

Reducing the incidence of bronchopulmonary dysplasia

A BAPM Quality Improvement Toolkit

December 2023

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Abbreviations

AHSN	Academic Health Sciences Network
ANS	Antenatal steroids
BAPM	British Association of Perinatal Medicine
BPD	Bronchopulmonary dysplasia
СРАР	Continuous Positive Airway Pressure
DBM	Donor Breast Milk
ENT	Ear Nose Throat
ESPGHAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
GA	Gestational Age
GIRFT	Getting It Right First Time
HFOV	High Frequency Oscillatory Ventilation
HQIP	Healthcare Quality Improvement Programme
IUGR	Intra-Uterine growth retardation
IVH	Intraventricular Hemorrhage
LISA	Less Invasive Surfactant Administration
LTV	Long Term Ventilation
MatNeoSIP	Maternity and Neonatal Safety Improvement Programme
MBM/MOM	Maternal Breast Milk /Mother's Own Milk
MDT	Multidisciplinary Team
MIST	Minimally Invasive Surfactant Therapy
NEC	Necrotising enterocolitis
NICE	National Institute for Health and Care Excellence
NIV	Non-invasive ventilation
NNAP	National Neonatal Audit Programme
NSQI	Neonatal Services Quality Indicators
ODN	Operational Delivery Network
PCS	Post natal corticosteroids
PDA	Patent Ductus Arteriosus
PDSA	Plan Do Study Act
PEEP	Positive End Expiratory Pressure
PIP	Peak inspiratory pressure
PMA	Post Menstrual age
QI	Quality Improvement
RCT	Randomised controlled trial
RDS	Respiratory Distress Syndrome
RCPCH	Royal College of Paediatrics and Child Health
ROP	Retinopathy of prematurity
SPC	Statistical process control
SPSP-MCQIC	Scottish Patient Safety Program Maternity and Children Quality
	Improvement Collaborative
UKNC	United Kingdom Neonatal Collaborative
VAP	Ventilation Associated Pneumonia
VTV	Volume Targeted Ventilation

Overview

The focus of this toolkit is to identify and support the implementation of best practices, interventions and strategies to reduce the incidence of bronchopulmonary dysplasia (BPD).

Why?

- BPD can be associated with adverse neurodevelopmental and respiratory outcomes continuing into childhood, requiring hospital admissions and considerable healthcare support.
- Incidence of BPD shows an increasing trend across the world and the UK reports some of the highest rates among European countries.
- Nearly 70% of single centre and collaborative structured quality improvement initiatives reported successful reduction of BPD rates.

Introduction

The British Association of Perinatal Medicine (BAPM) aims to improve standards of perinatal care by supporting all those involved in providing this care to optimise their knowledge and skills. The National Neonatal Audit Programme (NNAP) (1) sets evidence-based standards on key clinical outcomes and in turn identifies areas for quality improvement (QI) concerning the delivery and outcomes of neonatal care. With these shared goals in mind, the BAPM, the NNAP and other key stakeholder organisations in perinatal care have collaborated in national quality improvement initiatives to target key NNAP measures.

The <u>BAPM website</u> offers a range of free QI resources, links to easy-to-use templates and e-learning, QI tutorials and a forum for shared learning(2). The toolkit does not intend to replicate any existing local or national QI activity undertaken in focus but to complement these endeavours with a practical step-by-step guide.

This toolkit is aimed at individuals and teams who are involved in quality improvement to reduce BPD rates:

- If you have the resources to undertake a full change management QI project but have little knowledge or experience you may want to read this toolkit in its entirety.
- If you have some QI experience from other projects but know a limited amount about reducing BPD rates you may wish to focus on the key recommendations.
- If you know a lot about reducing BPD rates but lack QI knowledge you may choose to focus on understanding the overview of the improvement journey.
- If you are tasked with collecting/ understanding or interpreting data and don't know where to start look at Phase Four: Test and measure improvement.
- If your QI project team is a mix of all of the above there should be something in this toolkit for everyone to get your project started.

Definition of the condition

The most commonly used definition of BPD, the definition used by NNAP, and the one which we will use for the purpose of this toolkit, is here.

Definition:

BPD is the requirement of respiratory support at 36 weeks PMA in an infant born before 32 weeks.

