National Neonatal Network

Guideline

Management of Extreme Preterm Infants (22+0 to 23+6 weeks)

Scottish Perinatal Network

NEONATAL

Document Control Sheet

Title	Management of Extreme Preterm Infants (22+0 to 23+6 weeks)
Lead Author(s)	Refer Annex A
Date Published/ Issued	11.01.2024
Date Effective From	11.01.2024
Version/Issue Number	1.0
Document Type	National Neonatal Network, National Guidance
Document Status	Final
Owner	National Neonatal Network (NNN)
Approver	NNN Guideline Oversight Group
Approval Date	09.01.2024
Contact	nss.perinatalnetwork@nhs.scot
File Location	K:\09 PCF\NSD\Strategic Networks\Perinatal\Workstreams\NeoGdlns\SLWG ExtrPrtrmInf

Revision History:

Version	Date	Summary of Changes	Name	Changes Marked
1.0	09.01.2024	None - original version		

Disclaimer

The recommendations in this guideline represent the view of the National Neonatal Network Guideline Development Group, arrived at after careful consideration of the evidence available. When exercising their clinical judgement, healthcare professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of the families using their service. It is not mandatory to follow the guideline recommendations and it remains the responsibility of the healthcare professional to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Contents

1: Network Principles Underpinning this Consensus Framework

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

- Perinatal Care for pregnancies and babies applicable to this framework will be delivered by NICU centres as described within the Best Start Model. (A)
- In-utero and/or ex-utero transfers will be to NICU centres. (A) [2,3,5]
- NICUs must prioritise capacity for such high-risk extreme premature babies and ensure a process to mitigate against transferring out women or babies at this gestation to alternative units. (A)
- NICU centres will provide perinatal support including shared decision making to LNUs and SCUs. (A) [1,4]
- NICUs will provide care in line with the recommendations detailed within this framework facilitating a consistency of practice across Scotland. (A)
- NICUs will participate in audit and case reviews on an annual basis to review outcomes and share learning to inform future planning of care delivery for this population of babies. (A)

References

1 BAPM. (2019). Perinatal management of Extreme Preterm Birth before 27 weeks of gestation - A BAPM framework for Practice. https://hubble-live-assets.s3.amazonaws.com/bapm/file_asset/file/30/Extreme_Preterm_28-11-19_FINAL.pdf

2 BAPM. (2021). Optimal Arrangements for Neonatal Intensive Care Units in the UK including guidance on their Medical Staffing: A BAPM Framework for Practice. https://hubble-live-assets.s3.amazonaws.com/bapm/file_asset/file/131/Optimal_Arrangement_for_NICUs_revision_10-6-21.pdf.

3 Kaempf, J., et al. (2021). Continued improvement in morbidity reduction in extremely premature infants. Arch Dis Child Fetal Neonatal Ed, 106, F265–F270. doi:10.1136/archdischild-2020-319961.

4 Safer Care Victoria. (2021). Extreme prematurity guidelines. 20201222 Extreme Prematurity Guideline_FINAL.pdf (safercare.vic.gov.au).

5 Smith, J., et al. (2014). The effects of designation and volume of neonatal care on mortality and morbidity outcomes of very preterm infants in England: A retrospective population-based cohort study. BMJ Open, 4, e004856. doi:10.1136/bmjopen-2014-004856.

2: Antenatal Communication and Maternal / Neonatal Transport

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

- An antenatal collaborative perinatal discussion including senior obstetric, midwifery, neonatal staff and the parents should occur where possible and include review of any known risk factors that impact on the predicted chance of survival, recognising the specific challenges of rural locations. (A)
- The possibility of loss of the baby before birth or during labour should be part of this conversation. A resulting plan for active (survival focused) or palliative (comfort focused) care should be based on these discussions. This should be supported with written information. (A) [2,6,7,12,13,15]
- If survival focused care is offered, parallel care planning and an anticipatory care plan may be beneficial from the start-see section 9 guidance. (B)
- Parental discussions should occur locally, and in-utero transfer should be arranged if active survival focused care agreed and not available locally. Local Palliative care could be offered otherwise. (A) [2,13]
- Conversations should be documented and communicated to all members of the perinatal team. These should be regularly reviewed to enable the focus of care to change as gestation progresses if appropriate. (A) [2]
- After full discussion with parents outlining the guarded outcomes in this group of infants, a parental wish for survival focused care should be respected, with agreement to commit to full intensive care (e.g. antenatal optimisation, IUT/postnatal transfer and expressing etc), this should be supported with written information given to parents. (A) [2]
- Professional collaboration/support in delivering these conversations will be offered to LNUs and SCUs who do not routinely provide care for infants at this gestation by contacting their pathway NICU neonatologist and obstetrician. (A) [2,13]
- Comfort focused palliative care pathway will be supported where this is the parental wish for babies < 24 weeks with adverse prognostic indicators. (A) [2,9,13]
- If in-utero transfer is planned, a risk assessment utilising the SPN risk assessment tool for IUT should be undertaken which will include maternal history to guide the appropriateness, safety and timing of in-utero transfer. Transfers should only occur to allow delivery from 22 weeks gestation (A) [14]

- In the event of birth in a LNU or SCU where survival focused care is planned, transfer should be offered and arranged promptly following delivery to the pathway NICU. The decision to transfer postnatally should involve parents and should involve the NICU obstetrician/neonatologist and transport team. This should be supported with written information. (A) [2,13]
- If a precipitate delivery occurs with no time for antenatal optimisation and discussions - it is appropriate to offer survival focused care as default while discussions are ongoing, dependent on available facilities. The ongoing direction of care; either survival focused care or comfort focused and transport decisions should be based on parental wishes, infant's condition and following extensive discussion (local team, NICU obstetrician / neonatologist, transport team). (A)
- If survival focused care is planned the pregnancy and birth should be managed with the aim of optimising perinatal condition. This includes maternal administration of a full course antenatal corticosteroids from 22+0 weeks and Magnesium Sulphate if preterm birth anticipated. Antibiotics as per RCOG guidance. (A) [1, 2, 3, 4, 5, 6, 10, 11, 12, 13, 14, 15]
- Tocolysis to facilitate transfer or to allow completion of antenatal steroids should be considered and documented. (A) [1, 2, 4, 11]
- Caesarean birth is best avoided unless for maternal indications. (B)
- Electronic fetal monitoring is not felt to be helpful at this gestation, but intermittent monitoring of the heart is helpful to direct need for neonatal interventions. (A)
- The Scottish Perinatal Network guidance on "in-utero transfers" - covering both maternal and fetal indications and transport pathways - should be followed. (A) [14]
- It is not appropriate to attempt to provide active treatment to babies born before 22+0 weeks of gestation. (A) [2, 13]

References

1. Ågren J. (2022) The proactive approach to mother-infant dyads at 22-24 weeks of gestation: Perspectives from a Swedish center. Semin Perinatol. 2022 Feb;46(1):151536. doi: 10.1016/j.semperi.2021.151536. Epub 2021 Nov 10. PMID: 34844786.
2. BAPM. (2019). Perinatal management of Extreme Preterm Birth before 27 weeks of gestation - A BAPM framework for Practice. https://hubble-live-assets.s3.amazonaws.com/bapm/file_asset/file/30/Extreme_Preterm_28-11-19_FINAL.pdf
3. Chawla S, Wyckoff MH, Rysavy MA, Patel RM, Chowdhury D, Natarajan G, Laptook AR, Lakshminrusimha S, Bell EF, Shankaran S, Van Meurs KP, Ambalavanan N, Greenberg RG, Younge N, Werner EF, Das A, Carlo WA; (2022) Association of Antenatal Steroid Exposure at 21 to 22 Weeks of Gestation With Neonatal Survival and Survival Without Morbidities. JAMA Netw Open. 2022 Sep 1;5(9):e2233331. doi: 10.1001/jamanetworkopen.2022.33331. PMID: 36156145; PMCID: PMC9513645.
4. Helou YE, Buhimschi IA, Romano-Keeler J, Buhimschi CS. (2022) Controversies in treatment practices of the mother-infant dyad at the limit of viability. Semin Perinatol. 2022 Feb;46(1):151539. doi: 10.1016/j.semperi.2021.151539. Epub 2021 Nov 10. PMID: 34887106.
5. Hughes, RG, Brocklehurst, P, Steer, PJ, Heath, P, Stenson, BM on behalf of the Royal College of Obstetricians and Gynaecologists. (2017) Prevention of early-onset neonatal group B streptococcal disease. Green-top Guideline No. 36. BJOG 2017; 124: e280–e305.

6. Kaempf, J., et al. (2021). Continued improvement in morbidity reduction in extremely premature infants. Arch Dis Child Fetal Neonatal Ed, 106, F265–F270. doi:10.1136/archdischild-2020-319961
7. Linehan LA, Walsh J, Morris A, Kenny L, O'Donoghue K, Dempsey E, Russell N. (2016) Neonatal and maternal outcomes following midtrimester preterm premature rupture of the membranes: a retrospective cohort study. BMC Pregnancy Childbirth. 2016 Jan 29;16:25. doi: 10.1186/s12884-016-0813-3. PMID: 26831896; PMCID: PMC4734873.
8. Lorthe E, Torchin H, Delorme P, Ancel PY, Marchand-Martin L, Foix-L'Hélias L, Benhammou V, Gire C, d'Ercole C, Winer N, Sentilhes L, Subtil D, Goffinet F, Kayem G. (2018) Preterm premature rupture of membranes at 22-25 weeks' gestation: perinatal and 2-year outcomes within a national population-based study (EPIPAGE-2). Am J Obstet Gynecol. 2018 Sep;219(3):298.e1-298.e14. doi: 10.1016/j.ajog.2018.05.029. Epub 2018 May 29. PMID: 29852153.
9. MBRRACE. (2020). National clinical guidance for the determination of signs of life following spontaneous birth before 24+0 weeks of gestation where, following discussion with the parents, active survival-focused care is not appropriate.
10. Mori R, Kusuda S, Fujimura M; (2011) Neonatal Research Network Japan. Antenatal corticosteroids promote survival of extremely preterm infants born at 22 to 23 weeks of gestation. J Pediatr. 2011 Jul;159(1):110-114.e1. doi: 10.1016/j.jpeds.2010.12.039. Epub 2011 Feb 22. PMID: 21334006.
11. NICE. (2022). Preterm labour and birth. [NG25]. https://www.nice.org.uk/guidance/ng25/resources/preterm-labour-and-birth-pdf-1837333576645.
12. Queensland Government. (2014). Perinatal care at the threshold of viability: Guideline. Perinatal care of extremely preterm baby (health.qld.gov.au).
13. Safer Care Victoria. (2021). Extreme prematurity guidelines. 20201222 Extreme Prematurity Guideline_FINAL.pdf (safercare.vic.gov.au).
14. Scottish Perinatal Network Transport Group. (2023). In-utero Transfers in Scotland: Consultant-led Unit to Consultant-led Unit. https://www.perinatalnetwork.scot/wp-content/uploads/2023/03/In-Utero-Transfers-in-Scotland-CLU-to-CLU.pdf
15. Usuda H, Carter S, Takahashi T, Newnham JP, Fee EL, Jobe AH, Kemp MW. (2022) Perinatal care for the extremely preterm infant. Semin Fetal Neonatal Med. 2022 Apr;27(2):101334. doi: 10.1016/j.siny.2022.101334. Epub 2022 Apr 15. PMID: 35577715.
16. Watson SI, Arulampalam W, Petrou S, et al. (2014) The effects of designation and volume of neonatal care on mortality and morbidity outcomes of very preterm infants in England: retrospective population-based cohort study. BMJ Open 2014;4:e004856. doi: 10.1136/bmjopen-2014-004856

3: Delivery Room, Early NNU, Golden Hours and Access

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

Preparation and Pause

- A delivery room **prompt** should be used for all preterm births to ensure the entire perinatal team is prepared and all equipment is available and checked [1,2,3]. (A)
- This should include:
  - **HISTORY:** A brief summary clarifying the history, indications for delivery and antenatal optimisation measures achieved
  - **EQUIPMENT:** RESUSCITAIRE, AIRWAY, THERMAL CARE, MONITORING, TRANSPORT INCUBATOR (if used)
  - **ALLOCATE ROLES:** SUPPORTING DCC, AIRWAY, THERMAL CARE, MONITORING
  - **PAUSE:** A preterm pause should be performed involving the entire perinatal team, communicating a clear plan for the birth & stabilisation. The four most vital shared goals must be highlighted:
    1. **Deferred cord clamping (DCC)**
    2. **Gentle transition**
    3. **Achieving normothermia**
    4. **Supporting early milk expression**

    Any contraindications to DCC must be clearly communicated during the preterm pause, otherwise the default will be for at least 60 seconds of deferred cord clamping.

Stabilisation

DCC

- DCC of at least 60 seconds should be performed for all babies unless an absolute contraindication, or if there are no signs of life, follow local guidance [6, 9, 10, 11, 12, 13, 17, 20, 22]. (A)
- The neonatal team member leading DCC should be by the bedside assessing the infant and supporting the team throughout. Aim to maintain where possible neutral airway position and gently stimulate the infant. (A)
- Timing of clamping of the cord should be directed by both the neonatal and obstetric teams. (A)
- All babies should be delivered into a plastic bag. Consider provision of additional thermal care during DCC if feasible. Use plastic cord clamps, avoiding large metal theatre instruments being in contact with the infant (B)

Airway

- Resuscitation should be performed as per NLS guidance & with consideration of maturity and condition**.** (A) [15]
- Stabilisation and airway management should be led by a clinician with extensive resuscitation experience – either a senior middle grade or consultant. (A) [10, 11]
- Aim to support a gentle transition with facemask PEEP of 6-8 cm H_2O in 30% oxygen initially, followed by IPPV 25cm H_20 if required, or intubate immediately if clinically indicated[11,13, 14, 15, 19, 20, 22,]. (A)
- Intubation should be performed by a senior **experienced intubator** with a size 2 or 2.5mm ETT, likely length 5.5-6 cm max (A). Both 00 and 000 Laryngoscope blades should be available. (A)
- After clinical confirmation of intubation, give surfactant without delay. (A)
- ET fixation should be undertaken as per unit policy. Consideration to be given on practicalities due to size and extreme preterm skin. (A)
- Use minimal inflation pressures to achieve saturation targets and adequate heart rate and convert the infant to volume targeted ventilation as soon as possible[19, 22]. (A)

Thermoregulation on resuscitaire [3, 10, 11, 20, 22]

- Ensure the infant remains in the plastic bag throughout stabilisation (A) and directly under radiant heat.
- Attach a temperature probe and monitor temperature closely throughout stabilisation (this is ideal and should occur in NICUs, it is accepted that LNU/SCBUs may not be able to achieve this). (A)
- Ensure strict thermoregulatory measures are adhered to. (A)

Monitoring

- Attach pre-ductal saturation monitoring to right hand (A) [15]
- If good cardiac trace via saturation probe, ECG leads are not essential (A)

Family Delivery Room Contact

- If an infant is clinically stable and normothermic following stabilisation measures, a brief cuddle or contact with parents prior to transfer to NICU should be prioritised and offered. (B)

Advanced Resuscitation

Although evidence is lacking, performing CPR and using resuscitation drugs in this population of babies is unlikely to be effective both in the short-term acute outcome or improve longer term outcomes and would generally not be appropriate in this group of extremely premature infants.

If the infant is felt to be too small, immature, or too clinically unwell, it is reasonable not to undertake resuscitative measures in the best interests of the infant. Joint discussions with the clinical team and parents should help guide these decisions.

