

Neonatal Pain Assessment & Management

Guideline

Version	Date	Author(s)	Changes	Approved by	Review
1	29/05/2025	Claire Adamson- Clinical nurse manager Colette Jacobs –ANNP Julie-Clare Becher - Neonatal consultant Emily Petrie – Clinical educator		Neonatal Guideline meeting	



Contents

Introduction	
Background	Page 3
Service Aims	Page 3
Responsibilities	
Values	
Procedure	Page 4
Non-Pharmacological measures	Page 4 Page 7 Page 8
Neonatal Pain Assessment Scale	Page 10
Appendixes	
References	Page 16



Introduction

This guideline is in place to ensure that all babies admitted to the neonatal unit receive standardised pain and comfort care appropriate to their individual needs. The NPASS assessment tool should be used on admission for every infant and as per guidance thereafter throughout their stay within the neonatal unit.

Background

Although neonates are not able to verbalise pain, evidence suggest that neonates experience pain in various ways without having the ability to adapt to painful stimuli. Neonatal pain can be grouped into the following:

Acute

Chronic

Repetitive

Exposure to pain may be harmful to the developing brain, especially in preterm babies. It is also evident that changes in the pain sensitivity of babies who experienced suboptimal pain management continue into later life.

Appropriately providing pain control for neonates can be challenging due to the diverse perception of pain symptoms among health care providers. To address this, pain assessment tools have been developed to provide a structured and comprehensive way to monitor pain and guide individualised pain control. One such assessment tool is the Neonatal Pain Agitation and Sedation Scale (NPASS)

Service aims

This guideline aims to provide an understanding of the causes and classification of neonatal pain. Also, how the effect and experience of pain may be improved by effective use of an assessment tools (NPASS) to guide both non-pharmacological and pharmacological pain management interventions.

Responsibilities

For the attention of all Nursing and Medical staff within neonatal Services responsible for patient care.

Values

The neonatal service upholds the core NHS Lothian values of care and compassion, dignity and respect, quality, teamwork, openness, honesty and responsibility.

Procedure



Causes of neonatal pain and interventions

There are a wide range of causes of pain to the neonate. It is important that each procedure/event is assessed, and appropriate analgesia/support is given.

Pain increases the risk of physiological instability which may lead to higher blood pressure, intraventricular haemorrhage (IVH) and associated brain injury in the short term. Research suggests that long term consequences of experiencing acute pain can alter pain responses in later life.

Acute Pain

Includes time-limited interventions such as the following:

- Eye Examinations
- Surgery
- Endotracheal intubation and/or suctioning
- Heel prick
- Removal of dressings
- IV cannulation and/or venepuncture
- Lumbar puncture
- Ventricular tap
- Dressing of minor wounds

Interventions to Minimise Acute Pain:

- Being well prepared limits the time of disturbance during procedures.
- Support of junior staff during procedures to keep intervention times as short as possible.
- Monitor infants for signs of non-tolerance with NPASS.
- Most experienced staff to perform procedures on high-risk infants, i.e. extreme premature infants.
- In infants who are post-operative or clinically unwell higher doses of analgesia may be indicated and should be discussed with the senior medical team.

ENVIRONMENTAL	NON-PHARMACOLOGICAL	PHARMACOLOGICAL
Close incubator doors gently	Breastmilk	Sucrose
Set alarms at appropriate level	Non-nutritive sucking	Morphine Bolus*
Low noise levels in cot space	Swaddling	Morphine Infusion*
Encourage parental voice at cot side	Skin-to-skin/parental	
	holding	
Avoid telephones/radios/pagers near	Using adhesive remover	
incubators	for dressings	
Use incubator covers/drapes to decrease		
light levels appropriate for gestation		



Chronic Pain

Chronic pain is defined as episodes associated with longer exposure to possible painful stimuli.

Causes:

Due to the challenges in assessing long term chronic pain in babies with conditions such as bronchopulmonary dysplasia, assessment of chronic pain has been identified as an area of ongoing research interest.

