

# The Hierarchy of Evidence

**The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynyk and Fineout-Overholt (2011).**

- I Evidence obtained from a systematic review of all relevant randomised control trials.
- II Evidence obtained from at least one well designed randomised control trial.
- III Evidence obtained from well-designed controlled trials without randomisation.
- IV Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case- series
- V Evidence obtained from systematic reviews of descriptive and qualitative studies
- VI Evidence obtained from single descriptive and qualitative studies
- VII Expert opinion from clinicians, authorities and/or reports of expert committees or based on physiology

Melynyk, B. & Fineout-Overholt, E. (2011). *Evidence-based practice in nursing & healthcare: A guide to best practice (2<sup>nd</sup> ed.)*. Philadelphia: Wolters Kluwer, Lippincott Williams & Wilkins.

National Health and Medical Research Council (2009). *NHMRC levels of evidence and grades for recommendations for developers of guidelines* (2009). Australian Government: NHMRC.  
[http://www.nhmrc.gov.au/files\\_nhmrc/file/guidelines/evidence\\_statement\\_form.pdf](http://www.nhmrc.gov.au/files_nhmrc/file/guidelines/evidence_statement_form.pdf)

OCEBM Levels of Evidence Working Group Oxford (2011). *The Oxford 2011 Levels of Evidence*. Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=1025>

Reference (include title, author, journal title, year of publication, volume and issue, pages)	Evidence level (I-VII)	Key findings, outcomes or recommendations
Chang. J, Filoteo. L and Nasr. A.S. Comparing the analgesic effects of 4 nonpharmacologic interventions on term newborns undergoing heel lance- A randomized controlled trial, 2020, J Perinat Neonat Nurs, vol 34 (4), 338-345.	I	Randomized trial compared the analgesic effect of 4 nonpharmacologic interventions (breastfeeding, oral sucrose, nonnutritive sucking and skin to skin contact) on term newborns between 24 and 48 hours who underwent a heel lance. All of these interventions are clinically applicable and acceptable when caring for a newborn during a minor painful procedure.
Marceau J.R, Murray. H, Nanan R. Efficacy of Oral Sucrose in Infants of Methadone-Maintained Mothers. 2010, Neonatology. 97. 67-70.	IV	Previous report suggested that the taste induced analgesia was sub optimal in methadone exposed infants. Prospective observational study- 52 infants included (26 methadone exposed infants) Given 0.05ml of 24% sucrose 2 mins before heal lance procedure and 0.05ml at the time of the procedure and 0.05 every 1-2 mins until completion. The study found no differences in pain responses of methadone exposed infants when given sucrose during heal lance procedures.
Banga. S, Datta. V, Rehan. H.S and Bhakhri. Effect of sucrose analgesia, for repeated painful procedures, on short-term neurobehavioural outcome of preterm neonates: a randomized controlled trial. 2016. Journal of tropical pediatrics, 62, 101-106	II	93 newborns analyzed in a blind randomized controlled trial to receive either sucrose or distilled water for every potentially painful procedure during the first 7 days of enrollment. Study used the Neurobehavioral assessment of preterm infants scale at 40 weeks postconceptional age to determine neurodevelopmental status. There was no statistical difference of neurobehavioral outcome observed between the sucrose and water groups.
Stevens. B, Yamada. J, Gibbins. S, Harrison. D, Dianne. K, Taddio.A, McNair.C, Willan. A, Ballantyne. M, Widger. K, Sidoni. S, Eastbrooks. C, Synnes. A, Squires. J, Victor. C and Riahi. S. The minimally effective dose of sucrose for procedural pain relief in neonates: a randomized controlled trial, 2018, BMC paediatrics, 18:85	II	245 neonates from 4 Canadian tertiary NICUs at 24-42 wks gestation. Randomised to receive 0.1, 0.5 and 1ml during a heal lance procedure. No difference in pain scores at 30 and 60 secs. Therefore, concluded that the minimally effective dose for sucrose is 0.1 mL In order to assess sustained effectiveness, further research is needed.
Campbell-Yeo. M, Johnston.C, Disher. T, Caddell. K, Vincer.M, Walker.C-D, Latimer.M, Steiner.D.L and Inglis.D. Sustained efficacy of kangaroo care for repeated painful procedures over neonatal intensive care unit hospitalization: a single-blind randomized controlled trial. 2019, 160: 2580-2258.	II	Stable preterm infants were randomized to receive kangaroo care and water, kangaroo care and 24% sucrose or 24% sucrose before routine procedures throughout their NICU stay. Premature infant pain profile scores were assessed at 30, 60 or 90 seconds. Maternal kangaroo care seems to remain efficacious as a pain relieving intervention for infants delivered between 27 and 36 weeks of GA and seems to have comparative efficacy to kangaroo care plus sucrose or sucrose alone.