- If offering advanced resuscitative techniques, they should be performed as per NLS guidance [15]. (A)
- If the infant remains bradycardic despite effective lung inflation, intubation & surfactant, a formal assessment at 10 minutes of age should be performed, and a discussion with

parents should be had with around the appropriateness of ongoing resuscitative efforts and instead ensuring comfort for baby and family. (A)
- In the absence of signs of life by 20 minutes, discontinuing resuscitation would be regarded as acceptable. (A)

Neonatal Unit

Preparation
- Ensure the neonatal unit is set up to facilitate efficient stabilisation. (A)
- All equipment should be prepared including an incubator, ventilator, humidifier, monitoring, naso/oro-gastric tube, line trolley, parenteral nutrition, lipid and drugs (A).

Admission Pause
- Perform a brief pause on admission to make a systematic plan for the infant, and to allocate tasks and responsibilities.
- Clarify shared goals including rapid access, early administration of drugs and fluids & avoidance of hypocarbia.
- Ensure procedures are carried out by **skilled practitioners** to **minimise handling** and avoid **secondary hypothermia** (Avoid removing babies from their delivery room plastic bag until all procedures are undertaken).

Lines
- Aim to site umbilical arterial and venous lines as soon as possible. If any potential delay or difficulties, a peripheral cannula (PVC) can be inserted initially[20]. (A)
- If born in LNU/SCBU, umbilical line insertion should not be prolonged or delay transfer, a PVC is acceptable. (A)
- To avoid chemical burns, carefully ensure the correct cleaning solution is used on preterm skin, avoid alcohol and use lower concentration chlorhexidine solutions, as per local guidance. (A)
- Lines should be well secured as per local guidance and avoiding contact with skin. Particular care should be taken securing lines in babies requiring transfer. (A)

Bloods
- Routine bloods should be taken as soon as possible including full blood count, group & save, gas, blood spot +/- blood cultures & CRP if indicated. Consider obtaining from the placenta or cord following delivery to minimise blood losses (A)
- Coagulation screens should only be performed if concerns about bleeding/DIC from sepsis, or if very significant bruising. (A)

Fluids
- Commence parenteral nutrition and lipids as soon as possible after birth[1,18]. (A)
- Close attention should be made to regularly assess the fluid status of the infant, who will likely need rapid escalation of fluid volumes. (A)

Drugs
- CAFFEINE: Prescribed as per local drug monograph[19,22]. (A)
- ANTIBIOTICS: If indicated and as per local unit policy. (A)
- ANTIFUNGAL PROPHYLAXIS: follow local policy. (A)

- VITAMIN K (A)
- STEROIDS: Consider early prophylactic hydrocortisone, especially if no antenatal steroid given, or if there is a history of chorioamnionitis[4,5]. (B)

Cranial Ultrasound

- A cranial ultrasound should be performed within the first 24 hours[16]. (A)
- Perform early if anaemia or clinical concern.
- Time scan to minimise handling & avoid early hypothermia.
- If born in an LNU or SCBU, ensure cranial scans do not delay transfer, however perform earlier if there are questions around the appropriateness of transfer or ongoing intensive care. (A)

Breast Milk

- Ensure mother is supported to express in the first two hours after birth (A)
- Give colostrum as soon as possible for mouth care and trophic feeds[7,10,11,13]. (A)
- Use standardised feeding protocols to guide feeding plan[2,7,8,10,11,13,21,22]. (A)

References

1. Alexandre Lapillonne et al., (2018) ESPGHAN/ESPEN/ESPR/CSPEN guidelines on paediatric parenteral nutrition: Lipids. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on paediatric parenteral nutrition: Lipids (clinicalnutritionjournal.com)
2. Ågren J. (2021). The proactive approach to mother-infant dyads at 22-24 weeks of gestation: Perspectives from a Swedish center. Seminars in Perinatology. doi:10.1016/j.semperi.2021.151536.
3. BAPM/NNAP. (2020). Improving Normothermia in Very Preterm Infants - A Quality Improvement Toolkit. Normothermia Toolkit | British Association of Perinatal Medicine (bapm.org
4. Baud O, Maury L, Lebail F, Ramful D, El Moussawi F, Nicaise C, Zupan-Simunek V, Coursol A, Beuchée A, Bolot P, Andrini P, Mohamed D, Alberti C (2016). Effect of early low-dose hydrocortisone on survival without bronchopulmonary dysplasia in extremely preterm infants (PREMILOC): a double-blind, placebo-controlled, multicentre, randomised trial. The Lancet, Vol 387.
5. Baud O, Trousson C, Biran V, Leroy E, Mohamed D, Alberti C (2017). Association Between Early Low-Dose Hydrocortisone Therapy in Extremely Preterm Neonates and Neurodevelopmental Outcomes at 2 Years of Age. JAMA, 317(13), 1329-1337. doi:10.1001/jama.2017.2692.
6. Fogarty M, Osborn DA, Askie L, Seidler AL, Hunter K, Lui K, Simes J, Tarnow-Mordi W (2018). Delayed vs early umbilical cord clamping for preterm infants: a systematic review and meta-analysis. American Journal of Obstetrics & Gynaecology
7. Gephart SM, Hanson C, Wetzel CM, Fleiner M, Umberger E, Martin L, Rao S, Agrawal A, Marin T, Kirmani K, Quinn M, Quinn J, Dudding KM, Clay T, Sauberan J, Eskenazi Y, Porter C, Msowoya AL, Wyles C, Avenado-Ruiz M, Vo S, Reber KM, Duchon J (2017). NEC-zero recommendations from scoping review of evidence to prevent and foster timely recognition of necrotizing enterocolitis. Maternal Health, Neonatology and Perinatology, 3:23. doi: 10.1186/s40748-017-0062-0.
8. Isayama T (2019). The clinical management and outcomes of extremely preterm infants in Japan: past, present, and future. Translational Pediatrics, 8(3), 199-211. doi: 10.21037/tp.2019.07.10.
9. Kaempf JW, Schmidt NM, Rogers S, Novack C, Friant M, Wang L, Tipping N (2017). The quest for sustained multiple morbidity reduction in very low-birth-weight infants: the Antifragility project. Journal of Perinatology. doi:10.1038/jp.2017.7.
10. Kaempf JW, Morris M, Austin J, Steffen E, Wang L, Dunn M (2019). Sustained quality improvement collaboration and composite morbidity reduction in extremely low gestational age newborns. Acta Paediatrica, 108, pp. 2199–2207

11. Kaempf, J., et al. (2021). Continued improvement in morbidity reduction in extremely premature infants. Arch Dis Child Fetal Neonatal Ed, 106, F265–F270. doi:10.1136/archdischild-2020-319961.
12. Lamberska T, Luksova M, Smisek J, Vankova J, Plavka R (2015). Premature infants born at less than 25 weeks of gestation may be compromised by currently recommended resuscitation techniques. Acta Paediatrica.
13. Lee SK, Shah PS, Singhal N, Aziz K, Synnes A, McMillan D, Seshia MM (2014). Association of a quality improvement program with neonatal outcomes in extremely preterm infants: a prospective cohort study. CMAJ. DOI:10.1503/cmaj.140399.
14. Lee HC, Powers RJ, Bennett MV, Finer NN, Halamek LP, Nisbet C, Crockett M, Chance K, Blackney D, von Köhler C, Kurtin P, Sharek PJ (2014). Implementation Methods for Delivery Room Management: A Quality Improvement Comparison Study. Pediatrics, 134, e1378. DOI: 10.1542/peds.2014-0863
15. Madar J, Roehr CC, Ainsworth S, Ersdal H, Morley C, Rüdiger M, Skåre C, Szczapa T, Te Pas A, Trevisanuto D, Urlesberger B, Wilkinson D, Wyllie JP (2021). ILCOR -Newborn Life Support Algorithm 2021. Newborn Life Support Algorithm 2021.pdf
16. Mohammad K, Scott JN, Leijser LM, Zein H, Afifi J, Piedboeuf B, de Vries LS, van Wezel-Meijler G, Lee SK, Shah PS (2021). Consensus Approach for Standardizing the Screening and Classification of Preterm Brain Injury Diagnosed With Cranial Ultrasound: A Canadian Perspective. Frontiers in Pediatrics.
17. Morgan A S, Mendonca M, Thiele N, David A L. (2022). Management and outcomes of extreme preterm birth. BMJ, 376, e055924. doi: 10.1136/bmj-2021-055924.
18. NICE (2018). Neonatal Parenteral Nutrition. https://www.nice.org.uk/guidance/NG154
19. NICE (2019). Specialist neonatal respiratory care for babies born preterm. nice.org.uk/guidance/ng124
20. Safer Care Victoria (2021). Extreme prematurity guidelines. 20201222 Extreme Prematurity Guideline_FINAL.pdf (safercare.vic.gov.au)
21. Stevens TP, Shields E, Campbell D, Combs A, Horgan M, La Gamma EF, Xiong K, Kacica M (2018). Statewide Initiative to Reduce Postnatal Growth Restriction among Infants <31 Weeks of Gestation. J Pediatr, 197, 82-89.e2. doi: 10.1016/j.jpeds.2018.01.074.
22. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Te Pas A, Plavka R, Roehr CC, Saugstad OD, Simeoni U, Speer CP, Vento M, Visser GHA, Halliday H (2019). European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update. Neonatology, 115, 432–451.

4: Respiratory Management

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

Ventilation

- Minimise dead space – shortened ET tube, no ETCO2 as standard care (A)
- Mode of ventilation
  - volume targeted, start at 5ml/kg if on conventional ventilation. (A)
  - minimise ventilation while avoiding atelectasis[6,10,17]. (A)
  - consider HFOV – as first line or as rescue (B) [3,10,12]
- Avoid hypocarbia-adjust ventilation rapidly and repeat gas within the hour [10,11,15]. (A)
- Allow permissive hypercarbia[6,10,11,13]. (A)
- Minimise sedation (B), avoid midazolam. (B)
- Avoid muscle relaxation (A). If felt unavoidable, try bolus dose(s) rather than infusion. (A)
- Minimise suction, avoid routine suction. (A)

Extubation

- Avoid extubation in first 72 hours (highest risk of IVH). (A)
- Reasonable to avoid extubation in first weeks unless local NICU has good track record extubating babies <600g (unsuccessful extubations increase mortality and respiratory morbidity)[4,8]. (B)
- Extubate to non-invasive respiratory support – likely NIPPV[7,12,14,16]. (B)
- NAVA or nHFOV if available are other options and may be superior[12,14]. (C)
- Orogastric tubes are preferable to nasogastric tubes until stable off ventilator. (A)
- Extubation attempts need to be carefully planned, risks of multiple intubations and extubations need to be balanced with risks of prolonged ventilation[4,8]. (A)
- Consider using HFNC during intubation/reintubation attempts[5]. (B)

Steroids

- Routine use of postnatal corticosteroids is not recommended. (A)
- However, steroids either to prevent or treat early BPD, may increase the rate of survival without severe BPD but carry significant short- and long-term risks (B) [1,2,10,17]
- Treatment options need to be decided on a unit level and often individualised per patient with discussion with family.
  - Prophylactic
    - Consider early prophylactic hydrocortisone (B) especially if chorioamnionitis[1,2]
  - Treatment of evolving BPD
    - Consider low dose dexamethasone (DART) [10,17]

- if possible not before day 14.
- If ventilatory requirements are modest but the infant is not big enough in size or with good enough respiratory drive to extubate, consider delaying dexamethasone. (B)
- If no response after 72 hours consider stopping.
- May need more than one course of DART.
- Consider higher doses of dexamethasone if does not respond to DART (B)
- Consider nebulised budesonide to avoid re-ventilation. (B)
- Keep account of cumulative steroid dose (A) – total dose and duration should be minimised.

Diuretics

A trial of diuretics may be considered if evolving lung disease or PDA. If no improvement after a few days, stop. Watch carefully for AKI especially with furosemide [10] (B)

Non-invasive Respiratory Support

- Ensure rolling programme of nursing education on mask/prongs placement. (A)
- Observe for nasal trauma. (A)
- Wean support slowly guided by work of breathing and FiO2. (A)
- Step down of support NIPPV – CPAP – high flow[1, 5, 7, 14, 16]. (A)
- Consider higher flow rates on HFNC (8-12 l/min) when needed post term. (B)
- Optimise nutrition, see section below[6]. (A)
- Consider inhaled or enteral steroids if destabilising on non-invasive support and heading towards ventilation or slow to wean.[17] (B)
- Consider assessing for Pulmonary Hypertension in severe BPD.[5] (B)

Longer Term

- Offer RSV prophylaxis to infants with BPD.[9] (A)
- Parents should be:
    - Advised that the infant is at risk of respiratory deteriorations/admissions with respiratory viruses. (A)
    - Advised to avoid exposure to cigarette smoke, vaping, viruses or other respiratory infections. (A)
    - Encourage vaccinations including flu/pertussis. (A)
    - Considering encourage healthy diet and exercise long term. (B)

References

1. Baud O, Maury L, Lebail F, Ramful D, El Moussawi F, Nicaise C, Zupan-Simunek V, Coursol A, Beuchée A, Bolot P, Andrini P, Mohamed D, Alberti C (2016). Effect of early low-dose hydrocortisone on survival without bronchopulmonary dysplasia in extremely preterm infants (PREMILOC): a double-blind, placebo-controlled, multicentre, randomised trial. The Lancet, Vol 387.
2. Baud O, Trousson C, Biran V, Leroy E, Mohamed D, Alberti C (2017). Association Between Early Low-Dose Hydrocortisone Therapy in Extremely Preterm Neonates and Neurodevelopmental Outcomes at 2 Years of Age. JAMA, 317(13), 1329-1337. doi:10.1001/jama.2017.2692.

3. Burch K, Rhine W, Baker R, Litman F, Kaempf JW, Schwarz E, Sun S, Payne NR, Sharek PJ 2003). Implementing Potentially Better Practices to Reduce Lung Injury in Neonates. Pediatrics, Vol. 111, No.4.
4. Chawla S, Natarajan G, Shankaran S, Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. (2017). Markers of Successful Extubation in Extremely Preterm Infants, and Morbidity After Failed Extubation. J Pediatr, 189, 113-119.e2. doi: 10.1016/j.jpeds.2017.04.050.
5. Hodgson KA, Owen LS, Kamlin COF, Roberts CT, Newman SE, Francis KL, Donath SM, Davis PG, Manley BJ (2022). Nasal High-Flow Therapy during Neonatal Endotracheal Intubation. N Engl J Med, 386(17).
6. Kaempf, J., et al. (2021). Continued improvement in morbidity reduction in extremely premature infants. Arch Dis Child Fetal Neonatal Ed, 106, F265–F270. doi:10.1136/archdischild-2020-319961
7. Lemyre B, David P.G. (2023). Cochrane Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation. https://doi.org/10.1002/14651858.CD003212.pub3
8. Manley BJ, Doyle LW, Owen LS, Davis PG. (2016). Extubating Extremely Preterm Infants: Predictors of Success and Outcomes following Failure. J Pediatr, 173, 45-9. doi: 10.1016/j.jpeds.2016.02.016.
9. National Neonatal Network Scotland (2022). Home oxygen therapy for Neonates-Clinical guideline. https://www.perinatalnetwork.scot/wp-content/uploads/2022/04/National-Neonatal-Network-Home-Oxygen-Guideline-V1.0.pdf
10. NICE (2019). Specialist neonatal respiratory care for babies born preterm. nice.org.uk/guidance/ng124
11. Norman M, Jonsson B, Wallström L, Sindelar R (2022). Respiratory support of infants born at 22–24 weeks of gestational age. Seminars in Fetal and Neonatal Medicine
12. Owen LS, Manley BJ, Hodgson KA, Roberts CT. (2021). Impact of early respiratory care for extremely preterm infants. Seminars in Perinatology, 45(8), 151478. doi: 10.1016/j.semperi.2021.151478.X
13. Payne NR, LaCorte M, Sun S, Karna P, Lewis-Hunstiger M, Goldsmith JP (2006). Evaluation and Development of Potentially Better Practices to Reduce Bronchopulmonary Dysplasia in Very Low Birth Weight Infants. Pediatrics, 118(Supplement 2), S65. DOI: 10.1542/peds.2006-0913B.
14. Ramaswamy VV, More K, Roehr CC, Bandiya P, Nangia S (2020) Efficacy of non-invasive respiratory support modes for primary respiratory support in preterm neonates with respiratory distress syndrome: Systematic review and network meta-analysis. Pediatric Pulmonology, 55, 2940–2963
15. Sindelar R, Nakanishi H, Stanford AH, Colaizy TT, Klein JM (2021). Respiratory management for extremely premature infants born at 22 to 23 weeks of gestation in proactive centers in Sweden, Japan, and USA. Seminars in Perinatology.
16. Solevåg AL, Cheung PY, Schmölzer GM (2021). Bi-Level Noninvasive Ventilation in Neonatal Respiratory Distress Syndrome: A Systematic Review and Meta-Analysis. Neonatology, 118, 264–273.
17. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, Te Pas A, Plavka R, Roehr CC, Saugstad OD, Simeoni U, Speer CP, Vento M, Visser GHA, Halliday HL (2019). European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update. Neonatology, 115, 432–451.