However, for the purpose of this guideline chronic pain is described as prolonged painful experiences within the neonatal unit environment i.e.

- Invasive ventilation for prolonged periods
- Non-invasive respiratory support
- Post-operative or undergoing surgical management i.e. gastroschisis, sepsis, NEC
- Cooling treatment in HIE
- Chest drain
- Skin breakdown
- Stoma sites
- Invasive lines present
- Gastric feeding tubes

Interventions to Minimise Chronic Pain:

- Monitor for signs of pain with NPASS.
- Remove any invasive lines as soon as reasonably possible.
- Prevention of skin breakdown in infants on non-invasive respiratory support- see guideline
- Most experienced staff performing procedures on high-risk infants, i.e. extreme premature infants.

ENVIRONMENTAL	NON-PHARMACOLOGICAL	PHARMACOLOGICAL
Close incubator doors gently	Breast milk	Sucrose
Set alarms at appropriate level	Non-nutritive sucking	Paracetamol*
Low level noise in cot space	Swaddling	Morphine infusion*
Encourage parental voice at cot side	Skin-to-skin/Parental holding	Oramorph*
Avoid telephones/radios/pagers near		
incubators		
Use incubator covers/drapes to decrease		
light levels as appropriate for gestation		

^{*}In discussion with consultant team



Repetitive Pain

Pain inducing procedures experienced on a regular basis. This may involve a combination of acute and chronic painful stimuli.

Includes:

- Heel prick, i.e. regular blood glucose monitoring
- Endotracheal suctioning
- Dressing changes during wound care
- Stoma bag changes

Interventions to Minimise Repetitive Pain

- Monitor for signs of non-tolerance with NPASS.
- Most experienced staff performing procedures on high-risk infants, i.e. extreme premature infants.

ENVIRONMENTAL	NON-PHARMACOLOGICAL	PHARMACOLOGICAL
Close incubator doors gently	Breastmilk	Sucrose
Set alarms at appropriate level	Non-nutritive sucking	
Low noise levels at cot space	Swaddling	
Encourage parental voice at cot space	Skin-to-skin/Parental holding	
Avoid telephones/radios/pagers near		
incubators		
Use incubator covers/drapes to decrease		
light levels as appropriate for gestation		

Preventing and/or Limiting exposure to Pain

The following measures are considered to limit exposure to uncomfortable and/or painful procedures:

- Multiple painful or distressing procedures should be done on different days, i.e. ROP examinations and immunisations.
- Consider the timing of 'routine' blood sampling and appropriateness.
- Identify actual or potential sources of pain or discomfort
- Consider non-pharmacologic interventions first where there is no identified cause for pain/discomfort.
- NPASS assessment should be carried out after any interventions to address pain/discomfort to evaluate their efficacy.

Interventions to reduce pain experience and Improve Comfort

A wide range of research-based evidence has shown that various non-pharmacological and pharmacological interventions can be effective in reducing pain and discomfort in preterm and term infants exposed to painful stimuli.

Depending on clinical condition and the nature and length of the intended procedure, pain could be managed either non-pharmacologically or pharmacologically or with a combination of both.



NON-PHARMACOLOGICAL INTERVENTIONS

Non-pharmacological interventions applied appropriately, has been seen to decrease painful experience while being easily implemented and safe if done effectively (Shen et al. 2022). It also promotes family integrated care by encouraging parental involvement which has been linked to improve outcomes for families of babies receiving neonatal care. (Ulsten et al. 2022)

- Parental touch and involvement
- Containment holding
- Swaddling
- Kangaroo care
- Familiar odour such as bonding squares
- Non-nutritive sucking
- Breast feeding

Research shows that where mothers were present during painful procedures, infants were more likely to receive effective pain management strategies, highlighting a positive influence of parents. Parent driven strategies require staff to initiate and support it, and the healthcare team needs to be aware of their responsibility to facilitate such beneficial interactions between parent and baby.

