Partnering to Improve Health Care Quality for Mothers and Babies

NAS PHARMACOLOGIC MANAGEMENT

William Driscoll, DO (University of Florida/Jacksonville)

Doug Hardy, MD (Winnie Palmer)

Lance Wyble, MD (MEDNAX, Inc. - Bay Care)

Welcome!

- Please enter your Audio PIN on your phone so we can un-mute you for discussion
- If you have a question, please enter it in the Question box or Raise your hand to be unmuted
- This webinar is being recorded
- Please provide feedback on our post-webinar survey

Our speakers



William Driscoll, DO



Lance Wyble, MD, MPH



Doug Hardy, MD

Thank you!

Learning objectives

- Discuss pros & cons of the most commonly used medications in NAS
 - 1st line: Morphine, Methadone
 - 2nd line: Phenobarbital, Clonidine
- 2. Discuss benefits of complying with a standardized guideline
- 3. Describe individual hospital pharmacologic guidelines
- 4. Understand how to develop a process map to communicate pharmacologic management

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PHARMACOLOGIC MANAGEMENT

Ist line: Morphine, Methadone

NAS Therapies in US NICUs

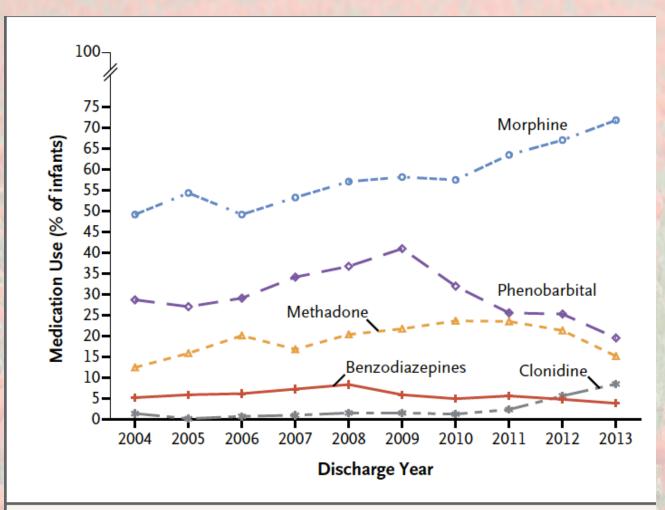


Figure 3. Medication Use in Infants with the Neonatal Abstinence Syndrome.

- Morphine & methadone are most commonly used therapies
- Buprenorphine may become more common over time
- New studies support role of clonidine alone in treatment of NAS

Morphine

ADVANTAGES

- Can be weaned more quickly in general due to its short half life
 - Shorter course of treatment
 - Shorter hospitalization
- Can be more easily given after discharge if necessary

DISADVANTAGES

 Short half life means diligent treatment and scoring during capture and weaning

Methadone

0.05-0.2 mg/kg every 12-24 hours

ADVANTAGES	DISADVANTAGES
 Longer half life means fewer daily doses 	 Long half-life may delay weaning Longer course of treatment Longer hospital stay Can lead to torsades de pointe in patients with congenital prolonged QT syndrome

Morphine vs. methadone

- No good comparisons between morphine
 & methadone as primary therapy for NAS
- Multiple reviews comparing NAS treatment with morphine or methadone have found conflicting results regarding length of stay
- Retrospective review of 36 infants treated with morphine or methadone for NAS found higher Cognitive and Gross Motor domains on Bayley-III for those treated with morphine

Takeaways

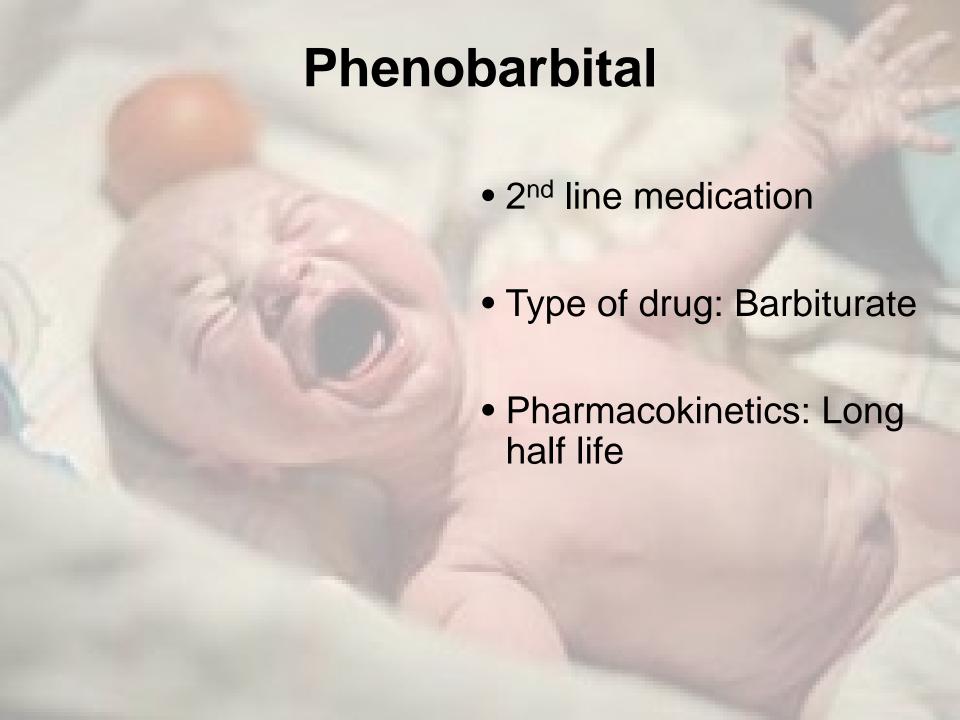
 Maternal methadone dose DOES NOT foretell likelihood of NAS in infant

 Non-pharmacologic measures are critical to successful treatment

 Centers have been successful with morphine or methadone – get a protocol and STICK TO IT Partnering to Improve Health Care Quality for Mothers and Babies

PHARMACOLOGIC MANAGEMENT

2nd Line: Phenobarbital, Clonidine



Phenobarbital

ADVANTAGES	DISADVANTAGES
 Decreased length of hospital stay (i.e., discharge home on phenobarbital) 	 Enteral formulation contains 10% alcohol Potential prolonged medication exposure

- Data on morphine/clonidine combination vs. morphine/phenobarbital combination
 - Phenobarbital combination had shorter hospital length of stay, but overall longer medication treatment time

Phenobarbital: Use in NAS

Polysubstance exposed neonate

- Commonly used dosing:
 - Loading dose of 20 mg/kg (given in 1 or 2 doses)
 - Maintenance dose of 5 mg/kg/day