Variations in the definition of BPD

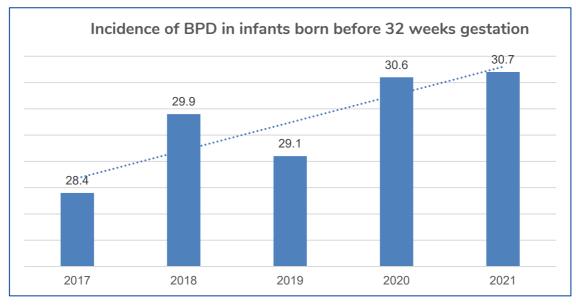
Several variations in the definition of BPD have been suggested in literature. Reports have suggested that the definition that best predicts early childhood respiratory morbidity, categorised disease severity according to the mode of respiratory support administered at 36 weeks' postmenstrual age, regardless of supplemental oxygen use(3). There is currently an international Delphi process is underway to achieve a uniform BPD definition and address the current variation in how BPD and its severity are defined.

For the purpose of standardization, it is recommended that you use a consistent BPD definition based on national benchmarking measures, as suggested by the NNAP, when assessing the impact of interventions as part of QI projects.

Why is this toolkit required?

Bronchopulmonary dysplasia (BPD) remains one of the most frequent and important consequences of prematurity and the most common adverse health outcome, exerting a significant impact on mortality, long term morbidities and healthcare cost. Despite numerous clinical trials and introduction of novel interventions and strategies, the global incidence of BPD has not shown a trend towards reduction.

• There exists wide variability in global incidences of BPD, ranging from 10%-89%, with the UK historically reporting some of the highest incidences of BPD among European countries (4). The NNAP annual reports over the last 5 years show steady increasing trend in the reported BPD rates across the UK. (Graph 1)



Graph 1: Incidence of BPD

Figures obtained courtesy NNAP annual reports.

• Quality improvement combines evidence with contextual knowledge to change organisational culture and individual behaviour and has been shown to foster sustained improvement in the neonatal unit (5). A systematic review of multiple single centre and collaborative QI initiatives has shown that BPD rates can be improved(5).

Long term adverse outcomes and health economics

- Premature infants with BPD have a greater incidence of adverse neurological and respiratory outcomes compared to those without BPD. Large cohort studies have reported that BPD was strongly associated with mild, moderate and severe overall neurodevelopmental disabilities even at 5-6 years of follow up, as well as being associated with developmental coordination disorders, behavioural difficulties and lower IQ score. (6)
- A significant proportion of preterm infants with BPD require chronic or long term invasive or non-invasive respiratory support. Around a third of infants with BPD are discharged home on oxygen (7). Some of these infants continue receiving respiratory support in a paediatric intensive care (PICU) or high-dependency (HDU) setting and constitute a significant proportion of children on long term ventilation (LTV).

- It has been reported that BPD exerts a significant strain on the health economics and that there exists an inverse association between gestation and economic burden irrespective of country and date(8). The reported expenditures, however, do not consider the additional costs incurred by local commissioning, training of carers, housing rearrangements and ongoing care that are required for ongoing multi-disciplinary support.
- Symptoms of psychological distress are common in parents of preterm infants, and still more so when infants experience prolonged respiratory illness. Parental healthcare related quality of life is lower when infants have frequent symptoms and acute care usage because of BPD.
 (9)

What is covered in this toolkit?

- The focus of this toolkit is to support implementation or adoption of best practices aimed at **prevention** of BPD among preterm infants born at less than 32 weeks gestational age (GA). *This toolkit will not aim to discuss principles of management of established BPD*.
- These interventions or practices will be based on **five core strategy elements** (these elements are color-coded as themes throughout the toolkit) as outlined below.
- As is the case with most clinical toolkit or bundle elements, not all interventions or strategies will necessarily have the same weight of evidence behind them. The idea of this toolkit to provide or highlight the best practice elements from each domain and briefly outline the evidence base. The focus, however, has been more on identifying barriers to these best practice elements and how to circumvent these through a QI approach.

