

# WHAT WORKS IN NAS TREATMENT



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# DISCLOSURE

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I have no conflicts of interest (financial or otherwise) that are germane to this presentation.

Our center will be participating in a multi-center NIH-funded study comparing the efficacy of methadone and oral morphine in the treatment of NAS.

# EFFECTS OF OPIOIDS ON FETUS/CHILD

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Slight increase in risk of congenital heart disease, neural tube defects, and gastroschisis (odds ratios 1.8-2.7:1)

Decreased fetal growth

Neurobehavioral abnormalities at birth (NAS)

Long term effects – small and variable increase in:

- Behavioral problems

- Attention deficit disorder

- Memory/perception issues

Unknown effects on IQ and executive functioning

# TOPICS OF INTEREST: PREVENTION

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## Primary prevention:

Contraception

Education of providers and the public

Role for inpatient medically supervised maternal detoxification?

Effect of maternal drug(s) on likelihood, timing, and severity of NAS

## Secondary prevention:

Prenatal identification of at risk infants

Monitoring of at risk infants

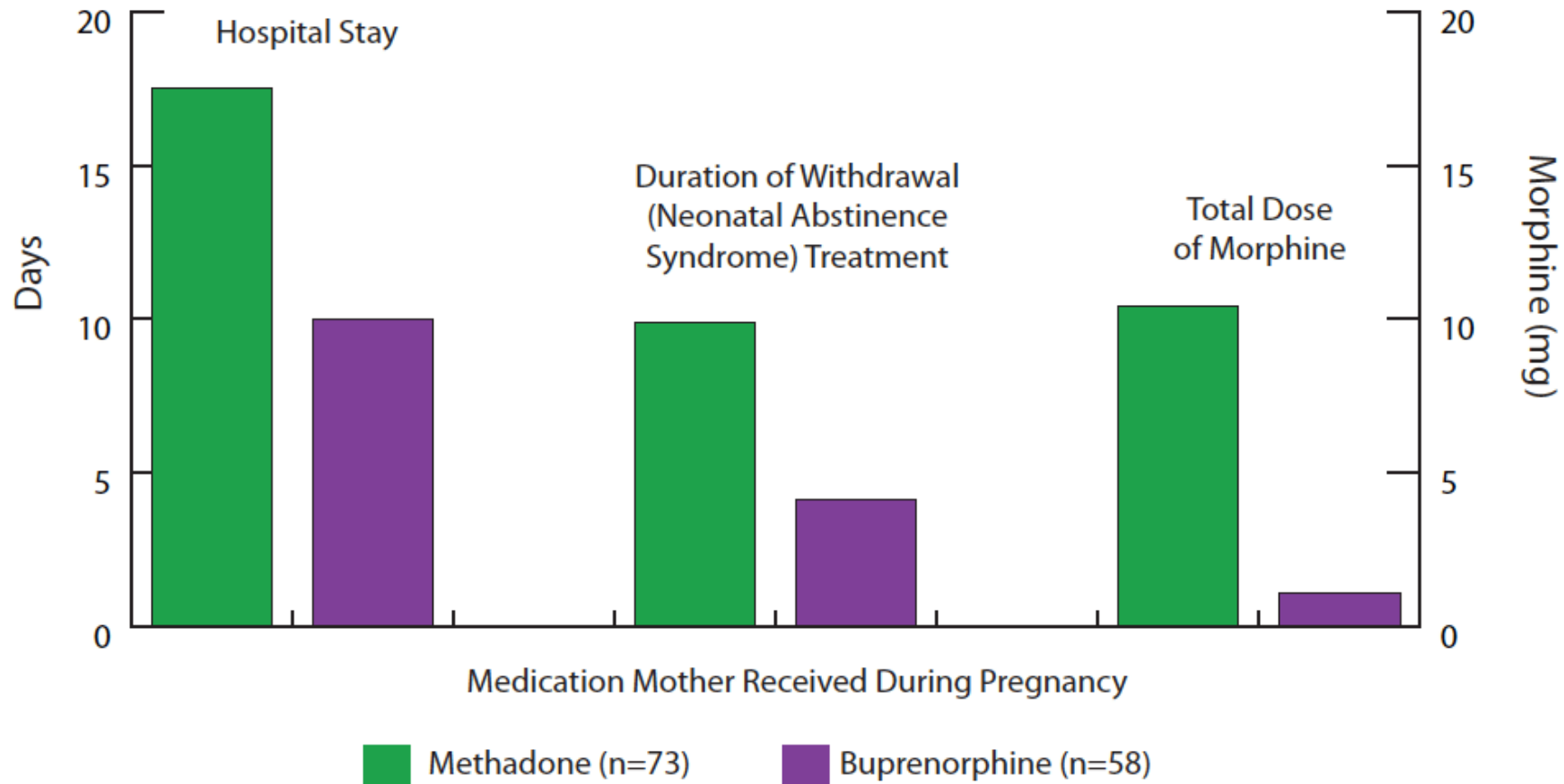
# MATERNAL OPIOIDS

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OPIOID:	HEROIN	METHADONE	BUPRENORPHINE
Half-life	Short (2-6 hours)	Long (24 hours)	Long (24+ hours)
Onset of signs	Usually < 24 hours	Usually 24-48 hours but may be 3-7 days	Usually 24-72 hours
Severity of signs	Mild-moderate	Moderate-severe	Mild-moderate
Likelihood of NAS	Lowest (50-70%)	Highest (up to 94%)	Intermediate

# METHADONE VS. BUPRENORPHINE

Mothers' Buprenorphine Treatment During Pregnancy Benefits Infants



# VARIABILITY OF NAS

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Maternal factors: Drug, amount, frequency, cofactors (e.g., benzos, EtOH, cocaine, marijuana), stress, other co-morbidities

Placental factors

Infant factors: Gestational age, co-morbidities, environmental and caregiver differences, efficacy of treatment

