

# Pharmacologic Treatments for NAS

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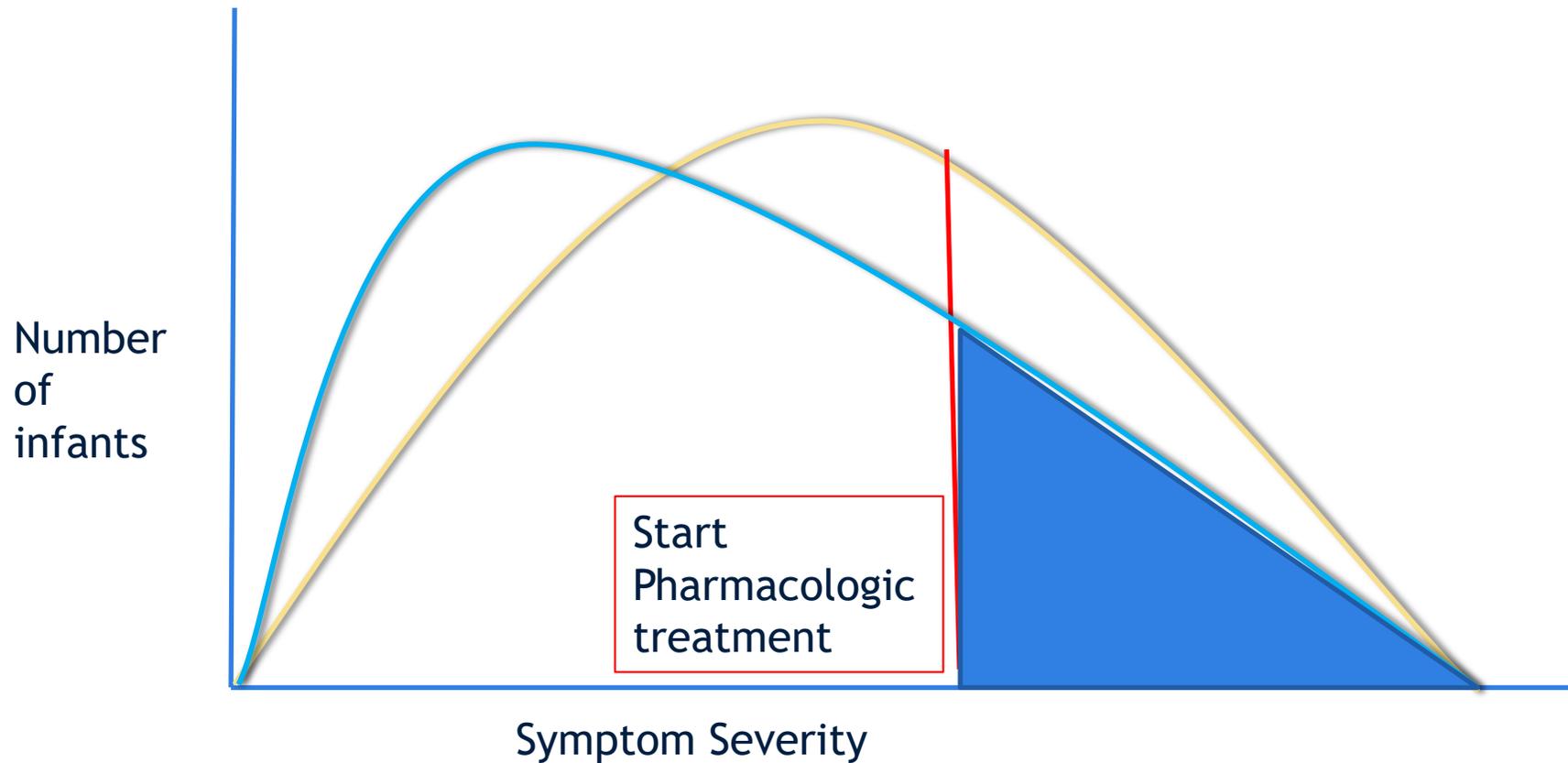


# FIRST PRINCIPLES

- Use standardized protocol
- Maximize non-pharmacologic approaches on all infants
- Continuous quality assessment

Non-pharm Treatments	Specific interventions
Foster maternal infant bonding	<p>Breast feeding</p> <p>Rooming in</p>
Foster enteral feeding	<p>Lactation support</p> <p>Small, calorically dense formula feeds</p> <p>On demand feeding, low lactose</p>
Environmental control	<p>Swaddling</p> <p>Low light, minimize distraction</p> <p>Low patient to nurse ratio</p>
Tactile measures	<p>Support skin to skin contact</p> <p>Volunteer cuddlers</p> <p>Music/physical therapy</p> <p>Acupuncture</p>
Parental trust building	<p>Outpatient links</p> <p>Staff Training</p>

# Non Pharm Treatments Can Shift Curve to the Left



# Intensity of pharmacologic treatment?

## Treating More

Longer hospitalization

Resources

Maternal stigma

Impaired dyad bonding?