Clonidine

- 2nd line medication
- Type of drug: CNS alpha₂ receptor agonist

- Pharmacokinetics
 - Inhibits sympathetic outflow
 - Reduces catecholamine release

Clonidine

ADVANTAGES	DISADVANTAGES
Reduced LOS when combined with other NAS medications	 Reduced blood pressure & heart rate (reduced catecholamine release) Weaned too quickly → rebound hypertension & tachycardia

Clonidine: Use in NAS

- Used to treat withdrawal in neonates, children,
 & adults
- Conflicting data on morphine alone vs. morphine/clonidine combination
- Commonly used dosing: unknown
 - Reports of every 3, 4, or 6 hours
 - Reports of continuous drug delivery

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BENEFITS OF COMPLIANCE WITH A STANDARDIZED GUIDELINE

Ohio Perinatal Quality Collaborative Improves Care of Neonatal Narcotic Abstinence Syndrome

Walsh MC, Crowley M, Wexelblatt S, et al. Pediatrics. 2018;141(4): e20170900

Multi-modal quality improvement initiative

GOAL 1	Standardize identification, <u>non</u> pharmacologic & pharmacologic treatment in Level 2 & 3 NICUs
GOAL 2	Reduce the use of & length of treatment in same Level 2 & 3 NICUs
GOAL 3	Reduce hospital length of stay in pharmacologically treated newborns with NAS

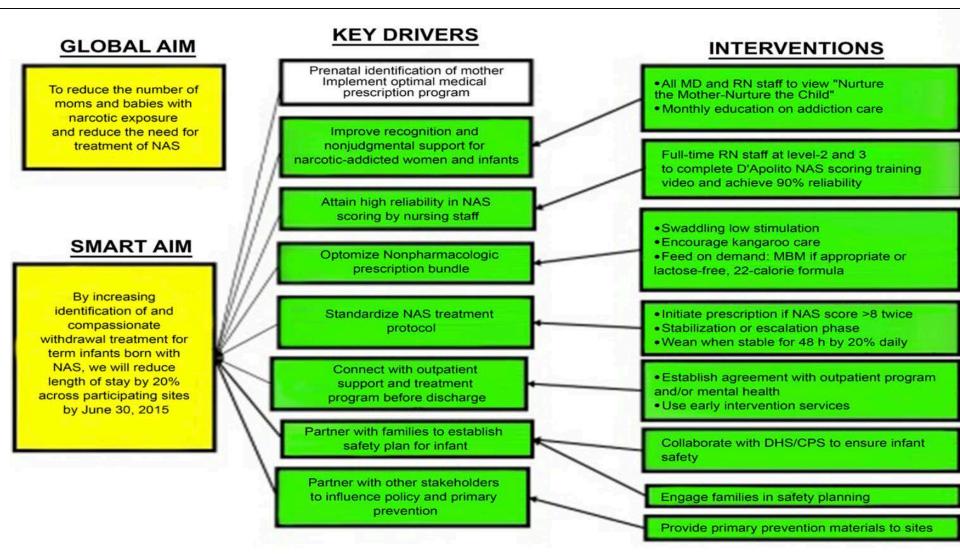


FIGURE 1

Key driver diagram for OPQC to Improve the Care of Newborns with In-Utero Narcotic Exposure. CPS, Child Protective Services; DHS, Department of Hulbert Services; MBM, maternal breast milk; MD, medical doctor; RN, registered nurse.

Walsh MC, Crowley M, Wexelblatt S, et al. Ohio Perinatal Quality Collaborative Improves Care of Neonatal Narcotic Abstinence Syndrome. *Pediatrics*. 2018;141(4):e20170900

Compliance	PRE- intervention	POST- intervention
Nonpharmacologic bundle	37%	59%
Pharmacologic bundle	59%	68%

- Ninety-six percent of Ohio NICU's participated
- Nearly half of babies received pharmacologic treatment

Nonpharmacologic ALL OR NONE

1: Swaddling

2: Low Stimulation or Rooming In

3: Breast milk and/or Low Lactose

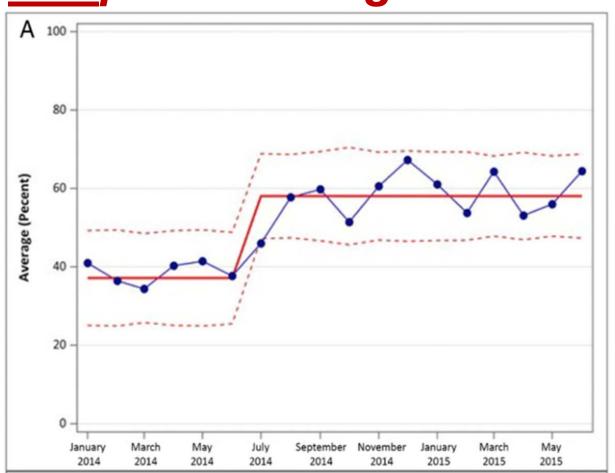
Pharmacologic ALL OR NONE

- 1: Treatment initiated appropriately
- 2: Unit primary opiate given
- 3: Weaning begun 48hr after stabilization

Pharmacologic Intermediate process

- 1: Frequency of dose escalation
- 2: Failed weaning
- 3: Percent of infants with either or both

Nonpharmacologic bundle compliance

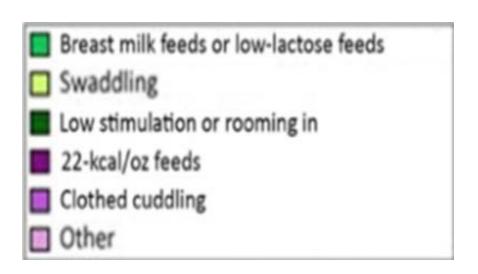


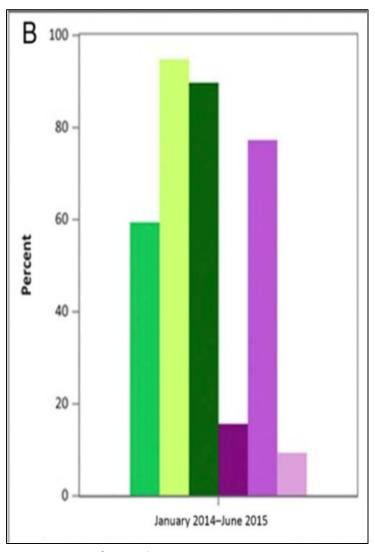
- Significant improvements in this bundle
- Centerline shift: increase by 21% from 37% to 59%