Family Education

- Parents need to feel confident that their baby is having the most appropriate pain/comfort care.
- Assess the family's knowledge and perception about pain in infants and its management.
- Support their decisions; empower them to make good decisions for their baby.
- Answer their questions honestly.
- Guide parents in how they can touch and interact with their baby.
- Encourage parents to comfort their baby and involve parents during procedures where possible.
- Teach the family to understand their baby's signs of attention and stress.
- Explain the side-effects of pain medication.

PHARMACOLOGICAL INTERVENTIONS

In cases where non-pharmacological interventions are not appropriate or effective in providing adequate pain management, pharmacological interventions may be indicated. Careful consideration should be given in the use of analgesia especially in the preterm population due to their fragile renal and hepatic systems (Perry et al. 2018). Research evidence around the longer-term effects of analgesia in preterm infants suggest following a cautious approach in the use of pharmacological pain management. Some studies indicate longer term neurodevelopmental effects of pain medication. (Selvanathan et al. 2024)

- Sucrose
- Paracetamol (Acetaminophen)
- Morphine (Opioids)
- Lidocaine (Amino Amide)



Sucrose

- Effective in reducing procedural pain, i.e. heel prick, venepuncture and IM injection
- More effective when used alongside non-nutritive sucking or breastfeeding
- Use as per local guideline (Stevens et al. 2016)

Paracetamol

- Paracetamol has been shown to be effective in providing pain relief after surgery in neonates.
- Can be used in combination with opioids.
- Careful consideration should be given in babies where there are hepatic concerns such as hyperbilirubinemia refer to local guideline. (Allegaert, 2020)

Morphine (Opioid)

Widely used for the treatment of acute pain within the NNU

Can be used to treat pain associated with a range of conditions including:

- Post-Surgery (Operative), i.e. Laparotomy, Insertion of VAD
- Post procedural, i.e. ROP treatment
- Infection, i.e. NEC, Meningitis or other causes of sepsis
- Critically illness, i.e. HIE undergoing Therapeutic Cooling Therapy
- Treatment of Neonatal Withdrawal Symptoms in conditions such as
- Neonatal Abstinence Syndrome (NAS)

Careful consideration should be given to when and for how long opioids are given in especially preterm babies due to the associated side-effects.

The use of opioids should be reviewed daily and weaned as appropriate.

Babies who received Morphine for an extended period should be weaned gradually before stopping the medication due to risk of drug withdrawal. (Refer to morphine guideline)

Associated Side-Effects:

- Hypotension
- Respiratory Depression
- Urinary Retention
- Feeding Intolerance due to slowed gut motility
- Drug Dependence

Lidocaine

Lidocaine is indicated for procedures such as chest drain insertion where it is administered subcutaneously as a local anaesthetic (as per local guideline).



ADDITIONAL CONSIDERATIONS:

Muscle Relaxed Infants

Due to the difficulty in assessing pain and/or discomfort in infants who are paralysed, consideration should be given to appropriate analyses which may include continuous infusion or bolus.

In muscle relaxed infants, physiological indicators such as heart rate and blood pressure should be closely monitored, as this may be the only signs of pain or discomfort.

Ventilated Infants

- **Morphine is not routinely used as analgesia in ventilated infants due to the known side-effects in the neonatal population.
- All newly ventilated neonates will be assessed as to their need for analgesia.
- Effective treatment of pain and/or distress is important in the supportive care of ventilated infants. Pain and stress can lead to ventilator asynchrony, suboptimal ventilation and cardiovascular instability and increased risk for pneumothorax and IVH.
- Non-pharmacological measures such as careful positioning/ handling, use of synchronised ventilation modes and clearing of secretions may be very effective in minimising pain and distress in ventilated infants
- Suctioning should be kept to a minimum, but if needed then swaddling or containment should be used during the procedure by a second person
- If an infant is already on an infusion of morphine and ventilated or post-surgery, it is important to still consider alternative methods to relieve pain when further procedures are required.
- Optimise ventilation. Monitoring of endotracheal tube position, auscultation of chest, blood gas and chest x-ray are useful tools in supporting effective ventilation.