Genetic and epigenetic factors

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# TOPICS OF INTEREST: TREATMENT

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Treatment issues:

Quantification of severity of NAS

Goals of treatment

Non-pharmacologic approach

Role of breast feeding

When to use pharmacologic treatment

What drug(s); what dosage regimens; how to wean

Role of outpatient management; post-discharge follow-up

# Finnegan Score

SYSTEMS	SIGNS AND SYMPTOMS	SCORE	DAILY WT.														
			AM 2	4	6	8	10	12	PM 2	4	6	8	10	12			
CENTRAL NERVOUS SYSTEM DISTURBANCES	High Pitched Cry	2															
	Continuous High Pitched Cry	3															
	Sleeps < 1 Hour After Feeding	3															
	Sleeps < 2 Hours After Feeding	2															
	Hyperactive Moro Reflex	2															
	Markedly Hyperactive Moro Reflex	3															
	Mild Tremors Disturbed	2															
	Moderate Severe Tremors Disturbed	3															
	Mild Tremors Undisturbed	1															
	Moderate Severe Tremors Undisturbed	2															
	Increased Muscle Tone	2															
	Excoriation (specify area): _____	1															
	Myoclonic Jerks	3															
	Generalized Convulsions	3															
METABOLIC VASOMOTOR/ RESPIRATORY DISTURBANCES	Sweating	1															
	Fever < 101 <sup>o</sup> F (39.3 <sup>o</sup> C)	1															
	Fever > 101 <sup>o</sup> F (39.3 <sup>o</sup> C)	2															
	Frequent Yawning (> 3-4 times/interval)	1															
	Mottling	1															
	Nasal Stuffiness	1															
	Sneezing (> 3-4 times/interval)	1															
	Nasal Flaring	2															
	Respiratory Rate > 60/min	1															
Respiration Rate > 60/min with Retractions	2																
GASTROINTESTINAL DISTURBANCES	Excessive Sucking	1															
	Poor Feeding	2															
	Regurgitation	2															
	Projectile Vomiting	3															
	Loose Stools	2															
Watery Stools	3																
SUMMARY	<b>TOTAL SCORE</b>																
	<b>SCORER'S INITIALS</b>																
	<b>STATUS OF THERAPY</b>																

