance medication facilitates retention of patients and reduces substance use compared to no medication
- Biggest concern with opioid agonist medication during pregnancy is the potential for occurrence of neonatal abstinence syndrome (NAS) – a treatable condition

23 **Why Use Opioid Medications?**

With opioid medications we are not replacing one addiction for another. Opioid medications are long-acting medication that help with:

- ✓ CRAVING
An individual's cravings are controlled
- ✓ COMPULSION
Individual is no longer compulsively using opioids
- ✓ CONTROL
Medication-assisted treatment gives back control to the individual
- ✓ CONSEQUENCES
Medication assisted treatment helps the individual focus on rebuilding her life

➔ *An individual receiving opioid pharmacotherapy must be monitored by a medical team that evaluates adequacy of medication dosage and general health and well-being of the individual.*

24 **Methadone: Dosing during Pregnancy**



- In the 1970s, a positive relationship between maternal methadone dose and NAS severity was reported
- Recommendations to maintain pregnant women on methadone doses between 20 to 40 mg
- 3 decades of research shows an inconsistent relationship between maternal methadone dose and NAS severity
- The latest systematic review and meta-analysis concluded that the "Severity of the neonatal abstinence syndrome does not appear to differ according to whether mothers are on high- or low-dose methadone maintenance therapy."

(Review in Cleary et al., *Addiction*, 2010)

25 **Methadone: Dosing during Pregnancy**

Split Dosing

- Maternal Results
 - increase drug negative urines during treatment
 - Increased adherence with treatment
 - decrease withdrawal symptoms in mother
 - No change in maternal heart rate, vagal tone or skin conductance
- Fetal Results
 - Minimizes the reduction in breathing
 - Minimizes the reduction in movement
 - Fetal movement-fetal heart rate coupling less suppressed





(DePetrillo et al., 1995; Swift et al., 1989; Wittmann et al., 1991; Jansson et al., 2009; McCarthy)
Credit: "Human Fetus" by ddpavumba; "Smiling Pregnant Female Holding Her Tummy" by Imagerymajestic

26 **Methadone: NAS**

Methadone-associated NAS

NAS signs	55-90%
Requiring medication	~ 60%
NAS appears	45 to 72 hrs
NAS peaks	40 to 120 hrs




- Most common medication for treatment is morphine
- Most common assessment tool is a "modified" Finnegan scale
- No current standard uniform protocol for treatment

Credit: "Sleeping Asian Baby" by hin255

27 **Methadone: Breastfeeding**

Breastfeeding in Methadone-Stabilized Mothers

- Methadone detected in breast milk in very low levels
- Methadone concentrations in breast milk are unrelated to maternal methadone dose
- The amount of methadone ingested by the infant is low
- The amount of methadone ingested by the infant remains low even 6 months later
- Several studies show relationships between breastfeeding and reduced NAS severity and duration
- Hepatitis C is not a contraindication for breastfeeding
- Contraindications: HIV+, unstable recovery




(D'Apollito, 2013; AAP 2012; McQueen et al., 2011; Jansson et al., 2007; Jansson et al., 2010)
Credit: "Mother Is Breast Feeding For Her Baby" by Jomphong

28 **Methadone: Child Development**

Research focusing on the effects of prenatal exposure to methadone has been inconsistent

- Long-term effects on physical growth have not been demonstrated
- Although some research has shown that methadone-exposed school-age children to be less interactive, more aggressive, and showing poorer achievement than children not so exposed, other research has failed to show any differences in either cognitive or social development
- The issue is confounded by the fact that children exposed to methadone in utero may experience a nutritional, family, and parenting history quite different than children not so exposed
- 2014 meta-analysis showed "no significant impairments for cognitive, psychomotor or observed behavioural outcomes for chronic intra-uterine exposed infants and pre-school children compared to non-exposed infants and children."



(Baldacchino et al., BMC Psychiatry 2014; Behnke et al., Pediatrics, 2013; Farid et al., Curr Neuropharm, 2008)
Credit: "Lady Doctor Measuring Girls Height" by David Castillo

29 **Methadone: Summary**

50 years of documented benefits of methadone during pregnancy

- Induction is relatively simple
- Adequate doses are needed to prevent withdrawal and other opioid use
- Indicators of fetal well-being are less compromised with split-dosing
- NAS is worse with heavier smoking
- Breastfeeding is compatible with methadone

(Reviews in Jones et al., *Drugs*, 2012, and *Addiction*, 2012)

30 **Buprenorphine**

- A derivative of the opioid alkaloid thebaine
- Schedule III opioid
- μ -opioid receptor partial agonist
- primarily antagonistic actions on κ -opioid and δ -opioid receptors
- Half-life estimated to fall in the range of 24-60 hours

(Reviews in Jones et al., *Drugs*, 2012, and *Addiction*, 2012)

31 **Buprenorphine and Pregnancy**

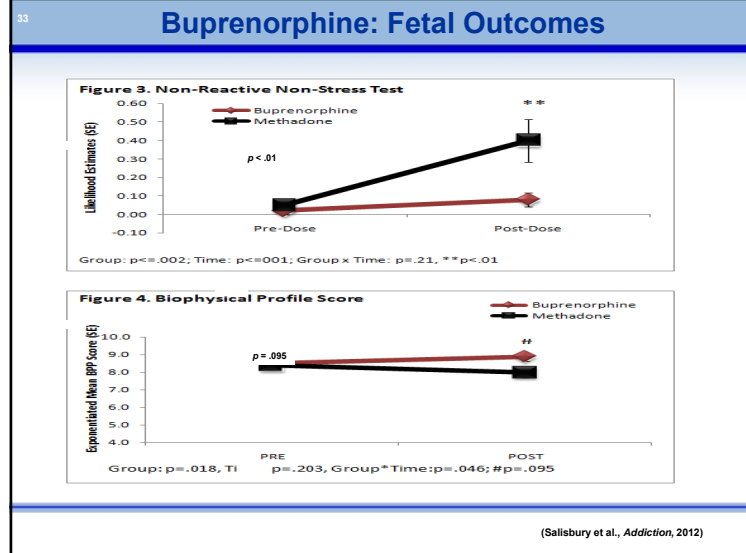
- Since 1995, over 40 published reports of prenatal exposure to buprenorphine maintenance
- Approximately 750 babies prenatally exposed to buprenorphine (number of cases per report ranged from 1 to 159; *Median*=14)
- Dose range 0.4 to 32 mg
- 88% reported concomitant drug use