<p>McNair. C, Campbell-Yeo. M, Johnston. C and Taddio.A, Nonpharmacologic management of pain during common needle puncture procedures in infants, Current research evidence and practical considerations: An Update, 2019, Clin Perinatol 46, 709-730.</p>	<p>V</p>	<p>It is important to treat needle pain in infants, to reduce distress and suffering and reduce long term negative impact on brain development and functioning.</p> <ul style="list-style-type: none"> <li>• Swaddling and containment aims to limit the infant’s boundaries, promote self-regulation, and attenuate physiologic and behavioral stress caused by acute pain.</li> <li>• Breastfeeding- systematic review including 21 studies- breastfeeding was more effective than holding, skin to skin and sweet tasting solutions in full term infants.</li> <li>• Breastmilk- Another review found that breastmilk alone does not seem to be as beneficial as breastfeeding.</li> <li>• Pacifier and non-nutritive sucking- systematic review showed sufficient evidence that sucking is efficacious compared to no treatment in reducing pain-related distress in preterm infants and improving immediate pain related regulation in preterm and term infants up to 1 month of age.</li> <li>• Skin to skin- research suggests a clear role in neonatal pain management.</li> <li>• Sucrose- administration with a pacifier stimulates non-nutritive sucking, which may improve effectiveness. Onset of action is quick (seconds) but peak at 2 mins and duration of action is up to 10 mins.</li> </ul>
<p>Committee on fetus and newborn and section on anesthesiology and pain medicine. Prevention and management of procedural pain in the neonate: An update. American academy of pediatrics, Pediatric vol 137, 2.</p>	<p>V</p>	<p>A meta analysis of 57 studies including &gt;4730 infants 25-44 weeks GA concluded that sucrose is safe and effective for reducing procedural pain from a single event.</p>
<p>Lago. P, Cavicchiolo. M.E, Mian T, Dalcengio. V, Allegro. A, Daverio.M, Frigo. A.C, Repeating a dose of sucrose for heal prick procedure in preterms is not effective in reducing pain: a randomized controlled trial, Eur J peditri, 2020, 179 (2): 293-301</p>	<p>I</p>	<p>72 infants randomized to receive a double dose of sucrose 2 mins prior to a painful procedure. Repeating a dose of 24% sucrose is not effective at reducing pain during the recovery phase of a skin breaking procedure.</p>

<p>Stevens, B., Yamanda, J., Lee G., &amp; Ohlsson, A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews, 2013, Issue 1 Art. No.: CD001069.DOI:10.1002/14651858.CD001069.pub4.</p>	<p>I</p>	<p>Systematic review of 57 RCT's in which neonates term (29) preterm (27) or both (1) received sucrose for procedural pain.</p> <p><b>Sucrose is safe and effective for reducing procedural pain from single events</b>          Sucrose is most effective for heel lancing and has some effectiveness for venipuncture.</p> <p><b>Optimal dosing yet to be established, inconsistency in effective sucrose dosing evidence:</b></p> <ul style="list-style-type: none"> <li>• Recommended use of sucrose 0.012 to 0.12 g (0.05ml to 0.5ml of 24% sucrose) be administered <b>approximately two minutes prior</b> to single heel lances and venipunctures in neonates.</li> <li>• <b>The peak effect appears to occur at two minutes and lasts approximately four minutes;</b> the analgesic effect may wear off for prolonged procedures.</li> <li>• Small doses of 24% sucrose (0.01 to 0.02 ml) are efficacious in very-low birthweight infants while larger doses (0.24 to 0.50 ml) reduce crying time in term infants.</li> <li>• <b>Sucrose was effective</b> in reducing crying behaviours, grimacing, and vagal tone. Unidimensional, multidimensional and composite pain scores were reduced during heel lance with <b>volumes and concentrations ranging from 0.5 to 2 mL of 12% to 50% solution.</b></li> </ul> <p><b>Further investigation required:</b></p> <ul style="list-style-type: none"> <li>• The repeated administration of sucrose in neonates</li> <li>• The use of sucrose with other interventions e.g. NNS and kangaroo care</li> <li>• The minimal effective dose of sucrose during a single painful procedure</li> <li>• Sucrose use in extremely preterm, unstable, ventilated neonates ( or a combination)</li> <li>• The effectiveness of sucrose for longer procedures such as ROP examinations, bladder catheterisation, venipuncture and circumcision.</li> <li>• The effect of repeated sucrose administration on immediate (pain intensity) and long-term (neurodevelopmental) outcomes</li> <li>• No studies reported on long-term neurodevelopmental outcomes</li> </ul>
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<p>Harrison, D., Yamada, J., Adams-Webber, T., Ohlsson, A., Beyene, J., Stevens, B. Sweet tasting solutions for reduction of needle related procedural pain in children aged one to 16 years. Cochrane Database of Systematic Reviews, 2015, Issue 5. Art. No.: CD008408.DOI:10.1002/14651858.CD008408.pub3.</p>	<p>I</p>	<p>Systematic review of RCT's, 7 Published and 1 unpublished, in which children aged one year to 16 years, received a sweet tasting solution or substance for needle-related procedural pain.</p> <p><b>Efficacy of sweet tasting solutions or substances for reducing needle-related procedural pain in children beyond one year of age:</b></p> <ul style="list-style-type: none"> <li>• The evidence is insufficient and conflicting in determining the analgesic effects of sweet tasting solutions or substances during acutely painful procedures in young children ( one to four years of age)</li> <li>• There is no evidence of analgesic effects of sweet taste in school-aged children.</li> </ul>
<p>Beuno, M., Yamada, J., Harrison, D., Khan, S., Ohlsson, A., Adams-Webber, T., Beyene, J., and Stevens, B. (2013). A systematic review and meta-analyses of non-sucrose sweet solutions for pain relief in neonates. Pain Research Management, 18(3), 151-163.</p>	<p>I</p>	<p>Systematic review and meta-analyses of thirty-eight studies (3785 neonates) Glucose was investigated in 35 trials, with doses ranging from 0.2 mL to 2 mL of 5% to 50% solutions. Other solutions studied were artificial sweeteners, fructose, glycine, honey and maltitol.</p> <p><b>Efficacy and safety of sweet-tasting solutions other than sucrose during acute procedural pain in neonates:</b></p> <ul style="list-style-type: none"> <li>• Glucose reduces pain scores and crying during single heel lance and venipuncture.</li> <li>• 20% to 30% glucose solutions have analgesic effect and can be an alternative to sucrose for procedural pain reduction in healthy term and preterm neonates undergoing a single heel lance and venipuncture</li> </ul> <p><b>Further investigation to establish the efficacy and safety of non-sucrose solutions:</b></p> <ul style="list-style-type: none"> <li>• Current research demonstrates considerable variability in outcome measurements, due to the volumes and concentrations of non-sucrose solutions administered</li> <li>• No studies measured the effects of repeated doses of glucose for procedural pain</li> </ul>