5: Cardiovascular and Haemodynamics

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Aims

To use an approach to haemodynamic monitoring and support to reduce the incidence of serious and common adverse outcomes in infants born at 22-23 week gestation. These including death, pulmonary haemorrhage, brain injury, NEC and chronic respiratory failure.

Evidence: incorporated into the main document and referenced.

Useful Additional Resources

Appendix 1: provides normative blood pressure values, details of inotropes, hypotension flow charts in response to echo and multiparameter monitoring and suggested bedside algorithm for NIRS.

Recommendations

Perinatal Optimisation and Delivery Room Care (A)

- Optimal perinatal and delivery room care, with delayed cord clamping and transition are key to early cardiovascular stability[33].

Admission to NICU General Care

- Umbilical arterial line and venous line placement wherever possible. These can be left in place for 7-10 days and are critical to fluid/nutritional support of these infants (A)
- Goal posting of umbilical lines, attaching them to the abdomen by placing Duoderm on the abdominal skin and goal posting tape to this, should be undertaken as standard at approximately 72 hours i.e. before the umbilical separates avoiding line displacement. (A)
- Avoid any sustained hypocalcaemia < 2 mmol/l (corrected) or < 1 (ionised) (B)
- Avoid very rapid fluid boluses where possible (A)
- Consider checking clotting screen if the infant is very badly bruised or at clinical risk of severe clotting impairment putting them at further risk of IVH **OR** if hypotensive use FFP or cryoprecitate as volume (B)
- Haemoglobin: consider lower early target of between 12g – 14g /dl for 1st 72 hours[11] (B)

Specific Haemodynamic Care (B)

- Fundamentally based on clinical assessment, gases and multiparameter monitoring.
- If hypotensive consider findings and likely pathophysiology in context of integrated flow Chart 1
- Also consider echocardiographic assessment and cerebral NIRS to provide a fuller understanding of pathophysiology, brain oxygenation, appropriate treatments and responses. (B)

Monitoring

- **Arterial Blood Pressure (BP) monitoring (A)** via UAC is standard part of care. Where not possible, placement of peripheral arterial lines will depend on the size and stability of the infant. (A)
  - BP should be considered along with clinical phenotype (see Appendix Chart 1)
  - There is limited normative BP data for 22 and 23 weeks GA but reference charts are available (Appendix 1: Tables 1 &2).
  - Extrapolation of mean BP down from data at 24 weeks, suggests lower mean BP thresholds should generally be > GA + 2mmHg. (A)
  - All early BP should be interpreted with caution as early BP is poorly concordant with flow and end organ perfusion, particularly in the first 24 hours when low flow states are common and the brain is most vulnerable to IVH[19,32]. (A)
  - Responses should never be made in isolation from other measures of perfusion: including Lactate, Hb, urine output, capillary refill (CRF) time and where in use cerebral NIRS. (A)
  - Low BP is a common scenario and, after a single fluid bolus, dobutamine up to maximum 10microg/kg/min is generally a good approach. (B)
  - Consideration should always be given to other non-cardiac pathophysiology such as over ventilation or pneumothorax. (A)
  - Consideration should be given to both **systolic and diastolic** components as indicators of cause of hypotension or compromise when considering response beyond a single slow bolus of fluid (Appendix 1 Table 3 and Appendix 2 Chart 1). (A)
  - "Inotropes" should be selected based on characteristics (vasotropes, chronotropes, inotropes, lusitropes) and underlying pathophysiology (Appendix 1 Table 4 & Appendix 2 Chart 1).
  - Consider hydrocortisone particularly if more than one inotropic agent is required. (A)
  - If additional support for low BP is required, consider low dose adrenaline (particularly if LV / RV dysfunction) or noradrenaline for septic shock with tachycardia. (B)
  - Dopamine has a limited role, should be avoided in pulmonary hypertension and should only be used in cautiously with dobutamine as may lead to excessive tachycardia. If second line agents for hypotension are required adrenaline or noradrenaline maybe more appropriate. (B)
  - Infants with LV dysfunction may require sedation, particularly if high BP or high systemic vascular resistance. (B)

- **ECG:** typically best avoided for at 1st 72 hours for skin integrity issues. (A)

- **Cerebral NIRS monitoring (B)**

This is an area of growing practice; use is evolving but not routine. Pilot trials have demonstrated the ability to reduce cerebral hypoxia (4) but a large pragmatic RCT did not show a reduction in cranial ultrasound changes or death if used in the first 72 hours of life [14]. However secondary outcomes exploring unintended adverse effects and skin damage were reassuring [14].

Consider commencing where skin integrity and experience with more mature infants allows to guide intervention/ support.(B)

  - Consider monitoring cerebral saturations (NIRS) where possible from birth for at least the first 72 hours of life and/or during periods of haemodynamic instability. [32]
  - Cerebral NIRS can be helpful in the absence of arterial BP monitoring.
  - NIRS hypoxic thresholds must selected for the specific manufacturer's device and probe (Appendix 1: Table 5).
  - Responses to hypoxic thresholds should include utilisation of bedside clinical algorithms of evidence based interventions (Appendix 2: Chart 1).
  - Units using NIRS should audit carefully and in collaboration with other centres.

- **Echocardiographic assessment (B)**

  During the transitional phase from fetal to neonatal circulation, pulmonary vascular resistance decreases rapidly, followed by the increased systemic vascular resistance due to the separation from the placenta. Extremely preterm infants have greater difficulty adapting to these changes. Preterm infants born at 22-24 weeks of gestation have fewer myocardial muscle fibres (30%) with poor myocardial contractility and responses to catecholamines. In addition, a PDA superimposes and exacerbates unstable hemodynamic conditions[31]. Publications from North America , Japan[15,16,31] and Europe[9] describe neonatal functional echocardiography as part of a range of interventions associated with excellent outcomes[15,16,31] at 22-25 weeks or improved outcomes generally in preterms[27]. Whilst outcomes may represent other aspects of care, or population findings, more recently there are improvements associated with the introduction of echo assessment[29]. Echo can also guide appropriate care during periods of acute destabilisation and has an important role in monitoring for later development of pulmonary hypertension.

  Echo must be carried out with care and attention to infection control principles. (B)

  - Units that can provide routine echo assessment should consider echo based circulatory management as an additional key component of care.
  - Echocardiographic haemodynamic assessment, where skills are available, should be considered in the first 12-36 hours of life or for infants requiring more than one inotrope, clinical suspicion of a PDA or any acutely deteriorating infant.
  - There is no one size fits all solution to haemodynamic instability which is disease and physiology dependant; thoughtful use of Charts 1-3 (Appendix 2), integrating clinical background and other aspects of multi modal monitoring are required.
  - Structured recording of assessments and interventions along with peer review are vital to improving care and outcomes.

Specific Interventions

1. Early prophylactic indomethacin (C)

Indomethacin is highly effective in PDA closure and reducing pulmonary haemorrhage[17,24]. Additionally, indomethacin has independent effects on capillary stability and cerebral flow, resulting in reductions in major IVH if used prophylactically[24]. The same effects are not apparent with ibuprofen and paracetamol. Two-year outcome studies and Cochrane review did not show benefits in development or survival compared with routine open label use to manage PDA in RCTs[10] but more recent cohort studies demonstrate reductions in early hypotension and BPD with prophylactic use compared to later PDA treatment [21,22]. The American Academy of paediatrics recommend against routine prophylactic administration to reduce major IVH. However, the risk benefit of giving at 12 hours, in very high-risk infants with no cardiovascular contraindication on echo assessment, is still debated[28]. Effects in reducing IVH can be obtained with a single dose[5] and prophylactic indomethacin remains in use in North America and Japan at very low gestations. In two recent publications of parental health related preferences parents were interviewed and listed reduction in major IVH as their main priority. When presented with options on indomethacin, ibuprofen, paracetamol from prophylaxis compared with watch and see options early indomethacin was the preferred option[1,25].

Indomethacin is not in routine use in Scotland or UK.

- **Not for current adoption**
- Could be reviewed in future based ongoing audit and review of outcomes.

2. A. Medical management of PDA (B)

Assessment of clinical trial data alone would justify either treatment or watch and wait approaches.

Cochrane reviews of PDA management[26], and recent clinical trials, show no evidence of long-term benefit from PDA treatment[7,13,30]. The challenges of clinical trials have been considerable and maybe affected by clinician bias[23], PDA assessment, treatment efficacy and contamination of control arms leaving little difference in actual PDA exposure. Many clinicians chose not to treat whilst others have adopted a more individual pathophysiology-based approach to treatment accepting short term benefits on inotropes, pulmonary haemorrhage and lung compliance[7,17,21,22]. Untreated, a moderate or large PDA, is likely to remain open for several months and will have a protracted physiological effect on the circulation. There is secondary analysis evidence that prolonged exposure in ventilated babies is associated with increased incidence of severe BPD[6,8,] and there are concerns about potential impact on brain growth[20]. Centres with considerable experience in managing 22-23 week infants report excellent outcomes and include hemodynamic assessment and early closure of moderate to large PDA as an important part of their treatment strategies[15,16, 27,31]. There is some longitudinal evidence to support this but there are also likely to be other population or practice factors and managing PDA is only a part of haemodynamic management.

Where medical treatment is practised the following should be considered.
Medical treatment, if considered, is optimal in the first 2 weeks.

- Early 18 -72 hours (B) (Appendix 2 chart 3)

- Consider haemodynamic assessment and management of moderate/ large PDAs[3,15,16,17,21,22,27.]
- Avoid extubation in the presence of a very large PDA in the first week.
- Ibuprofen is usually the drug of choice and can be used safely with low dose (Premiloc) hydrocortisone beyond 24 hours of life.[4] Paracetamol probably has little efficacy in this GA group but is an option and can be used when ibuprofen is contraindicated, can be used with ibuprofen in refractory cases or as a trial of response whilst establishing some enteral feeds and assessing the ongoing need to close a PDA in the first 72 hours of life.[22]

- Late 72 hrs - 10 days (B)
  - Consider medical closure of moderate to large PDA in infants approaching end of the 1st week to reduce challenges of later closure, optimise brain growth and severe grades of BPD (if ventilated).[1,5,10,13,25,]
- Watch and wait (B). The PDA may close spontaneously but at this gestation is likely to remain open for several months.

B. Interventional closure of PDA

- Persistent PDA should have a full cardiology review and be considered for closure as per guideline PDA ligation guideline (https://www.perinatalnetwork.scot).
- Device closure by interventional catheterisation is limited to babies >6kg in Scotland (although this is currently under review).

3. Management of hypotension or poor perfusion states (B)

- Consider referring to NIRS algorithm (for cerebral saturations below threshold), echo and hypotension flow charts (Appendix 2 Charts 1-4).

Management of acute pulmonary hypertension (PPHN) and right ventricle dysfunction (A),

There is no evidence of benefit to routine use of inhaled Nitric Oxide (iNO) in preterm infants to prevent lung diseases [3]. There are concerns it may cause intracranial haemorrhage and pulmonary haemorrhage. There is some limited evidence for the use of iNO in specific groups of preterm infants including those born following preterm prolonged rupture of membranes and those with echocardiographic criteria of PPHN physiology [18].

- Use when severe pulmonary hypertension and right ventricular dysfunction (not left ventricle physiology); ideally after echocardiography assessment but also in the context of pulmonary hypoplasia and respiratory failure.
- Consider starting at low doses of 5ppm and titrate against response.
- Review frequently as pulmonary pressures ductal physiology can change rapidly.
- Avoid dopamine in management of PPHN – inotrope support will depend on pathophysiology, but low dose adrenaline is generally preferred.
- Follow hypotension flow charts if associated hypotension.

Screening for Late Pulmonary Hypertension (A)

Pulmonary hypertension can develop in association with BPD and has a poor outcome.

- Consider formal echo review if worsening respiratory condition. An echo should be performed at 36 weeks corrected and prior to discharge if not undertaken earlier [2].
- Management of pulmonary hypertension should generally be supportive. However, if severe/ persistent consider prompt specialist respiratory and cardiology review.

References

1. AlFaleh K, Alluwaimi E, Alosaimi A, et al. (2015) A prospective study of maternal preference for indomethacin prophylaxis versus symptomatic treatment of a patent ductus arteriosus in preterm infants. BMC Pediatr. 2015;15:47.
2. Arjaans S, Haarman MG, Roofthooft MTR, et al. (2021) Fate of pulmonary hypertension associated with bronchopulmonary dysplasia beyond 36 weeks postmenstrual age. Arch Dis Child Fetal Neonatal Ed. 2021;106:45-50.
3. Barrington KJ, Finer N, Pennaforte T. (2017) Inhaled nitric oxide for respiratory failure in preterm infants. Cochrane Database of Systematic Reviews. 2017, Issue 1.
4. Baud O, Maury L, Lebail F, et al. (2016) Effect of early low-dose hydrocortisone on survival without bronchopulmonary dysplasia in extremely preterm infants (PREMILOC): a double-blind, placebo-controlled, multicentre, randomized trial. Lancet. 2016;387:1827-36.
5. Bhat R, Zayek M, Maertens P, Eyal F. (2019) A single-dose indomethacin prophylaxis for reducing perinatal brain injury in extremely low birth weight infants: a non-inferiority analysis. J Perinatol. 2019 Nov;39(11):1462-1471.
6. Bussmann N, Smith A, Breatnach CR, McCallion N, Cleary B, Franklin O, McNamara PJ, El-Khuffash A. (2021) Patent ductus arteriosus shunt elimination results in a reduction in adverse outcomes: a post hoc analysis of the PDA RCT cohort. J Perinatol. 2021 May;41(5):1134-1141.
7. Clyman RI, Liebowitz M, Kaempf J, et al. (2019) PDA-TOLERATE Trial: An Exploratory Randomized Controlled Trial of Treatment of Moderate-to-Large Patent Ductus Arteriosus at 1 Week of Age. J Pediatr. 2019 Feb;205:41-48.
8. Clyman RI, Liebowitz M, Kaempf J, et al. (2021) Prolonged Tracheal Intubation and the Association Between Patent Ductus Arteriosus and Bronchopulmonary Dysplasia: A Secondary Analysis of the PDA-TOLERATE trial. J Pediatr. 2021 Feb;229:283-288.
9. Clyman RI, Hills NK, Cambonie G, et al. (2022) Patent ductus arteriosus, tracheal ventilation, and the risk of bronchopulmonary dysplasia. Pediatr Res. 2022 Feb;91(3):652-658.
10. Evans P, O'Reilly D, Flyer JN, Soll R, Mitra S. (2021) Indomethacin for symptomatic patent ductus arteriosus in preterm infants. Cochrane Database of Systematic Reviews. 2021, Issue 1.
11. Forestier F, Daffos F, Galactèros F, et al. (1986) Hematological Values of 163 Normal Fetuses between 18 and 30 Weeks of Gestation. Pediatr Res. 1986;20:342–346.
12. Giesinger RE, Rios DR, Chatmethakul T, et al. (2023) Impact of Early Hemodynamic Screening on Extremely Preterm Outcomes in a High-Performance Center. Am J Respir Crit Care Med. 2023 Aug 1;208(3):290-300.
13. Gupta S, Juszczak E, Subhedar N, et al. (2022) Does selective early treatment of Patent Ductus Arteriosus (PDA) with ibuprofen reduce death or Bronchopulmonary Dysplasia (BPD) at 36 weeks in extreme preterm babies? A Randomised Controlled Trial (Baby-OSCAR Trial). Archives of Disease in Childhood. 2022;107.
14. Hansen ML, Pellicer A, Hyttel-Sørensen S, et al. (2023) Cerebral Oximetry Monitoring in Extremely Preterm Infants. N Engl J Med. 2023 Apr 20;388(16):1501-1511.
15. Isayama T. (2019) The clinical management and outcomes of extremely preterm infants in Japan: past, present, and future. Transl Pediatr. 2019 Jul;8(3):199-211.
16. John M. Dagle, Matthew A. Rysavy, Stephen K. Hunter, et al. (2022) Cardiorespiratory management of infants born at 22 weeks' gestation: The Iowa approach. Seminars in Perinatology. 2022.

