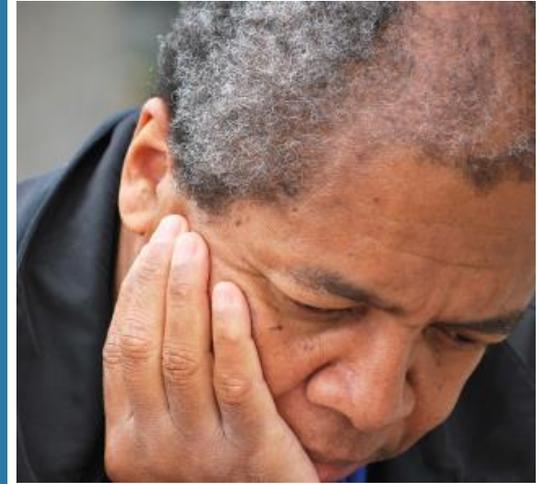


Intervening Early in the Lives of Children: Implications of Substance Exposure During Pregnancy

Hendree E Jones, PhD, September 24, 2015, and Charleston,
West Virginia



Intervening Early in the Lives of Children: Implications of Substance Exposure During Pregnancy



Hendrée E. Jones, PhD

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Objectives

- 1. Participants will compare and contrast the ways neonatal opioid withdrawal is identified, assessed, and treated**
- 2. Participants will identify different evidence-based strategies to help support resilience among children who have been prenatally opioid-exposed**

Neonatal Opioid Withdrawal: Early History

- 1875 to 1900 multiple reports of congenital morphinism – most died, no specific treatment offered
- 1903 report about congenital morphinism –treated infant with morphine

Queries and Minor Notes.

JAMA, 1903

ANONYMOUS COMMUNICATIONS will not be noticed. Queries for this column must be accompanied by the writer's name and address, but the request of the writer not to publish his name will be faithfully observed.

FETAL MORPHIIN ADDICTION.

COLORADO, April 10, 1903.

To the Editor:—Concerning a very peculiar case in my regular work I wish a little information: April 3 I delivered a multipara of a nine pound boy. The mother had been addicted to the use of morphin for the past three years. The child appeared to be healthy and perfect in every respect with excretions normal. On the second day it began to cry, and cried continuously for two days and nights despite the free use of paregoric. At the end of that time the baby had become so weak that I was unable to give it any

Timeline of Neonatal Opioid Withdrawal History

- **1964 Methadone introduced as pharmacotherapy**
- **1965 Goodfriend et al. report neonatal withdrawal signs**
- **1971 Zelson et al reported frequency of signs on neonatal withdrawal in 259 of 384 infants born to drug-abusing mothers**
- **1975 Desmond and Wilson publish Neonatal Abstinence Syndrome: Recognition and Diagnosis**
- **1975 Finnegan et al. publish a neonatal abstinence syndrome tool**

NOWS: Signs and Symptoms

- **Signs of withdrawal typically start after 24-96 hours after birth depending upon the specific opioid exposure**
- **Central nervous system signs**
 - Tremors
 - Irritability, high-pitched crying
 - Sleep disturbances
 - Tight muscles tone, hyperactive reflexes
 - Myoclonic jerks (sometimes misinterpreted as seizures), seizures - rare
- **Autonomic signs**
 - Sweating, fever, yawning and sneezing
 - Rapid breathing, nasal congestion
- **Gastrointestinal signs**
 - Poor feeding, vomiting and loose stools or diarrhea

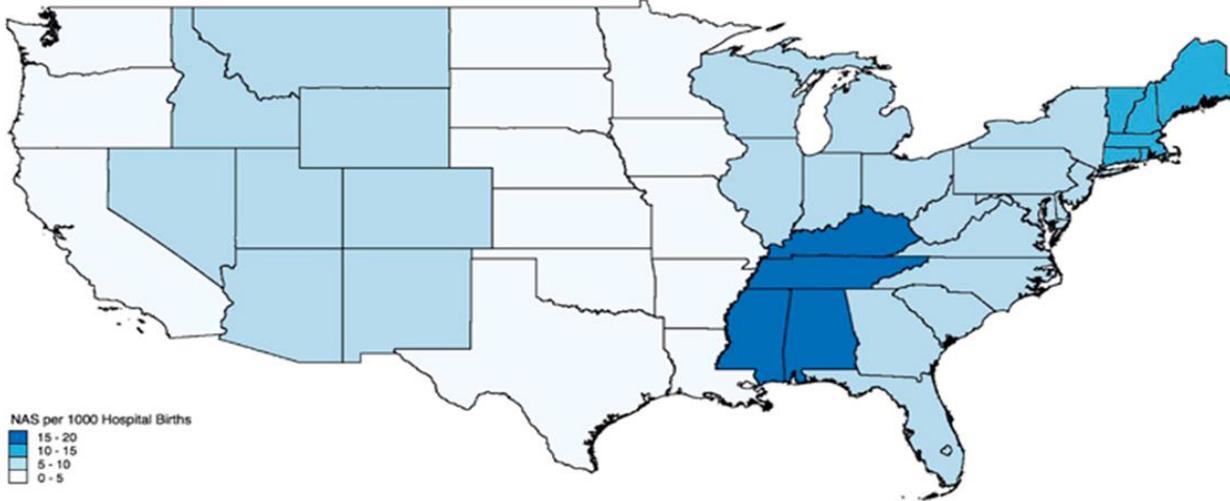
NOWS: Untreated

What would happen if NOWS is untreated?

- **Depends upon the severity**
- **There are many infants who do not receive medication for NOWS and their outcome is good**
- **However, an irritable, crying baby who does not sleep and cannot feed will be at risk for**
 - **Dehydration**
 - **Abusive trauma**
 - **Interrupted attachment and maybe failure of attachment**
- **Excessive irritability and dehydration are very likely to lead the caregiver to seek medical attention**
- **An infant may die without treatment – however, in an extensive literature search, the only reported deaths occurred over 100 years ago**
- **NOWS does not necessarily lead to poor neurodevelopmental outcomes**

NOWS: Increasing in the USA

Neonatal Abstinence Syndrome per 1000 Hospital Births by US Census Division, 2012



NAS per 1000 Hospital Births

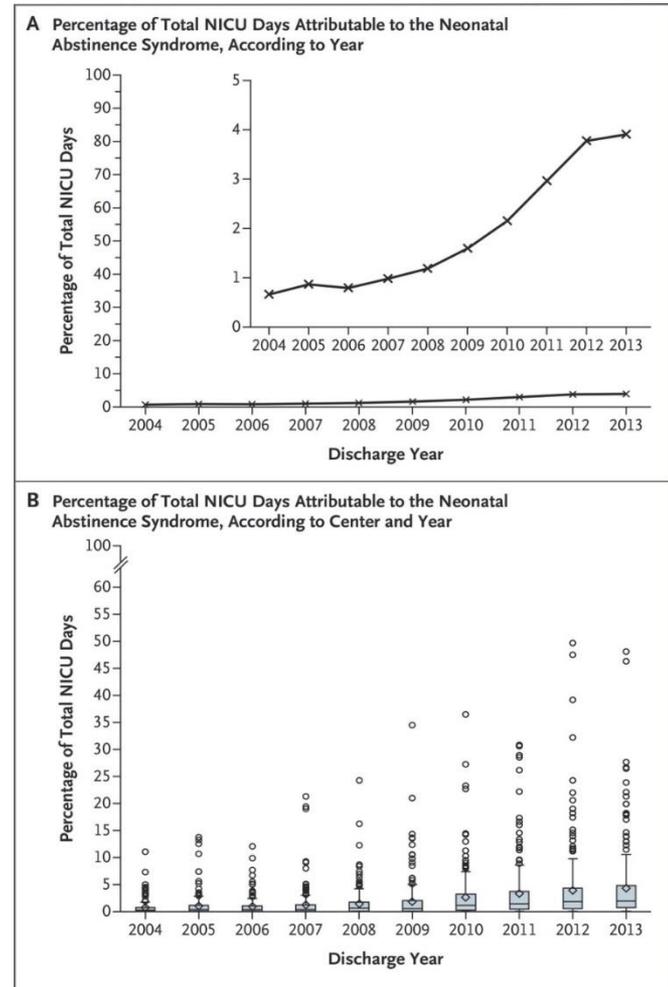
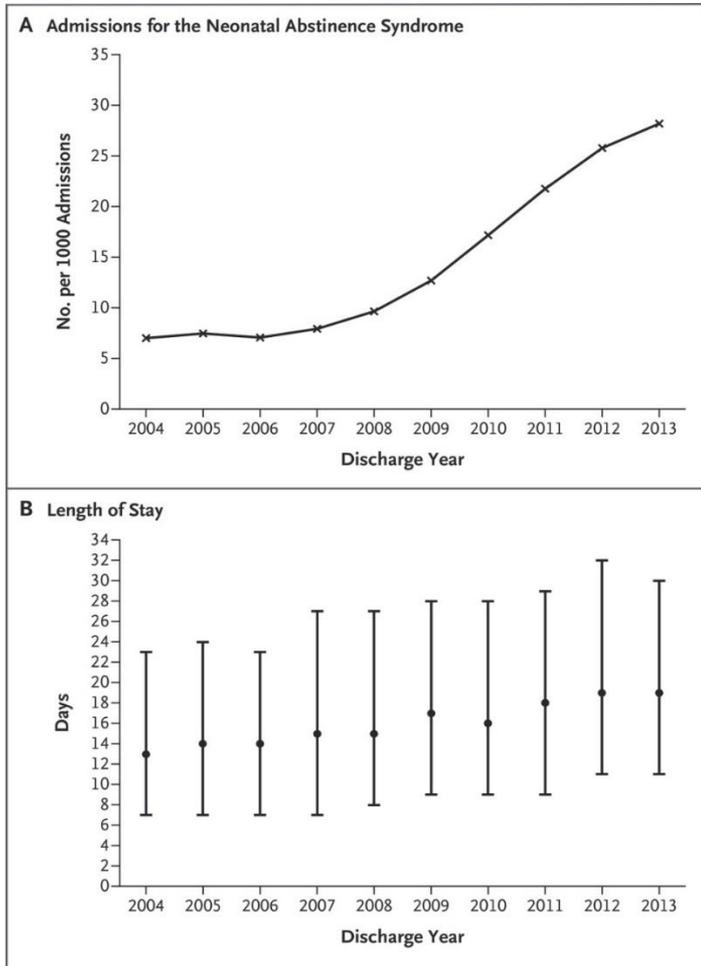
- 15 - 20
- 10 - 15
- 5 - 10
- 0 - 5