Walsh MC, Crowley M, Wexelblatt S, et al. Ohio Perinatal Quality Collaborative Improves Care of Neonatal Narcotic Abstinence Syndrome. *Pediatrics*. 2018;141(4):e20170900

Nonpharmacologic bundle compliance

Criteria met in individual elements



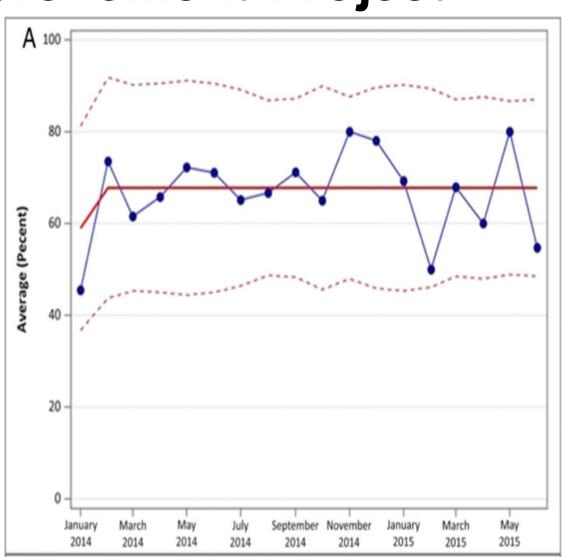


Walsh MC, Crowley M, Wexelblatt S, et al. Ohio Perinatal Quality Collaborative Improves Care of Neonatal Narcotic Abstinence Syndrome. *Pediatrics*. 2018;141(4):e20170900

Pharmacologic bundle compliance

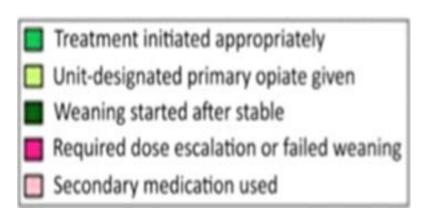
- Outcome only reported for Morphine in this bundle
- Centerline shift: Increase from 59% to 68%

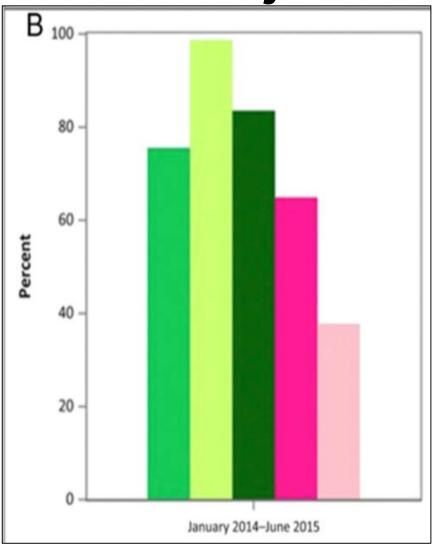
*Missing Methadone cohort (i.e. Underreporting true compliance)



Pharmacologic bundle compliance

Criteria met in individual elements





Pharmacologic Intermediate process

- Significant decrease in failed weaning/dose escalation
- Centerline shift: Decrease from 67% to 59%

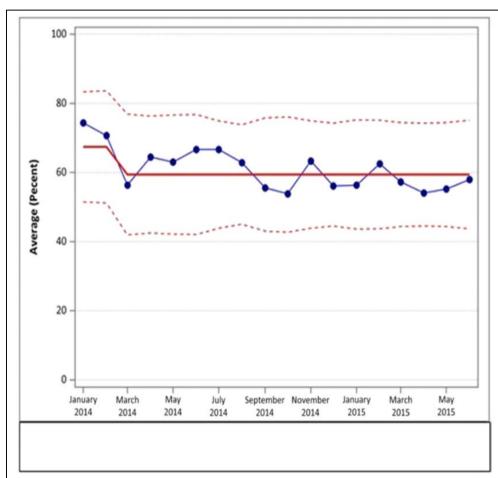
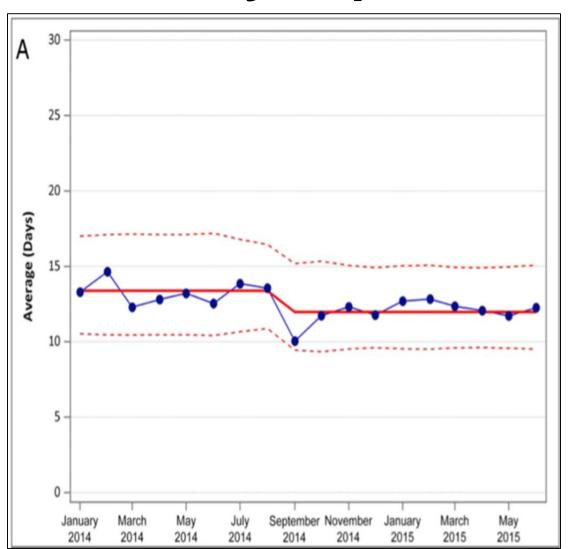


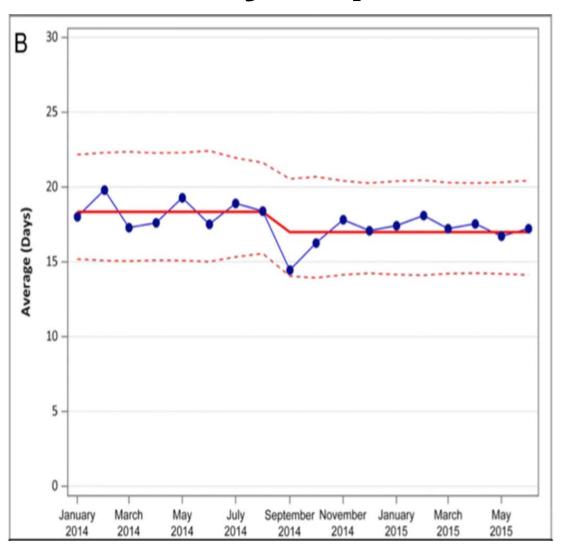
FIGURE 4

Proportion of infants with NAS failing a weaning step or requiring an opioid dose escalation: control chart showing a shift in centerline in March 2014.



