



Updates/changes to the recommended OPQC NAS Protocol

Introduction: These protocols are a synthesis of the best available, although limited evidence, and an analysis of practice variation across the state of Ohio in a cohort of over 6800 term infants (≥ 37 weeks GA) with maternal narcotic exposure. The updated methadone protocol is based initially on pharmacokinetic data¹³ and then subsequent published improvement with implementation of the protocol¹⁴. Changes from the Ohio Children's Hospital Association (OCHA - pilot project)⁹ recommended protocol include:

- The non-pharmacological treatment formula feeding recommendation is based upon OPQC's QI initiative using a factorial design testing the impact of formula (LLF vs. No LLF and 22 kcal vs. 19 kcal) on care of infants with NAS.
- The Methadone updates are based on a pharmacokinetic informed protocol that demonstrated lower length of treatment and length of stay.
- Morphine updates include escalation/rescue doses that are *score based*.
- The pharmacological treatment updates are based on enteral dosing. IV dosing for Morphine differs and is included as a footnote in the rare occurrence an NAS infant is NPO.
- Phenobarbital is listed as the recommended secondary drug option. It is included in the protocol because centers have the most experience with it, but evidence is lacking for all secondary agents. Due to this fact, some centers may elect to use clonidine. Each center should select one agent and use the same drug consistently as an adjunct therapy. Should Clonidine be selected as the secondary medication of choice, it is NOT recommended that an infant be discharged home on the drug.



Ohio Perinatal Quality Collaborative:

Enteral Methadone or Morphine Protocol for

Neonatal Abstinence Syndrome (NAS) from Maternal Exposure

Introduction: These protocols are a synthesis of the best available, although limited evidence, and an analysis of practice variation across the state of Ohio in a cohort of over 6800 term infants (≥ 37 weeks GA) with maternal narcotic exposure. The updated methadone protocol is based initially on pharmacokinetic data ¹³ and then subsequent published improvement with implementation of the protocol ¹⁴.

These are viewed as potentially better protocols that humanely and safely wean infants off narcotics over a 2-3 week period.

Overview of Stages of treatment:

Non-pharmacologic bundle:	Swaddle, skin to skin, decreased stimulation breast feed or 22kcal formula
Pharmacologic bundle:	
• Initiate	• Select Methadone or Morphine PO • Finnegan scores >8 q3hrs THREE times or scores ≥ 12 TWO times in a row
• Escalate	• If Finnegan scores remain elevated, increase dosage based on infant's score
• Stabilize	• Maintain dose for 24 hrs (Methadone) • Maintain dose for 48 hrs (Morphine)
• Wean	• Wean every 24 hrs based on Finnegan scores • Wean by step daily (Methadone) • Wean by 10% stabilizing dose daily (Morphine)
• Discharge	• Discharge 48 hrs off of Methadone or Morphine

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1. **Scoring:** All Infants will be scored every 3-4 hours around feedings with the modified Finnegan Scoring System. Begin scoring prior to 12 hours of life.

1a. There are some experts who recommend using the *average* of Finnegan scores over a 24 hour period in the stabilization and weaning phase to minimize the impact of minor variations on dosing.

1b. Centers should develop a plan for periodic refresher training for all nurses on the modified Finnegan scoring system using the D'Apolito Reliability Training system, and a training system for on-boarding new nursing staff. Recommend dual scoring to be done once a day minimum, in addition to periodic refresher training on the Finnegan scoring tools.

1c. Adjust trigger scores when > 3 weeks old: Research has shown that NAS scores increase over time as the infant matures, so > 21 days all Trigger thresholds should be increased by 2.

2. **Non-Pharmacologic Treatments:** All infants with NAS will be treated with a bundle of non-pharmacologic interventions including decreased stimulation, swaddling, continuous holding and frequent feeds.

2a. Each institution should develop a policy for the use of Mother's Own Milk. Consideration of supporting breast feeding may be given if the mother is active in a treatment program and mother's addiction specialist supports breast feeding.

2b. If MBM is not used, use of a term 22kcal/oz formula to meet the exceptional caloric needs and combat the documented weight loss seen in NAS infants is recommended. Use of non-lactose containing formula is at the discretion of the individual unit. High calorie (22 kcal/oz) formula may be discontinued when the infant completes pharmacologic treatment or if the infant has excessive weight gain.