2012:

- **21,732 newborns**
- **~\$1.5 billion**
- **81.5% Medicaid**
- **↑ complications**

US Census Division	NAS Rate per 1000 Births (95% CI)
New England	13.7 (12.5-14.5)
Middle Atlantic	6.8 (5.9-7.6)
East North Central	6.9 (6.0-7.8)
West North Central	3.4 (3.0-3.8)
South Atlantic	6.9 (6.3-7.4)
East South Central	16.2 (12.4-18.9)
West South Central	2.6 (2.3-2.9)
Mountain	5.1 (4.6-5.5)
Pacific	3.0 (2.7-3.3)

NOWS: Increasing Admissions



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**

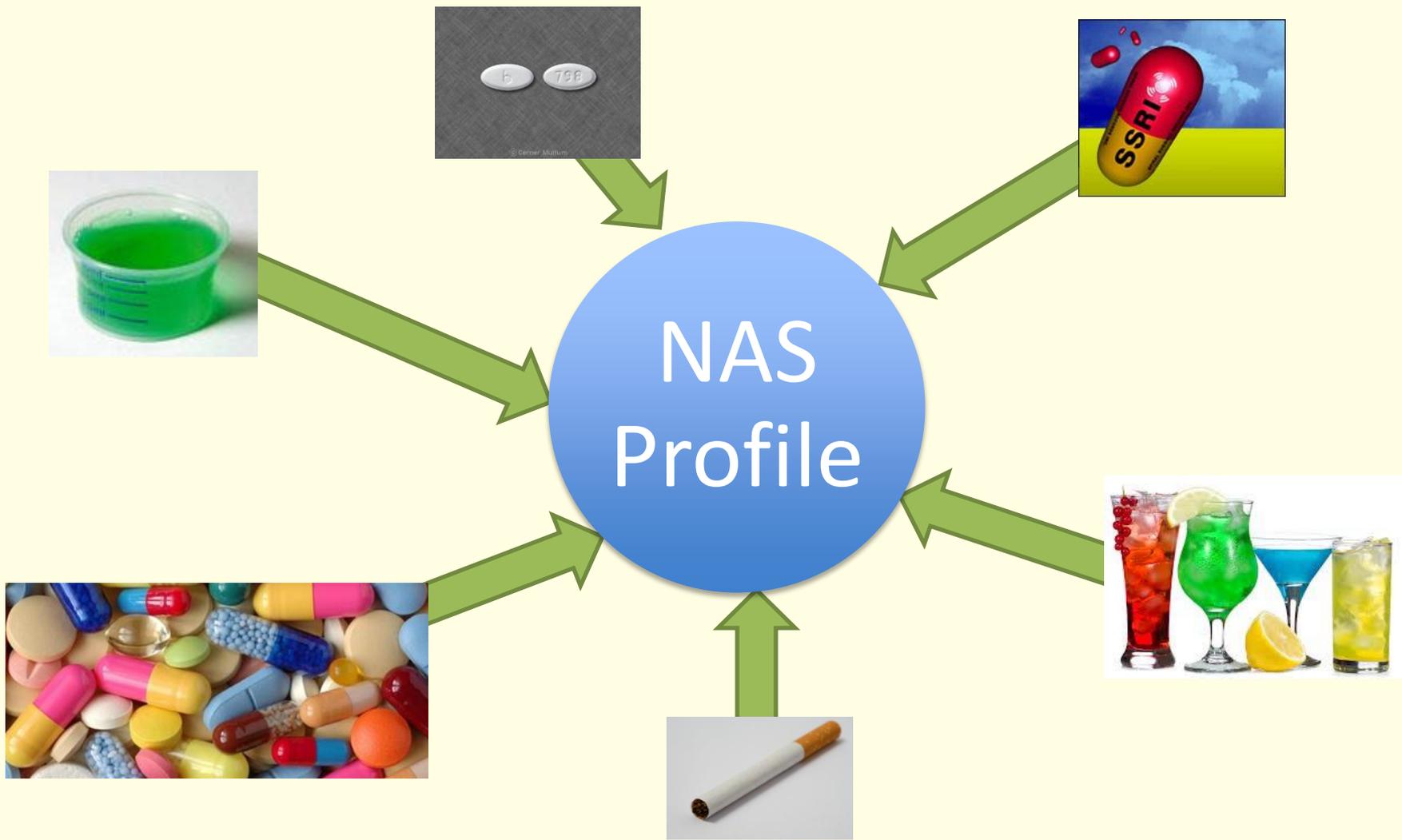
- The NAS assessment and medication initiation and weaning protocols
- Not breastfeeding
- Rooming in or separating mother and baby