Average length of treatment decreased from 33.8 to 21.3 days

Walsh MC, Crowley M, Wexelblatt S, et al. Ohio Perinatal Quality Collaborative Improves Care of Neonatal Narcotic Abstinence Syndrome. *Pediatrics*. 2018;141(4):e20170900



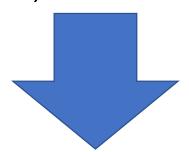
Average
length of stay
decreased
from
18.3 to 17 days

Walsh MC, Crowley M, Wexelblatt S, et al. Ohio Perinatal Quality Collaborative Improves Care of Neonatal Narcotic Abstinence Syndrome. *Pediatrics*. 2018;141(4):e20170900

Takeaways

- High reliability achieved with <u>unit-specific opioid</u> (99%)
- High reliability achieved with <u>weaning protocol</u> (87%)
- Total compliance measure was reduced by the component of treatment initiation (68%), influenced by Finnegan scoring

Therefore, high confidence that



Promoting a uniform, standardized approach to pharmacologic treatment is effective in reducing variability & outcomes

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INDIVIDUAL HOSPITAL GUIDELINES

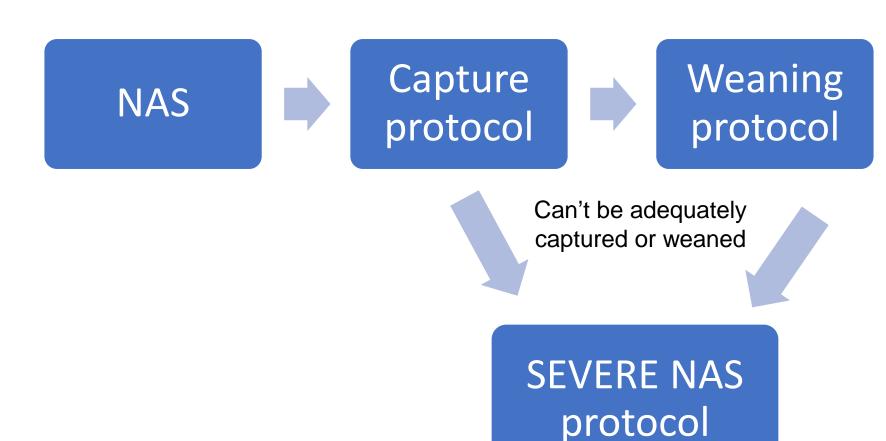
- University of Florida/Jacksonville
- Winnie Palmer
- Baycare

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NAS PROTOCOL/GUIDELINES

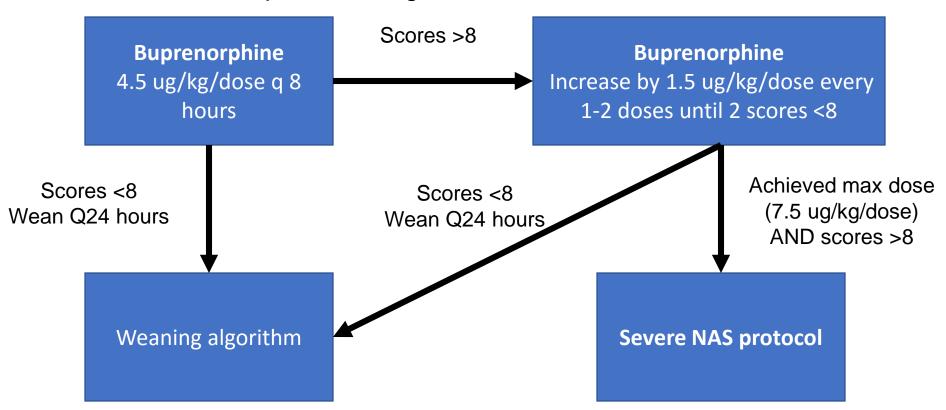
UF Health/Jacksonville

UF/Jacksonville



CAPTURE protocol

Initiate buprenorphine when 2 consecutive scores >8 or 1 score >12 despite maximization of non-pharmacologic measures.



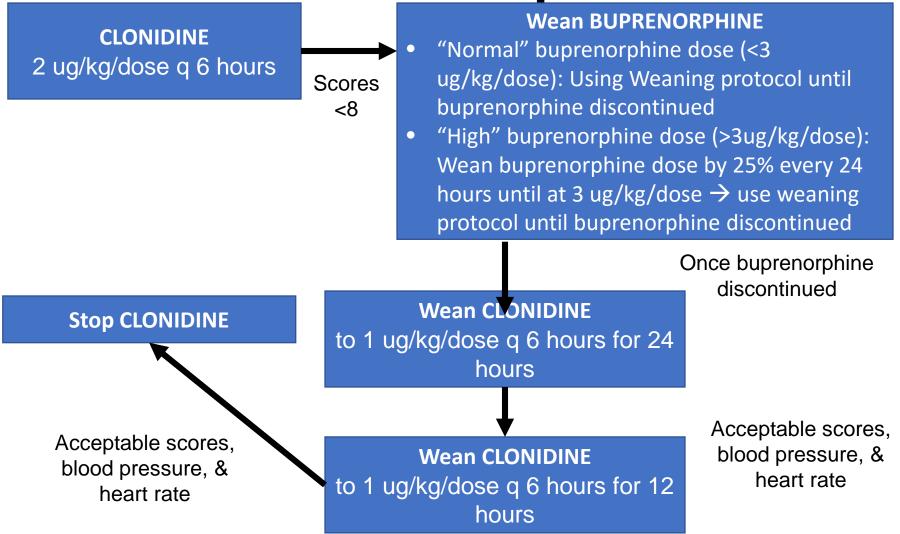
- Buprenorphine concentration: 75 ug/ml: compounded with 30% ethanol and simple syrup. If volume greater than 0.5 ml give in 2 separate aliquots with pacifier (2 minutes apart) to help absorption.
- Once captured, consider PT/OT consultation

WEANING **BUPRENORPHINE** protocol Wean to 3 ug/kg Q8 hours for 24 hours Buprenorphine 4.5 ug/kg/dose q 8 **BUPRENORPHINE** hours Wean to 1.5 ug/kg Q8 hours for 24 hours Scores <8 Wean Q24 hours **BUPRENORPHINE** Wean to 1.5 ug/kg Q12 hours for 24 hours Weaning algorithm STOP BUPRENORPHINE

NOTES:

- Caregiver rooming (if appropriate and room available) has been shown to facilitate timely weaning.
- If scores average >8 DO NOT wean.
- If scores average <6 consider weaning the dose as early as 16 hours
- Go to Severe NAS protocol if patient can't be weaned every 2-3 days
- Once medication is discontinued observed patient for 1-2 days.