3. **Pharmacologic Treatment:** Each center should pick either Methadone or Morphine as their primary opioid for pharmacologic treatment and use this for ALL NAS infants treated in that center.

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Methadone:

3a. NAS Methadone Initiation:

- Start pharmacologic treatment for infants with 3 consecutive Finnegan scores > 8, or 2 consecutive Finnegan scores \geq 12.

	Methadone Dose	Dosing Interval	Number of Doses
Step 1	0.1 mg/kg	Q6	4
Step 2	0.07 mg/kg	Q12	2
Step 3	0.05 mg/kg	Q12	2
Step 4	0.04 mg/kg	Q12	2
Step 5	0.03 mg/kg	Q12	2
Step 6	0.02 mg/kg	Q12	2
Step 7	0.01 mg/kg	Q12	2
Step 8	0.01 mg/kg	Q24	1

3b. NAS Methadone Escalation:

- If infant fails step 1 (scores >12) consider steps 1A through 1C.

	Methadone Dose	Dosing Interval	Number of Doses
Step 1A	0.1 mg/kg	Q4	6
Step 1B	0.1 mg/kg	Q8	3
Step 1C	0.1 mg/kg	Q12	2

Adjunct Therapy/Second Drug: Phenobarbital

Phenobarbital is included in this protocol as the majority of sites had the most experience with it, but evidence is lacking for all secondary agents¹². Due to this fact, some centers may elect to use clonidine. Each center should select one agent and use the same drug consistently as adjunct therapy.

Consider starting phenobarbital if:

- Polysubstance exposure is suspected/confirmed: (benzodiazepines, barbiturates, antipsychotics, antidepressants, other sedatives/hypnotics, tobacco) AND
 - CNS findings predominate, rather than GI findings on NAS subscale e.g. tremors, increased muscle tone, etc.
 - Unable to wean for 2 consecutive days.

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Loading dose:

- 10 mg/kg/dose po every 12hr x 2 doses OR 20 mg/kg/dose x 1
 - Enteral formulation contains 10% alcohol.
 - Dividing po dose may decrease risk of emesis and/or sedation.

Maintenance dose:

- 5 mg/kg/dose po once daily – do not adjust for weight

Phenobarbital Wean: Two approaches may be used. (Neither has been directly studied.) Each center should pick one method.

- A. Discontinue when on second to last step of morphine wean to assess for tolerance of discontinuation. Given long half-life of phenobarbital this will wear off gradually over 4 days.
- B. Discharging infant home on phenobarbital with subsequent weaning to be done either in Neo Clinic or by infant's PCP. (Given the high alcohol concentration limiting exposure may be the best practice. Hypnotic or nicotine withdrawal occurs rapidly and generally is completed by day 5- thus longer phenobarbital exposure may not be needed.)

3c. NAS Methadone Weaning:

- Wean to next step if average Finnegan score is < 8 for the past 24 hours.
- If average Finnegan score is 8-12, do not wean.
- If average Finnegan score is > 12, consider an extra dose of methadone at the current step, or return to the previous step.

3d. NAS Methadone Discharge:

- Observe for 48 hours off methadone.

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Morphine

4a. NAS Morphine Initiation: 0.05mg/kg/dose q3h po

4b. NAS Morphine Escalation

- Increase dose every 3 hrs until controlled (average NAS \leq 8 in 24 hours).
- Rescue Dose: If infant has 2 scores in a row of 9-12, increase Morphine by 0.02mg/kg/dose
- If infant has 2 scores in a row >12 increase morphine by 0.04 mg/kg/dose
- Please refer to Adjunct Therapy if dose becomes ≥ 0.3 mg/kg/dose

Adjunct Therapy/Second Drug: Phenobarbital

Consider starting phenobarbital if:

- Polysubstance exposure is suspected/confirmed: (benzodiazepines, barbiturates, antipsychotics, antidepressants, other sedatives/hypnotics, tobacco) AND
 - CNS findings predominate, rather than GI findings on NAS subscale e.g. tremors, increased muscle tone, etc.
 - Morphine dose exceeds 0.3 mg/kg/dose with NAS score > 8 ; OR unable to wean for 2 consecutive days.