DOCUMENTATION

Document:

- Pain assessment NPASS tool is located under "Scoring" on Badger for babies
- Type of pain intervention
- Family involvement
- Within one hour post intervention to determine effectiveness of the strategy
- All pharmacological pain relief should be recorded

The documentation should include:

- Reason for its initiation
- Response to the medication
- Rationale for continuing or weaning
- Rationale for discontinuing
- Any senior discussion re pain concerns where appropriate



Document and report any adverse side-effects from pharmacological interventions including:

- Deviations from baseline pain assessment/ measurement
- Assessment showing no pain relief
- Tolerance or dependence to pharmacological agents
- Respiratory depression and desaturation
- Apnoea requiring stimulation and/or neopuff
- Bradycardia
- Hypotension
- Muscle rigidity
- Suspect ileus (reduced bowel sounds and/or abdominal distension)
- Urinary retention for more than eight hours

THE NEONATAL PAIN ASSESSMENT SCALE (NPASS)

The main aim of using NPASS is to prevent and limit long term neurological injury caused by exposure to pain.

NPASS was developed specifically for the neonatal population. It aids in objectively and comprehensively assessing pain and sedation in preterm, term and postoperative surgical infants in an easy and non-invasive manner. Evidence has shown that using NPASS provides a useful tool to quantify pain/discomfort and guide appropriate pain control interventions.

All medical and nursing staff providing care to babies within the neonatal unit should be applying NPASS during routine and acute care of babies. Parents should be encouraged to observe for and discuss any signs of pain and/or discomfort with healthcare staff to ensure prompt review and implementing measures to improve comfort.

Due to the different levels of acuity the frequency of assessment should be adjusted according to the level of care of each baby.

Interventions to address pain or discomfort should be considered and discussed with senior staff based on regular assessment.

Applying NPASS in the clinical setting

Guidance for the frequency for NPASS assessment as follows:

- 1. On admission to the Neonatal Unit.
- 2. At shift changes
- 3. Before and after potentially painful procedures.
- 4. After implementing each measure aimed at addressing pain concerns.
- 5. Throughout longer painful procedures.
- 6. Four hourly/as required if the infant is receiving analgesic support
- 7. Analgesia/Sedation PRN: within 30-60 minutes post analgesia to assess response.
- 8. Post-operative: Hourly for 24-48 hours and then 4 hourly.
- 9. At any point during when a nursing or medical staff member or parent considers it necessary

NHS Lothian

Interpretation of NPASS scores

IMPORTANT

Infants > 35 weeks – Document NPASS assessments on Badger by using the NPASS tool found within the scoring section. Filling in the form will generate a score which can be used to inform pain /comfort care and interventions.

Infants <35 weeks – Document NPASS on paper form. Fill in the form and calculate the score before adding additional points for gestation as recommended below:

- +3 if < 28 weeks corrected gestational age (CGA)
- +2 if 28 31 CGA
- o +1 if 32 35 CGA

Pain is scored from $0 \rightarrow +2$ for each element and the score added up- See appendix 1 NPASS diagram

The total pain score is documented as a positive number $0 \rightarrow +10$.

It is important to consider trends and changes in scoring which can indicate physiological changes prompting review and action.

Scores > 3 indicate interventions or treatment

In known painful procedures, interventions should be introduced prior to procedure and monitored throughout with the aim to keep scores ≤ 3.

Consideration and Assessment of Sedation during Pain Assessment

Although Sedatives are not included in the Pain guideline, the NPASS Scale includes Sedation as part of its assessment of pain/discomfort. This section will briefly describe the considerations around Sedation and its assessment.