SEVERE NAS protocol



- Use for patients who can't be adequately captured or weaned efficiently.
- Ensure all non-pharmacologic measures are maximized (parent/cuddler holding, rooming in)
- Notify NAS experts of severe NAS case

Notes with Severe NAS protocol

Clonidine

- Measure blood pressure Q6 hours while on clonidine & for 1-2 days after clonidine is discontinued.
- Hold clonidine dose if mean blood pressure < 40 mmHg and/or heart rate <100 bpm.
- If patient doesn't respond to buprenorphine & clonidine use Phenobarbital
 - Load with Phenobarbital (10 mg/kg) x2 doses 12 hours apart
 - Start maintenance dose of 2.5 mg/kg twice a day
 - Once average scores are <8 wean buprenorphine 1st, clonidine 2nd, & phenobarbital 3rd
- Once off all medications, the severe NAS patient should be monitored for 2 days for rebound NAS signs.

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NAS PROTOCOL/GUIDELINES

Winnie Palmer

Neonatal Abstinence Syndrome Management

NAS Scoring

Begin scoring every 3 hours once NAS is suspected
If maternal narcotic use is known, begin scoring on admission

Non-pharmacologic therapy

Non-p	harmaco	ologic therapy is critical to treatment of NAS and with appropriate and timely intervention, it may reduce or eliminate the infant's need for
pharm	nacologic	therapy. Initiate non-pharmacologic therapy below as soon as scoring is started:
	Dark a	nd quiet Room Assignment
	0	Notify appropriate charge nurse for room assignment to one of the preferred rooms for NAS babies
	Swadd	ling, pacifier, holding, gentle up and down rocking
	0	Parents and family are the ideal caretakers when able and available, rooming-in is preferred
	0	Volunteers should be called when the family is unavailable particularly in the early stages

- Attend to any infant needs quickly (wet or soiled diaper, dropping pacifier, etc.)
- ☐ Frequent feeds if able to feed ad lib
- ☐ Encourage breast feeding if no contraindications noted and no other drug abuse documented
- □ NO CD PLAYERS and NO MECHANICAL ROCKERS (mamaRoo is approved)

Initiation of Pharmacologic Therapy:

Single score > 8: Attend to any infant needs (feeding, diaper change, etc.), wait 1 hour and repeat scoring (FOR FIRST ELEVATED SCORE ONLY)

- **❖** If repeat score ≤ 8, continue with non-pharmacologic intervention
- ❖ If repeat score is > 8, initiate Morphine at dose that corresponds to the higher score; MD/NNP to be notified of score q 3 hours.

Subsequent scores > 8: Use the "Escalation" column to increase Morphine until scores < 8 (see chart); MD/NNP need to be called with score q 3 hours so morphine dose is increase accordingly until infant is controlled. Once infant is receiving morphine, escalate dose with single scores > 8. DO NOT REPEAT scoring after 1 hour as per protocol for the initial elevated score.

- ♦ Maximum morphine dose = 0.1 mg/kg/dose
- ❖ If morphine is at 0.1 mg/kg/dose and scores continue to be > 8, Clonidine is added at 1 mcg/kg/dose every 6 hours.
- ❖ If scores continue to be > 8, increase Clonidine to 2 mcg/kg/dose every 6 hours. Clonidine may be escalated to 3 mcg/kg/dose q 6 hours for persistently elevated scores.
- If scores remain elevated with increasing pharmacologic therapy, consider that there may be additional non-opioid drug exposure contributing to the infant's clinical picture.

NAS Score	Initial morphine Dosing	Escalation	Re-escalation (post wean initiation)					
0-8	Not Indicated	Continue same dose	Continue same dose					
9-12	0.04 mg q 3 hours	Increase morphine by 0.02 mg	Increase morphine by 0.01 mg					
13-16	0.08 mg q 3 hours	Increase morphine by 0.04 mg	Increase morphine by 0.02 mg					
17-20	0.12 mg q 3 hours	Increase morphine by 0.06 mg	Increase morphine by 0.03 mg					
21-24	0.16 mg q 3 hours	Increase morphine by 0.08 mg	Increase morphine by 0.04 mg					
25 or higher	0.20 mg q 3 hours	Increase morphine by 0.1 mg	Increase morphine by 0.05 mg					
Morphine is the Agent of Choice for NICU NAS								

Weaning of Pharmacologic Therapy

Initiate tapering with NAS scores ≤ 8 for 48 hours

- ❖ Decrease morphine by 0.02 mg every 24 hours (May decrease more rapidly with scores < 5)
- ❖ Once off morphine for 24 hours with scores ≤ 8, reduce Clonidine dose by 50% for 24 hours, then discontinue.

Re-escalation of Pharmacologic Therapy

If scores increase to > 8 once weaning has begun, re-escalate morphine dose with each score > 8 using the "Re-escalation" column above

Morphine - initiation

Begin morphine with 2 scores > 8, 1 hour apart

- 9-12 = 0.04 mg every 3-4 hours
- 13-16 = 0.08 mg every 3-4 hours
- 17-20 = 0.12 mg every 3-4 hours
- 21-24 = 0.16 mg every 3-4 hours
- $\geq 25 = 0.20 \text{ mg every } 3-4 \text{ hours}$

Morphine – continuation therapy

- For each subsequent score > 8, increase dose by:
 - 9-12 = 0.02 mg every 3-4 hours
 - 13-16 = 0.04 mg every 3-4 hours
 - 17-20 = 0.06 mg every 3-4 hours
 - 21-24 = 0.08 mg every 3-4 hours
 - \geq 25 = 0.1 mg every 3-4 hours
- Subsequent dosing every 3-4 hours
- If morphine reaches 0.1 mg/kg every 3-4 hours and scores are still > 8, add Clonidine at 1 mcg/kg every 6 hours. May increase to 2-3 mcg/kg q 6 hr

Morphine - weaning

- Once scores are ≤8 for 48 hours, may begin to wean morphine by 0.02 mg every 24
 - May decrease more rapidly with scores <5
- Once off morphine for 24 hours with scores
 ≤8, reduce Clonidine dose b 50% for 24 hours, then discontinue Clonidine

Morphine - re-escalation

- If scores increase to > 8 on 2 occasions after weaning was started, increase dose with each score >8 by:
 - 9-12 = 0.01 mg every 3-4 hours
 - 13-16 = 0.02 mg every 3-4 hours
 - 17-20 = 0.03 mg every 3-4 hours
 - 21-24 = 0.04 mg every 3-4 hours
 - $\ge 25 = 0.05$ mg every 3-4 hours

Clonidine - weaning

- If clonidine was given, continue at the maximum dose until morphine has been stopped for 24 hours.
- Wean by 50% and watch for tachycardia or hypertension or increased NAS scores
- If stable for 24 hours, discontinue clonidine and observe for another 24-48 hours.