17. Khalid Alfaleh et al. (2008) Prevention and 18-Month Outcomes of Serious Pulmonary Hemorrhage in Extremely Low Birth Weight Infants: Results From the Trial of Indomethacin Prophylaxis in Preterms. Pediatrics. 2008;121(2).
18. Kinsella JP, Steinhorn RH, Krishnan US, et al. (2016) Recommendations for the Use of Inhaled Nitric Oxide Therapy in Premature Newborns with Severe Pulmonary Hypertension. J Pediatr. 2016 Mar;170:312-4.
19. Kluckow M, Evans N. (2000) Low superior vena cava flow and intraventricular hemorrhage in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2000 May;82(3):F188-94.
20. Lemmers PM, Benders MJ, D'Ascenzo R, et al. (2016) Patent Ductus Arteriosus and Brain Volume. Pediatrics. 2016 Apr;137(4):e20153090.
21. Liebowitz M, Koo J, Wickremasinghe A, Allen IE, Clyman RI. (2017) Effects of Prophylactic Indomethacin on Vasopressor-Dependent Hypotension in Extremely Preterm Infants. J Pediatr. 2017 Mar;182:21-27.
22. Liebowitz M, Clyman RI. (2017) Prophylactic Indomethacin Compared with Delayed Conservative Management of the Patent Ductus Arteriosus in Extremely Preterm Infants: Effects on Neonatal Outcomes. J Pediatr. 2017 Aug;187:119-126.
23. Liebowitz M, Kaempf J, Erdeve O, Bulbul A, Håkansson S, Lindqvist J, Farooqi A, Katheria A, Sauberan J, Singh J, Nelson K, Wickremasinghe A, Dong L, Hassinger DC, Aucott SW, Hayashi M, Heuchan AM, Carey WA, Derrick M, Wolf IS, Kimball A, Sankar M, Leone T, Perez J, Serize A, Clyman RI. (2019) Comparative effectiveness of drugs used to constrict the patent ductus arteriosus: a secondary analysis of the PDA-TOLERATE trial. J Perinatol. 2019 May;39(5):599-607.
24. Ment LR, Vohr BR, Makuch RW, et al. (2014) Prevention of intraventricular hemorrhage by indomethacin in male preterm infants. J Pediatr. 2004;145:832–4.
25. Mitra S, Hatfield T, Campbell-Yeo M, Dorling J, Johnston BC. (2023) Evaluation of Health-Related Values and Preferences of Adults Who Were Preterm Infants and Parents of Preterm Infants Concerning Use of Prophylactic Cyclooxygenase Inhibitor Drugs. JAMA Netw Open. 2023 Mar 1;6(3):e232273.
26. Mitra S, de Boode WP, Weisz DE, Shah PS. (2023) Interventions for patent ductus arteriosus (PDA) in preterm infants: an overview of Cochrane Systematic Reviews.Cochrane Database of Systematic Reviews. 2023, Issue 4.
27. Motojima Y, Nishimura E, Kabe K, et al. (2023) Management and outcomes of periviable neonates born at 22 weeks of gestation: a single-center experience in Japan. Research Square. 2023.
28. Reese J, Shelton EL, Slaughter JC, McNamara PJ. (2017) Prophylactic Indomethacin Revisited. J Pediatr. 2017 Jul;186:11-14.e1.
29. Rozé J, Cambonie G, Marchand-Martin L, et al. (2015) Association Between Early Screening for Patent Ductus Arteriosus and In-Hospital Mortality Among Extremely Preterm Infants. JAMA. 2015;313(24):2441–2448.
30. Rozé JC, Cambonie G, Le Thuaut A, et al. (2021) Effect of Early Targeted Treatment of Ductus Arteriosus with Ibuprofen on Survival Without Cerebral Palsy at 2 Years in Infants with Extreme Prematurity: A Randomized Clinical Trial. J Pediatr. 2021 Jun;233:33-42.e2.
31. Satoshi Kusuda, Shinya Hirano, Tomohiko Nakamura. (2022) Creating experiences from active treatment towards extremely preterm infants born at less than 25 weeks in Japan. Seminars in Perinatology. 2022.
32. Simon Hyttel-Sorensen. (2015) Cerebral near-infrared spectroscopy oximetry in extremely preterm infants: phase II randomized clinical trial. BMJ. 2015;350:g7635.
33. Sommers R, Stonestreet BS, Oh W, Laptook A, Yanowitz TD, Raker C, Mercer J. (2012) Hemodynamic effects of delayed cord clamping in premature infants. Pediatrics. 2012 Mar;129(3):e667-72.

6: Fluids and Nutrition

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

Fluids/Nutrition Management [4,17]

- Fluids should start at 120-140 ml/kg/day, (Likely IWL of 60-100ml/kg/day). (A) [2,14]
- Urine output and fluid balance should be monitored at least 6 hourly, with fluid balance aims set on ward round. (A)
- Weigh infant daily, aiming for 7-10% weight loss in the first few days; liberalize fluid allowance when weight loss >5%. (B)
- Fluid requirements may rise very rapidly and may exceed 200ml/kg/day in the early days after birth.
- Total energy should at least cover resting energy expenditure 40-60kcal/kg/day, increase to at least 75kcal/kg/day by day 3, and aim at 90-120kcal/kg/day later in anabolic phase. (A) [4,17]
- Amino acids should start at 1.5-2g/kg/day and increase to 2.5-4 g/kg/day by day 3. (A) [4,5,8,15,17]
- Consider decreasing amino acids if Urea >10 mmol/l (B)
- Lipid Should start at 2 g/kg/day and increase to 3.5 g/kg/day by day 3, weaning back as per local protocol as enteral feeds are tolerated. (A)[4,17]
- As a minimum triglyceride should be checked 72 hours after starting lipid, then 48 hours after maximum dose lipid infusion, then weekly if in the normal range. IV lipids should be provided in a quantity not to exceed serum triglyceride level of 3 mmol/l.
- Infants should start on sodium free bag PN running at a maximum of 83 ml/kg/day asap after birth and transition to sodium containing bag when >48 hours or when sodium falls below 145 mmol/l or when weight loss >5%. Sodium from other drugs and infusions should also be kept to a minimum where possible. Arterial line continuous infusion fluid should be of 0.45% sodium chloride/heparin solutions. (A) [4,11,14,17]
- Carbohydrates should start 4-8 mg/kg/min (5.8-11.5 g/Kg/day) and increase to 8-10 mg/kg/min (11.5-12.7 g/Kg/day) by day 3. (B) [4,17]
- Consider decreasing carbohydrates if significant hyperglycaemia by reducing total PN and replacing with a lower sugar load or reducing PN glucose concentration and or beginning insulin. Consider how this affects amino acids and electrolytes and aim to keep in the normal range. (A) [12,13,19] Significant hyperglycaemia cut-offs:

    - Any Blood Glucose measurement of ≥20 mmol/L
    - Persistent Blood Glucose values of ≥15 mmol/L
    - Persistent Blood Glucose values of > 12 mmol/L with glycosuria ≥ 3+ on urinary dipstick testing
- Potassium up to 2 mmol/kd/day may be tolerated and even desirable from the beginning, but serum levels need to be monitored as individual differences are significant due to catabolism/anabolism, urine output, and intracellular/extracellular shifts. (A)
- Avoid hyperchloraemia from fluids, infusions and fluid boluses. Aim to keep chloride less than or equal to the sum of Sodium and Potassium ions combined. Consider replacing chloride anions with acetate in PN and/or utilize phosphate to deliver sodium or potassium without increasing chloride load. (A)
- Start Phosphate at >=0.5 mmol/kg/day and increase to 2 mmol/kg/day by day 4, monitor bone profile and aim to keep in the normal range adding additional phosphate if required. (A) [4,17]
- Combined solution such as SMOF lipid with vitamins may be used with dose of vitamins varying with the lipid intake. (A) [4,17]
- Ideally individual nutrition should be available in institutions looking after extreme preterm babies as altering intake of different components independently is often required, e.g. decreasing carbohydrates while increasing amino acids and maintaining delivery of Calcium, Phosphate or electrolytes is optimal. (A) Individual nutrition is ideally provided by an aseptic pharmacy daily (A) or with breaks in service not exceeding 48 hours.
- Nutrition is ideally prescribed prospectively according to recommendations and individual circumstances including all components. Nutrition should be documented in a form that facilitates audit. NICUs should have access to a dietician who will monitor growth measurements and advise on optimal nutrition to meet recommendations. (A) [10]

Feeds

- Start feeds on day 1 (trophic feeds). (A) [1,6,8,9,10,15]
- 1-2 hourly feeds (3). (B) [6]
- Use probiotics. (B) [6,10,18]
- Promote expressing and using of fresh milk. (A) [1,9,10,16]
- If there is any shortfall of maternal expressed breast milk, after 24-48 hours, it is recommended that donor expressed milk is used to make up any shortfall, rather than formula, where parents consent. [1,9,18]
- Use local guidance for advancing enteral feed volumes, managing possible intolerance and fortification schedule. (A) [9,10,16]
- Use an individual feeding plan with increments of 18-30 ml/kg/d. (A) [1,3,4,19]
- Fortify expressed breast milk after 150 ml/kg/day tolerated. (B)

Other

- Record all blood sampling volumes, flushes, and drugs in fluid balance. (B) [5]
- Blood sampling stewardship-strict sampling volumes, blood sampling plans (how often) to be documented on twice daily ward rounds, aim to rely on near patient results if they are within normal range. [5]
- Consultant lead blood sampling stewardship aiming to undertake minimum blood sampling (Unless there is specific clinical concern or parameters that are abnormal there is no specific reason to take more bloods unless discussed with attending consultant). (A) [5] Suggested minimum sampling:
    - At birth (could be obtained from the cord):
        - FBC, Group and DAT, gas
        - Coagulation is not standard unless concerns about bleeding/DIC from sepsis
    - There after:
        - Blood gas frequency as recommended by attending consultant
        - Observe Hb and electrolytes daily on gas if in normal range while on PN
        - Jaundice monitoring will require lab samples until falling spontaneously.
        - Lab U&E's, LFT's, Bone profile, FBC weekly otherwise
        - Triglycerides as above
- Avoid pharmacologic treatment of reflux. (A) [16]
- Minimize antibiotic exposure, using antibiotic stewardship. (A) [16]
- Consider using 0.45% Sodium Chloride/heparin arterial and line flushes NaCl 0.9%. (B)

References

1. Acta Paediatrica (2019) "Sustained quality improvement collaboration and composite morbidity reduction in extremely low gestational age newborns." DOI:10.1111/apa.14895
2. Als, H., Gilkerson, L., Duffy, F. H., McAnulty, G. B., Buehler, D. M., Vandenberg, K.,& Ringer, S. A. (1998). Transepidermal water loss in infants born at 24 and 25 weeks of gestation. Acta Paediatrica, 87, 1158-1160.
3. Bamat, N. A., Munson, D. A., Cheesman, K. K., & Whitener, B. L. (2019). Sustained quality improvement collaboration and composite morbidity reduction in extremely low gestational age newborns. Acta Paediatrica. doi:10.1111/apa.14895.
4. ESPGHAN (European Society for Pediatric Gastroenterology, Hepatology, and Nutrition) (2020) Guidelines. https://espghan.info/published-guidelines/
5. Harabor, A., & Kelleher, J. (2021). Effects of blood sampling stewardship and erythropoietin administration in extremely low birth weight infants-a quality improvement non-controlled before-and-after retrospective study. European Journal of Paediatrics, 180(5), 1617-1626. doi: 10.1007/s00431-020-03925-9.
6. Isayama, T. (2019). The clinical management and outcomes of extremely preterm infants in Japan: past, present, and future. Translational Paediatrics, 8(3), 199-211.

7. Johnson, M. J., Leaf, A. A., & Pearson, F. (2021). Feeding Strategies in Preterm Very Low Birth-Weight Infants: State-of-the-Science Review. Advances in Neonatal Care, 21(6), 493-502. doi: 10.1097/ANC.0000000000000849.
8. Jonsson, B., & Westrup, B. (2021). The proactive approach to mother-infant dyads at 22-24 weeks of gestation: Perspectives from a Swedish center. Seminars in Perinatology. https://doi.org/10.1016/j.semperi.2021.151536
9. Kaempf, J., et al. (2018). Statewide Initiative to Reduce Postnatal Growth Restriction among Infants <31 Weeks of Gestation. The Journal of Paediatrics, 197, 82-89.e2. doi: 10.1016/j.jpeds.2018.01.074.
10. Kaempf, J., & et al. (2021). Continued improvement in morbidity reduction in extremely premature infants. Archives of Disease in Childhood - Fetal and Neonatal Edition, 106, F265-F270. doi:10.1136/archdischild-2020-319961
11. Kim, S. J., Kim, H. S., Seo, D. M., & Choi, C. W. (2015). Early Sodium and Fluid Intake and Severe Intraventricular Hemorrhage in Extremely Low Birth Weight Infants. Journal of Korean Medical Science, 30(3), 283-289. http://dx.doi.org/10.3346/jkms.2015.30.3.283
12. Kling, P. J., Taing, K. M., Donohue, P. K., & Devaskar, S. U. (2006). Gluconeogenesis continues in premature infants receiving total parenteral nutrition. The Journal of Pediatrics, 148(5), 585-587.
13. Kling, P. J., Taing, K. M., Donohue, P. K., Devaskar, S. U. (2007). Gluconeogenesis is Not Regulated by Either Glucose or Insulin in Extremely Low Birth Weight Infants Receiving Total Parenteral Nutrition. Pediatric Research, 61, 465-470.
14. Lechevalier, N., & Lapillonne, A. (2021). Fluid management considerations in extremely preterm infants born at 22-24 weeks of gestation. Seminars in Perinatology.
15. Lee, S. M., Chang, Y. S., Bennett, S. H., & Morse, S. B. (2014). Association of a quality improvement program with neonatal outcomes in extremely preterm infants: a prospective cohort study. Canadian Medical Association Journal, 186(5), E193-E202. doi:10.1503/cmaj.140399.
16. Menon, G., & Sutcliffe, A. G. (2017). NEC-zero recommendations from a scoping review of evidence to prevent and foster timely recognition of necrotizing enterocolitis. Maternal Health, Neonatology, and Perinatology, 3, 23. doi: 10.1186/s40748-017-0062-0.
17. National Institute for Health and Care Excellence (2018). Neonatal Parenteral Nutrition. Available at: https://www.nice.org.uk/guidance/NG154
18. Profit, J., Gould, J. B., Bennett, M., Goldstein, B. A., Draper, D., Phibbs, C. S. & Lee, H. C. (2017). The quest for sustained multiple morbidity reduction in very low-birth-weight infants: the Antifragility project. Journal of Perinatology. doi:10.1038/jp.2017.7
19. Zamir I, Stoltz Sjöström E, Ahlsson F, Hansen-Pupp I, Serenius F, Domellöf M. (2021) Neonatal hyperglycaemia is associated with worse neurodevelopmental outcomes in extremely preterm infants. Arch Dis Child Fetal Neonatal Ed. 2021 Sep;106(5):460-466. doi: 10.1136/archdischild-2020-319926. Epub 2021 Apr 16.