- Sedatives do not relieve pain, although some may increase the effects of opioids.
- Sedatives should not be given instead of analgesia for pain.
- Sedatives must always be used with caution and side effects must be considered which may include abnormal neurological movement and negative effects on neurological outcomes.
- It may not be appropriate to assess sedation with every pain assessment, i.e. babies who are not receiving any analgesia.
- If a baby appears sedated in the absence of sedatives this may be due to other causes such as
 infection, altered neurology etc. Any changes in sedation level should be urgently discussed
 with senior staff to ensure prompt review.
- It is important to consider that preterm babies exposed to extended periods of untreated pain stimuli may appear sedated or lethargic.
- Assessment for sedation should not be done for infants receiving muscle relaxants.
- Physiological indicators such as heart rate and blood pressure may be the only sign that babies need to be reviewed for pain.



Sedation Assessment

- Sedation is scored in addition to pain for each behavioural and physiological criteria to assess the infant's response to stimuli.
- Sedation does not need to be assessed/ scored with every pain assessment unless indicated.
- Sedation is scored from 0 -2 for each behavioural and physiological criteria, then totalled and noted as a negative score (0 -10)
 - o A score of 0 is given if the infant's response to stimuli is normal for their gestational age
- Desired levels of sedation vary according to the situation
 - o "Deep sedation" score of -10 to -5 as goal
 - "Light sedation" score of -5 to -2 as goal
 - Deep sedation is not recommended unless an infant is receiving ventilator support, related to the high potential for apnoea and hypoventilation
- A negative score without the administration of opioids/ sedatives may indicate:
 - The premature infant's response to prolonged or persistent pain/stress
 - Neurologic depression, sepsis, or other pathology

Paralysis Assessment

- It is impossible to behaviourally evaluate a paralysed infant for pain
- Increases in heart rate and blood pressure may be the only indicator of a need for more analgesia
- Analgesics should be administered continuously by drip or around-the-clock dosing
- Higher, more frequent doses may be required if the infant is post-op, has a chest drain, or other pathology (such as NEC) that would normally cause pain



Appendix 1. The Neonatal Pain and Sedation Assessment Scale (NPASS)

	NPASS Pain Assessment Scale				
Assessment	Sec	dation	Normal	Pain/Agitation	
Criteria	-2	-1	0	+1	+2
Crying/ Irritability	No cry with painful stimuli, i.e. needlestick, ETT/nasal suction/care giving	Moans or cries minimally with painful stimuli, i.e. needlestick, ETT/nasal suction/cares	Appropriate crying with normal stimuli. Not irritable.	Irritable or crying at intervals. Consolable	High-pitched or silent-continuous cry Inconsolable
Behaviour State	N o arousal to any stimuli N o spontaneous movement	Arouses minimally to stimuli Little spontaneous movement	Appropriate for gestational age	Restless, squirming Awakens frequently with minimal stimuli	Arching, kicking Constantly awake or Arouses minimally / no movement(not sedated)
Facial expression	M outh is lax No expression	M inimal expression with stimuli	R elaxed Appropriate	A ny pain expression intermit-tent	Any pain expression continual
Extremities Tone	N o grasp reflexes Flaccid tone	W eak grasp reflex D ecreased muscle tone	Relaxed hands and feet Normal tone	Intermit-tent clenched toes, fists or finger splay Body is not tense	Continual clenched toes, fists or finger splay Body is tense
Vital signs HR, RR, BP and Sa02	N o variability with stimuli H ypoventilation or apnoea	< 10% variability of baseline with stimuli	W ithin baseline or normal for gestational age	Increased by 10- 20% from baseline Sa02 76-85% with stimulation- quick increase	Increase > 20% from baseline with stimulation – slow increase Out of sync with ventilator
Premature Pain Assessment	Premature +3 if < 28 weeks gestation/corrected age +2 if 28-31 weeks gestation/corrected age				



Appendix 2 Expanded Scoring Criteria

Crying / Irritability -2 → No response to painful stimuli, e.g.:

No cry with needle sticks

No reaction to ETT or nares suctioning

No response to care giving

- Moans, sighs, or cries (audible or silent) minimally to painful stimuli, e.g. needle sticks, ETT or nares suctioning, care giving
- 0 → Not irritable appropriate crying
 - · Cries briefly with normal stimuli
 - Easily consoled
 - Normal for gestational age
- +1 → Infant is irritable/crying at intervals but can be consoled
 - If intubated intermittent silent cry
- +2 → Any of the following:
 - · Cry is high-pitched
 - · Infant cries inconsolably
 - · If intubated silent continuous cry

Behavior / State

- -2 → Does not arouse or react to any stimuli:
 - · Eyes continually shut or open
 - · No spontaneous criterous movement
- -1 → Little spontaneous movement, arouses briefly and/or minimally to any stimuli:
 - · Opens eyes briefly
 - · Reacts to suctioning
 - · Withdraws to pain
- 0 → Behavior and state are gestational age appropriate
- +1 → Any of the following:
 - · Restless, squirming
 - · Awakens frequently/easily with minimal or no stimuli
- +2 → Any of the following:
 - Kicking
 - Arching
 - Constantly awake
 - No movement or minimal arousal with stimulation (inappropriate for gestational age or clinical situation, i.e. post-operative)

Extremities / Tone

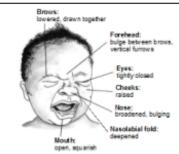
- -2 → Any of the following:
 - · No palmar or planter grasp can be elicited
 - Flaccid tone
- -1 → Any of the following:
 - · Weak palmar or planter grasp can be elicited
 - Decreased tone
- 0 → Relaxed hands and feet normal palmar or sole grasp elicited – appropriate tone for gestational age
- +1 → Intermittent (<30 seconds duration) observation of toes and/or hands as clenched or fingers splayed
 - Body is not tense
- +2 → Any of the following:
 - Frequent (≥30 seconds duration) observation of toes and/or hands as clenched, or fingers splayed
 - Body is tense/stiff

Vital Signs: HR, BP, RR, & O2 Saturations

- -2 → Any of the following:
 - · No variability in vital signs with stimuli
 - Hypoventilation
 - Apnea
 - Ventilated infant no spontaneous respiratory effort
- -1 → Vital signs show little variability with stimuli less than 10% from baseline
- Vital signs and/or oxygen saturations are within normal limits with normal variability – or normal for gestational age
- +1 → Any of the following:
 - · HR, RR, and/or BP are 10-20% above baseline
 - With care/stimuli infant desaturates minimally to moderately (SaO₂ 76-85%) and recovers quickly (within 2 minutes)
- +2 → Any of the following:
 - · HR, RR, and/or BP are > 20% above baseline
 - With care/stimuli infant desaturates severely (SaO₂ < 75%) and recovers slowly (> 2 minutes)
 - Infant is out of synchrony with the ventilator fighting the ventilator

Facial Expression

- -2 → Any of the following:
 - Mouth is lax
 - Drooling
 - · No facial expression at rest or with stimuli
- Minimal facial expression with stimuli
- 0 → Face is relaxed at rest but not lax normal expression with stimuli
- +1 → Any pain face expression observed intermittently
- +2 → Any pain face expression is continual