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NAS PROTOCOL/GUIDELINES

Baycare
St Joseph's Women's Hospital

Early medication protocol: Morphine

Scores DURING FIRST 1-2 days of withdrawal

- ≥8 intermittently or 1 scores ≥12
- → start Morphine dose 0.04 mg/kg/dose q3 hours
- Consistent scores >12
- → start Morphine at 0.06 mg/kg/dose q3 hours

Medication escalation: Morphine

 Scores DURING FIRST 1-2 days of treatment for withdrawal

- Continues with high NAS scores (2 scores of 9-12 or 1 score >12)
- →increase Morphine dose by 0.01-0.02 mg/kg/dose q 3h
 MAX Morphine dose used 0.08mg/kg/dose q3h
- Must assess the effect for 12 hours before another increase

Medication escalation: Adding Clonidine

- Add Clonidine when
 - Morphine at 0.08 mg/kg/dose
 - IF 2 scores 9-12 or 1 score >12
- Start Clonidine at 1 mcg/kg/dose q3h
- Must assess the effect for 12 hours before another increase.
- Clonidine monitoring: blood pressure & heart rate before dose administered
 - Hold Clonidine dose if heart rate <100 bpm or systolic blood pressure <60 mmHg

Medication escalation: Clonidine

- Increase Clonidine dose IF 2 scores 9-12 or 1 score >12
- Can increase Clonidine
 - 1st increase to 2 mcg/kg/dose q3 hours
 - 2nd increase to 2.5 mcg/kg/dose q3 hours
 - 3rd increase to 3 mcg/kg/dose q3 hours
- Must assess the effect for 12 hours before another increase
- Clonidine monitoring: blood pressure & heart rate before dose administered
 - Hold Clonidine dose if heart rate <100 bpm or systolic blood pressure <60 mmHg

Medication escalation: High doses of Morphine & Clonidine

When Morphine at 0.08 mg/kg/dose & Clonidine at 3 mcg/kg/dose

IF Morphine preferred

Increase Morphine to 0.09 mg/kg/dose q3 hours, then to 0.1 mg/kg/dose, then to 0.11 mg/kg, then to 0.12 mg/kg/dose

THIS DOSE MAY LEAD TO IATROGENIC CONCERNS

Must assess the effect for 12 hours before EACH increase

IF Clonidine preferred

Increase Clonidine doses 3.5mcg/kg/dose, then 4mcg/kg/dose

Medication weaning: Morphine

ALWAYS wean morphine BEFORE Clonidine

(regardless of Morphine dose)

- Decrease Morphine by ~10% for every 18-30 hours that scores AVERAGE <8
- When Morphine is at 0.09 mg/kg/dose q3 hours, go to 0.08 mg/kg/dose q3 hours, then to 0.07 mg/kg/dose, 0.06 mg/kg/dose, 0.05 mg/kg/dose...
- If scores are higher after weaning, assess the effect for 12 hours before returning to the previous dose

Medication weaning: Morphine

ALWAYS wean morphine BEFORE Clonidine (regardless of Morphine dose)

- Once Morphine is at 0.04-0.05 mg/kg/dose Q3 hours, frequency can be spaced (still before Clonidine weaning)
- Decrease Morphine frequency to q6 hours for 18-30 hours
 - IF scores AVERAGE ≤8 can continue weaning frequency (e.g., if at 0.05 mg/kg/dose q3 hours wean to q6 hours, then q12 hours, then discontinue)
- If scores are higher after weaning, assess the effect for 12 hours before returning to the previous interval

Medication weaning: Clonidine

- Once Morphine has been discontinued for 18-30 hours, consider Clonidine weaning
- Decrease Clonidine dose by 1 mcg/kg/dose changes
- Decrease Clonidine frequency once at 1 mcg/kg/dose
 - Start at q6 hour frequency for 18-30 hours
 - IF scores AVERAGE ≤8 can continue weaning frequency (e.g., if at q6 hours wean to q12 hours, then discontinue)
- If scores are higher after weaning, assess the effect for 12 hours before returning to the previous interval

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USING PROCESS MAPPING IN NAS

Maya Balakrishnan & Karen Fugate

THE GRAND SCHEME OF THINGS:

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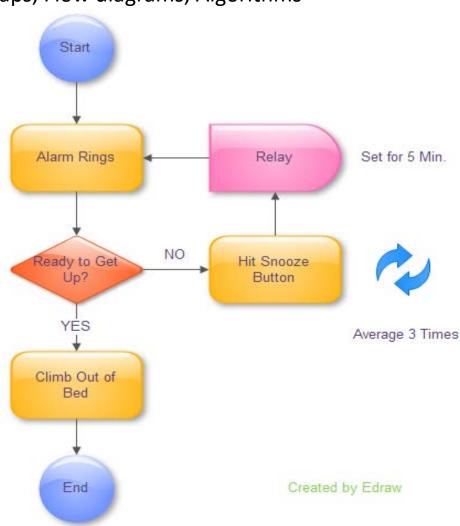
extres)

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What is a process flow map?

AKA, Flowcharts, Flow maps, Flow diagrams, Algorithms

- Tool in your toolbox
- Easy-to-understand visual model of a process
- Standardizes a process
- Can improve efficiency
- Sequence of steps to get from "A" → "B"



Why use a process flow map for NAS management?