7: Infection Prevention and Skin Care

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

Reducing Healthcare Associated Infection

- In the delivery room -care should be taken to ensure team members hands are clean[12]. (A)
- If screening the infant for infection at birth, consider taking septic screen from umbilical cord or freshly placed umbilical line to avoid unnecessary skin breaks. (A)
- After a caesarean birth where indication was maternal only (no infection risk factors), a septic screen and antibiotics is not considered standard[9,15,]. (A)
- Antibiotics should be reviewed around 36 hours after starting and consideration of discontinuing the course where infection is felt to be clinically unlikely, backed up by inflammatory markers[,1,7,14,15]. (A)
- Strict Hand washing policies should be followed - Hands and forearms: Bare Below the Elbow (BBE)[13,14] (A):
- Education on gentle handling should be offered to parents while supporting the positive influences of parental touch and presence[10]. (A)
- Avoid entering incubator unless clear reason – minimal, gentle handling should be maintained where possible. (A)
- Local/national central line insertion checklist and maintenance bundle guidance should be followed[1,3,7]. (A)
- All invasive procedures should be done using Aseptic Non Touch Technique; ideally all staff (medical and nursing) dealing with these lines should have done the NES module on this and undertaken local observed practice[11]. (A/B)

Skin Care

- Minimise medical device/adhesive or solution related skin trauma (A):
    - Where possible avoid peripheral lines while UVC in situ, where used careful consideration of tape selection should be undertaken.[8]
    - Use the smallest piece of tape/dressing to achieve desired goal [2,10,11]
    - Don't use ECG probes or tape on hands as standard
    - If using skin temperature probes, lay the flat surface of the temperature probe against the skin and cover with smallest size of silicone or hydrocolloid dressing

- Avoid direct contact with new-born skin with any adhesive probes. (e.g. "double backed" tape or deactivate adhesive with cotton balls when full adhesion not required e.g. when using pulse oximetry)
- If using hydrogel, silicone or hydrocolloid dressings as cushioning beneath equipment, they should be left in place for a minimum of 24 hours when their natural adhesiveness begins to diminish and they are then more easily removed; note when using dressing, you will not be able to assess the skin under the dressing.[11]
- Avoid bandaging or using plasters on area post heel pricks/venepuncture. Use pressure with a cotton ball or gauze to halt bleeding
- When removing adhesives:
  - Avoid using solvents (e.g. alcohol) to weaken adhesive due to potential toxicity
  - Slowly fold adhesive back onto itself while moistening the adhesive-skin surface with warm water or a silicone-based alcohol-free adhesive remover e.g. Appeel, Peel-Easy, mineral oil or petrolatum-based emollients; select the best remover and removal technique for the type of adhesive
  - If using transparent dressings, stretch to release adherence, then peel back horizontally - avoid friction to avoid skin trauma.
  - Follow local unit skin aseptic product guidance and wipe off strategy (A) [11]

- Use a Nursing Skin Care Package (A) [5,11]:
  - Identify risks for skin breakdown:
    - Extreme prematurity.
    - Medical devices/probes/lines.
    - Sedating/muscle relaxing medication.
    - Medical conditions.
  - Assessment/report on skin integrity.
    - Inspect skin on front and back and undertake a skin injury risk assessment on admission and at the first opportunity when beginning a shift e.g. with first set of 'cares' and with changes in skin condition.
  - Report skin quality, assessment, interventions and outcomes at handover and during the shift if problems arise.
  - Care procedures to promote and protect skin for injury
    - Avoid pressure/probes damaging skin.
    - Change saturation probe/TCM probe site 4 hourly as tolerated, in first few days.
    - Nappies should be left loose or unfastened. If skin breaking down on bottom leave nappy open to air or apply orabase/petrolatum based mixture.
    - Nasal septum observation on NCPAP – rotate between mask and prongs to change pressure areas 4-6 hourly or more frequently if skin breakdown is present. Assess for pressure damage with every mask and prong rotation.
    - Assess pressure areas e.g. occiput and ears, under NCPAP hat once per shift

- Protect skin and bony prominences with low adhesive sheeting (e.g. Parafricta), and or gel filled mattress. Limit number of layers between the infant and sheets
- Change the infant's position using sheeting to relieve pressure and avoid friction and shear injury.
- Use special mattresses-airbed/silk sheets. Use of Fluidised positioner to maintain the infant in midline position. E.g. https://parafricta.com/neonatal-sheet-by-parafricta-40-p.asp
- Avoid routine use of topical emollients[6]. If used coconut oil is recommended[5].
- Separate bottles for emollients if using same product for perineal protection.
- Incubator humidity should be 80-90% as per local policy and weaning protocol in place as per local guidance.

o On admission undertake scoring/documentation for skin
  - In Badgernet EPR go to: Obs/monitoring → Nursing obs → Skin
  - If using paper documentation consider:
    - Northampton Neonatal Skin Assessment tool
    - Skin Injury Risk Assessment Record (SIRA)
    - Neonatal Skin Risk Assessment (NSRA) tool
    - Neonatal Tissue Viability Assessment Tool
o Frequency of ongoing skin assessment depends on the condition of the infant.
o Various skin ongoing assessment tools exist; document assessment in relevant part of the infant's record. Consider:
  - In Badgernet EPR go to: Obs/monitoring → Nursing obs → Formal Skin Assessment 1
  - If using paper documentation consider:
    - Neonatal Skin Condition Score (NSCS)
    - Braden Q Scale
    - Glamorgan Scale
    - Neonatal Skin Risk Assessment and Management Tool (SRAMT)
o Treatment suggestions following skin breakdown- various common issues: (see Appendix 3 and 4)
  - To treat damaged skin – select products that are advocated by the local tissue viability team and formulary
    - Cover superficial wounds and abrasions with low adherence wound contact dressing (e.g. Mepitel, Lomatuell pro) or hydrocolloid (e.g. DuoDerm Extra Thin) wound care products.
    - Cover low or high exudate wounds with hydrogel (e.g. Purilon) then vapour permeable dressing (e.g. Tegaderm) or hydrocolloid or silicone dressing.
    - Cover clean granulating wounds with low to high exudate with hydrocolloid (e.g. DuoDerm Extra Thin) or low adherence wound contact dressing (e.g. Mepitel, Kliniderm foam silicone lite).

        - Cover epitheliasing wounds that have no to low exudate with hydrocolloid (DuoDerm Extra Thin) or vapour permeable dressing (Tegaderm).
        - Cover extravasation injuries and extensive wounds with medical grade honey, covered with honey infused hydrocolloid dressing or petrolatum impregnated gauze and then a low adherent dressing (Mepitel).
    - As prophylaxis or treatment for infected skin:
        - Consider using anti-fungal prophylaxis as prescribed.
        - Necrotising fasciitis is a particular problem (presenting as pressure sores with overlying black eschars or rash with florid white exudate) and may be cause by aspergillosis-have a low index for escalating fungal treatment to treatment doses from prophylactic.
        - Use IV antibiotic for gram positive organisms as prescribed
- From birth and during antibiotic courses with broad spectrum antibiotics follow local/national fungal prophylaxis guidance -If using fluconazole prophylaxis consider topical antifungal in addition. (A)
- Escalation of antifungal treatment if significant deterioration with skin lesions. (A)
- Staff Education (A/B):
    - Skin Care Education package;
    - Study days;
    - Skin Integrity Team/Champions.

References

1. Acta Paediatrica (2019) "Sustained quality improvement collaboration and composite morbidity reduction in extremely low gestational age newborns." DOI:10.1111/apa.14895
2. BC Canada Skin Care for Preterm Infant (2017). Skin care for preterm infant less than 32 weeks. Skin Care for Preterm Infant NN.14.03 (cw.bc.ca)
3. CMAJ (2014). "Association of a quality improvement program with neonatal outcomes in extremely preterm infants: a prospective cohort study." DOI:10.1503/cmaj.140399
4. Government (2022) Good IPC practice for the cleaning and handling of incubators and other equipment in neonatal units. Good IPC practice for the cleaning and handling of incubators and other equipment in neonatal units.
5. Government of Western Australia (2020) Skin care of extremely preterm skin clinical pathway. Skin Care Extremely Preterm Skin Clinical Pathway (health.wa.gov.au)
6. Johnson DE (2020) Extremely Preterm Infant Skin Care. Advances in Neonatal Care, 2020, 16(5S), pp. S26-S32.
7. Journal of Perinatology (2017) "The quest for sustained multiple morbidity reduction in very low-birth-weight infants: the Antifragility project." doi:10.1038/jp.2017.7
8. Lund, C. (2014). Medical Adhesives in the NICU. Newborn and Infant Nursing Reviews, 14(4), 160-165. https://doi.org/10.1053/j.nainr.2014.10.001
9. Maternal Health, Neonatology and Perinatology (2017) NEC-zero recommendations from scoping review of evidence to prevent and foster timely recognition of necrotizing enterocolitis. [DOI: 10.1186/s40748-017-0062-0](DOI: 10.1186/s40748-017-0062-0)
10. New Zealand Newborn Clinical Network (2019) Practice recommendations for skin care of neonates < 28 weeks gestation.

11. North Devon Health (2019) Skin-care-for-Neonates-guidelines-May-19. Skin-care-for-Neonates-guidelines-May-19.pdf (northdevonhealth.nhs.uk)
12. NHS England (2023) Chapter 1: Standard infection control precautions (SICPs). Standard-Infection-Control-Precautions.pdf (tewv.nhs.uk)
13. NHS Scotland (2008). Dress Code CEL 53 (2008) – NHS Scotland Dress Code
14. NICE (2021). Neonatal infection: antibiotics for prevention and treatment. Neonatal infection: antibiotics for prevention and treatment (nice.org.uk)
15. Seminars in Perinatology, (2021) The proactive approach to mother-infant dyads at 22-24 weeks of gestation: Perspectives from a Swedish center. https://doi.org/10.1016/j.semperi.2021.151536

8: Neuro-Critical

Recommendation allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

- Maintain head in midline 15-20 degrees up, supine position for 72 hours. Avoid head in side position with 90 degrees tilt, avoid prone position unless clinically indicated by consultant in charge with use of positioner[1,6,7]. (A) -Extrapolated evidence level B, Class 11a.
- Minimal handling. Aim for responsive care every 6-8 hours including any required procedures e.g. CrUSS, gases, bloods (saturation probs may need changing more often to avoid burns, see skin care section). More frequent intervention at consultant discretion[1,7]. (A) - Extrapolated evidence level B, Class 11a.
- Central lines: aspiration and flushing of UAC/UVC is done slowly over minimum of 30 seconds to avoid rapid fluctuations of cerebral haemodynamics[1]. (A) - Extrapolated evidence level B, Class 11a.
- 2-person technique to do care including change of nappies to avoid head down position and elevation of legs as per neuroprotective care bundle. (A)-Extrapolated evidence level B, Class 11a.
- Cranial US performed on D1 & 3 as a minimum by an experienced clinician able to minimize time spent and handling. Subsequent scans as per unit protocols. This should not delay transfer if infant needs transfer[3]. (A) -Extrapolated evidence level C, Class 11a.
- Minimise exposure to sensory stimuli (bright light, noise, cold and pain) and use of appropriate analgesia/sedation if required as per clinical team and local unit policy[4]. (B) Extrapolated evidence level C, Class 11a.
- Encourage parental positive skin touch in the first 72 hrs. (A) Encourage skin to skin as clinically appropriate as per unit policy after first 72 hrs. (B) Extrapolated evidence level C, Class 11a.
- Maintain normal temperature and avoid hypothermia[6,8]. (B) Extrapolated evidence level C, Class 11a.
- Consider NIRS monitoring as an adjunct haemodynamics monitoring tool as per local unit protocol. (B) Extrapolated evidence level C, Class 11a.
- Avoid hypoglycaemia and hyperglycaemia, treat rapidly when occurs and repeat glucose within 1 hour when it does occur[2]. (A)
- Avoid hypocarbia (PCO_2 <4.5 kPa), making ventilation changes and repeating gas within the hour, until PCO_2 in the normal range. (A)

References

1. de Bijl-Marcus K, Brouwer AJ, De Vries LS, Groenendaal F, Wezel-Meijler GV. (2020) Neonatal care bundles are associated with a reduction in the incidence of intraventricular haemorrhage in preterm infants: a multicentre cohort study. Arch Dis Child Fetal Neonatal Ed. 2020 Jul;105(4):419-424. doi: 10.1136/archdischild-2018-316692. Epub 2019 Nov 15.
2. Howes A, Hilditch C, Keir A. (2019) What clinical practice strategies have been shown to decrease incidence rates of intraventricular haemorrhage in preterm infants? J Paediatr Child Health. 2019 Oct;55(10):1269-1278. doi: 10.1111/jpc.14613. pp1269–1278
3. Kaempf JW, Morris M, Austin J, Steffen E, Wang L, Dunn M. (2019) Sustained quality improvement collaboration and composite morbidity reduction in extremely low gestational age newborns. Acta Paediatr. 2019 Dec;108(12):2199-2207. doi: 10.1111/apa.14895. Epub 2019 Jul 22., pp. 2199–2207
4. Mohammad K, Scott JN, Leijser LM, Zein H, Afifi J, Piedboeuf B, de Vries LS, van Wezel-Meijler G, Lee SK, Shah PS. (2021) Consensus Approach for Standardizing the Screening and Classification of Preterm Brain Injury Diagnosed With Cranial Ultrasound: A Canadian Perspective. Front Pediatr. 2021 Mar 8;9:618236. doi: 10.3389/fped.2021.618236.
5. Murthy P, Zein H, Thomas S, Scott JN, Abou Mehrem A, Esser MJ, Lodha A, Metcalfe C, Kowal D, Irvine L, Scotland J, Leijser L, Mohammad K. (2020) Neuroprotection Care Bundle Implementation to Decrease Acute Brain Injury in Preterm Infants. Pediatr Neurol. 2020 Sep;110:42-48. doi: 10.1016/j.pediatrneurol.2020.04.016. Epub 2020 May 1.
6. Ryan M, Lacaze-Masmonteil T, Mohammad K. (2019) Neuroprotection from acute brain injury in preterm infants. Paediatr Child Health. 2019 Jul;24(4):276-290. doi: 10.1093/pch/pxz056. Epub 2019 Jun 21.
7. Travers CP, Gentle S, Freeman AE, Nichols K, Shukla VV, Purvis D, Dolma K, Winter L, Ambalavanan N, Carlo WA, Lal CV. (2022) A Quality Improvement Bundle to Improve Outcomes in Extremely Preterm Infants in the First Week. Pediatrics. 2022 Feb 1;149(2):e2020037341. doi: 10.1542/peds.2020-037341
8. Zamir I, Stoltz Sjöström E, Ahlsson F, Hansen-Pupp I, Serenius F, Domellöf M. (2021) Neonatal hyperglycaemia is associated with worse neurodevelopmental outcomes in extremely preterm infants. Arch Dis Child Fetal Neonatal Ed. 2021 Sep;106(5):460-466. doi: 10.1136/archdischild-2020-319926. Epub 2021 Apr 16.