Long term effects?

## Treating Less

Impaired weight gain

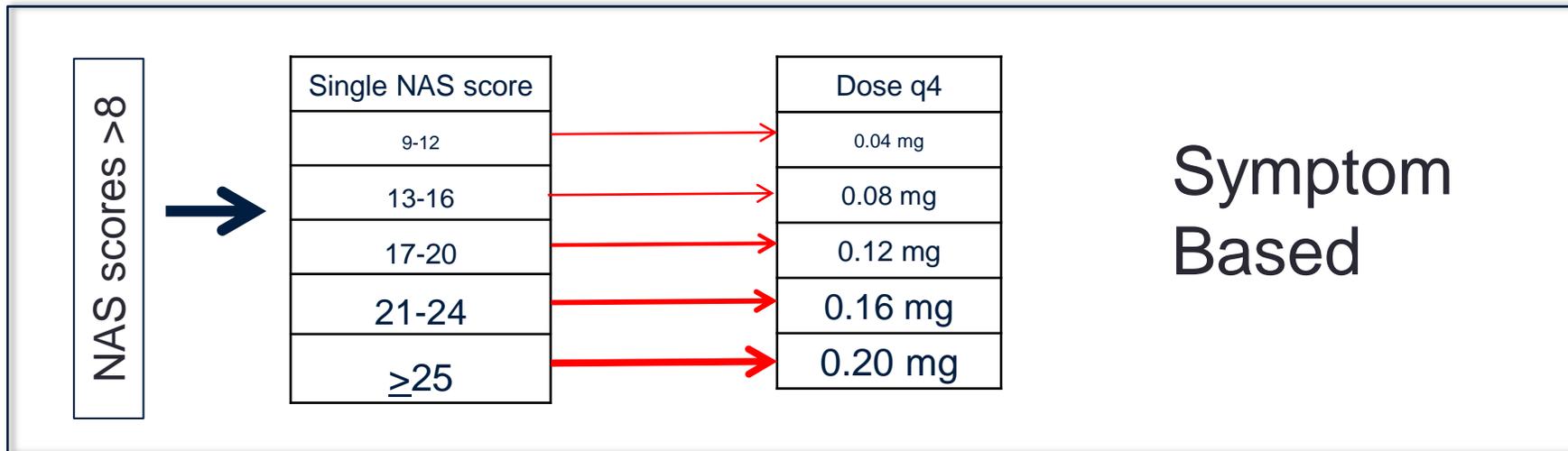
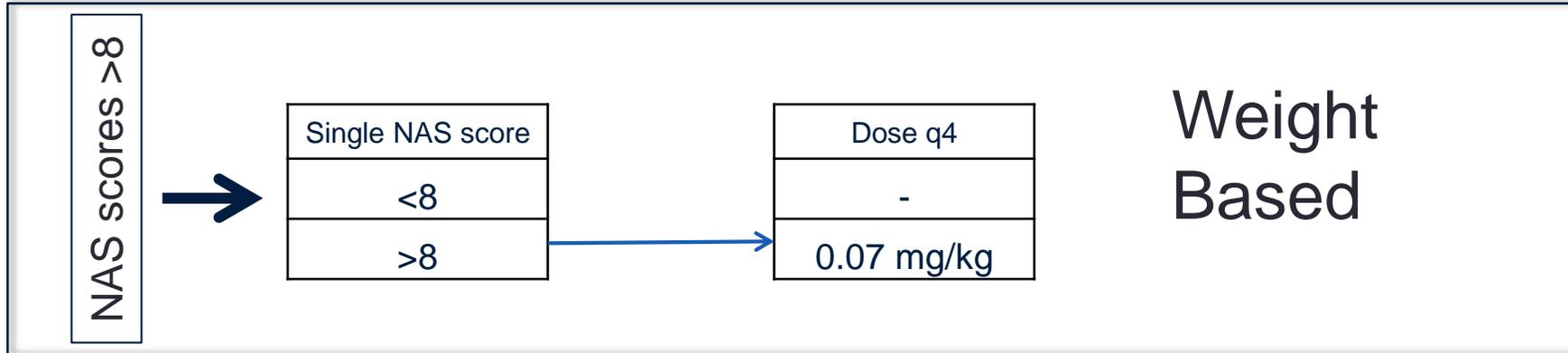
Seizure risk

Discomfort

Maternal stress

Long term effects?