(Reviews in Jones et al., *Drugs*, 2012, and *Addiction*, 2012)


32 **Buprenorphine: Maternal Outcomes**

- ✦ Research with buprenorphine not as extensive as with methadone
- ✦ Well-tolerated and generally safe
- ✦ In contrast to the research with methadone, little research has compared buprenorphine to an untreated control group
- ✦ Rather, buprenorphine has been compared in both retrospective and prospective studies to methadone
- ✦ Majority of research would suggest that maternal outcomes are not in any way different than for methadone

(Reviews in Jones et al., *Drugs*, 2012, and *Addiction*, 2012)



- 34 **Buprenorphine: NAS**
- Incidence rate for NAS is estimated to be 50% – about the same as for methadone
 - NAS onset approximately 48 hours
 - Peaking within approximately 72-96 hours
 - Exceptions to this onset history have been the few neonates with NAS onset of 8-10 days postnatal age
 - such a protracted withdrawal syndrome may be due to withdrawal from concomitant drug exposure (e.g., benzodiazepines) rather than a direct effect of buprenorphine withdrawal
 - Correlation between buprenorphine dose and NAS severity has been inconsistent
 - Time of first dose of NAS treatment medication has been shown to be later with buprenorphine than methadone (71 hrs vs 34 hrs, respectively)
- (Reviews in Jones et al., *Drugs*, 2012, and *Addiction*, 2012.; Gaalema et al., *DAD*, 2013)

- 35 **Buprenorphine: Breastfeeding**
- Buprenorphine is found in breast milk 2 hours post-maternal dosing
 - Concentration of buprenorphine in breast milk is low
 - Amount of buprenorphine or norbuprenorphine the infant receives via breast milk is only 1%
 - Most recent guidelines: “the amounts of buprenorphine in human milk are small and unlikely to have negative effects on the developing infant”
 - “The advantages of breast feeding prevail despite the risks of an infant opiate intoxication caused by methadone or buprenorphine.”
- 
- (Atkinson et al., 1990; Marquet et al., 1997; Johnson, et al., 2001; Grimm et al., 2005; Lindemalm et al., 2009; Jansson et al., 2009; Müller et al., 2011)
Credit: “Mother Is Breast Feeding For Her Baby” by Jomphong

- 36 **Buprenorphine: Child Development**
- Research on the neonatal consequences of prenatal exposure to buprenorphine is quite limited
 - Not enough births have been followed for a sufficient period of time to collect convincing data regarding factors such as cognitive and social development
 - Same issue of confounding parental and family factors in teasing apart developmental effect
- (Reviews in Jones et al., *Drugs*, 2012, and *Addiction*, 2012)

MOTHER: Sites

Lead Site Johns Hopkins University PI: H. Jones
 Brown University PI: B. Lester
 Thomas Jefferson University PI: K. Kaltenbach
 University of Vermont PI: S. Heil
 University of Vienna PI: G. Fischer
 University of Toronto PI: P. Selby
 Vanderbilt University PI: P. Martin
 Wayne State University PI: S. Stine
 Coordinating Center University of Maryland PI: A. Arria

MOTHER: Buprenorphine v. Methadone

- Compared with methadone-exposed neonates, buprenorphine-exposed neonates
 - Required 89% less morphine to treat NAS
 - Spent 43% less time in the hospital
 - Spent 58% less time in the hospital being medicated for NAS
- Both medications in the context of comprehensive care produced similar maternal treatment and delivery outcomes

Notes: Significant results are circled. Site was a blocking factor in all analyses. The O'Brien-Fleming α spending function resulted in $\alpha = .0091$ for the inferential tests of the Medication Condition effect for the 5 primary outcome measures at the conclusion of the trial.

(Jones et al., *N Engl J Med*. 2010)

MOTHER: Buprenorphine v. Methadone

- Clinically meaningful attrition rate in buprenorphine condition
- Low rates of illicit drug use during pregnancy and at delivery
- Maternal outcomes similar in the 2 study conditions

Note: Bonferroni's principle was used to set familywise $\alpha = .003125$ (nominal $\alpha = .05/16$) for the secondary outcome measures.

(Jones et al., *N Engl J Med*. 2010)

MOTHER: Buprenorphine v. Methadone

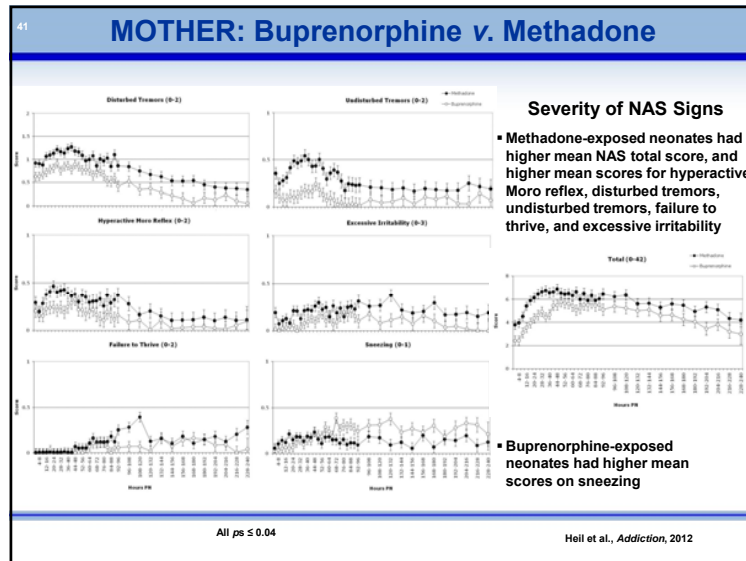
Incidence of NAS signs

N (%) of neonates who ever had a NAS score > 0

NAS sign	Methadone (n = 72)	Buprenorphine (n = 57)
NAS Total score	72 (100%)	57 (100%)
Disturbed tremors	72 (100%)	55 (97%)
Increased muscle tone	71 (99%)	57 (100%)
Sleep	65 (90%)	55 (97%)
Tachypnea	62 (86%)	51 (90%)
Fever	61 (85%)	53 (93%)
Undisturbed tremors	58 (81%)	36 (63%)
Hyperactive Moro reflex	55 (76%)	33 (58%)
Sneezing*	55 (76%)	53 (93%)
Crying	40 (56%)	32 (56%)
Excessive irritability	39 (54%)	38 (67%)
Poor feeding	39 (54%)	28 (49%)
Vomiting	38 (53%)	33 (58%)
Excoriation	34 (47%)	32 (56%)
Loose stools*	33 (46%)	40 (70%)
Nasal stuffiness*	20 (28%)	29 (51%)
Frequent yawning	15 (21%)	17 (30%)
Sweating	15 (21%)	12 (21%)
Failure to thrive	12 (17%)	7 (12%)
Generalized seizure	0	2 (4%)