Adapted from Finnegan L. Neonatal abstinence syndrome: assessment and pharmacotherapy. Neonatal Therapy: An update, F. F. Rubaltelli and B. Granti, editors. Elsevier Science Publishers B. V. (Biomedical Division). 1986: 122-146

# GOALS OF TREATMENT

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Minimize signs of NAS

Ensure normal growth (rate of weight gain)

Establish normal sleep-wake cycles

Promote normal socialization (caretaker-child interactions)

Avoid known complications; e.g.,

- Fever
- Skin breakdown
- Seizures

# NON-PHARMACOLOGIC TREATMENT

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Swaddling

C-Position

Vertical rock

Head to toe movement

Percussion

Small frequent high caloric feedings; nursing when indicated

Minimize external environmental stimuli

Introduce stimuli gradually

Intravenous hydration as necessary

# CONCURRENT TREATMENT OF FAMILIES

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Recognize that mother always feels anxiety and guilt

Show empathy

Project a non-judgmental attitude

Evaluate maternal (and familial) psychosocial status

Work toward establishing good parental-infant bonding, teach parenting skills, with goals to:

- Avoid later child abuse and neglect
- Promote long-term supportive environment

Educate family about resources

# PHARMACOLOGIC TREATMENT

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Goal of pharmacologic treatment is to allow infant to tolerate mild signs of withdrawal (feed, sleep, interact)

Medications that have been used to treat NAS include:

- Morphine, methadone, buprenorphine (opioids)
- Phenobarbital (barbiturate)
- Diazepam, lorazepam, clonazepam (benzodiazepines)
- Clonidine ( $\alpha_2$ -adrenergic agonist)
- Chlorpromazine (phenothiazine)

# CURRENT PHARMACOLOGIC PRACTICE

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First line drug treatment (U.S. and U.K.): opioid (oral morphine > methadone), but significant use of phenobarbital

Initial dose is usually titrated to Finnegan scores

If signs of NAS are not relieved by maximum dose of single drug, a second drug is added (phenobarbital > clonidine > benzodiazepine)

Dose is weaned by 10-20% every 1-2 days so long as Finnegan scores are generally < 8

# CURRENT STATE OF EVIDENCE

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Existing trials do not clearly identify the most effective pharmacologic drug class or the most effective agent within a drug class (endpoints: treatment failure; length of stay; total dose of drug) and have methodological weaknesses

Protocols that use specific Finnegan scores to initiate therapy are based on precedent but not on evidence

However, adopting a protocol and adhering to it reduces the length of hospital stay



# CLONIDINE vs. PHENOBARB AS ADJUNCT

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Unblinded study of morphine plus clonidine vs. morphine plus phenobarbital (34 infants in each group)