Loading dose:

- 10 mg/kg/dose po every 12hr x 2 doses OR 20 mg/kg/dose x 1
 - Enteral formulation contains 10% alcohol.
 - Dividing po dose may decrease risk of emesis and/or sedation.

Maintenance dose:

- 5 mg/kg/dose po once daily – do not adjust for weight

Phenobarbital Wean: Two approaches may be used. (Neither has been directly studied.) Each center should pick one method.

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- B. Discharging infant home on phenobarbital with subsequent weaning to be done either in Neo Clinic or by infant's PCP. (Given the high alcohol concentration limiting exposure may be the best practice. Hypnotic or nicotine withdrawal occurs rapidly and generally is completed by day 5- thus longer phenobarbital exposure may not be needed.)

4c. NAS Morphine Stabilization

- All scores remain ≤ 8 for minimum 48 hours.
- 72 hours of stabilization may be used if infant has had to increase above 0.4mg/kg dose or if phenobarbital added.

4d. NAS Morphine Wean and Backslide

- Once stabilized on same dose for 48 hours, use this dose as the starting point of the wean.
- Begin weaning the dose by 10% (of the original dose when the first wean was started) every 24 hours.
- Drug may be discontinued when a single dose is < 0.02 mg/kg/dose. Please see below for example.

Example:

Infant X (wt: 3.2 kg) required 2 dose increases of his morphine to get his NAS scores consistently ≤ 8 . He has now been on the dose of 0.32 mg (0.1 mg/kg/dose) po q3hr for 72 hours. Team would like to begin weaning. As long as his scores remain consistently ≤ 8 , please decrease by 10% every 24hrs.

Day 1: 0.29 mg q3hr (0.09 mg/kg)

Day 2: 0.26 mg q3hr (0.08 mg/kg)

Day 3: 0.22 mg q3hr (0.07 mg/kg)

Day 4: 0.19 mg q3hr (0.06 mg/kg)

Day 5: 0.16 mg q3hr (0.05 mg/kg)

Day 6: 0.13 mg q3hr (0.04 mg/kg)

Day 7: 0.1 mg q3hr (0.03 mg/kg)