*p < .02

Heil et al., *Addiction*, 2012





- 42 **Summary: Buprenorphine**
- MOTHER provided the first RCT data to support the safety and efficacy of methadone
 - Maternal outcomes are similar between medications
 - Pain management and breastfeeding recommendations are similar between medications
 - In terms of NAS severity, buprenorphine can be a front-line medication option for managing opioid-dependence for pregnant women who are new to treatment or maintained on buprenorphine pre-pregnancy
 - NAS, its treatment and elucidating factors that exacerbate and minimize it, remains a significant clinical issue for prenatally opioid-exposed neonates
 - Currently there is great variation in terms of medications and use of tools.

43 **NAS: Factors**

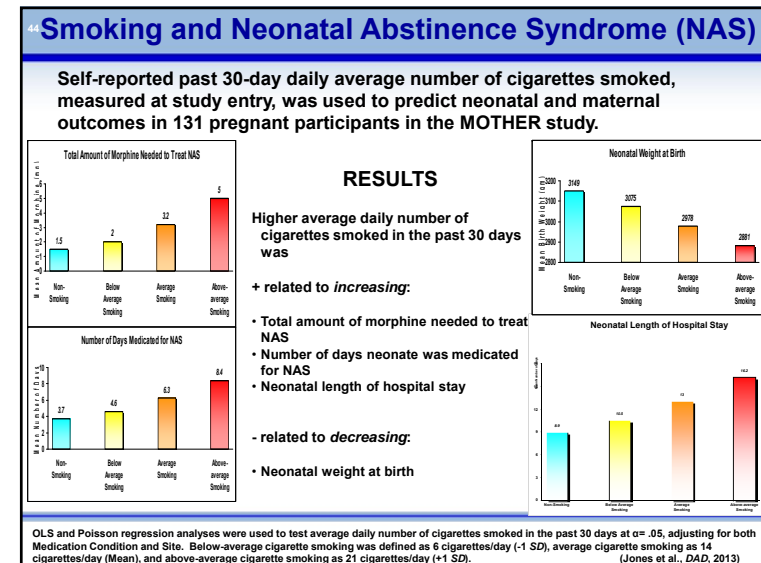
Other factors that contribute to severity of NAS in neonates exposed to opioid agonists in utero:

- **Genetics**
- **Other Substances**
 - Cigarette smoking
 - Benzodiazepines
 - SSRIs
- **Hospital Protocols**
 - The NAS assessment and medication initiation and weaning protocols
 - Not breastfeeding
 - Rooming in or separating mother and baby

(Jansson and Velez, *Curr Opin Pediatrics*, 2012)

Credit: "Woman Smoking E-cigarette" by patrisyu; "Embryonic Development" by dream designs




Benefits and Risks of Pharmacotherapy		
	Methadone	Buprenorphine
Availability	Methadone clinic	Doctor's office with an "X number"
Frequency of dosing	daily	daily
Abuse liability	abused	abused
Cost	\$	\$\$
Reduced HIV drug risk behaviors	♣	♣
Greater birthweight than no treatment	♣	♣
Recommended for pregnancy	♣	♣
Independent replication of results	♣	♣
Fetal behavior	♣ (with split dosing)	♣
Neonatal Abstinence Syndrome	♠	♠

Program Components for Women	
<ul style="list-style-type: none"> Considers the needs of women in all aspects of program design and delivery, including location, staffing, program development, program content, and program materials Provides safe and comfortable environments in which women develop supportive relationships that allow them to address their recovery needs Services need to include: <ul style="list-style-type: none"> Outreach and engagement Screening Detoxification Crisis intervention Assessment Treatment planning Case management 	
<ul style="list-style-type: none"> Substance use counseling and education Trauma specific and informed services Medical and mental health care Pharmacotherapy Drug monitoring Continuing care 	
<p>→ Program should be accredited by an outside body like CARF or JHACO</p>	

UNC Horizons Program

Where women and their children find



.... *Help*
... *Hope*
... *Healing*

UNC Horizons Program

UNC Horizons' mission is to provide world class empowering and transformative interdisciplinary care to women and their children affected by substance use disorders

49 **UNC Horizons Program**

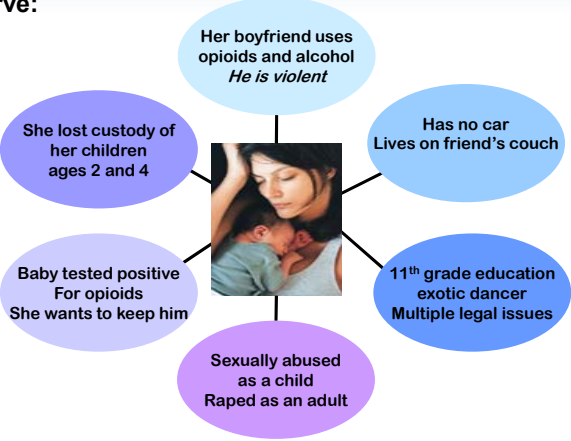
Who We Serve:

Last year we treated 233 women, including 57 women with 66 children in our residential program and 45 women in our prenatal clinic.