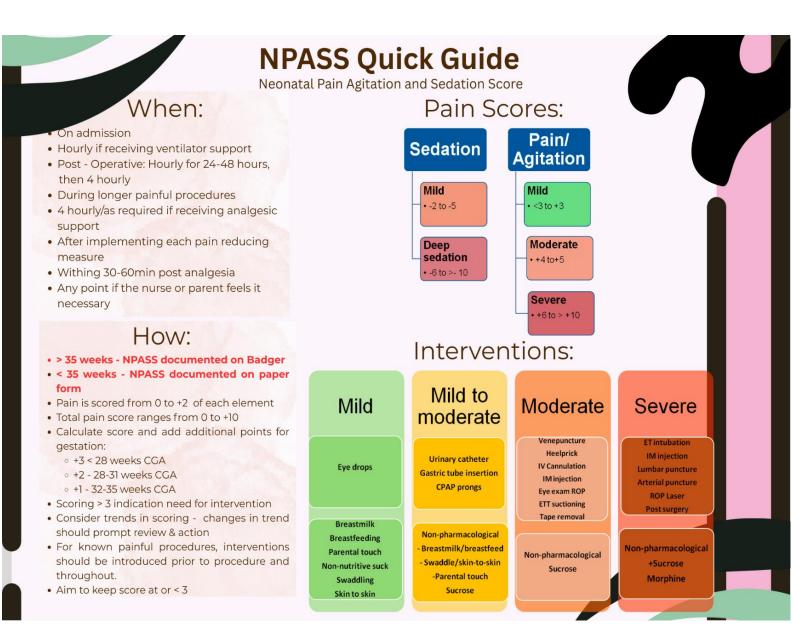
Facial expression of physical distress and pain in the infant

**Reputate of personner two young Co. TeacCt. Young on Whaty's

Close Name of Person Name (\$2.1,200, Young St. Laue



Appendix 3: Prepare and support babies during painful hospital procedures





REFERENCES:

- 1. Allegaert K. A Critical Review on the Relevance of Paracetamol for Procedural Pain Management in Neonates. Front Pediatr. 2020 Mar 18;8:89. doi: 10.3389/fped.2020.00089. PMID: 32257982; PMCID: PMC7093493.
- 2. Garcia-Rodriguez MT, Bujan-Bravo S, Seijo-Bestilleiro R, Gonzalez-Martin C. Pain assessment and management in the newborn: A systematized review. World J Clin Cases. 2021 Jul 26;9(21):5921-5931. doi: 10.12998/wjcc.v9.i21.5921. PMID: 34368310; PMCID: PMC8316969.
- 3. Grunau RE, Holsti L, Peters JW. Long-term consequences of pain in human neonates. Semin Fetal Neonatal Med. 2006 Aug;11(4):268-75. doi: 10.1016/j.siny.2006.02.007. Epub 2006 Apr 24. PMID: 16632415.
- 4. Hillman BA, Tabrizi MN, Gauda EB, Carson KA, Aucott SW. The Neonatal Pain, Agitation and Sedation Scale and the bedside nurse's assessment of neonates. J Perinatol. 2015 Feb;35(2):128-31. doi: 10.1038/jp.2014.154. Epub 2014 Aug 21. PMID: 25144158; PMCID: PMC5526063.
- 5. Hummel, P., Puchalski, M., Creech, S. *et al.* Clinical reliability and validity of the N-PASS: neonatal pain, agitation and sedation scale with prolonged pain. *J Perinatol* **28**, 55–60 (2008). https://doi.org/10.1038/sj.jp.7211861
- 6. Lago P, Garetti E, Merazzi D, et al. Guidelines for procedural pain in the newborn. Acta Paediatr (Oslo, Norway: 1992). 2009;98(6):932–9. doi:10.1111/j.1651-2227.2009.01291.x. *A foundational systematic review of procedural pain prevention and treatment of NICU neonatal patients*. [PMC free article] [PubMed]
- 7. Laudiano-Dray, Maria Pureza^{a,*}; Pillai Riddell, Rebecca^{b,c}; Jones, Laura^a; Iyer, Rajeshwari^a; Whitehead, Kimberley^a; Fitzgerald, Maria^a; Fabrizi, Lorenzo^a; Meek, Judith^d. Quantification of neonatal procedural pain severity: a platform for estimating total pain burden in individual infants. PAIN 161(6):p 1270-1277, June 2020. | DOI: 10.1097/j.pain.000000000001814
- 8. Llerena A, Tran K, Choudhary D, Hausmann J, Goldgof D, Sun Y, Prescott SM. Neonatal pain assessment: Do we have the right tools? Front Pediatr. 2023 Feb 2;10:1022751. doi: 10.3389/fped.2022.1022751. PMID: 36819198; PMCID: PMC9932268.
- 9. Li Q, Tan X, Li X, Tang W, Mei L, Cheng G, Zou Y. Efficacy and safety of combined oral sucrose and non-nutritive sucking in pain management for infants: A systematic review and meta-analysis. PLoS One. 2022 May 6;17(5):e0268033. doi: 10.1371/journal.pone.0268033. PMID: 35522649; PMCID: PMC9075656.
- 10. Morgan, M.E., Kukora, S., Nemshak, M. *et al.* Neonatal Pain, Agitation, and Sedation Scale's use, reliability, and validity: a systematic review. *J Perinatol* **40**, 1753–1763 (2020). https://doi.org/10.1038/s41372-020-00840-7
- 11. McPherson, C., Ortinau, C.M. & Vesoulis, Z. Practical approaches to sedation and analgesia in the newborn. *J Perinatol* **41**, 383–395 (2021). https://doi.org/10.1038/s41372-020-00878-7
- 12. Morgan, M.E., Kukora, S., Nemshak, M. *et al.* Neonatal Pain, Agitation, and Sedation Scale's use, reliability, and validity: a systematic review. *J Perinatol* **40**, 1753–1763 (2020). https://doi.org/10.1038/s41372-020-00840-7
- 13. Olsson E, Ahl H, Bengtsson K, Vejayaram DN, Norman E, Bruschettini M, Eriksson M. The use and reporting of neonatal pain scales: a systematic review of randomized trials. Pain. 2021 Feb 1;162(2):353-360. doi: 10.1097/j.pain.000000000000002046. PMID: 32826760; PMCID: PMC7808360.
- 14. Perry M, Tan Z, Chen J, Weidig T, Xu W, Cong XS. Neonatal Pain: Perceptions and Current Practice. Crit Care Nurs Clin North Am. 2018 Dec;30(4):549-561. doi: 10.1016/j.cnc.2018.07.013. PMID: 30447813; PMCID: PMC6570422.