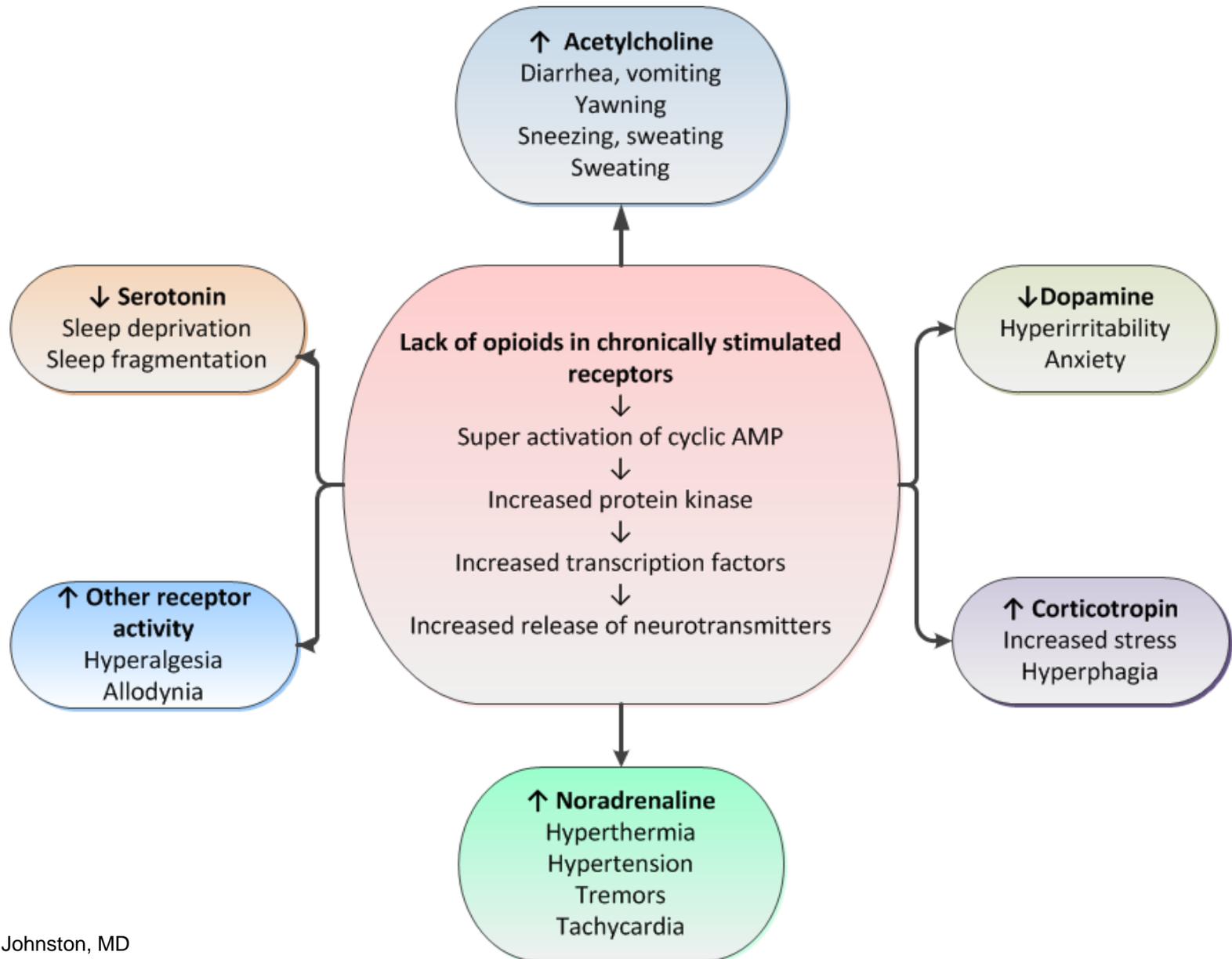
MOTHER: NAS Predictors

- **53% of the total sample required treatment for NAS**
- **Receipt of NAS treatment for infants was predicted by:**
 - **infant birthweight**
 - **greater maternal nicotine use**
- **Total medication dose needed to treat NAS was predicted by:**
 - **Maternal use of SSRIs**
 - **higher nicotine use**
 - **fewer days of study medication received also predicted.**
- **No variables predicted length of treatment for NAS**

NAS ≠ NAS ≠ NAS



Pathophysiology of Neonatal Opioid Withdrawal



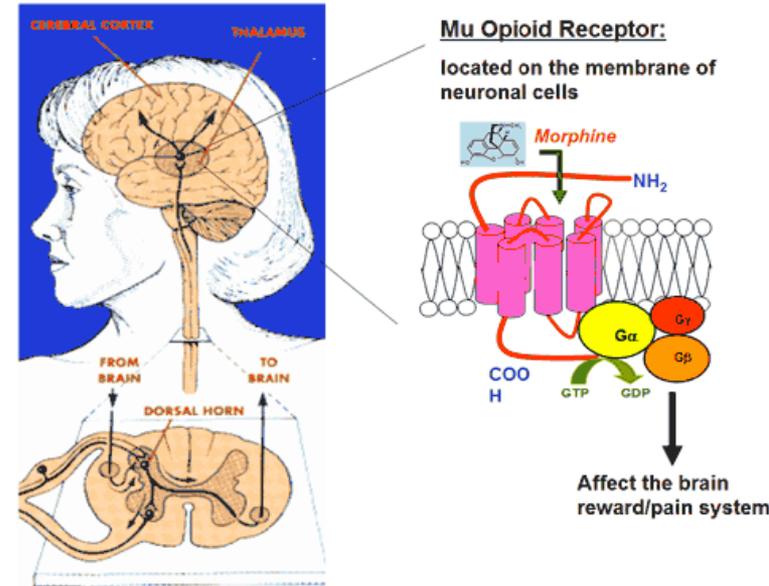
Credit: Anne Johnston, MD

Adapted from Prabhakar Kocherlakota Pediatrics 2014;

NAS: Factors

A study of newborns with NAS found a relationship between allelic variants of OPRM1 (opioid receptor μ_1), COMT (catechol-o-methyltransferase) which affect autonomic instability during withdrawal, and ABCB1 (multidrug resistance):

- Variants in the OPRM1 and COMT genes were associated with a shorter length of hospital stay and less need for treatment.
- Associations with the ABCB1 were not significant



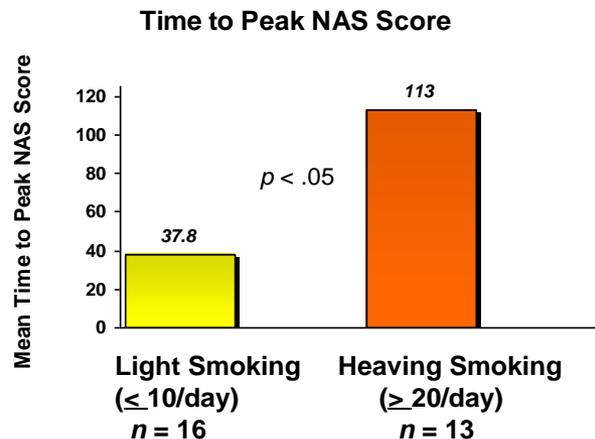
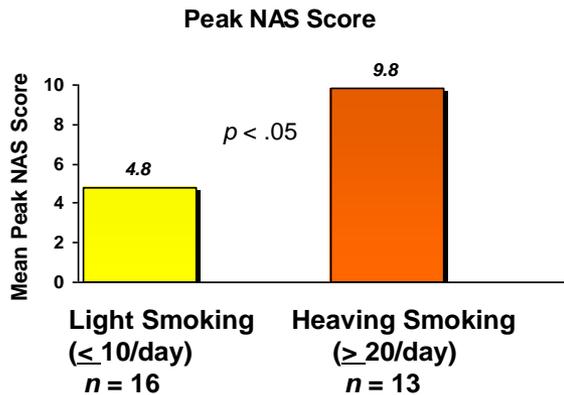
NAS: Factors

- **To determine whether concurrent in utero exposure to buprenorphine and antidepressants impacts the course of neonatal abstinence syndrome (NAS) in infants.**
- **A retrospective cohort study of 148 infants who were exposed to buprenorphine during pregnancy. Univariate and bivariate analyses were used to examine associations between concurrent maternal use of buprenorphine and antidepressants as compared to maternal use of buprenorphine alone.**
- **The time to onset of NAS resolution was significantly longer in infants exposed to both buprenorphine and antidepressants during pregnancy when compared to infants exposed to buprenorphine alone (129.8 h v. 70.2 h, $p = .042$).**
- **Women who are prescribed both antidepressants and buprenorphine during pregnancy should be counseled about the possibility of a prolonged course of neonatal abstinence syndrome.**

Smoking and NAS

Heavier cigarette smoking has been found to be related to:

- ▶ peak NAS score and time to peak NAS score in neonates of methadone-maintained women
- ▶ lower neonatal birth weight, smaller birth length, and greater NAS severity in neonates of opioid-maintained pregnant women
- ▶ NAS symptoms and duration of hospitalization in neonates of methadone-maintained women
- ▶ NAS symptoms and unrelated to any NAS treatment in neonates of methadone-maintained women
- ▶ duration of NAS treatment in neonates of methadone-maintained pregnant women but not in neonates of buprenorphine-maintained pregnant women



Choo et al., Drug Alcohol Depend. 2004;75(3):253-60.

Bakstad et al., Eur Addict Res 2009;15(3):128-134.

Winklbaaur et al., Eur Addict Res 2009;15(3):153-6.

Miles et al., J Reprod Med 2006;51(7):567-572.