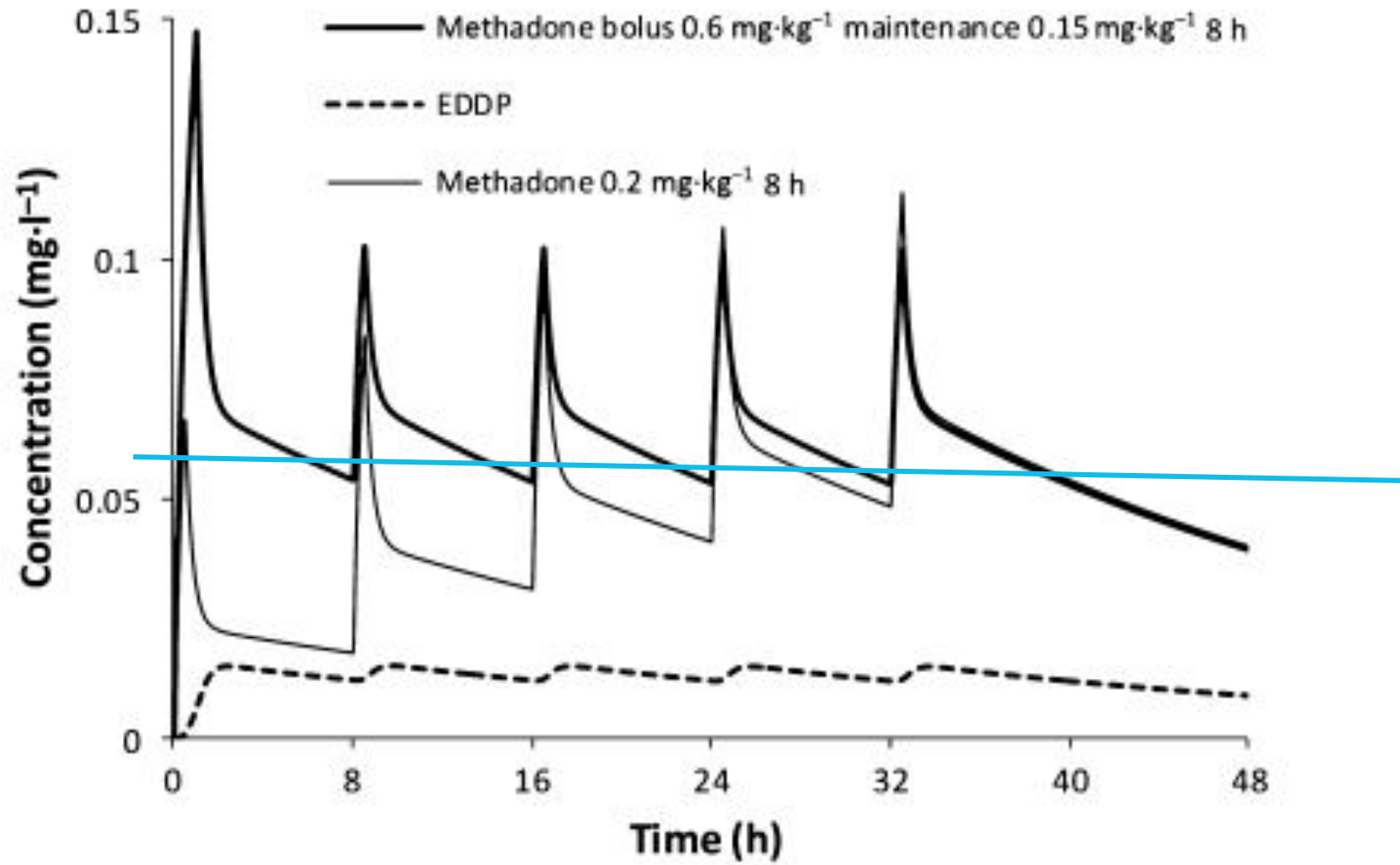
Primary outcome: days of morphine therapy

Protocol: Clonidine weaned in hospital but infants could be discharged home on phenobarbital

Results: Phenobarbital continued for mean of 3.8 (range, 1-8) months

	CLONIDINE	PHENOBARBITAL	P VALUE
Days of morphine	18.2	13.6	0.037
Morphine (mg)	5.7	4.6	0.069

# METHADONE PHARMACOKINETICS



# OTHER ISSUES

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## Breast feeding

## Hospital rooming-in

- Facilitate rooming-in by parents, caregivers
- Encourage breast feeding
- Minimize pharmacologic treatment
- Tolerate higher NAS scores: goal is not to eliminate signs!

## Outpatient management

- Occurs in some areas of the country by necessity
- Literature (much is European) documents excessive lengths of treatment; high use of phenobarbital
- Requires excellent family selection and close follow-up: only takes one serious morbidity to dismantle a program
- Two “recent” reported experiences (Australia; Ohio)

# SUMMARY POINTS ABOUT TREATMENT

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Substantial variability in resources for non-pharmacologic treatment

Significant variability in NAS assessment and criteria to initiate pharmacologic treatment

Existing data are insufficient to identify optimal initial drug treatment

Optimal adjunctive therapy remains controversial

Having a treatment/weaning protocol decreases LOS

Improved assessment of integrated prenatal drug exposure may allow tailoring of postnatal treatment

Analysis of genetic and epigenetic information may identify babies at highest risk for severe withdrawal

# QUESTIONS