Clarify current state

- Basis for discussion
- Standardize a process

Communicate a process

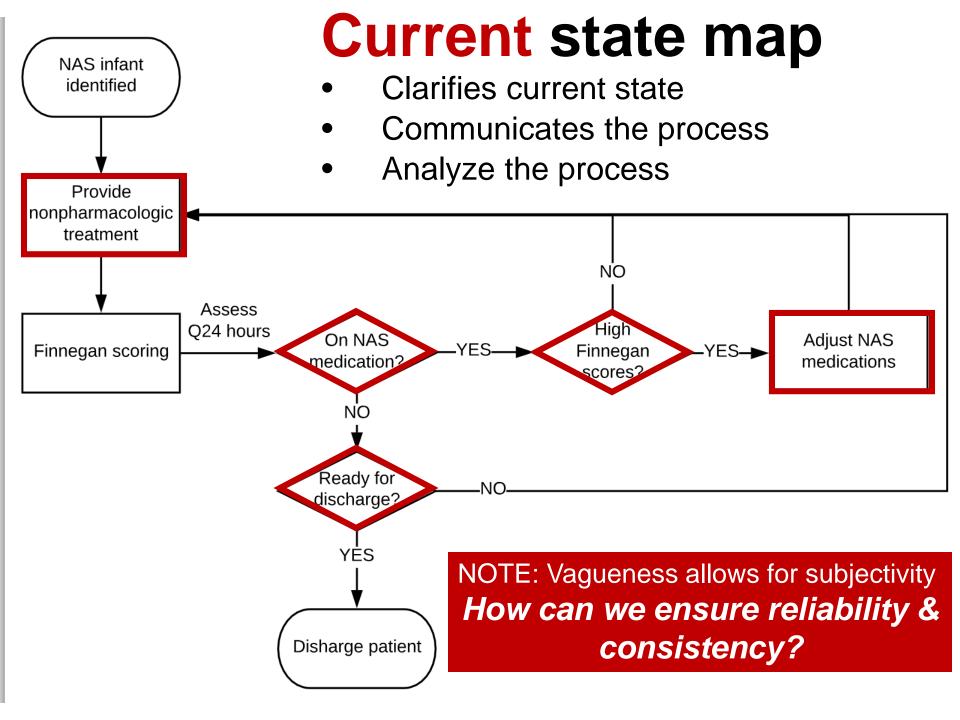
Clarify process for team & others

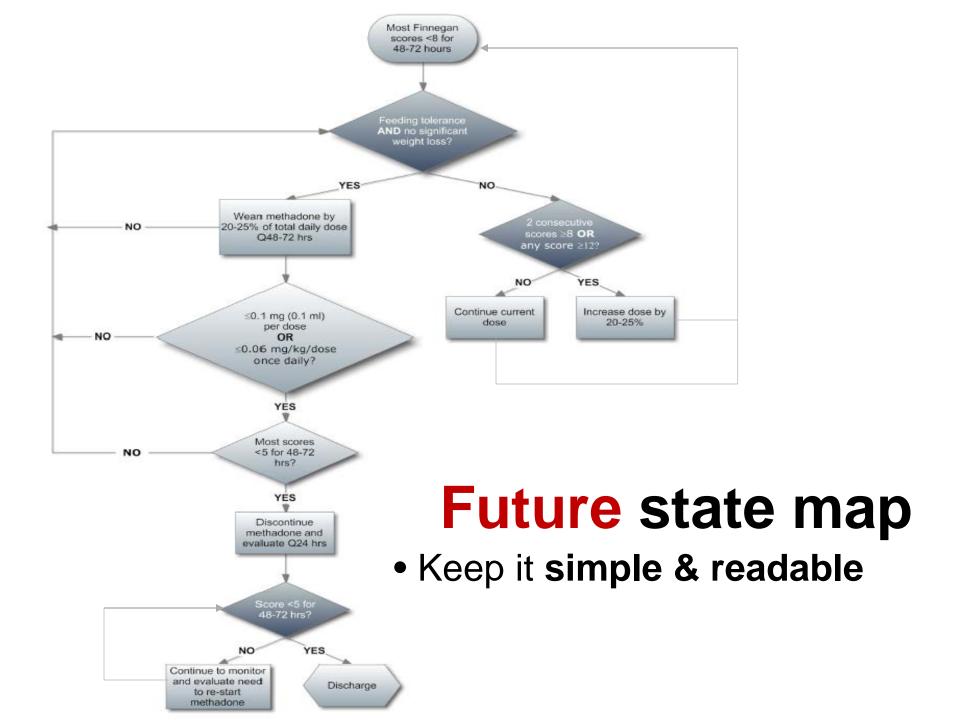
Analyze a process

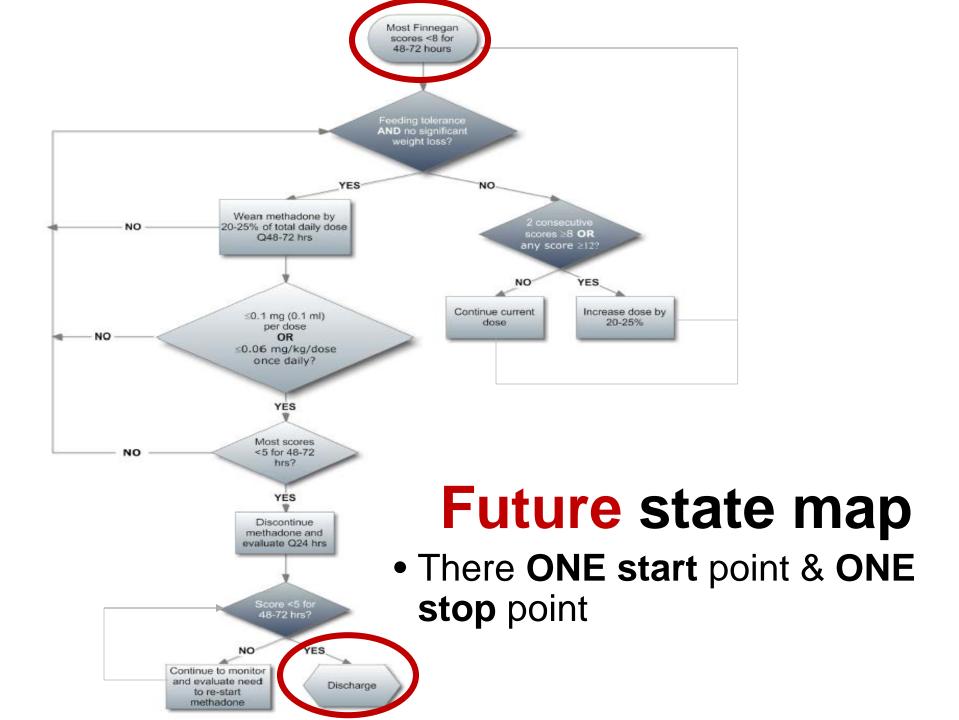
 Opportunities, inefficiencies, bottlenecks