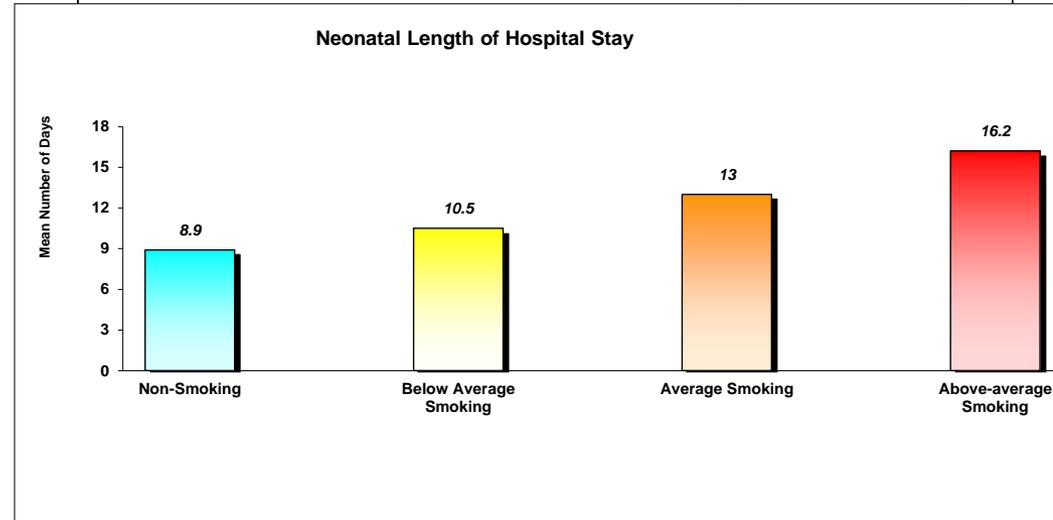
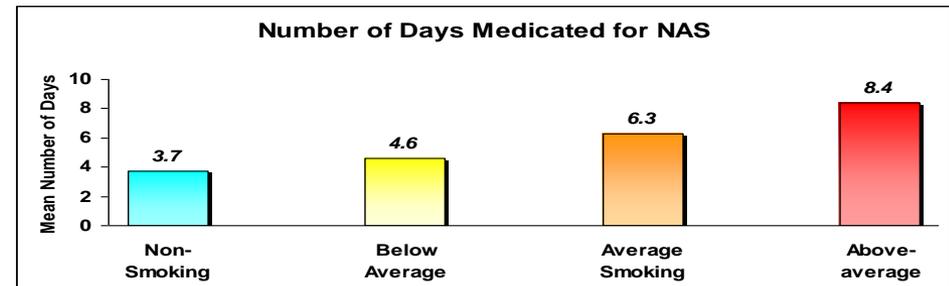
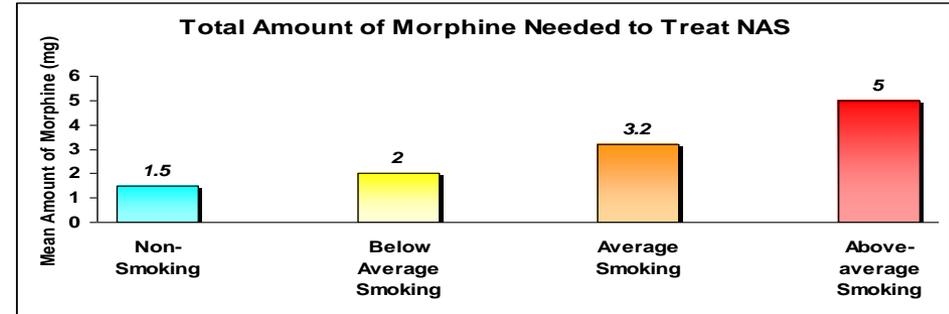
Jansson et al., Drug Alcohol Depend. 2010;109(1-3):198-204.

MOTHER Study: Cigarette Smoking NAS

RESULTS

Average number of cigarettes smoked in the past 30 days was significantly *positively* related to:

- Total amount of morphine needed to treat NAS
- Number of days neonate was medicated for NAS
- Neonatal length of hospital stay



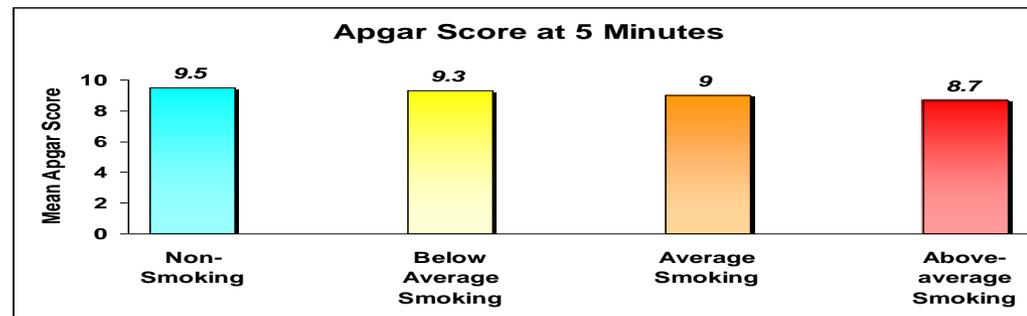
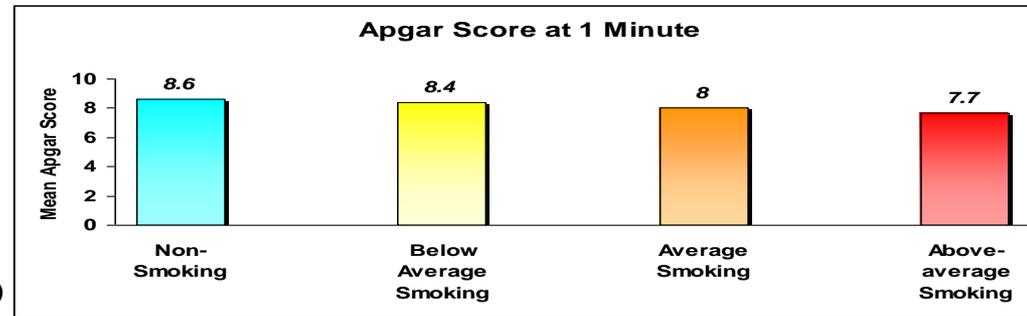
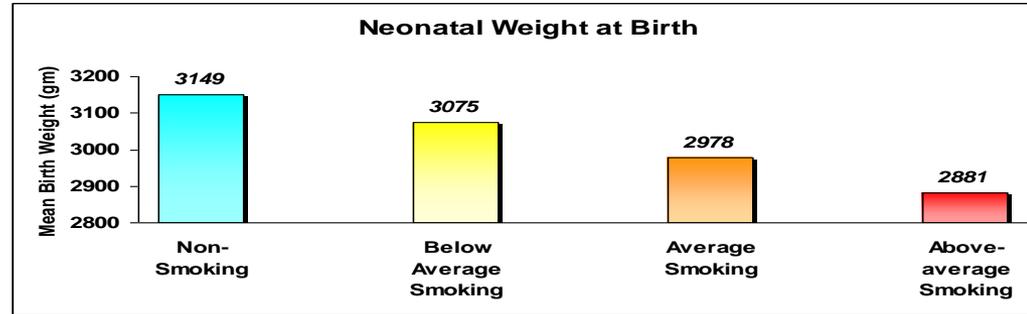
OLS and Poisson regression analyses were used to test average number of cigarettes smoked in the past 30 days at $\alpha = .05$, adjusting for both Medication Condition and Site. Below-average cigarette smoking was defined as 6 cigarettes/day (-1 SD), average cigarette smoking as 14 cigarettes/day (Mean), and above-average cigarette smoking as 21 cigarettes/day (+1 SD).
Jones et al., DAD, 2012

MOTHER Study: Other Outcomes

RESULTS

Average number of cigarettes smoked in the past 30 days was significantly negatively related to:

- Neonatal weight at birth
- Apgar score at 1 minute
- Apgar score at 5 minutes
- Maternal weight gain, study entry to delivery



OLS and Poisson regression analyses were used to test average number of cigarettes smoked in the past 30 days at $\alpha = .05$, adjusting for both Medication Condition and Site. Below-average cigarette smoking was defined as 6 cigarettes/day (-1 SD), average cigarette smoking as 14 cigarettes/day (Mean), and above-average cigarette smoking as 21 cigarettes/day (+1 SD).

MOTHER Study: Cigarette Smoking

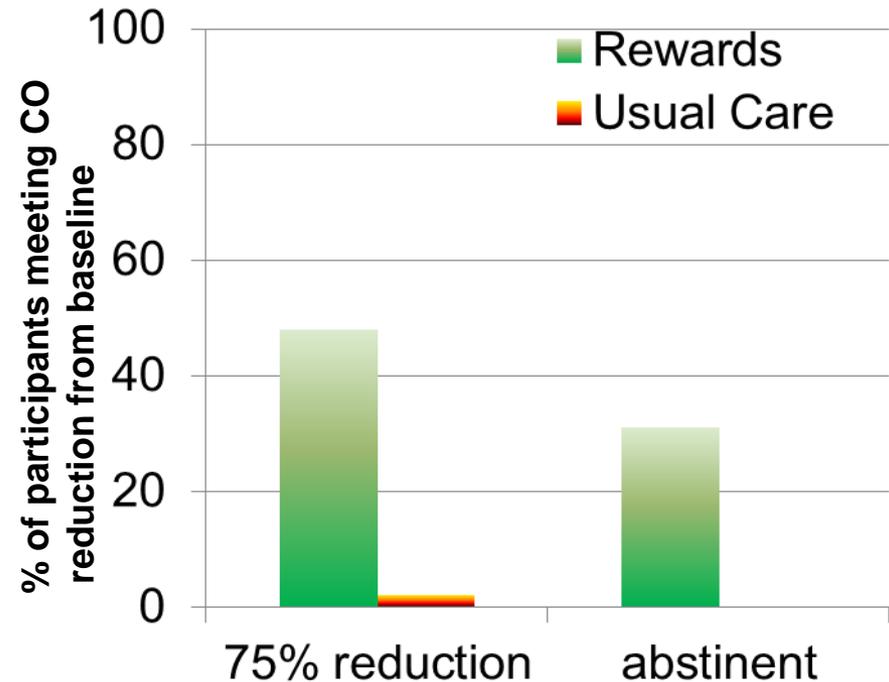
A Practical Viewpoint on the Results

Relative to a pregnant woman in opioid agonist treatment who didn't smoke during her pregnancy, a pregnant woman in opioid agonist treatment who smokes a pack of cigarettes a day on average during her pregnancy would likely face:

- More than triple the total amount of morphine needed to treat her neonate's NAS
- More than double the number of days required to treat her neonate's NAS
- Almost double the length of hospital stay for her neonate
- A more than 8% decrease in her neonate's birth weight
- A decrease of almost 1 point in her neonate's Apgar scores at 1 minute
- A more than ½ point decrease in her neonate's Apgar scores at 5 minutes
- A more than 3 kg (more than 7 lbs) decrease in her own weight gain during pregnancy

Reducing Cigarette Smoking in Methadone-treated Pregnant Patients

- Providing monetary rewards for meeting smoking reduction targets over 12 weeks
- Took baseline and then measured CO 3 times a week.
- Rewards given for reducing by:
 - 25% for 3 wks
 - 50% for 3 wks
 - 75% for 3 wks
 - smoking abstinence for 3 wks



Scoring tools for NOWS/NAS

Finnegan Neonatal Abstinence Scoring System

31 items

Symptoms are weighted

Guidelines for pharmacologic treatment at score of 8 or greater

MOTHER score (modified Finnegan score)

19 items (which contribute to total score)

Items weighted differently

Some Finnegan items eliminated and others added

Guidelines for treatment based on score rather than weight

Lipsitz Neonatal Drug-Withdrawal Scoring System

11 items

Items scored for severity and gives guidelines for treatment

The Neonatal Withdrawal Inventory – 8 point checklist

The Neonatal Narcotic Withdrawal Index – 6 signs plus others

NOW Assessment: MOTHER NAS Scale

Appendix Figure 2. Maternal Opioid Treatment: Human Experimental Research (MOTHER) Neonatal Abstinence Measure

PATIENT ID#		Morphine Maintenance								
Dose given q 3-4 hrs with feeds; do not exceed 4 hrs between doses		<ul style="list-style-type: none"> Maintain dose if score 0-8 Increase dose by 0.02 if score is 9-12 (rescore before dosing) Increase dose by 0.04 if score 13-16 Increase score by 0.06 if score 17-20 								
SCORE Morphine (0.04mg/0.1ml) DOSE FOR INITIATION		Weaning Instructions:								
0-8	0	<ul style="list-style-type: none"> Maintain on dose 48 hrs before starting weaning Wean 0.02 mg morphine every day for a score is 0-8 Defer wean for score e 9-12 								
9-12	0.04 mg/dose	Re-escalation								
13-16	0.08 mg/dose	<ul style="list-style-type: none"> If neonate scores 9-12 re-score as described for initiation If second score is in 9-12 increase morphine 0.01 mg q3-4 hrs If 2 consecutive scores 13-16, increase 0.02 mg q3-4 hrs If 2 consecutive scores in 17-20, increase 0.04 mg q3-4 hrs etc 								
17-20	0.12 mg/dose									
21-24	0.16 mg/dose									
25 or above	0.20mg/dose									
Morphine Initiation:										
<ul style="list-style-type: none"> If neonate scores 9-12 re-score after feeding or within the hour and if re-score is 9-12 start treatment based on highest score. If re-score is 0-8, do not initiate treatment. If initial score is 13 or greater, start treatment immediately without reassessment. 										
Timing of Scoring: Hospitalized infants scored every 3-4 hrs before feeds. Reassessment Occurs immediately after feeds or within 1 hour.										
Discharged (e.g., in GCRC) infants scored twice a day scores must be separated by 8 hrs)										
****NOTE: Discharged infants are to be admitted to hospital if the infant receives a single score of 9 or more****										
SIGNS AND SYMPTOMS		Score	Date/time							
Please note presence (pr) or absence (ab) of items where indicated. Include observations for the past 4 hour period.										
Crying: excessive high pitched		2								
Crying: Continuous high pitched		3								
Sleeps < 1 hour after feeding		3								
Sleeps < 2 hours after feeding		2								
Sleeps < 3 hours after feeding		1								
Hyperactive Moro Reflex		1								
Markedly Hyperactive Moro Reflex		2								
Mild Tremors: Disturbed		1								
Moderate-Severe Tremors: Disturbed		2								
Mild Tremors: Undisturbed		1								
Moderate-Severe Tremors: Undisturbed		2								
Myoclonic jerks	present/absent		Qpr Qab							
Increased Muscle Tone		1-2								
Excoriation (indicate specific area):		1 - 2								
Mottling	present/absent		Qpr Qab							
Generalized Seizure (or convulsion)		8								
Convulsions	present/absent		Qpr Qab							
Fever ≥ 37.3 C (99.2 F)		1								
Fever >38.4 (101.2 F)	present/absent		Qpr Qab							
Frequent Yawning (4 or more successive times)		1								
Sweating		1								
Nasal Stuffiness		1								
Sneezing (4 or more successive times)		1								
Tachypnea (Respiratory Rate> 60/min)		2								
Retractions	present/absent		Qpr Qab							
Nasal flaring	present/absent		Qpr Qab							
Poor Feeding		2								
Excessive sucking	present/absent		Qpr Qab							
Vomiting (or regurgitation)		2								
Projectile vomiting	present/absent		Qpr Qab							
Loose Stools		2								
Watery Stools	present/absent		Qpr Qab							
Failure to Thrive (Current weight ≥ 10% below birth weight) 90% BWT=		2 (record weight in score box 1 x day)								
Excessive Irritability		1 - 3								
TOTAL SCORE										
CURRENT MORPHINE DOSE	Dose in mg Time Given									
STATUS OF TREATMENT*	N, I, M, W, R									
INITIALS of SCORER										

Note: Code Status of Treatment as follows: N="No treatment", I="Initiation", M="Maintenance", W="Weaning", R=" Re-Escalation"

- NAS score is not the sole determining factor in the decision to start pharmacotherapy for NAS
- Score can be affected by
 - State of infant
 - Painful stimuli
 - Order of score
 - "Motive" of scorer

NOW: Measurement and Response

- All NOW instruments have common features of summing item scores and/or weighting the severity of presenting signs
- NOW evaluation is recommended every 3 to 4 hours during hospitalization; surveillance should last for several days after birth and for entire hospitalization
- Scores above a threshold trigger medication initiation to reduce NOW severity – no or delayed treatment can result in morbidity or mortality
- Stabilization on medication promotes regular eating and sleeping patterns, weight gain, and improved interaction with caregivers
- Medication amount is increased then gradually decreased until the neonate is stable without medication

NOWS: Pharmacologic Treatment

- **Short-acting opioids (morphine sulfate, dilute tincture of opium)**
 - Inpatient treatment
 - “standard of care”
 - Symptom based versus weight based
 - Endorsed by the AAP (2012)
- **Methadone**
 - Inpatient treatment and inpatient to outpatient treatment
 - Symptom versus weight based
 - Allows for shorter length of stay (with outpatient treatment)
 - Endorsed by the AAP (2012)
 - (Several studies including MS Brown et al (2015) which revealed shortened duration of treatment with methadone)
- **Dilute tincture of opium and phenobarbital (Coyle et al, 2002)**
 - Decreased severity of withdrawal, decreased length of stay
- **Buprenorphine (Kraft et al, 2011)**
 - Shorter length of stay in buprenorphine treated infants
 - Well tolerated
- **Clonidine (Agthe et al, 2009)**
 - Oral clonidine as adjunct to short-acting opioids
 - Shortens the duration of therapy, no short-term cardiovascular side effects observed

NOWS: Non-pharmacologic Treatment

- **Breastfeeding is associated with reduced severity of withdrawal, delayed onset, decreased need for Rx (Abdel-Latif et al, 2006)**
- **Rooming-in decreased the need for Rx, length of Rx, and LOS (Abrahams et al, 2007)**
- **Water beds decreased amount of medication needed (Oro et al, 1988)**
- **Acupuncture (Filippelli et al, 2012)**
- **Kangaroo therapy or skin to skin**
- **Decreased environmental stimuli**
- **Frequent small demand feeds**
- **Pacifiers**
- **Swaddling, containment, holding, vertical rocking**
- **Provider, nursing attitudes**