- 100% are covered by Medicaid or are uninsured
- 33% have less than a high-school education
- ~40% pregnant at intake
- ~90% have at least one child under 18 (majority under 2)
- Over 50% of those women with children have had recent Child Protective Services (CPS) involvement

50 **UNC Horizons Program**

Who We Serve:



Her boyfriend uses opioids and alcohol
He is violent

She lost custody of her children ages 2 and 4

Has no car
Lives on friend's couch

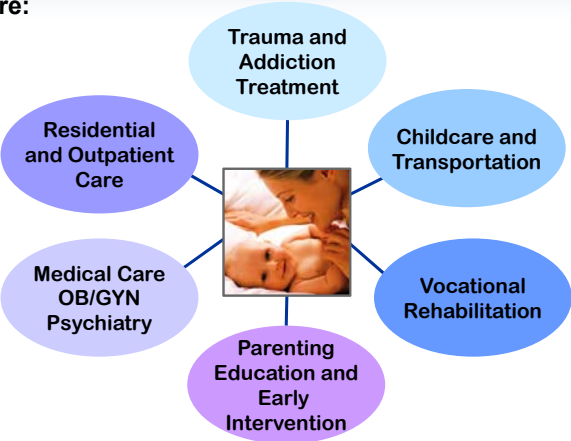
11th grade education
exotic dancer
Multiple legal issues

Sexually abused as a child
Raped as an adult

Baby tested positive For opioids
She wants to keep him

51 **UNC Horizons Program**

Model of Care:



Trauma and Addiction Treatment

Childcare and Transportation

Vocational Rehabilitation

Parenting Education and Early Intervention

Medical Care OB/GYN Psychiatry

Residential and Outpatient Care

52 **UNC Horizons Program**

- ▲ Substance Abuse Comprehensive Outpatient Treatment
- ▲ Substance Abuse Intensive Outpatient Treatment

Elements Common to both services:

- ♦ Multiple evidence-based practices
- ♦ Childcare
- ♦ Psychiatry
- ♦ Case management
- ♦ Individual counseling
- ♦ Parenting
- ♦ Crisis contingency planning
- ♦ Disease management
- ♦ Transportation
- ♦ OB/GYN care
- ♦ Peer support
- ♦ Group counseling
- ♦ Urine drug screening

53 **UNC Horizons Program**

Residential Programs

- Up to a one-year program with 6-month aftercare
- Apartments in 2 Chapel Hill complexes
- Transitional apartments
- Services:
 - ♦ Childcare services
 - ♦ Case management
 - ♦ Individual counseling
 - ♦ Urine drug screens
 - ♦ Disease management
 - ♦ Transportation
 - ♦ Peer-support
 - ♦ Parenting/ Family therapy
 - ♦ Crisis contingency plans

Goals:

- ▲ Recovery and self-care related to addiction and trauma
- ▲ Employment
- ▲ Parenting

54 **UNC Horizons Program**

Early Intervention and Therapeutic Services for Children

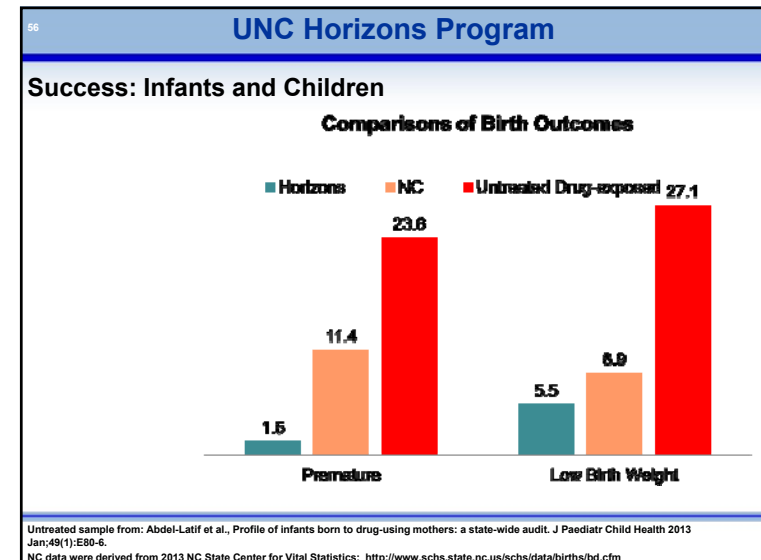
- All children receive age-appropriate mental health and social/emotional assessments; and individual, group, and/or family therapy as needed
- All children screened for speech and language, occupational therapy, physical therapy, dental, hearing and vision and referred for developmental evaluations
- About 90% of the residential children ages 0-5 qualify for and receive early intervention services

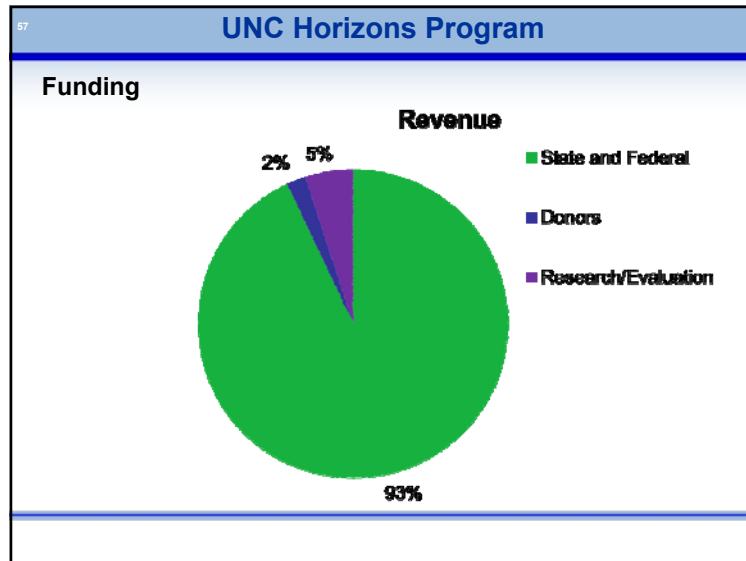
55 **UNC Horizons Program**

Success: Infants and Children

Child Protective Service Involvement:

- Outpatient women and children who complete the program: 75% of families had positive changes (e.g., closed cases, children reunited)
- Residential women and children who complete the program: 100% of families with cases had positive changes (regained custody, cases closed)





58 **UNC Horizons Program**

UNC Horizons Estimated Cost, Cost Avoidance, and Cost Savings Associated with Maternal and Child Care, 2013-2014 Fiscal Year

Outcomes	Number of Births	Number of Events	Cost of Event	Cost Savings
Child				
Premature Delivery: Delivery Cost	35	0	\$2,784	\$97,440
Premature Delivery: Hospital Care	35	0	\$19,211	\$672,385
Child Abuse/Neglect: Direct	35	0	\$28,674 lifetime	\$1,003,590 lifetime
Child Abuse/Neglect: Indirect	35	0	\$40,367 lifetime	\$1,412,845 lifetime
Foster Care	35	0	\$47,522 lifetime	\$1,663,270 lifetime
Maternal				
Preterm Delivery: Maternal	35	0	\$4,621	\$161,735
Incarceration	35	0	\$32,590 yearly	\$1,140,650 yearly
Medical care associated with intimate partner violence: rape	35	0	\$2,552 per incident	\$89,320 per incident
Medical care associated with intimate partner violence: physical assault	35	0	\$3,253 per incident	\$113,855 per incident



60 **Take-home Messages**

- ▶ Opioid addiction is a treatable illness
- ▶ Pregnant women with opioid use disorders have medication options from which to choose as a part of a comprehensive treatment program
- ▶ Women-centered treatment programs that focus on the needs of the women, her fetus, and her family offer the promise of addressing the multiple and complex needs of women with opioid use disorders

Credit: "balanced stones" by Pakhnyushchyy.