9: Family centred support (including palliative care) and neonatal team support

Recommendation Allocations

(A) Practices that should virtually always be practiced.
(B) Evidence of benefit unclear – variation in practice likely.
(C) Unknown efficacy and safety - items that still need evidence and may be practiced as part of extended practice from infants born more mature or part of ethically approved research.

Recommendations

Family centred support-General principles

- Neonatal services and pathways for parents should align with a **trauma-informed approach** to family and staff wellbeing[11]. (A)
- Families should have access to **formalised psychosocial support**, in line with Best Start[15] recommendations, Delivering Effective Services in Perinatal and Infant Mental Health[16] (2019), and National Bereavement Care Neonatal Death Pathway.
    - Services should consider how to deliver support **equitably**, regardless of length or level of stay or medical outcome[10]. (A)
- Staff teams should access training in psychosocial interventions for supporting neonatal families that draw on models such as '**psychological first aid'**. The emotional support provided by neonatal unit staff at the cot side can ensure that families fundamentally[6]: (A)
    - Feel supported via their experience of day-to-day communication with staff teams
    - Feel emotionally 'contained' through opportunities to talk about experiences if they choose to, with staff.
    - Have opportunities to have difficult attributions or beliefs compassionately heard and responded to e.g. 'It's my fault'
- Parents of infants born extremely preterm will be impacted across different domains including stress responses, anticipatory grief processes, the transition to parenthood, and relationship building with their new baby. Neonatal teams can:
    - Adopt **Family Integrated Care** principles and practices including supporting families to be involved in delivering hands-on care, if they choose/can[2] (A)
    - Support families to take part in cares informed by and consistent with the principles of **developmental care** (A)
    - Acknowledge the individual ways that emotional complexity can manifest for parents at difficult times and are mindful that family choices may not always align with staff expectations (A)
    - Recognise every "first thing" as a first for the family (A)

    - Parents may or may not be ready to be addressed by terms such as "Mum" or "Dad" –ask parents how they would like to be referred to and record this, so this is used consistently with follow-up checks with parents as care progresses and advice updated accordingly (A)
    - Ask parents if they would like to use milestone cards or alternative means of marking moments to support the **building of a psychological narrative of events** (A)
- Staff to support **family communication** with tools or aids (A)
    - vCreate
    - Communication boards
- Support the space to **promote bonding and parenting**, whilst acknowledging that some parents may not be ready/able – "Make the most of every moment" (A)
    - Begin making memories from birth (don't wait until death is imminent or has occurred)
    - Package of care at admission – footprints, photo, bonding squares, bookbug bag
    - Welcome the baby as a little person ("congratulations" may not be appropriate but 'welcome to the world' may be a helpful alternative; take care not to use negative language "I'm so sorry your baby has come so early")
- If parents have had a multiple birth, they face the challenge of preparing for the possibility their baby/babies may die whilst caring for their other baby/babies. Support the family by focussing equally on the baby/babies who may die and the sibling or siblings[10]. (A)

Family centred support - Palliative care

- All maternity and neonatal teams should be able to provide quality **comfort-focused care** at birth to families who have chosen this pathway, after a collaborative discussion (see Group 1 recommendations) as described in the BAPM FfP, and neonatal teams should be able to deliver supportive **end-of-life and bereavement care**. Both comfort-focused care and end-of-life care should align with principles in the National Bereavement Care Pathway for Neonatal Death[1,10]. (A)
    - Suggest palliative care leads/champions in Midwifery, Neonatal Nursing and Neonatology (A/B)
- Suggest **parallel care planning** (delivery of intensive care whilst planning care of anticipated complications/deteriorations/death) routinely at these gestations from admission[7]. (A/B)
    - Document this in an **anticipatory care plan** (**ACP**) which embodies individualised shared decision-making and of which parents hold a copy[4,8].
- Use the right team to discuss parallel care planning. The right team is compassionate, confident, skilled and trained[8,10]. (A)
- Support consistent family communication with/by:
    - continuity of staff (medical and nursing) where possible
    - providing parents with written transcripts of professional conversations[10] (A/B)

- If an infant dies unexpectedly and quickly, staff should focus on explaining the known facts to parents, providing supportive end of life care and memory making[10]. (A)
- Ongoing care after death[10] (A)
    - Continue to support family time (hospital, hospice, home) with use of cuddle cot
    - Offer bereavement support, share information about key contact, CHAS
    - Discuss Perinatal Mortality Review Tool and Post-mortem
    - Discuss lactation support and Scottish Milk Bank memory milk gift
    - Support family in transfer of care to mortuary team (e.g., in pram, Moses basket etc)
    - Introduce third parties and recognise benefit of peer support

Family centred support – Bereavement care

- If an infant sadly dies, units should ensure there are pathways in place to meet the emotional needs of bereaved families that are consistent with National Bereavement Care Neonatal Death Pathway[10]. (A)
- Neonatal services and pathways for bereaved parents should align with a **trauma-informed approach** to family and staff wellbeing[11]. (A)
- Teams should be aware of the emotional processes around grief which should be normalised and not pathologized within a mental health framework[12]. (A)
    - Families should be supported to access appropriate specialist grief supports for parents and for siblings.
    - Pathways should be in place to provide access to mental health assessment and treatment, should mental health needs or risks emerge following a bereavement.
- Families affected by previous baby loss should have access to supports should this experience impact on emotional health in a **next pregnancy**[16]. (A)

Psychological support for the neonatal team

Neonatal staff teams are routinely involved in delivery of complex care with families managing significant stress. The interpersonal demands on staff will include sensitive delivery of medical information and complex decision making alongside compassionately receiving and holding the family's expression of their stress responses and anticipatory grief processes which will unfold concurrently with the transition to parenthood and relationship building with their new baby. Levels of staff burnout (state of physical, emotional, and mental exhaustion caused by long-term involvement in emotionally demanding situations) can be high in healthcare settings with rates in NICU's varying by profession and ranging from 7.5-54.4%[14]. Risk factors for medical staff have been reported to include less time in post, negative beliefs around quality of life with disability, and recurrent thoughts of deaths[3].

Care of staff wellbeing will have three broad functions:

- To provide staff with a culture of 'psychological safety' which supports the **self-management of psychological processes and dynamics in self and with others**[10]. (A) To this end units should:
    - Aim to provide an emotionally supportive environment for staff where challenges can be discussed openly, and individual needs are acknowledged and met
    - A trauma-informed approach to family and staff wellbeing should be implemented and monitored[11].
    - Hold spaces to acknowledge difficult events and normalise reflective spaces/practice groups
        - Responsive after an event (Peer Support) and/or
        - Regular access to reflective practice as psychological first aid
    - Acknowledge staff grief after the death of an infant
- To ensure staff have access to supportive training and materials to deliver complex interpersonal tasks. (A) Units should consider and implement appropriate training for all staff in:
    - Normal responses to infant hospitalisation
    - Communication skills within a recognised framework that improves practice e.g., EC4H[5] training or simulation training[17]
    - Developmental care
    - Family integrated care
    - Perinatal and infant mental health
- To ensure staff are encouraged to self-monitor wellbeing, be mindful of 'warning signs' for burnout and mental distress, and have access to appropriate supports[9,10,13]. (A)

References

1. BAPM (2019) Perinatal Management of Extreme Preterm Birth Before 27 weeks of Gestation. Perinatal Management of Extreme Preterm Birth Before 27 weeks of Gestation (2019) | British Association of Perinatal Medicine (bapm.org)
2. BAPM (2021). Family Integrated Care. A framework for practice. Family Integrated Care | British Association of Perinatal Medicine (bapm.org)
3. Bellieni C, Righetti P, Ciampa R. (2010) Assessing burnout among neonatologists. J Matern Fetal Neonatal Med 2010; 25 (10): 2130–2134.
4. Cheong et al. (2018) Changes in long-term prognosis with increasing postnatal survival and the occurrence of postnatal morbidities in extremely preterm infants offered intensive care: a prospective observational study. The Lancet Child & Adolescent Health Vol 2. (12), pp. 872-879.
5. Effective Communication for Healthcare (2023) Having better conversations. Home - EC4H
6. Hall, S., Cross, J., Selix, N., et al. (2015) Recommendations for enhancing psychosocial support of NICU parents through staff education and support. J Perinatol 35, S29–S36 (2015). doi.org/10.1038/jp.2015.147
7. Hancock H, S et al. (2018) A randomised trial of early palliative care for maternal stress in infants prenatally diagnosed with single-ventricle heart disease. Cardiology in the Young. Ch28, pp. 561–570.

8. Health Improvement Scotland (2023) ihub Scotland. Preparation and Planning. Preparation and planning - Preparation and planning (ihub.scot)
9. National Wellbeing Hub Scotland (2023) "Find Help." wellbeinghub.scot
10. NBCP Scotland (2023). If a Baby May Die. SANDS If a baby may die | SANDS (nbcpscotland.org.uk)
11. NES (2021) National Trauma Training Programme. www.nes.scot.nhs.uk/our-work/trauma-national-trauma-training-programme
12. NES (2023) Support Around Death Scotland. Support Around Death Scotland | Support Around Death
13. Practitioner Health NHS (2023) A confidential mental health service for all regulated professionals working in health and social work/social care sectors in Scotland. Accessing The Service: Regulated NHS & Care Staff in Scotland (practitionerhealth.nhs.uk)
14. Profit J, Sharek P, Amspoker A, Kowalkowski M, Nisbet C, Thomas E et al. (2014) Burnout in the NICU setting and its relation to safety culture. BMJ Qual Saf 2014; 10: 806–813.
15. Scottish Government (2017) "The Best Start: Five-Year Plan for Maternity and Neonatal Care." The best start: five-year plan for maternity and neonatal care - gov.scot (www.gov.scot)
16. Scottish Government (2019) Perinatal and Infant Mental Health Programme Board: Delivery Plan 2019-2020. Perinatal and Infant Mental Health Programme Board: delivery plan 2019-2020 (www.gov.scot)
17. Taylor N, Nair V, Grimbley J. (2022) Better general paediatric and neonatal palliative care skills: simulation teaching. BMJ Supportive & Palliative Care Published Online First: 02 February 2022. doi: 10.1136/bmjspcare-2021-003389

Glossary

ACP - Anticipatory Care Plan

AKI – Acute Kidney Injury

BAPM FfP – British Association of Perinatal Medicine Framework for Practice

BBE - Bare Below the Elbow

BP – Blood Pressure

BPD - Bronchopulmonary dysplasia

CHAS- Children's Hospices Across Scotland

CPAP - Continuous Positive Airway Pressure

CPR - Cardiopulmonary Resuscitation

CRF - Capillary Refill

CrUSS - Cranial Ultrasonography

DART - Dexamethasone dosing: (a randomised trial) protocol for low dose dexamethasone

DAT – Direct Antibody Test

DCC – Deferred Cord Clamping

DIC - Disseminated Intravascular Coagulation

EC4H – Effective Communication for Healthcare

ECG – Electrocardiogram

EPR – Electronic Patient Record

ET - Endotracheal Tube

ETCO2 - End Tidal CO2

FBC – Full Blood Count

FFP - Fresh Frozen Plasma

FiO2 - Fraction of inspired oxygen

GA – Gestational Age

Hb – Haemoglobin

HFNC - High Flow Nasal Cannula

HFOV - High Frequency Oscillatory Ventilation

iNO – inhaled Nitric Oxide

IPPV - Intermittent Positive Pressure Ventilation

IUT – In-utero Transfer

IV – Intravenous

IVH - Intraventricular Haemorrhage

LFT's – Liver Function Tests

LNUs – Local Neonatal Units

LV / RV – Left Ventricle/ Right Ventricle

NaCl – Sodium Chloride

NAVA - Neurally-Adjusted Ventilatory Assist

NCPAP - Nasal Continuous Positive Airway Pressure

NEC - Necrotising Enterocolitis

NES – NHS National Education for Scotland

nHFOV - Non-invasive High-Frequency Oscillatory Ventilation

NICU – Neonatal Intensive Care Unit

NIPPV - Non-Invasive Positive Pressure Ventilation

NIRS - Near Infra-Red Spectroscopy

NLS – Newborn Life Support

NSCS - Neonatal Skin Condition Score

NSRA - Neonatal Skin Risk Assessment

PCO2 - Partial Pressure of Arterial Carbon Dioxide

PDA - Patent Ductus Arteriosus

PEEP - Positive End-Expiratory Pressure

PN - Parenteral Nutrition

PPHN - Persistent Pulmonary Hypertension of the Newborn

PVC - Peripheral Cannula

RCOG – Royal College of Obstetricians and Gynaecologists

RCT - Randomised Controlled Trials

RSV - Respiratory Syncytial Virus

SCUs – Special Care Units

SIRA - Skin Injury Risk Assessment Record

SPN – Scottish Perinatal Network

SRAMT - Neonatal Skin Risk Assessment and Management Tool

SVR - Systemic Vascular Resistance

TCM - Transcutaneous CO2 Monitoring

UAC/UVC - Umbilical Artery Catheter /Umbilical Vein Catheter

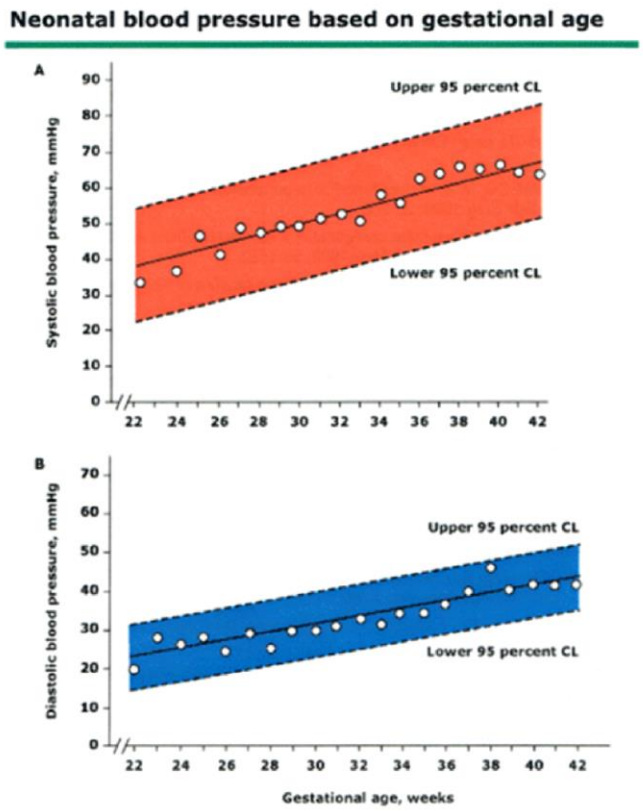
U&E's – Urea and Electrolytes

US – Ultrasound

UVC - Umbilical Venous Catheters

Appendix 1. Normative BP Values, inotropes, Hypotension and PDA flow charts and NIRS.