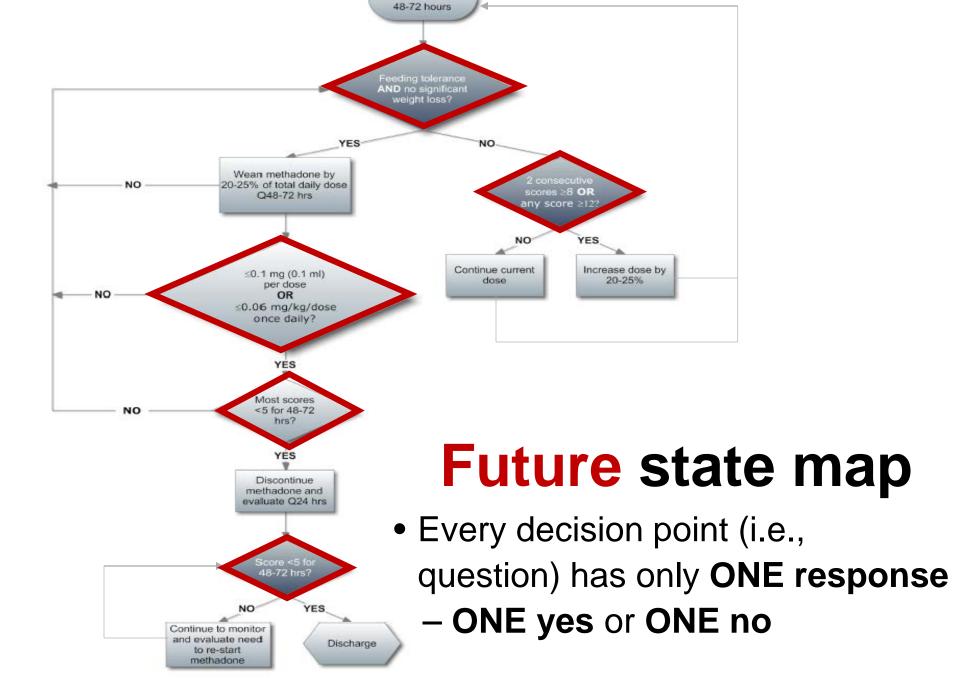
Process map symbols

 Start/End START Comment $\frac{Do}{this}$ \longrightarrow Check the The Weather Channel Weather Channel in on Cable Channel 61 Step If yes, follow this flow ves Rain Is this_ true? Stay Home Decision Predicted? ↓ If no, follow this flow Delay Do this → Play Golf Direction STOP

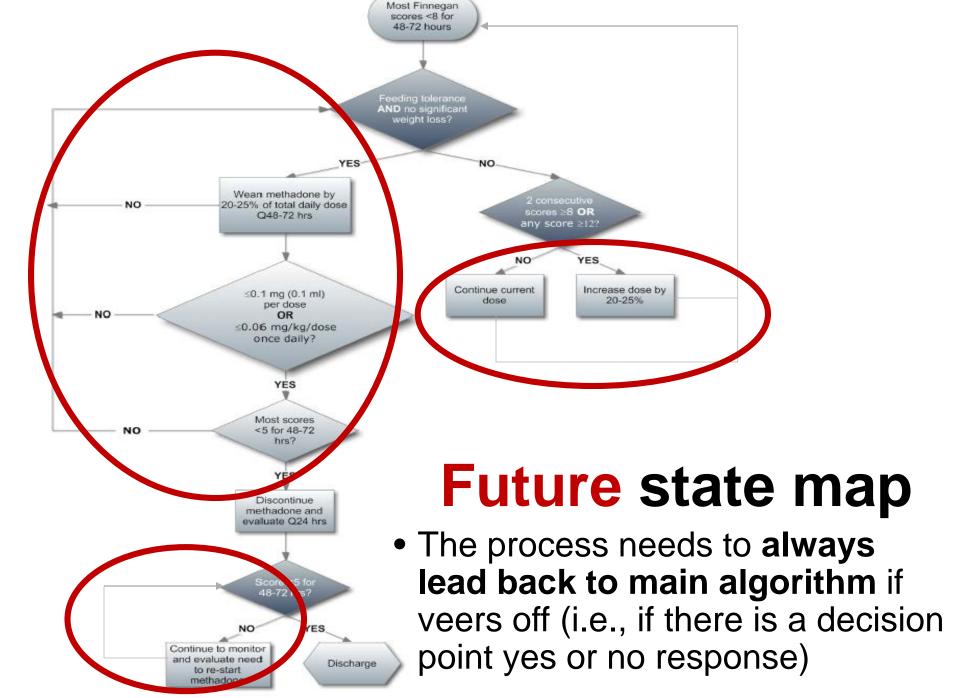








Most Finnegan scores <8 for



Tips on mapping

- "Walk" or observe the outlined process
- Sketch your map (sticky notes, butcher paper)
- → use an online application to create a Process map

Microsoft Word™, Excel™

• https://www.wikihow.com/Create-a-Process-Flowchart

Lucidchart.com (Free trial software)

https://www.lucidchart.com/

Our challenge to your team

Develop a pharmacologic treatment algorithm for NAS & share it with our FPQC teams



Quality Improvement

* ... > Current Residents & Fellows > Quality Improvement

Graduate Medical Education

Home	About GME	GME Programs	Residents & Fellows	Directors & Coordinators	Policies	Forms	Credentialing	Resources	
Housest	taff Handbook						11		
Stipend	& Benefits	Ç	Quality Improvement for Residents & Fellows						
Residen Program	t Assistance		About Quality Improver	nent Current QI Pro	jects	Resource	es Contac	t Us	
Residen Commit	t Advisory tee	V	hat is Quality	Improvement?					
Education	on Funds			alysis of performance and sys called "An Illustrated Look at				through this	
Taxi Ser	vices	U	SF Quality Im	provement Miss	ion				
Training Requirements			Guided by a focus on quality, patient safety, and co-production of care, our physicians will strive to continuously improve healthcare delivery in our communities. We are invested in co-producing doctors who continuously						
FL Medi	cal Licenses		prove healthcare delivery prove healthcare.	in our communities, we are in	ivested in co	o-producing	doctors who con	linuousiy	
Graduating/Exit Requirements			QI vs Research						
New Inn	ovations Login	VVI	nat are some differences t	petween QI and Research? R	ead more at	Quality Im	provement Versus	Research.	
Near Mis	ss Reporting								
Frequen	itly Asked ns								
Anonym	ous Reporting								
Researc	h Resources								

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Q & A

If you have a question, please enter it in the Question box or Raise your hand to be un-muted.

We can only unmute you if you have dialed your Audio PIN (shown on the GoToWebinar side bar).

Save the Date: April 4-5, Tampa FPQC 2019 Conference

- Racial/ethnic disparities in maternal mortality & morbidity Elizabeth Howell, MD, MPP
 Professor of Population Health Sciences & Policy, Obstetrics, Gynecology, and Reproductive Science, & Psychiatry, Mount Sinai Health System
- Parent topic Lelis Vernon NICU Mom, National Network of Perinatal Quality Collaboratives, Patient and Family Centered Care advocate
- Racial/ethnic disparities in NICU care quality Jochen Profit, MD
 Associate Professor of Pediatrics (Neonatology), Stanford University
- Change Management— Bethany Robertson, DNP, CNM Assistant Professor Clinical, Emory University

For More Information, go to www.fpqc.org









Next NAS Webinar

Tuesday, February 19 at 1:00 pm ET

Topic: Eat Sleep Console Scoring



THANK YOU!

Technical Assistance:

FPQC@health.usf.edu

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