81

Resources

- ▶ <http://www.youtube.com/watch?v=3HsmuxtsBZ8>
- ▶ DRMC Neonatal Abstinence Syndrome
- ▶ <http://pcmch.on.ca/LinkClick.aspx?fileticket=JTt9lpgEbN0%3D&tabid=40>
- ▶ <http://www.neoadvances.com/index.html>
- ▶ <http://www.vtoxford.org/home.aspx>
- ▶ http://www.health.qld.gov.au/qcg/documents/g_nas5-0.pdf
- ▶ http://www.uvm.edu/medicine/vchip/documents/VCHIP_5NEONATAL_GUIDELINES.pdf
- ▶ <http://pediatrics.aappublications.org/content/101/6/1079.full>
- ▶ <http://store.samhsa.gov/product/TIP-51-Substance-Abuse-Treatment-Addressing-the-Specific-Needs-of-Women/SMA13-4426>
- ▶ <http://store.samhsa.gov/product/Methadone-Treatment-for-Pregnant-Women/SMA09-4124>

Understanding and Treating Neonatal Abstinence Syndrome

Carl Seashore, MD

Associate Professor of Pediatrics

Medical Director, UNC Nursery



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Disclosures

I have no financial disclosures (I am a pediatrician)

I **will** discuss off-label use of medications (I am a pediatrician)



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Goals

- Recognize that neonatal abstinence syndrome is an important public health problem
- Understand when and why infants may be at risk for neonatal abstinence syndrome
- Understand the approach to treatment of infants at risk for and exhibiting symptoms of neonatal abstinence syndrome



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Background

"During the past decade, narcotic addiction in the United States has reached epidemic proportions."



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Background-History

"During the past decade, narcotic addiction in the United States has reached epidemic proportions."

-Finnegan, et al, 1975

Assessment and treatment of abstinence in the infant of the drug-dependent mother. Int J Clin Pharmacology.



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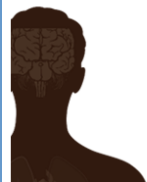


Background-Opiate explosion

Prescription Painkiller Overdoses

A growing epidemic, especially among women
July 2013

Vitalsigns™
CDC



48,000
Nearly 48,000 women died of prescription painkiller* overdoses between 1999 and 2010.



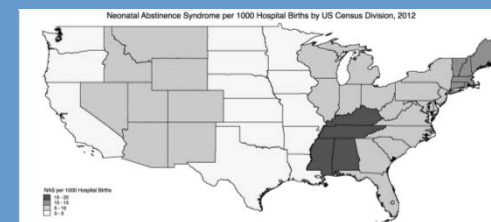
400%
Deaths from prescription painkiller overdoses among women have increased more than 400% since 1999, compared to 265% among men.



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Background-NAS



US Census Division	NAS Rate per 1000 Births (95% CI)
New England	13.7 (12.5-14.9)
Middle Atlantic	6.8 (5.8-7.8)
East North Central	6.9 (5.9-7.9)
West North Central	13.0 (11.8-14.2)
South Atlantic	16.2 (14.8-17.6)
East South Central	2.8 (2.2-3.4)
West South Central	5.1 (4.6-5.5)
Mountain	3.0 (2.7-3.3)
Pacific	2.7 (2.3-3.1)

Recent data illustrating the geographic distribution of NAS in the US.

Almost 22,000 babies:2012
Cost: \$1.5 Billion (hospital)
~80% Medicaid
More complications
Has not peaked

Patrick, et al Journal of Perinatology, 2015



Background-Treatment Team

NAS can occur in babies whose mothers are using prescribed or illicit opiates of any kind, including those on opiate replacement therapy as Dr. Jones outlined.

A **TEAM** is required to care for these families

- (ideally) Engage all players before delivery for planning
- Early testing in mother during gestation in addition to mother **AND** baby at delivery is key
- Evidence-based protocols exist for L&D and Newborn
- **Pain management plan for mother**



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Recognition-Prevention?

Screening Protocols can involve nurses and mothers

- Educating mother about NAS symptoms is empowering
- Help her (and family) help the baby
- Emphasize Non-pharmacologic treatments
- Support mom's desire to breastfeed
- Model soothing techniques



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Recognition-Parent Scoring

Date and Time			
Excessive crying	Less than 5 minutes More than 5 minutes	Sneezing Stuffy nose	More than 3 times in the past 4 hours 0-3 times in the past 4 hours
Sleepiness	None Sleeps: less than 1hr after feeding less than 2hrs after feeding less than 3hrs after feeding	Poor Feeding (not feeding often or not sucking well)	Present Not present Yes No
Tremors/Jitteriness	Mild tremors when disturbed Moderate/severe tremors when disturbed Mild tremors when UNDISTURBED Moderate/severe tremors when UNDISTURBED	Spit up Loose/Watery Stool	Yes, more than 2 times during or after a feeding Yes, projectile vomiting No, none or less than 2 times Yes No
Sweating	Present Not present	- More liquid than normal or any type of stool with a water ring on the diaper	(Save diapers for your nurse)
Yawning	More than 3 times in the past 4 hours 0-3 in the past 4 hours		



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Recognition-Tools

Use a standard screening tool for at-risk infants

- Finnegan is most widely used
 - MOTHER study (NEJM, 2010) used modified Finnegan
- Lipsitz, Neonatal Withdrawal Inventory, etc
- Vermont Oxford Network
- PQCNC project underway