Table 1. BP thresholds at the 3rd centile for gestational age



Reference: Zubrow AB et al , J Perinatology 1994; 16(6): 470-9

Table 2: Normative BP values

GA (weeks)	SYSTOLIC (mmHg)	MEAN (mmHg	DIASTOLIC (mmHg)
24	32	26	15
25	34	26	16
26	36	27	17
27	38	27	17
28	40	28	18
29	42	28	19
30	43	29	20
31	45	30	20
32	46	30	21
33	47	30	22
34	48	31	23
35	49	32	24
36	50	32	25

Reference: Giesinger et al Seminars in Perinatology 2016; 40:174-188

Table 3: Suggested interpretation of abnormalities BP referencing systolic and diastolic values

Systolic BP < 3rd Centile (narrow pulse pressure)	PPHN, cardiogenic shock(LV dysfunction, poor transition and high SVR or arrhythmias), early sepsis "cold" shock
Diastolic hypotension	PDA, systemic hypovolaemia, evolving warm shock
Systolic + diastolic hypotension	Very large PDA, established warm shock, severe PPHN, cardiogenic shock (arrhythmia or severe dysfunction)
Hypertension – may be narrow pulse pressure	Agitation: pain, imminent pulmonary haemorrhage, intracranial haemorrhage, kidney injury, impaired renal function, coarctation of the aorta, renal/aortic thrombosis

SVR = systemic vascular resistance

PDA= Patent ductus arteriosus

PPHN= persistent pulmonary hypertension of the newborn

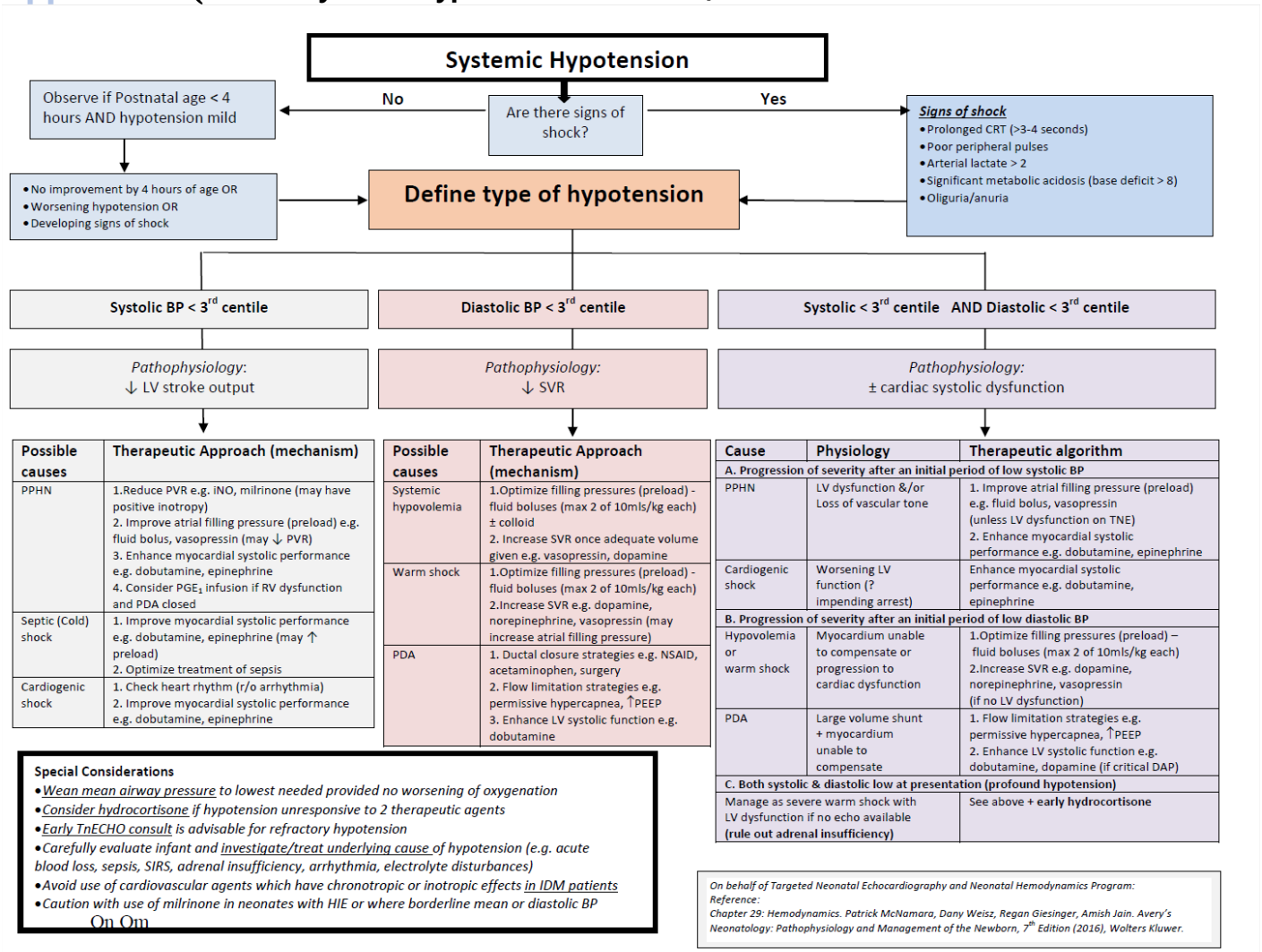
Table 4: Comparisons of net effects of "inotrope"agents

Agent	SV	SVR	PVR
Dopamine	↑	↑↑	↑↑↑
Norepinephrine	↑ / (no effect)	↑↑↑	↓ / (no effect)
Vasopressin	↓	↑↑↑	↓
Dobutamine	↑↑	no effect	no effect
Milrinone	↑↑		↓↓
Epinephrine	↑↑↑	↑↑↑	↑↑

SV = stroke volume, SVR = systemic vascular resistance, PVR = pulmonary vascular resistance

Reference: Giesinger et al Seminars in Perinatology 40 (174-188) 2016

Appendix 2 (Chart 1: systemic hypotension flow chart)



Possible causes	Therapeutic Approach (mechanism)
PPHN	1.Reduce PVR e.g. iNO, milrinone (may have positive inotropy) 2. Improve atrial filling pressure (preload) e.g. fluid bolus, vasopressin (may ↓ PVR) 3. Enhance myocardial systolic performance e.g. dobutamine, epinephrine 4. Consider PGE_1 infusion if RV dysfunction and PDA closed
Septic (Cold) shock	1. Improve myocardial systolic performance e.g. dobutamine, epinephrine (may ↑ preload) 2. Optimize treatment of sepsis
Cardiogenic shock	1. Check heart rhythm (r/o arrhythmia) 2. Improve myocardial systolic performance e.g. dobutamine, epinephrine

Possible causes	Therapeutic Approach (mechanism)
Systemic hypovolemia	1.Optimize filling pressures (preload) - fluid boluses (max 2 of 10mls/kg each) ± colloid 2. Increase SVR once adequate volume given e.g. vasopressin, dopamine
Warm shock	1.Optimize filling pressures (preload) - fluid boluses (max 2 of 10mls/kg each) 2.Increase SVR e.g. dopamine, norepinephrine, vasopressin (may increase atrial filling pressure)
PDA	1. Ductal closure strategies e.g. NSAID, acetaminophen, surgery 2. Flow limitation strategies e.g. permissive hypercapnea, ↑PEEP 3. Enhance LV systolic function e.g. dobutamine

Cause	Physiology	Therapeutic algorithm
A. Progression of severity after an initial period of low systolic BP		
PPHN	LV dysfunction &/or Loss of vascular tone	1. Improve atrial filling pressure (preload) e.g. fluid bolus, vasopressin (unless LV dysfunction on TNE) 2. Enhance myocardial systolic performance e.g. dobutamine, epinephrine
Cardiogenic shock	Worsening LV function (? impending arrest)	Enhance myocardial systolic performance e.g. dobutamine, epinephrine
B. Progression of severity after an initial period of low diastolic BP		
Hypovolemia or warm shock	Myocardium unable to compensate or progression to cardiac dysfunction	1.Optimize filling pressures (preload) – fluid boluses (max 2 of 10mls/kg each) 2.Increase SVR e.g. dopamine, norepinephrine, vasopressin (if no LV dysfunction)
PDA	Large volume shunt + myocardium unable to compensate	1. Flow limitation strategies e.g. permissive hypercapnea, ↑PEEP 2. Enhance LV systolic function e.g. dobutamine, dopamine (if critical DAP)
C. Both systolic & diastolic low at presentation (profound hypotension)		
Manage as severe warm shock with LV dysfunction if no echo available **(rule out adrenal insufficiency)**		See above + **early hydrocortisone**

Special Considerations

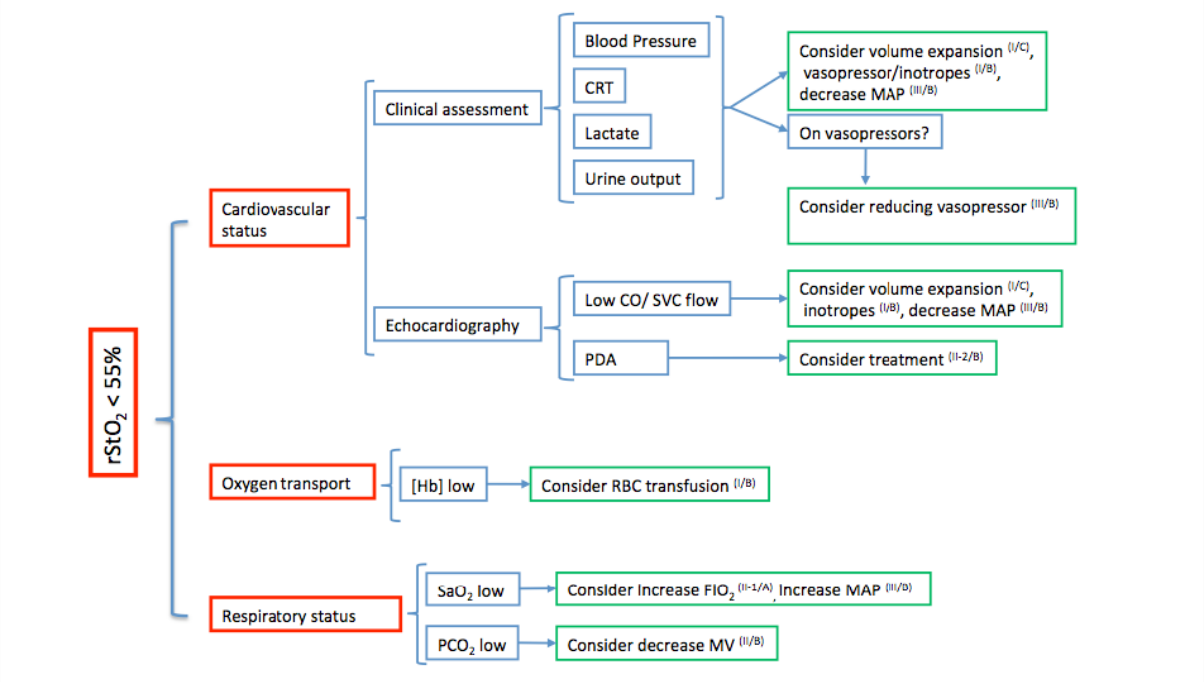
- *Wean mean airway pressure to lowest needed provided no worsening of oxygenation*
- *Consider hydrocortisone if hypotension unresponsive to 2 therapeutic agents*
- *Early TnECHO consult is advisable for refractory hypotension*
- *Carefully evaluate infant and investigate/treat underlying cause of hypotension (e.g. acute blood loss, sepsis, SIRS, adrenal insufficiency, arrhythmia, electrolyte disturbances)*
- *Avoid use of cardiovascular agents which have chronotropic or inotropic effects in IDM patients*
- *Caution with use of milrinone in neonates with HIE or where borderline mean or diastolic BP*

On Om

On behalf of Targeted Neonatal Echocardiography and Neonatal Hemodynamics Program:
Reference:
Chapter 29: Hemodynamics. Patrick McNamara, Dany Weisz, Regan Giesinger, Amish Jain. Avery's Neonatology: Pathophysiology and Management of the Newborn, 7th Edition (2016), Wolters Kluwer.

Reference: Giesinger et al Seminars in Perinatology 2016; 40:174-188

Chart 2: Clinical treatment guideline in response to low NIRS thresholds from SafeBoosC consortium

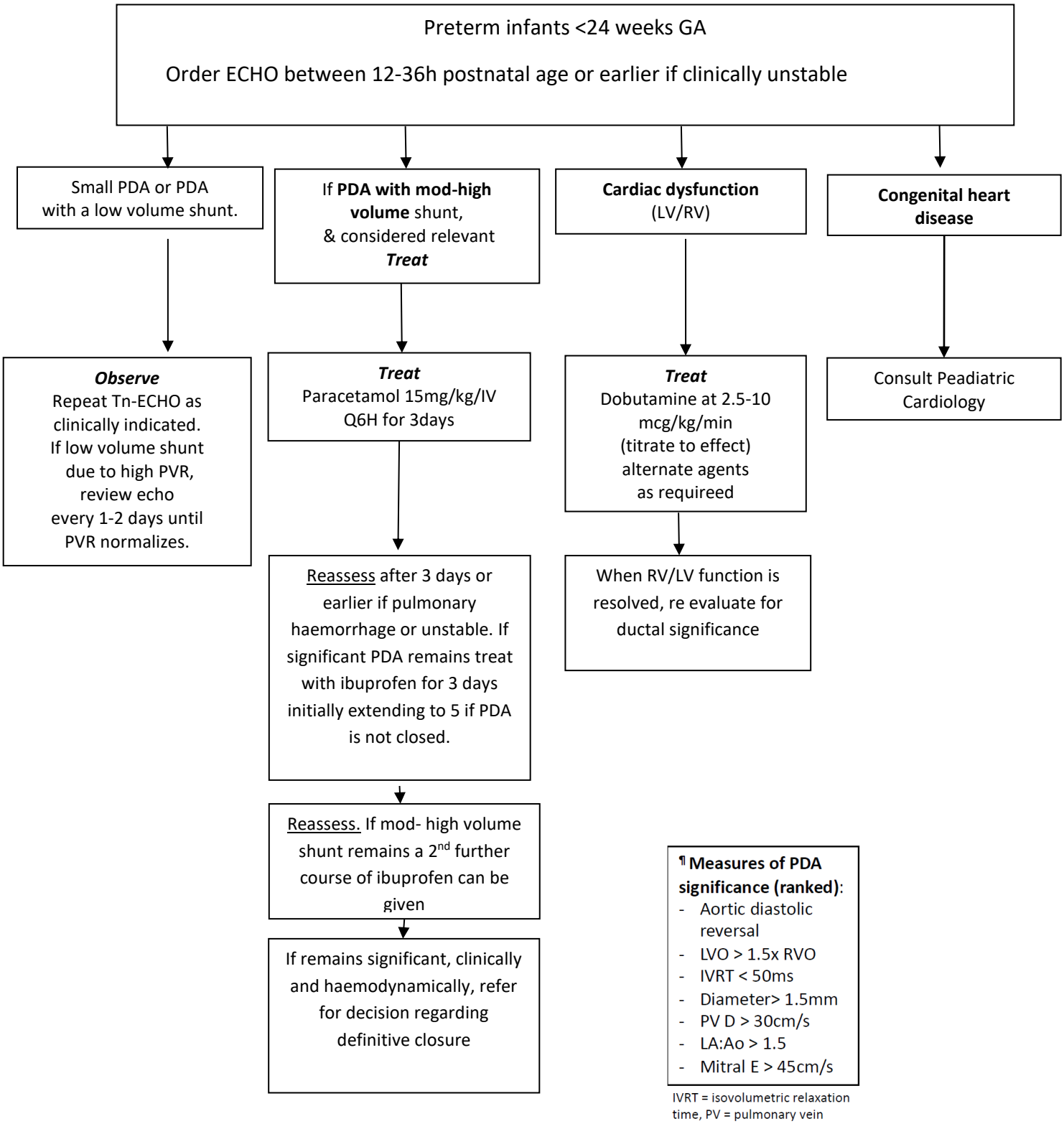


Treatment Guideline for SafeBoosCII &III RCTs. In brackets the level of evidence and recommendation for a given intervention (US preventive Services Task Force system 2001). Note the rSt02 value here is 55% but depends on the cerebral oximeter used (see Table 5).