Day 8: 0.06 mg q3hr (0.02 mg/kg) x 24hr and then stop

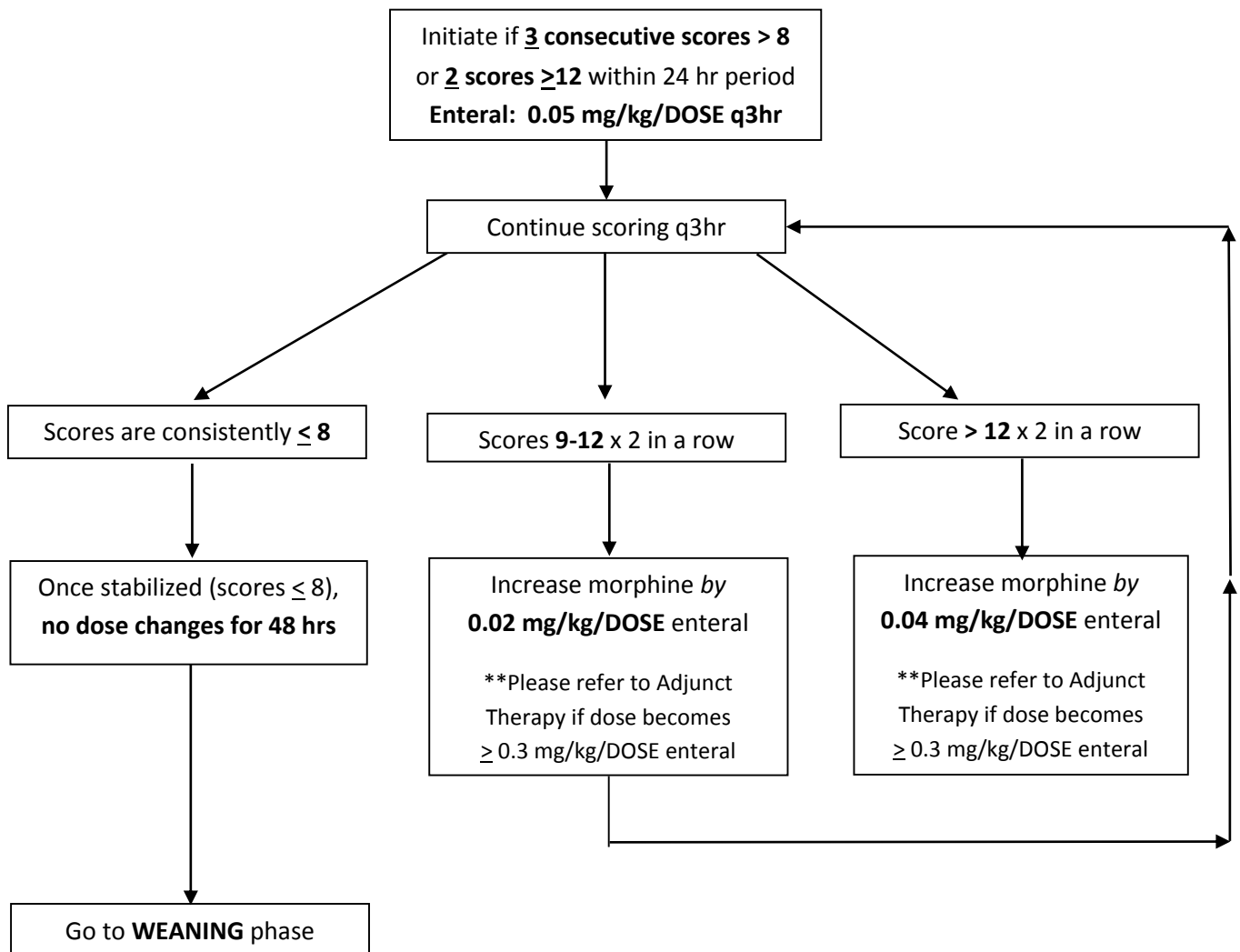
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4e. NAS Morphine Discharge

- Observe in-house x 48 hours off of morphine before discharge

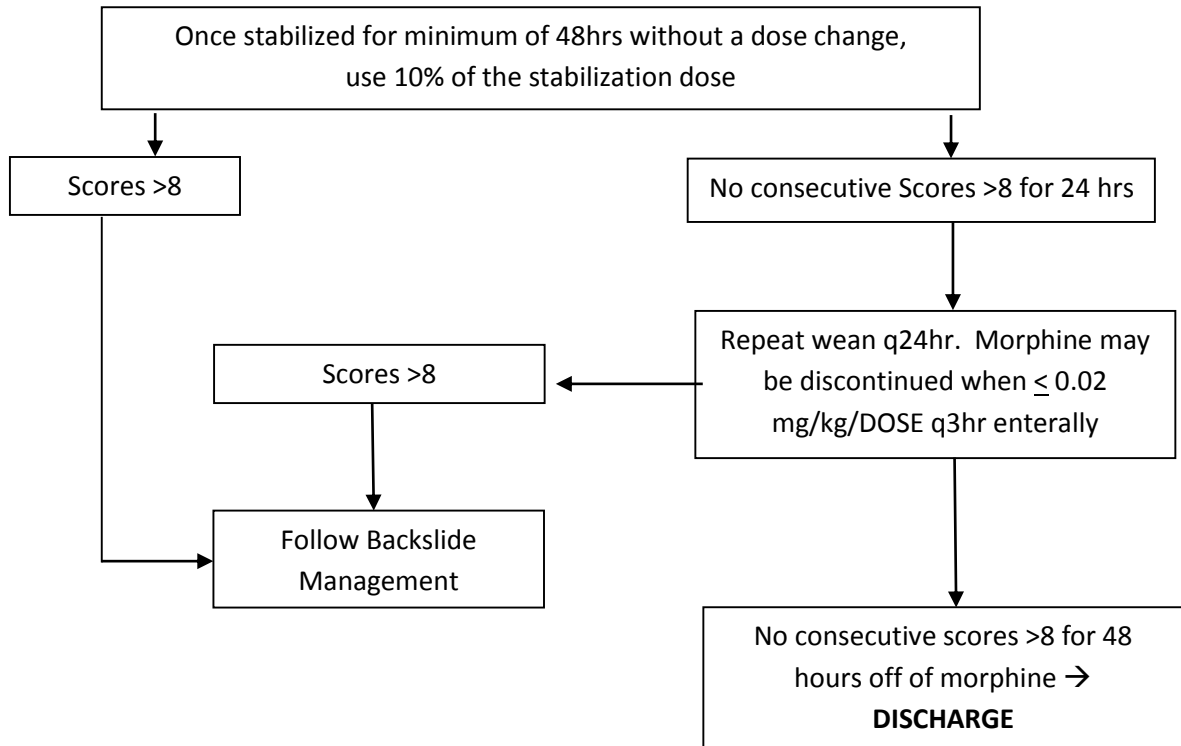
*The above protocol is for *enteral* dosing of Morphine. In the situation where an infant with NAS cannot have enteral morphine (ie gastrochisis, omphalocele, etc) IV morphine should be used. **IV and enteral morphine doses are not equivalent.** The IV initiation dose is 0.02mg/kg/dose every 3 hours. If the symptoms are not controlled, may increase the IV dose by 0.01mg/kg/dose every three hours until symptoms are controlled.