Management

Initiate non-pharmacologic treatment for at-risk infants

- Finnegan noted this in 1975 and it is true today
 - **Skin-to-skin, breastfeeding (if not illicit use)**
 - Swaddling, teaching parents soothing/coping
 - Minimize external stimuli - lights, TV, visitors, noise



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Management

TABLE 2 Comparison of Infants' Characteristics and Outcome of the 2 Study Groups

Characteristic	Breast Milk Group (n = 85)	Formula Group (n = 105)	P
Gestational age, wk, mean \pm SD	37.9 \pm 3.0	37.4 \pm 3.0	.246
Gestation <37 wk, n (%)	14 (16.5)	32 (30.5)	.041
Birth weight percentile, mean \pm SD	38.1 \pm 29.5	39.5 \pm 30.6	.750
Small for gestation ($<10^{\text{th}}$ percentile), n (%)	12 (14.1)	11 (10.5)	.595
Male gender, n (%)	52 (61.2)	52 (49.5)	.152
Child at risk, n (%)	27 (31.8)	72 (68.6)	$<.001$
Former case, n (%)	8 (9.4)	31 (29.5)	.001
Required treatment for NAS, n (%)	45 (52.9)	83 (79.0)	$<.001$
Required ≥ 2 medications to control NAS, n (%)	6 (7.0)	18 (17.1)	.065
Maximum dose of morphine mg/kg per day, mean \pm SD	0.57 \pm 0.22	0.59 \pm 0.22	.526
Duration of treatment, day, mean \pm SD	85.4 \pm 71.7	108.2 \pm 81.8	.185
Length of hospitalization, day, mean \pm SD	14.7 \pm 14.9	19.1 \pm 15.0	.049

Abdel-Latif et al, Pediatrics, 2006



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Management

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 - Skin-to-skin, breastfeeding (if not illicit use)
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Management

Pharmacologic treatment if symptoms/scores warrant

- Morphine oral solution is standard first-line treatment
 - Dosing regimens vary; use protocol approach
 - Range 0.24 mg/kg per day to 1.3 mg/kg per day (AAP)
 - Weight-based vs Symptom-based (MOTHER)
- Methadone used in some centers



Management

Pharmacologic treatment if symptoms/scores warrant(2)

- Escalate/Wean dosage based on scoring
- Clonidine as an adjuvant therapy (first-line use rare)
- Transition to Methadone for home care?
 - Depends on PCP, social supports
- Continue non-pharm interventions!!



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Management

Referral and Long-Term Follow-up for exposed infants

- Early Intervention, CDSA, other local resources
 - Early childhood development, ongoing "eyes" in home
 - MAT programs-mom's treatment does not end in L+D
 - We are fortunate with Horizons at UNC
 - Finding an appropriate PCP for baby



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Management

Referral and Long-Term Follow-up for exposed infants

- DSS involvement
 - This can and should be seen as supportive not punitive
 - Active illicit use should escalate involvement
 - Often past history with DSS precludes acceptance
- Preschool as child gets older



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Improvement!



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Neonatal Abstinence Syndrome: The Use of Clonidine as a Treatment Option. Laura Broome and Tsz-Yin So. NeoReviews 2011;12:e575-e584

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Effects of Breast Milk on the Severity and Outcome of Neonatal Abstinence Syndrome Among Infants of Drug-Dependent Mothers. Mohamed E. Abdel-Latif, MRCPCH, MPH, MEpi, Jason Pinner, MRCPCH, Sara Clews, RN, Fiona Cooke, RN, Kei Lui, FRACP, MD, Julee Oei, FRACP. Pediatrics 2006;117:e1163



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Pain as a 5th Vital Sign

Measuring Pain as the 5th Vital Sign Does Not Improve Quality of Pain Management

[Richard A Mularski](#), MD, MSHS,^{1,2} [Foy White-Chu](#), MD,³ [Devorah Overbay](#), MS, RN,⁴ [Lois Miller](#), PhD, RN,⁴ [Steven M Asch](#), MD, MPH,^{1,2} and [Linda Ganzini](#), MD, MPH^{5,6}



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Working with Mothers and Infants Post-Discharge

ANNE JOHNSTON, MD
*Neonatal Perinatal Medicine
Associate Professor of Pediatrics
University of Vermont*

May 13, 2015



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Children's Hospital

OBJECTIVES

- ✓ Neonatal antenatal approach to the pregnant opioid-dependent woman at the University of Vermont
- ✓ The choice of methadone for inpatient and outpatient treatment
- ✓ UVM outcomes



New York Times

In Annual Speech, Vermont Governor Shifts Focus to Drug Abuse

By Katherine O. Seelye Jan 8, 2014



UVM Children's Hospital Antenatal Visit With Neonatology

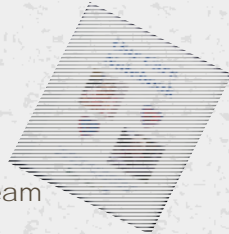
- Schedule 1 – 2 visits with NeoMed Clinic staff
- Written information (Care Notebook)
- <http://www.uvm.edu/medicine/vchip/?Page=ICONcarenotebook.html>
- Promote breastfeeding



"I SWEAR TO TELL THE TRUTH, THE WHOLE TRUTH, AND NOTHING BUT THE TRUTH, FROM MY PERSPECTIVE."

UVM Children's Hospital NeoMed Experience

- Alleviation of fear
 - Care Notebook
 - You are not alone...
 - Ask them for their stories
- Respect
 - Introductions to others on the team
 - "Tell me about yourself"
 - "What are your dreams / goals"
- Recognition of strengths
 - Hearts



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UVM Children's Hospital Why methadone for treatment of neonatal abstinence syndrome?

- Decreased frequency of dosing
- Less respiratory depression
- Less need for adjustment of dose

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UVM Children's Hospital Benefits /risks of newborn outpatient treatment program with methadone

Benefits

- Length of stay reduced
- Slow wean of methadone reduces symptoms of withdrawal
- Allows for more breastfeeding success
- Empowers family

Risks

- Safety concerns – overdose to baby, use by others
- Long half-life may lead to "overmedication" in hospital
- Often prolonged course – are we treating normal baby irritability with methadone?