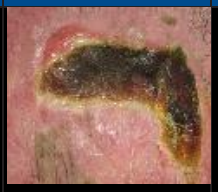
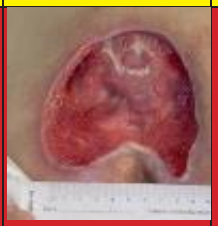
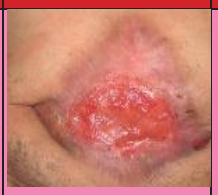
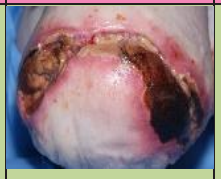
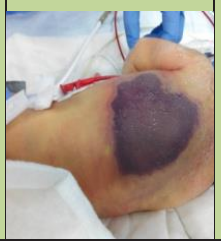
Table 5: Hypoxic thresholds for different NIRS devices

NIRS Device	Hypoxic threshold %
FORESIGHT small	66
FORESIGHT non-adhesive small	**67**
NIRO small	**61**
NIRO small re-usable	**63**
NIRO large	**62**
NIRO large re-usable	**62**
INVOS neo	**63**
SenSmart neo 8004CB-NA	**66**
Oxyprem 1.4: re-usable	**48**
O3 Pediatric	**64**
O3 Neonatal	**64**
Egos	**56**

Chart 3: Guideline for PDA screening and early haemodynamic management in extremely preterm infants



Appendix 3

COLOUR	EXAMPLE	CHARACTERISTICS	AIMS	PRIMARY DRESSINGS	SECONDARY DRESSINGS
BLACK NECROTIC TISSUE		• Dead tissue • Hard, black eschar • Brown leathery appearance	Rehydrate necrotic tissue to facilitate autolytic debridement. *Debridement only if holistic assessment permits	• Hydrogel • Honey dressing- Actilite, Medihoney. • Hydrocolloid – duoderm extra thin. • Hydro-responsive dressing – hydrosorb	• Hydrocolloid • Simple low absorbent dressing • Foam dressing if wound becomes wet or macerated
YELLOW SLOUGHY TISSUE		• Sloughy 48evitalized tissue, yellow in appearance • Can be soft, moist and stringy in consistency or more firm when dry	To remove slough from wound bed as this will hinder healing process	LOW EXUDATE • Hydrogel • Honey dressing – Actilite, Activon • Hydro-responsive dressing -Hydrosorb HIGH EXUDATE • Mixed fibre gel dressing – Aquacel.	• Wound pad • Simple absorbent dressing • Non-adhesive or adhesive foam, retention tape /bandage
RED GRANULATING TISSUE		• Granulating wound. • Shiny, moist with healthy red colouration and a 'lumpy' surface appearance due to new connective tissue and capillary buds	To protect the wound and maintain a warm, moist optimum healing environment through exudate management	LOW EXUDATE • Hydrogel • Hydrosorb • Duoderm extra thin HIGH EXUDATE • Mixed fibre gel dressing – Aquacel • Foam if superficial wound bed – Kliniderm foam	• Wound pad • Simple absorbent Dressing • Non-adhesive or adhesive foam, retention tape /bandage
PINK EPITHELIAL TISSUE		• Epithelialising wound. Epithelial cells migrating over healthy granulation • Shallow with low exudate. Pink/white in colour	Protection and prevention of trauma to fragile new cells	• Non-adherent dressing- Mepitel/ Mepitel One • Hydrocolloid – Duoderm Extra Thin	• Simple absorbent pad for low exudate • Foam dressing if remaining in place for more than 48hours
GREEN INFECTED TISSUE	 	• Deteriorating or static wound • Increased slough or necrosis • Increased levels of exudate • Malodour • Increased pain • Surrounding erythema • Hypergranulation (can include any of the above)	Reduce microbial load at wound bed. Debridement only if holistic assessment permits* Protect the wound whilst ensuring exudate levels are managed to protect surrounding skin.	LOW EXUDATE • Hydrogel • Honey dressing – Actilite, Activon • Hydro-responsive dressing -Hydrosorb HIGH EXUDATE • Mixed fibre gel dressing – Aquacel. • Alginate gel with antimicrobial – Flaminal hydro	• Wound pad with film • Adhesive foam or non- adhesive foam with retention tape/bandage • Super absorbent dressing if highly exuding

Appendix 4: NHSGGC Wound Classification Product Selection Guide

Type	Indications	Function	Precautions	Products
Barrier	Nappy Rash	Protects against moisture-associated skin damage Protects against epidermal stripping Protects against irritation from adhesives	May be difficult to assess wound with opaque preparations Residual cream or ointment should not be removed prior to reapplication	Conotrane Bepanthen Metanium White petrolatum Zinc oxide ointment Cavilon No-Sting barrier
Transparent polyurethane film	Skin tears Superficial wounds with little to no exudate	Prevents wound contamination Provides moist wound healing Promotes autolytic debridement Non-absorptive	Semi-permanent; not intended for frequent dressing changes May result in epidermal stripping (if adhesive present	Tegaderm Opsite
Contact layer	Skin tears Superficial wounds with little to no exudate Minimal to moderate exudative wounds Pressure ulcers Partial and full-thickness wounds	Prevents wound contamination Provides moist wound healing Allows transfer of exudate into absorbant dressing Nonabsorptive	Some contain softsilicone adhesive Requires secondary dressing	Mepitel Mepital-One DuoDerm Extra Thin Lomatuell pro
Hydrocolloid (gelatin, pectin, and/or carboxymethyl cellulose)	Minimal to moderate exudative wounds Pressure ulcers Partial and full-thickness wounds	Prevents wound contamination Promotes autolytic debridement Minimal absorption Ease of use	Caution in infected wounds May cause maceration of peri-wound May result in epidermal stripping (if adhesive present	Duoderm Tegasorb Duoderm extra thin Comfeel plus Comfeel plus transparent

Polyurethane foam and composite	Moderate to heavy exudative wounds Partial and full-thickness wounds Peristomal Pressure redistribution	Ease of removal (only if non-adherent or containing soft silicone adhesive) Ease of use Moderate absorption Pressure redistribution Comfortable	Not for use in dry wounds Requires a secondary dressing (unless compositie)	Kliniderm foam silicone lite or border lite Tegaderm foam Tegaderm foam adhesive Allevyn life
Hydrogel	Minimal exudate or dry wounds Partial and full-thickness wounds Burns	Pressure redistribution Reduce pain Promotes autolytic debridement Promotes epithelialization Adds moisture Minimal to moderate absorption Fills dead space Ease of removal	May over-hydrate wound May macerate peri-wound; consider applying skin sealant first as protection Requires secondary dressing	Sheet: Hydrosorb Amorphous: Intrasite
Hydrofiber (sodium carboxy-methyl cellulose)	Moderate to heavy exudative wounds Partial and full-thickness wounds Wound dehiscence Infected wounds	Promotes autolytic debridement Moderate to marked absorption Ease of removal	Requires secondary dressing	Aquacel
Alginate				Flaminal Hydro Flaminal Forte

Annex A: Guideline Development Group Membership

Antenatal, Communication and Maternal/Neonatal Transport

David Quine, Consultant Neonatologist, NHS Lothian (Chair)
Pamela Connolly, Neonatal Transport Nurse, ScotSTAR, NHS Forth Valley
Shona Cowan, Maternity and Fetal Medicine Consultant, NHS Lothian
Sharon Donachie, Senior Transport Charge Nurse, ScotSTAR
Lesley Jackson, Consultant Neonatologist, NHS GGC
Mahmoud Montasser, Consultant Neonatologist, NHS Lanarkshire
Judith Orme, Consultant Neonatologist, NHS Lothian
Joyce O'Shea, Consultant Neonatologist, NHS GGC
Lambrini Psiouri, Consultant Neonatologist, NHS Grampian
Hannah Porter, Lead Pharmacist, NHS Lothian
Lynsey Still, Consultant Neonatologist, NHS GGC
Sarah Stock, Clinical Career Development/Maternity and Fetal Medicine
Jessica Thompson, Research Midwife

Delivery Room, Early NNU, Golden Hours, and Access

Lynsey Still, Consultant Neonatologist, NHS GGC (Chair)
Carolyn Abernethy, Consultant Neonatologist, NHS GGC
Hester Blair, Neonatal Dietician, NHS Lothian
Pamela Connolly, Neonatal Transport Nurse, ScotSTAR, NHS Forth Valley
Shona Cowan, Consultant Obstetrics & Gynaecology, NHS Lothian
Kirsty Gracie, ST7 Paediatrics, NHS GGC
Melanie Gunning, Principal Clinical Psychologist, NHS Lothian, ERI
AnneMarie Heuchan, Consultant Neonatologist, NHS GGC
Allan Jackson, Consultant Neonatologist, NHS GGC
Lesley Jackson, Consultant Neonatologist, NHS GGC
Petr Kalous, Consultant Neonatologist, NHS Grampian
Amanda-Dawn Kimber, ANNP, NHS Tayside
Mahmoud Montasser, Consultant Neonatologist, NHS Lanarkshire
Peter Mulholland, Principal Pharmacist, NHS GGC
Kirstine Noonan-Stewart, ANNP, NHS Forth Valley
Judith Orme, Consultant Neonatologist, NHS Lothian
Joyce O'Shea, Consultant Neonatologist, NHS GGC
Anisa Patel, Neonatal Pharmacist, NHS GGC
David Quine, Consultant Neonatologist, NHS Lothian
Gillian Reid, ANNP, NHS Lanarkshire
Mithuna Urs, Consultant Paediatrician, NHS Highland

Respiratory

Joyce O'Shea, Consultant Neonatologist, NHS GGC (Chair)
Jonathan Coutts, Consultant Neonatal and Respiratory Paediatrician, NHS GGC

Shona Cowan, Consultant Obstetrics & Gynaecology, NHS Lothian
Lesley Jackson, Consultant Neonatologist, NHS GGC
Petr Kalous, Consultant Neonatologist, NHS Grampian
Gopala Krishnan, Consultant Neonatologist, NHS Lanarkshire
Tom McEwan, Principal Educator, NMAHP, NES
Mahmoud Montasser, Consultant Neonatologist, NHS Lanarkshire
Judith Orme, Consultant Neonatologist, NHS Lothian
Andrew Powls, Consultant Neonatologist, NHS GGC
David Quine, Consultant Neonatologist, NHS Lothian
Lynsey Still, Consultant Neonatologist, NHS GGC

Cardiovascular and Haemodynamics

Anne Marie Heuchan, Consultant Neonatologist, NHS GGC (Chair)
Lesley Jackson, Consultant Neonatologist, NHS GGC
Mahmoud Montasser, Consultant Neonatologist, NHS Lanarkshire
Kirstine Noonan-Stewart, ANNP, NHS Forth Valley
Judith Orme, Consultant Neonatologist, NHS Lothian
Joyce O'Shea, Consultant Neonatologist, NHS GGC
David Quine, Consultant Neonatologist, NHS Lothian
Helen Turner, PhD Research, NHS Lothian
Mithuna Urs, Consultant Paediatrician, NHS Highland
Philine Van der Heide, Consultant Neonatologist, NHS Highland

Fluids and Nutrition

Petr Kalous, Consultant Neonatologist, NHS Grampian (Chair)
Hester Blair, Neonatal Dietician, NHS Lothian
Gopala Krishnan, Consultant Neonatologist, NHS Lanarkshire
Anne Marie Heuchan, Consultant Neonatologist, NHS GGC
Lesley Jackson, Consultant Neonatologist, NHS GGC
Amanda-Dawn Kimber, ANNP, NHS Tayside
Mahmoud Montasser, Consultant Neonatologist, NHS Lanarkshire
Peter Mulholland, Principal Pharmacist, NHS GGC
Kirstine Noonan-Stewart, ANNP, NHS Forth Valley
Joyce O'Shea, Consultant Neonatologist, NHS GGC
David Quine, Consultant Neonatologist, NHS Lothian
Philine Van der Heide, Consultant Neonatologist, NHS Highland

Infection Prevention and Skin Care

David Quine, Consultant Neonatologist, NHS Lothian (Chair)
Lynda Bowen, Neonatal Nurse, NHS Grampian
Lisa Broomfield, Neonatal Nurse, NHS Lothian
Susan Cameron, Clinical Nurse Specialist NHS Lothian
Tracy Clinton, Staff Nurse, NHS GGC
Pamela Connolly, Neonatal Transport Nurse, ScotSTAR, NHS Forth Valley
Yvonne Freer, Clinical Reader, NHS Lothian
Gopala Krishnan, Consultant Neonatologist, NHS Lanarkshire

Donna Landels, Staff Nurse, NHS Fife
Susan Leggat, Charge Nurse
Tom McEwan, Principal Educator, NMAHP, NES
Fiona McKeown, Neonatal Physiotherapist, NHS Lothian
Lauren McMinn, Staff Nurse, Special Care Unit, NHS Fife
Kirstine Noonan-Stewart, ANNP, NHS GGC
Claire O'Brien, Principal Clinical Pharmacist
Kate Ranford, Staff Nurse, NHS Lanarkshire
Eilidh Ritchie, Neonatal Nurse, NHS Grampian
Laura Stirling, Clinical Nurse Specialist, NHS Lothian

Neuro-critical Care

Mahmoud Montasser, Consultant Neonatologist, NHS Lanarkshire (Chair)
Michelle Brooks, Practice Educator, NHS Lanarkshire
Jo Gallagher, ANNP, NHS Lanarkshire
Kirsty Gracie, ST7 Paediatrics, NHS GGC
AnneMarie Heuchan, Consultant Neonatologist, NHS GGC
Lesley Jackson, Consultant Neonatologist, NHS GGC
Fiona McKeown, Neonatal Physiotherapist, NHS Lothian
Kirstine Noonan-Stewart, ANNP, NHS GGC
David Quine, Consultant Neonatologist, NHS Lothian
Jacqueline Rooney, Pharmacist, NHS Lanarkshire
Helen Turner, PhD Research, NHS Lothian

Family Centred – Psychological Support – Parallel Planning

Judith Orme, Consultant Neonatologist, NHS Lothian (Chair)
Nicole Bauwens, Nursing and Midwifery, NHS Grampian
Pamela Connolly, Neonatal Transport Nurse, ScotSTAR, NHS Forth Valley
Melanie Gunning, Principal Clinical Psychologist, NHS Lothian, ERI
Joyce O'Shea, Consultant Neonatologist, NHS GGC
David Quine, Consultant Neonatologist, NHS Lothian
Lauren Williams, Paediatric Clinical Pharmacist, NHS GGC