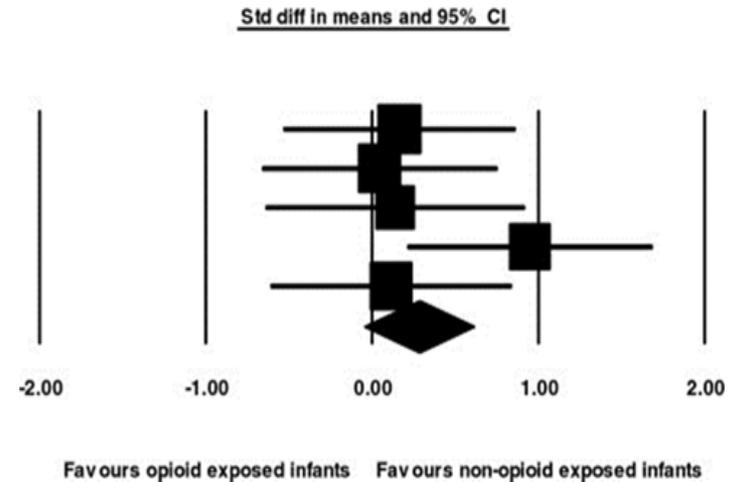
NOW: Recommendations

- ◆ **NOW occurs in the majority of all prenatally opioid-exposed neonates**
- ◆ **Medication to treat NOW is required in approximately 50% of the cases**
- ◆ **NOW following prenatal exposure to an opioid agonist is best assessed with a standard scoring tool and best treated with an opioid medication**
- ◆ **Patients and the providers who treat them will be best served through having a range of medication options from which to tailor treatment**
- ◆ **As treatment for maternal opioid dependence advances, so must neonatal treatment (i.e., buprenorphine in the infant may be an important medication for treatment of buprenorphine exposure in utero)**

Later Outcomes

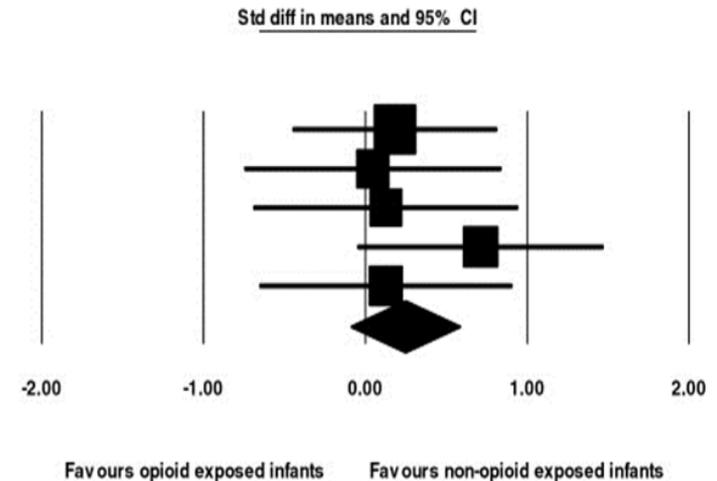
Psychomotor in opioid and non-opioid exposed infants

Study Name	Subgroup	Assessment
Hunt (2008)	1.5 years old	BSID (Psychomotor)
Burlowski (1998)	1 year old	GDS (Locomotor)
Moe (2002)	1 year old	BSID (Psychomotor)
Hans (2001)	1 year old	BSID (Psychomotor)
Hans (2001)	2 years old	BSID (Psychomotor)



Cognition in opioid and non-opioid exposed infants

Study Name	Subgroup	Assessment
Hunt (2008)	1.5 years old	BSID (Mental)
Burlowski (1998)	1 year old	GDS (DQ)
Moe (2002)	1 year old	BSID (Mental)
Hans (2001)	1 year old	BSID (Mental)
Hans (2001)	2 years old	BSID (Mental)

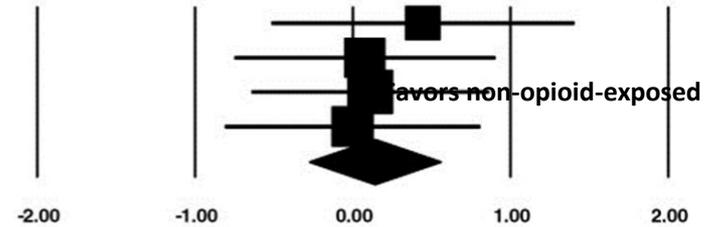


Later Outcomes (cont)

Cognition in opioid and non-opioid exposed infants

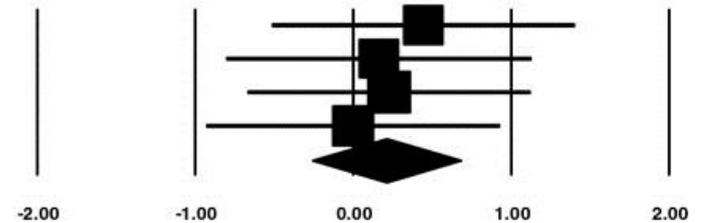
Study Name	Subgroup	Assessment
Hunt (2008)	3 years old	McCarthy
Ornoy (2001/2003)	5 years old	McCarthy
Moe (2002)	4.5 years old	McCarthy
Walhord (2007)	4.5 years old	McCarthy

Favors opioid-exposed



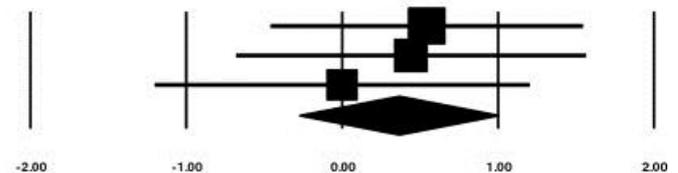
Psychomotor in opioid and non-opioid exposed infants

Study Name	Subgroup	Assessment
Hunt (2008)	3 years old	McCarthy Motor Scale
Ornoy (2001/2003)	5 years old	McCarthy Motor Scale
Moe (2002)	4.5 years old	McCarthy Motor Scale
Walhord (2007)	4.5 years old	McCarthy Motor Scale



Behaviour in opioid and non-opioid exposed infants

Study Name	Subgroup	Assessment
Hunt (2008)	3 years old	Vineland Social Maturity
Ornoy (2001/2003)	5 years old	Achenbach
Moe (2002)	4.5 years old	Achenbach



Prenatal Care

Post-Natal Care

Substance Abuse Treatment



Trauma-Informed

Staff trained on trauma-informed care:

- ✓ **Staff realizes the widespread impact of trauma and understands potential paths for healing**
- ✓ **Staff recognizes the signs and symptoms of trauma in staff, clients, and others involved with the system**
- ✓ **Staff responds by fully integrating knowledge about trauma into policies, procedures, practices, and settings**

Prenatal Horizons Clinic

- **Team includes: Nurse practitioner (NP), case manager, and therapist**
- **NP provides primary obstetrical care and manages women taking Suboxone prescribed by the OB**
- **Case manager provides assistance and access to community resources and services**
- **Therapists provides counseling**
- **Psychiatrist is available as-needed for evaluation and medication management**



- Team educates women on recovery and addiction and works to motivate women to participate in treatment
- Team collaborates with nursery staff to educate women about NAS
- Incentives to participate in services include:
 - Assistance with parking
 - Gas vouchers
 - Mommy Bucks
 - Transportation



Referral and Long-Term Follow-up for Exposed Infants

- **DSS involvement**
 - This can and should be seen as supportive, not punitive
 - Often past history with DSS precludes acceptance
- **CDSA referral from the nursery**
 - Can be difficult depending out county and resources
- **Ongoing treatment for mother and family**
 - Learn your local resources
- **Preschool when available**

Engage the Team

- **PCP, OB/GYN, Pediatrician**
 - 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 Labor & Delivery and Newborn
- **Anesthesiologist**
 - Pain management plan
- **Newborn Nursery Team**
 - Infant assessment, Finnegan Scales, non-pharmacologic treatments, encourage breastfeeding
- **Neonatal Critical Care Team**
 - Symptomatic Infants, Acute Withdrawal

UNC Horizons Postnatal Protocol

- Visit from child therapist within first week of delivery, even if in NICU
- Focus on infant strengths, learning infant cues (Hug Your Baby)
- Continue on going parent education (twice per week)
- At 6 weeks: Referrals for developmental assessments (Early Intervention) including Speech/Language, Occupational Therapy, Physical Therapy, and Social-Emotional Assessment
- Support Dyad: Weekly Child Parent Psychotherapy (CPP)



Further support via Parent Education during Substance Use Treatment

- Attachment-based parenting program: Circle of Security-Parenting© <http://circleofsecurity.net>
- Nurturing Parenting Program for Substance Abuse <http://www.nurturingparenting.com/>
- Hug Your Baby <http://www.hugyourbaby.org/>
- Child Parent Psychotherapy http://www.nctsn.org/sites/default/files/assets/pdfs/cpp_general.pdf

- ◆ **Parents need continued education and support at home**
- ◆ **In the first few months, these infants can be difficult to sooth/irritable, have difficulties transitioning and maintaining sleep, and have feeding issues**
- ◆ **This can put infants at risk for insecure attachment**
- ◆ **Parents frequently have other stressors**

Why focus on Attachment?