UVM Children's Hospital Inpatient treatment with methadone

- Initial dose 0.3 mg q12h to 0.6 mg q12h depending upon severity of symptoms
- Watch for lethargy!!!
- Stable dose for at least 48 hours prior to discharge
- Extensive family teaching regarding measurement of methadone dose

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UVM Children's Hospital Administration of methadone



Infrastructure: what works in Vermont

- Clinic staff with ability to "track infants down"
- Close relationships with obstetrics, substance abuse treatment providers, WIC, child protective services and home health nursing
- Single pharmacy to dispense methadone



NeoMed Clinic Staff



Nurse Clinician



Medical Assistant



Nurse Practitioner



Neonatal Fellow



Neonatologist



UVM Children's Hospital NeoMed

- ❑ First NeoMed clinic visit within 1 week of discharge
- ❑ Infants requiring medication for NAS are seen at least every 2 weeks
- ❑ Infants not requiring treatment follow up monthly for the first 4 months, then every 2-4 months until 12-18 months
- ❑ Bayley III Scales at 8-10 months
- ❑ Hepatitis C antibody at 18 months for exposed infants
- ❑ Multidisciplinary approach involving primary care provider, home health, early intervention, ChARM team, and maternal substance abuse provider



UVM Children's Hospital NeoMed clinic visits for infants on methadone

- 1st visit within 1 week to 10 days (usually no weaning before 1st visit)
- Must bring methadone to clinic visit, document amount remaining
- Caregiver demonstrates with syringe and air how much methadone they are administering
- Have caregiver demonstrate other doses
- Review storage, need for additional syringes, who is measuring and administering medicine



UVM Children's Hospital Agree on methadone weaning plan

- Review symptoms of "withdrawal" if any
- "Usual weans"
 - 0.02 mg every Monday and Thursday OR
 - 0.02 mg every Monday
- Provide written schedule for the weaning
- If any change in weaning schedule – first discuss with clinic



UVM Children's Hospital Sample methadone weaning schedule

Instructions:

Remember to bring your baby's methadone to each clinic visit

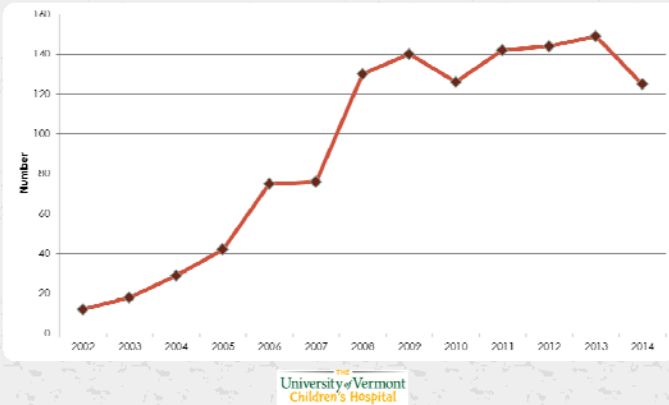
Day of the week	Date	Med	Dose	Frequency
Monday	2/4/13	Methadone dose (ml)	0.24	2x/day
Thursday	2/7/13	Methadone dose (ml)	0.22	2x/day
Monday	2/11/13	Methadone dose (ml)	0.2	2x/day
Thursday	2/14/13	Methadone dose (ml)	0.18	2x/day
Monday	2/18/13	Methadone dose (ml)	0.16	2x/day
Thursday	2/21/13	Methadone dose (ml)	0.14	2x/day
Monday	2/25/13	Methadone dose (ml)	0.12	2x/day
Thursday	2/28/13	Methadone dose (ml)	0.1	2x/day

UVM Children's Hospital Prescribing and dispensing methadone

- Use only one concentration (1 mg/mL)
- Use only one pharmacy
- Amount prescribed: 3 – 4 weeks
- We dispense in syringe connected to another syringe
- Recommend lock-box / lock-bag to store methadone

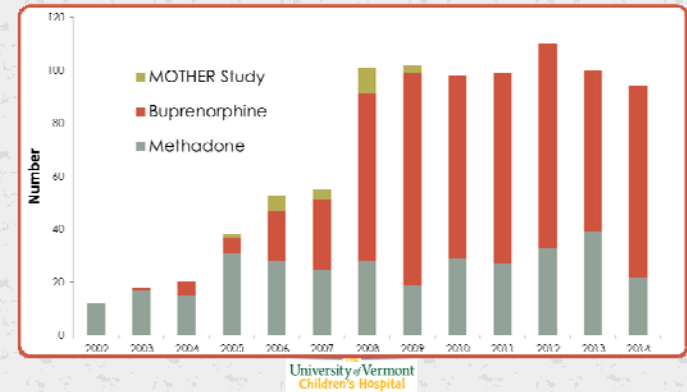


Total Opioid-exposed Newborns Followed at UVM Children's Hospital (1,208 newborns)



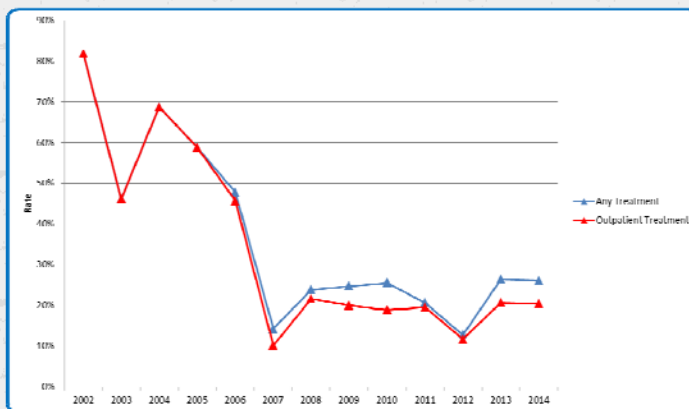
UVM Children's Hospital:

Infants born to opioid dependent women with substance abuse on methadone or **buprenorphine** at delivery (N = 876)



UVM Children's Hospital

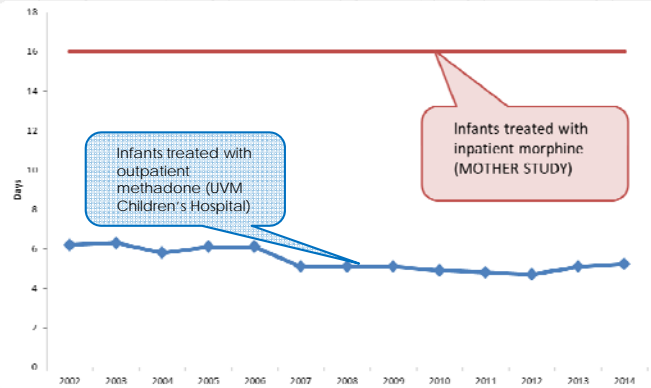
% Infants who received pharmacologic therapy