# Morphine: Weight vs Symptom Based



# Morphine vs Methadone median LOT

Author		Design	N	Morphine	Methadone	P
Lainwala	2005	Retrospective	46	36	40	NS
Hall	2014	Retrospective	383	16*	16*	NS
Young	2015	Retrospective	26	7*	38*	0.001
Brown	2015	Blinded RCT	31	21	14	0.008
Davis	2018	Blinded RCT	183	15	11.5	0.02
Tolia	2018	Retrospective	7667	23 <sup>#</sup>	18 <sup>#</sup>	<0.001

\*= mean, # = length of stay,  
 NS = not significant, RCT = randomized controlled trial

# Buprenorphine vs morphine or methadone

Study	Pub	Design	Buprenorphine			Comparator (N)	Reduction in length of treatment (days buprenorphine vs comparator)
			N	Initial dose ( $\mu\text{g}/\text{kg}/\text{day}$ )	Maximum dose ( $\mu\text{g}/\text{kg}/\text{day}$ )		
Kraft	2008	Randomized, open label	13	13.2	39	Morphine (13)	<b>32%</b> (22 vs 32)
Kraft	2011	Randomized, open label	12	15.3	60	Morphine (12)	<b>39%</b> (23 vs 38)
Kraft	2017	Blinded, randomized	30	15.3	60	Morphine (33)	<b>46%</b> (15 vs 28)
Hall	2016	Retrospective cohort	38	13.2	39	Methadone (163)	<b>33%</b> (9.3 vs 14)
Hall	2017	Retrospective cohort	174	13.5	22.5	Methadone or Morphine (186)	<b>29%</b> (7.4 vs 10.4)

# Ethanol

- Buprenorphine 30%
- Methadone 9%
- Morphine 0%
- Phenobarbital 15-30%

Drug	Ethanol content (%)
Acetaminophen with codeine elixir	7
Chlorothiazide oral suspension	0.50
Cyproheptadine hydrochloride syrup	5
Dexamethasone oral solution	30
Diazoxide oral suspension	7.25
Digoxin oral solution	10
Ferrous sulfate oral drops	0.20
Griseofulvin oral suspension	0.20
Hydroxyzine hydrochloride syrup	0.50
Lasix oral solution	11.50
Maalox oral suspension	< 0.5
Metoclopramide oral solution	< 0.1
Nystatin oral suspension	≤ 1
Phenobarbital elixir	15
Prednisolone oral solution	2
Propranolol hydrochloride	0.60
Ranitidine oral solution	7.70
Sulfamethoxazole and trimethoprim oral suspension	0.26
Zantac	7.50

# Non opioid adjuncts

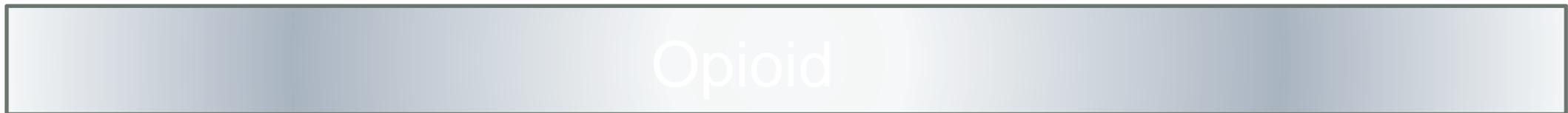
## Phenobarbital

- Binds GABA(A) receptor
- Global sedative properties
- Use is common
  - Phenobarbital used in 80% of neonatal seizures
  - 20-30,000 infants per year in US

## Clonidine

- Central alpha 2 adrenergic agonist
- Specific for opioid withdrawal
- Concerns for rebound hypertension on cessation

# Non-opioid adjunct models



# Key Considerations

- Which opioid?
- Which regimen?
  - *Starting dose*
  - *Up and down titration*
  - *Maximum dose*
- Which adjunct?
  - *When to start and stop*
- Which setting
  - *NICU*
  - *Peds floor*
  - *Outpatient*

# Ondansetron to reduce need for opioid pharm treatment

Single dose given to mother in labor followed by daily dose for infant  
-current clinical trial ongoing

 U.S. National Library of Medicine

*ClinicalTrials.gov*

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## Can Ondansetron Prevent Neonatal Abstinence Syndrome (NAS) in Babies Born to Narcotic-dependent Women (AIM2NAS)

**This study is currently recruiting participants.**

See [▶ Contacts and Locations](#)

*Verified October 2017 by David R. Drover, Stanford University*

**Sponsor:**

Stanford University

**ClinicalTrials.gov Identifier:**

NCT01965704

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