Researchers have found that mothers with substance abuse histories:

- **Have repeated relationship disruptions**
- **Report more irritable babies**
- **Are less sensitive in interactions**
- **Are less emotionally engaged**
- **Are less attentive**
- **Have less positive affect**

Children from families with substance abuse issues have higher rates of insecure and disorganized attachment.

Post-Natal Mental Health Assessments

- **Transdisciplinary Play-Based Assessment, Second Edition (TPBA2)**
- **Ages and Stages Questionnaire: Social-Emotional (ASQ:SE)**
- **PICCOLO (beginning at 10 months)**
- **Angels in the Nursery**

Circle of Security-Parenting Study[©]:

- Pretest to Posttest changes on emotion regulation, attributions, and discipline practices.
- Mean scores from pretest to posttest improved on all three quantitative measures.
- Significant RCI's were found on each measure.

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)**

Qualitative Outcomes: Post Natal Protocol

We have very high program satisfaction:

100% of clients have indicated that they either strongly agree or agree with every item on the satisfaction survey every year.

“How has the Child Parent Psychotherapy Program with Evette helped you and your family?”) are included below:

- *Helped to balance having 3 babies and the importance of giving them positive attention and positive interactions.*
- *Helped me to discipline without being harsh, i.e., 1,2,3 timeout, giving choices, and setting age appropriate limits and giving alternatives*
- *Helped me learn how to better recognize my child's different emotions and to be with them through it and to teach them its OK to feel how they are feeling but also to set limits on behavior.*
- *Help learn to bond with baby*
- *It has improved our relationship so much and our connection has been good since Ms. Evette has helped. Ms. Evette is doing a wonderful job.*

Qualitative Outcomes: Post Natal Protocol (cont)

- *I've learned better ways to handle stressful situations. Family now is happy, healthy, and fun. Awesome program.*
- *Learned coping skills, games, healthy living habits. My family now is very happy and we all have better relationships. Great, really helpful program.*
- *We got onto a plan to make V. sleep better, which was enjoyable for us. V. really bloomed and I believe she is now advanced for her age.*
- *I am a first time mother and I had no idea what was normal or abnormal. Evette has helped me build confidence as a mother. My daughter and I have bonded over the exercises we were given. She's very accessible and does home visits.*
- *It has taught me things to look for in my children, how to bond with them, and how to discipline without physical discipline*
- *She has helped me greatly understand my son and things he is going through. We get along so much better now.*
- *I have a better relationship with my child. Its made our home life a lot better and more controllable*

Qualitative Outcomes: Post Natal Protocol (last)

- *She has taught me patience and has sat down physically showed me how to interact with my daughter. I have seen great improvement with my daughter's behavior.*
- *Word cannot explain the miracles she's performed. She really....just can't explain it! Thank you!*
- *She has helped me understand why and what to expect. Approaching the child in the right way. How to handle situations that come up. How to build a stronger one on one relationship.*
- *Understand why they are acting that way. Know what to expect. How to build stronger relationship with child. Approaching situations and kids in a healthy manner.*

Summary

Treatment for NAS occurs during the pregnancy, post-delivery, and in the home

Treatment for mother, infant, *and* the dyad

Focus on strengthening attachment relationship

Focus on helping parents learn to read and respond to their infants cues

Referrals to early intervention paramount

Ask About Tobacco

- ◆ Tobacco use is a good indicator to ask about other drug use
- ◆ How you ask is as important as what you ask:
 - ◆ Open-ended questions
 - ◆ Non-judgmental approach



Smoking during pregnancy increases the risks of:

- deep venous thrombosis
- stroke
- pulmonary embolusmyocardial infarction
- pulmonary complications such as influenza, pneumonia, and bronchitis
- Increases in pregnancy-related risks include:
 - spontaneous pregnancy loss
 - ectopic pregnancy
 - placental abruption
 - placenta previa
 - preterm premature rupture of the membranes
 - stillbirth
 - preterm delivery
 - low birth weight

Fetal Effects

✦ No known teratogenic risk – although there has been the suggestion of some congenital abnormalities, including cleft lip or palate, urinary tract malformations, cardiac, cranial, and limb malformations

✦ There is also some suggestion of genotoxicity, producing chromosomal instability. De la Chica 12% of smokers and 3½% of non-smokers demonstrated genetic instability.

Neonatal Effects

Maternal smoking associated with:

- decreased birth weight
- decreased length of gestation

Maternal genotype may play a role here, particularly *CYP1A1* and *GSTT1* genotype

Child Effects

Behavioral outcomes (e.g., activity and inattention and externalizing behaviors, including conduct disorder and antisocial behavior).

In adolescents, increased attention deficit hyperactivity disorder, brain changes and nicotine addiction.

Tobacco: Breastfeeding

Nicotine and other compounds transfer to the infant via milk, as do chemicals via second-hand smoke. Increases in the incidence of respiratory allergy in infants and in SIDS are examples of significant well known risks of infant exposure to environmental tobacco smoke.

Most sources endorse promotion of breastfeeding in the setting of maternal smoking while vigorously supporting smoking cessation.

Some smoking cessation modalities (nicotine patch, nicotine gum, and possibly bupropion) are compatible with breastfeeding and can be encouraged in many circumstances.

➤ **Alcohol use during pregnancy increases the risks associated with:**

– **Fertility**

– **Fetal abnormalities**

– **Lactation**

➤ **and, may increase the risk of stillbirth: stillbirth increased eight-fold when drinking increased from 1 drink per week to 5 or more drinks per week**

Fetal Effects

◆ No known lower limit of safety for alcohol use during pregnancy that will prevent the common and most severe neonatal outcomes: fetal alcohol spectrum disorder (FASD) and stillbirth.

◆ *FASD* describes a broad range of adverse results for offspring of alcohol-using women, including alcohol-related birth defects (ARBDs), alcohol-related neurodevelopmental disorder (ARND), and fetal alcohol syndrome (FAS). ARBDs and ARND do not meet all the criteria of FAS, but describe offspring with structural or neurodevelopmental abnormalities resulting from alcohol use. FAS is defined by maternal drinking during pregnancy, fetal growth problems at any point in time, facial dysmorphism and central nervous system abnormalities

◆ *Prevalence of FAS is 10% to 50% in infants of heavy drinkers.*

Child Effects

- ◆ Child effects can be pervasive and life-long
- ◆ Beyond the effects associated with FASD, prenatal exposure to alcohol has been associated with increased risk for:
 - psychiatric disorders
 - substance use disorders
 - poor school performance
 - Inadequate social relations
 - legal problems

Alcohol: Breastfeeding

Alcohol is not stored in breastmilk but following maternal consumption, is concentrated in it due to its presence in maternal blood

'Pumping and dumping' does not remove alcohol from breast milk, because alcohol is not stored in breast milk

Most sources advise limiting alcohol intake to the equivalent of 8 ounces of wine or two beers, and waiting 2 hours after drinking to resume breastfeeding



Legal Does Not Mean Safe

- **Do not assume that the legality of a substance makes is related to the potential harms that a substance can have on the mother or fetus.**
- **Two of the substances that we have the most documentation on their harms include tobacco and alcohol.**
- **However, even for alcohol, risk factors (e.g., maternal age, genetics, nutrition) other than alcohol exist and serve to mediate, moderate or otherwise alter the effects of alcohol on the fetus and child.**
- **As with all substances, the potential effects on the mother, fetus and child must be viewed in the context of the social determinants of health including the overriding influence of poverty and its radiating effects.**

Co-occurring Disorders: Marijuana

- ▶ **Marijuana is a commonly used recreational substance whose use by pregnant women with and without opioid use disorder is likely to increase, perhaps substantially, given evolving changes in state laws regarding its regulation and sale.**
- ▶ **There are no good estimates of rates of use of marijuana among pregnant women, which vary between 3% and 20%. The rate in pregnant women with opioid use disorder is likely substantially higher.**
- ▶ **Research on the fetotoxic, teratogenic, and developmental effects of prenatal use of marijuana use has been failed to be conclusive.**
- ▶ **The general concern revolves around subtle cognitive deficits of children of exposed prenatally to marijuana. However, at present we know little about any form of a dose-response relationship.**
- ▶ **It does not seem that marijuana use is related to premature treatment termination.**