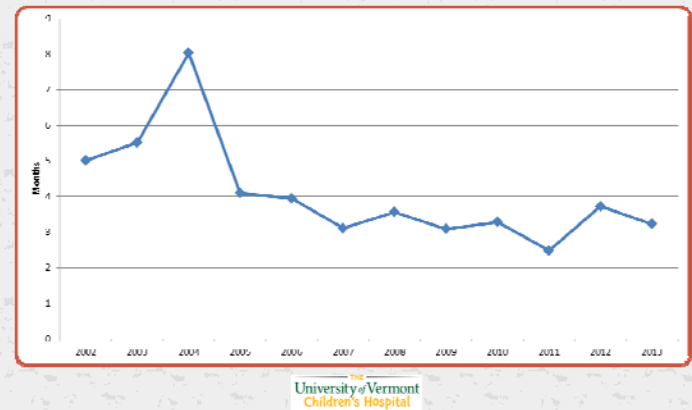
Why did pharmacologic treatment for NAS decrease?

- Better use of non-pharmacologic treatment
- Less subjectivity in NAS scoring
 - Through participating in MOTHER study
 - Decreased assumption of need for treatment
- Over time, the proportion of buprenorphine-treated pregnant women increased

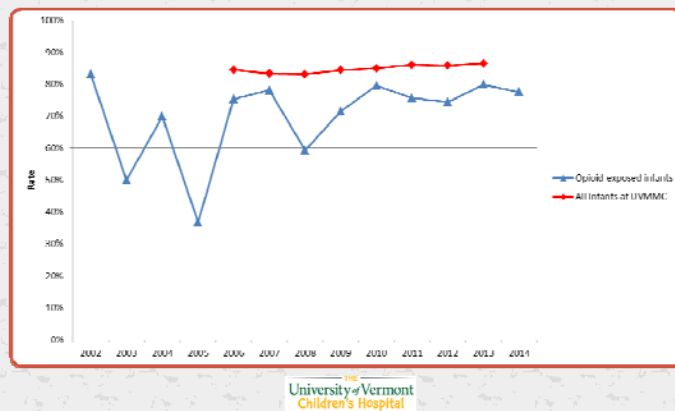
Mean Length of Hospital Stay



UVM Children's Hospital Mean Length of Infant Outpatient Treatment with Methadone

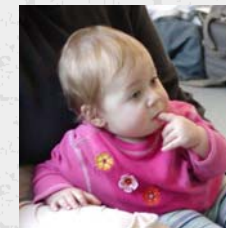


UVM Children's Hospital Breastfeeding at discharge



University of Vermont Children's Hospital: Bayley III Composite Scores at 7-14 months* (N=166)

	Cognitive	Language	Motor
Mean	107.8	105.4	104.7
Percentile Rank	66.3	62.7	60.0



* Term infants born at UVM Children's Hospital

UVM Children's Hospital
Deaths < 2 years of age
1,208 Opioid-exposed Newborns (2000 -2014)

#	Date of Death	Age @ Death	Cause of Death
1	05/2004	5 days	Shared sleeping
2	04/2006	4 months	SIDS
3	12/2008	6 months	Motor Vehicle Accident
4	01/2009	4 months	Shared sleeping
5	11/2009	5 months	Shared sleeping
6	03/2010	5 months	Hypoplastic Left Heart Syndrome
7	12/2010	6 weeks	Shared sleeping
8	05/2012	8 months	Motor Vehicle Accident
9	08/2013	3 months	Shared sleeping
10	09/2013	2 months	Shared sleeping
11	09/2013	19 days	Shared sleeping
12	11/2013	1 day	Extreme prematurity
13	04/2014	14 months	Head Injury (Non-accidental)

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Outcomes

- Average length of treatment: 3.2 months (2014)
- No infant deaths from methadone overdose
- 1 infant who received prn doses – disconjugate gaze, slightly lethargic – resolved immediately when weaning schedule was adhered to
- 1 infant transitioned over to oral morphine due to parents' inability to wean methadone at a certain level
- 1 infant required overnight hospitalization due to overdose by grandmother who had not been trained



UVM Children's Hospital
Learn from our experience

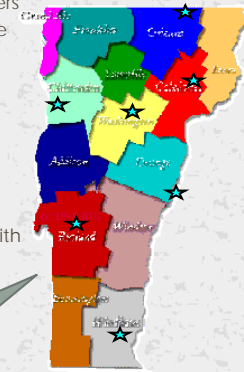
- As a rule, parents do not use their infant's methadone (they are usually on medication assisted treatment themselves)
- Beware of "prn dosing" of methadone by family
- If family cannot demonstrate the dose consistently – they may be altering the dose at their discretion
- If a spill occurs – have them take a picture with their cell phone
- Always ensure that caregiver has been trained in accurate methadone measurement
- Need to have close relationship with child protective services and be available for foster parent training



Vermont Experience: Overall

- ChARM Team: Children and Recovering Mothers
- Monthly multidisciplinary meetings with multiple agencies: impaneled
- High risk factors:
 - Increased distance to treatment center
 - Discontinuation of methadone / buprenorphine
 - Actively using partner
 - Abusive relationship with partner
- Women respond well to positive interactions with health care providers

★
methadone/buprenorphine
treatment centers



ACKNOWLEDGEMENTS

We would like to thank the infants and families we have had the pleasure of caring for – we continue to learn from them daily.



Children's Hospital

Discussion

Resources

3-Part Webinar Series

Medication Assisted Treatment for Families Affected by Substance Abuse Disorders

<http://www.cffutures.org/presentation/webinars/medication-assisted-treatment-families-affected-substance-abuse-disorders>

Medication Assisted Treatment During Pregnancy, Postnatal and Beyond

<http://www.cffutures.org/presentation/webinars/medication-assisted-treatment-during-pregnancy-postnatal-and-beyond>

Opioid Use in Pregnancy: A Community's Approach, The Children and Recovery Mothers (CHARM) Collaborative

<http://www.cffutures.org/presentation/webinars/opioid-use-pregnancy-communitys-approach-the-children-and-recovering-mothers-charm>



Contact the NCSACW for additional information:
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