<p>Shah, P., Herbozo, C., Aliwalas, L., Shah, V. Breastfeeding or breast milk for procedural pain in neonates. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD004950. DOI: 10.1002/14651858.CD004950.pub3.</p>	<p>I</p>	<p>Systematic review of 28 RCTs or quasi-RCTs of breastfeeding or supplemental breast milk versus no treatment/other measures in neonates, reporting on either physiologic markers of pain or validated pain scores.</p> <p><b>Breastfeeding or breast milk should be used to alleviate procedural pain in neonates:</b></p> <ul style="list-style-type: none"> <li>• In reducing procedural pain the administration of glucose/sucrose had similar effectiveness as breastfeeding</li> <li>• Breast milk by syringe was not as efficacious as breastfeeding</li> <li>• Effective for a single painful procedure compared to no intervention</li> </ul> <p><b>Future investigation required:</b></p> <ul style="list-style-type: none"> <li>• The effectiveness of breast milk for painful procedures in the preterm population</li> <li>• Efficacy and safety of repeated administration of breast milk or breastfeeding for painful procedures</li> </ul>
<p>Harrison, D. (2008). Oral sucrose for pain management in infants: Myths and misconceptions. Journal of Neonatal Nursing, 14(2), 39-46.</p>	<p>VII</p>	<ul style="list-style-type: none"> <li>• Oral sucrose, when administered to both healthy and sick hospitalised infants, in small volumes, prior to acute painful procedures is a safe, effective, economic, and feasible pain reduction strategy</li> <li>• <b>There is no evidence of increased risk of necrotising enterocolitis, dental caries, bacterial overgrowth or hyperglycemia associated with oral sucrose</b></li> <li>• Sucrose used for pain management is endorsed by the Baby Friendly Health Initiative (BFHI)</li> </ul>
<p>Matsuda, E. (2017) Sucrose as analgesia in neonates undergoing painful procedures, Cochrane Corner, Advanced Journal of Nursing, Vol 117, No 8.</p>	<p>I</p>	<p>Systematic review of 74 RCT's.</p> <ul style="list-style-type: none"> <li>• For neonates undergoing venipuncture, composite and multidimensional pain scores and cry variables were reduced by sucrose concentrations of 24% to 30%.</li> </ul>
<p>Stevens.B, Yamada.J, Ohlsson.A, Haliburton.S, July 2016, Sucrose for analgesia in newborn infants undergoing painful procedures, Cochrane neonatal group, the Cochrane library.</p>	<p>I</p>	<p>Systematic review (Cochrane review) looking at 74 studies enrolling 7049 infants.</p> <ul style="list-style-type: none"> <li>• Sucrose has been found to be effective in providing relief for single events procedures, such as heel lance, venipuncture and intramuscular injection in both term and preterm infants.</li> <li>• Does not provide effective pain relief for circumcision.</li> </ul>