Initiation, Escalation, Stabilization

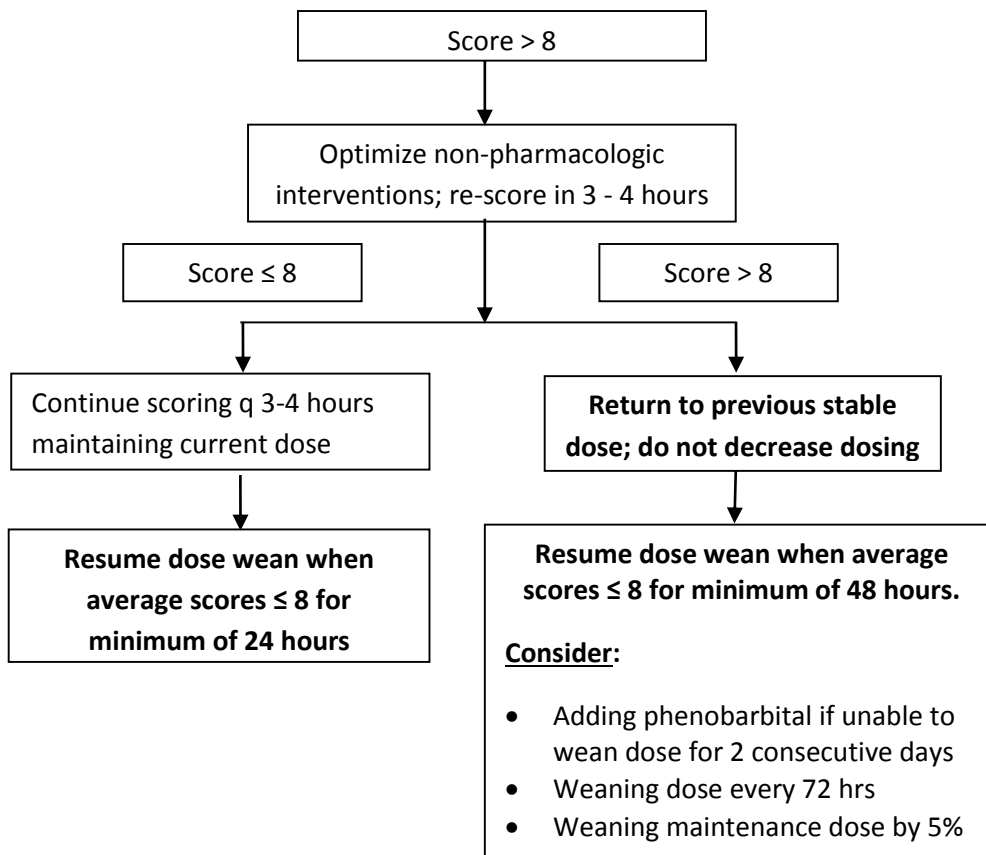


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Weaning



Backslide Management for scores >8



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Through collaborative use of improvement science methods, reduce preterm births & improve perinatal and preterm newborn outcomes in Ohio as quickly as possible.