Cannabis: Maternal Effects

- ✦ Marijuana smoke is most likely carcinogenic
 - ✦ Likely mutagenic in vivo and in vitro
 - ✦ Chronic marijuana smoking has been found to be related to:
 - chronic bronchitis
 - decreased lung function
 - increased risk of various oral cancers
 - ✦ long-term use has been related to subtle forms of cognitive impairment
 - ✦ Certain individuals seem to develop dependence
- ◆ There are no reliable data regarding stillbirth and maternal cannabis use
- ↪ *No research addresses these potential problems for pregnant women who use cannabis*

Fetal Effects

✦ There are some suggestions in the literature of teratologic effects of cannabis but there is too little research for definitive statements in this regard

Neonatal Effects

◆ There is *no* support in the literature at present that maternal use of cannabis is related to birth parameters, rates of preterm birth, neonatal intensive care unit (NICU) admission, or neonatal mortality

Child Effects

- ◆ Increased tremors, exaggerated and prolonged startle responses, and/or altered sleep patterns.
- ◆ Abstinence- and stress-related behaviors in 1-month-old neonates
- ◆ At 6 years of age, there are reports of increased impulsivity and hyperactivity
- ◆ At 10 years of age, there are reports of inattention, delinquency, impulsivity, increased hyperactivity
- ◆ Associated with deficits in problem-solving skills that require sustained attention and visual memory, analysis, and integration and with subtle deficits in learning and memory

Cannabis: Breastfeeding

Counsel mothers who admit to occasional or rare use to avoid further use or reduce their use as much as possible while breastfeeding, advise them as to its possible long-term neurobehavioral effects, and instruct them to avoid direct exposure of the infant to marijuana and its smoke.

Strongly advise mothers with a positive THC screen to discontinue exposure while breastfeeding and counsel them as to its possible long-term neurobehavioral effects.

Take into careful consideration and counsel on the potential risks of exposure of marijuana and benefits of breastfeeding to the infant.

The lack of long-term follow-up data on infants exposed to varying amounts of marijuana via human milk, coupled with concerns over negative neurodevelopmental outcomes, should prompt extremely careful consideration of the risks versus benefits of breastfeeding in the setting of moderate or chronic marijuana use.

Co-occurring Disorders: Cocaine and Amphetamines

- Cocaine is a very common co-occurring substance in patients in opioid agonist treatment, including pregnant women. Amphetamine, apparently less so.
- Despite the original concern about a “lost generation” of “crack babies” recent research has failed to support such a position, and the general conclusion is that the effects of cocaine on a child exposed to cocaine in utero maybe subtle and diffuse, at least in infants
- Research on the fetotoxic and teratogenic effects of maternal amphetamine use is largely lacking, although animal models suggest potential congenital abnormalities.
- *However, there is the increased risk of premature treatment termination associated with both cocaine and amphetamine use.*



Cocaine: Maternal

- Cocaine is known to impact the adrenergic system, producing increased heart rate and blood pressure, and systemic vasoconstriction
- These effects can be pronounced in pregnancy, and result in increased risks for:
 - Hypertensive emergencies
 - Placental abruption
- Cocaine has been found to be associated with a increased risk of stillbirth

Fetal Effects

⤴ Cocaine crosses the placenta and enters the fetal brain.

⤴ Fetus is broadly impacted by the vasoconstrictive effects of cocaine

⤴ Initial reports in both the popular press and the scientific literature suggested heightened teratogenicity associated with prenatal exposure to cocaine

↪ *However, these reports have not been borne out, and the single largest study of maternal cocaine use suggests that there is no heightened risk for congenital abnormalities associated with prenatal exposure to cocaine.*

↪ *Effects of cocaine may be subtle and enduring*

Neonatal Effects

- Maternal use of cocaine has been associated with: Preterm birth, low birth weight, small for gestational age, younger gestational age at delivery , and reduced birth weight

Child Effects

- ◆ Has been found to be associated with an increased risk of specific cognitive deficits
 - visual-spatial skills
 - general knowledge
 - arithmetic skills

Cocaine: Breastfeeding

- **Women who use cocaine should be discouraged from breastfeeding, as cocaine appears in breastmilk in sufficient quantities to cause toxicity**



Maternal Effects

- Amphetamine/methamphetamine use has pronounced deleterious short- and long-term impacts on humans
- However, the extent to which it complicates pregnancy is largely unknown due to lack of research
- There are no reliable data regarding stillbirth and maternal amphetamine/methamphetamine use

Amphetamines/Methamphetamines

Fetal Effects

- ◆ Likewise, there is little information regarding fetal effects of amphetamines/methamphetamines
- ◆ Results of animal studies have been conflicting
- ◆ Case reports suggest some congenital abnormalities in multiple organ systems
- ◆ Case-control studies have failed to support the findings of case reports

Neonatal Effects

- ✧ Maternal use increases the risk of:
 - preterm birth
 - low birth weight
 - small for gestational age
- ✧ Similar to cocaine, maternal amphetamines/methamphetamine use has been found to be related to:
 - decreased arousal
 - increased stress
 - poor quality of movement
 - likely in a dose-response manner

Child Effects

- ✧ Some suggestions in the literature of problems with attention, verbal and spatial memory, and visual-motor integration without verification

Breastfeeding

- ◆ **Women who use amphetamines/methamphetamines should be discouraged from breastfeeding**
- ◆ **Concentrations in breastmilk are estimated to be 3-7 times that in maternal blood**
- ◆ **Case reports suggest some evidence of toxicity in infants of mothers who are actively using amphetamines/methamphetamines**

Co-occurring Disorders: Benzos

- **Benzodiazepine use by pregnant women with opioid use disorder can occur both because of medical indications, under the direction of a health care provider, or through illicit use. Benzodiazepine use in the former case can lead to abuse.**
- **The prevalence of benzodiazepine use in either circumstance is not well documented, as little research has examined either situation.**
- **Moreover, pregnant women who develop withdrawal symptoms following cessation of alcohol use are often managed with a short-term use of a long-acting benzodiazepine, further complicating the issue.**
- **A withdrawal syndrome is known to occur in pregnant women following abrupt cessation from benzodiazepines, that may involve seizures and/or psychosis.**
- **Treatment for benzodiazepine use in pregnancy typically involves prescription of long-acting benzodiazepines with gradual reduction in dose over an extended period. An inpatient stay may be important to the success in treatment.**
- **Psychosocial treatment during the dose reduction period may play an important role in recovery.**

Maternal Effects

- ✦ Benzodiazepines may be used during pregnancy as pharmacotherapy for a medical problem
- ✦ It may also be used illicitly

- ✦ Benzodiazepines are known to produce sedation and relaxing effects, and reduce anxiety

- ✦ There are no reliable data regarding stillbirth and maternal benzodiazepine use

- ↳ *There are no known effects of benzodiazepines that produce unique or specific maternal effects*

Fetal Effects

There have been some suggestions in the literature of teratologic effects of benzodiazepines but recent research fail to support such conclusions.

↳ *The issue of fetal effects is complicated by the various pharmacologies of benzodiazepines that may have different fetal effects*

Neonatal/Child Effects

- Neonatal and child effects are similar to those effects found for opioids, so will be discussed when opioids are discussed

Breastfeeding

- **Women who use benzodiazepines should be cautioned about breastfeeding, because there is little information regarding its concentrations in breastmilk, its concentrations in blood plasma, and its behavioral effects on the neonate**



Opioids

Fetal Effects

- neural tube defects are of higher frequency in heroin-exposed fetuses
- no specific teratogenic syndrome identified, but heroin use may be associated with an increased risk of malformation
- An association between major congenital malformations and methadone exposure has been noted

Neonatal Effects

- ✦ perinatal mortality
- ✦ preterm birth
- ✦ low birth weight
- ✦ Neonatal Abstinence Syndrome (NAS)

Child Effects

- School-age children prenatally exposed to heroin may experience developmental delay
- These children may exhibit abnormal behaviors such as aggressiveness, hyperactivity, and disinhibition

► *Family and social environment is likely to be disadvantaged, with inadequate nutrition, poor parenting, and multiple substances of abuse, which may in part or in whole contribute to the problems in fetal, neonatal, and child development*

Take-home Messages

NOW is a treatable condition that requires more study to find optimal medications and treatment protocols

Treatment for mother, infant, *and* the dyad are important for children

Focus on strengthening attachment relationship

Focus on helping parents learn to read and respond to their infants cues

Referrals to early intervention paramount

Prenatal exposure to other substances are risk factors for- but not determinants of- poor child outcomes

Child resilience is bolstered by strong nurturing bonds





Questions
& Answers

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