- 15. RAJA, S. N.; CARR, D. B.; COHEN, M.; FINNERUP, N. B. *et al.* The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. **Pain (Amsterdam)**, 161, n. 9, p. 1976-1982, 2020.
- 16. Selvanathan, T., Miller, S.P. Brain health in preterm infants: importance of early-life pain and analgesia exposure. *Pediatr Res* (2024). https://doi.org/10.1038/s41390-024-03245-w
- 17. SHEN, Q.; HUANG, Z.; LENG, H.; LUO, X. *et al.* Efficacy and safety of non-pharmacological interventions for neonatal pain: an overview of systematic reviews. **BMJ open**, 12, n. 9, p. e062296-e062296, 2022.
- 18. Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev. 2016 Jul 16;7(7):CD001069. doi: 10.1002/14651858.CD001069.pub5. PMID: 27420164; PMCID: PMC6457867.
- 19. Ullsten A, Andreasson M, Eriksson M. State of the Art in Parent-Delivered Pain-Relieving Interventions in Neonatal Care: A Scoping Review. Front Pediatr. 2021 Apr 27;9:651846. doi: 10.3389/fped.2021.651846. PMID: 33987153; PMCID: PMC8112545.
- 20. Valeri BO, Holsti L, Linhares MB. Neonatal pain and developmental outcomes in children born preterm: a systematic review. Clin J Pain. 2015 Apr;31(4):355-62. doi: 10.1097/AJP.00000000000114. PMID: 24866853
- 21. Williams MD, Lascelles BDX. Early Neonatal Pain-A Review of Clinical and Experimental Implications on Painful Conditions Later in Life. Front Pediatr. 2020 Feb 7;8:30. doi: 10.3389/fped.2020.00030. PMID: 32117835; PMCID: PMC7020755