Table 1: Five core strategies to reduce the incidence of BPD

	Core elements
1	Perinatal Optimisation
	Interventions in the antenatal period and around time of delivery which can ensure an optimal start.
2	Early Respiratory support strategies in the delivery room and neonatal unit
	Approaches around early respiratory care which could potentially minimise lung injury.
3	Optimising care of other organ systems which might positively impact respiratory
	outcome
	This includes fluid and nutrition (particularly maternal breast milk provision),
	cardiovascular management, avoidance of late onset neonatal sepsis,
4	Pharmacological interventions
	To discuss use of medications / therapeutic modalities which have been shown to reduce
	incidence of BPD or improve respiratory outcomes.
5	Multi-disciplinary team and parental involvement
	Involvement of parents and allied health professionals in shared decision making

Key recommendations from core strategies and evidence supporting them to reduce BPD

The following table (Table 1) outlines key recommendations based on available evidence from the core elements named above and the strength of recommendation/ evidence as considered by the committee. **Detailed evidence summary and references for each core strategy/ intervention are described separately in the appendix.** The evidence sources have been categorised as journal references, professional recommendations or consensus guidelines and standards and quality Improvement Initiatives:

Core Strategy	Key interventions	Level of evidence
	 Optimal place of birth Infants before 27 weeks (before 28 weeks if multiples) and if estimated fetal weight <800grams should be born in neonatal intensive care unit (NICU) 	Not causally linked to reduction of BPD, but has been reported to have strong positive impact on outcome of survival and major co-morbidities, strongly recommended.
Perinatal Optimisation	 Optimally timed Antenatal steroids (ANS) A mother who delivers an infant between 22-33 weeks should ideally receive 1 full course of antenatal steroids within 1 week prior to delivery. Additional Resource: BAPM Antenatal Optimisation Toolkit 	There is high certainty of evidence than ANS reduce neonatal mortality and respiratory distress syndrome (RDS), but it is unclear whether they reduce BPD.
	 3. Optimal Cord Management: Clamping of the cord should be delayed for at least 60 seconds in infants born below 34 weeks 	No evidence to suggest that optimal management of cord reduces BPD, but there is high quality evidence that the practice reduces neonatal mortality. Strongly recommended practice.
	 4. Thermoregulation Achieving and maintaining normothermia is a key goal. This should involve use of plastic bag, radiant warmers and humidified gases in infants born below 32 weeks, Caution should be exerted to avoid hyperthermia 	High quality evidence, strongly recommended Additional Resource: BAPM Normothermia Toolkit.

	Delivery Room Practices	
	1. Gentle Lung Aeration:	
Early Respiratory support	 Spontaneously breathing preterm infants should be stabilised using CPAP using PEEP between 6-8cm H₂0. If apnoeic or bradycardic, ventilation breaths are recommended using a T-piece device with peak inspiratory pressure (PIP) set at 20-25cm H₂0 and positive end expiratory pressure (PEP) set at 6 cm H₂0. Humidified gas should be used where possible. Using an air oxygen blender, the FiO₂ should be commenced using the settings below according to gestation: <28 weeks - 30% 28-31 weeks - 21-30% 32 weeks and above - 21% During stabilisation, close attention should be paid to the pressures delivered to the baby, and settings adjusted 	Moderate quality evidence, strongly recommended as per national resuscitation guidelines.
strategies in delivery	according to clinical response, oxygen saturations, aiming for SpO ₂ of 80% by 5 minutes of life.	
room and neonatal unit	2 Non-Invasive Respiratory Support:	
	 2. Non-Invasive Respiratory Support: Primary mode of respiratory support in spontaneously breathing infants in the delivery room should be CPAP. In preterm infants with prolonged apnoea or instability, intubation should be considered in the delivery room. 	High quality evidence, strongly recommended.
	 Early intubation in the delivery room could be considered during stabilisation of extreme preterm infants born <24 weeks 	Expert consensus.

 Surfactant: (principles for delivery room and neonatal unit) 	
 Where intubation is required for stabilisation in preterm infants born before 30 weeks gestation, surfactant should be administered in the delivery room. 	High quality evidence, strongly recommended.
 Rescue surfactant should be administered early in the course of the disease. 	High quality evidence, strongly recommended.
 In infants stabilised on CPAP with PEEP >6 cm H₂O and FiO2 >30%, early surfactant rescue should be given. 	Moderate quality evidence, recommended based on expert consensus.
• Repeated dosing of surfactant should be considered when there is evidence of ongoing moderate to severe RDS.	High quality evidence, strongly recommended
With appropriate training and expertise lung ultrasound might be a more sensitive predictor of CPAP failure and surfactant requirement than FiO2 cut- off in the neonatal unit.	
• Less Invasive Surfactant Administration (LISA) should be the preferred method of surfactant administration in spontaneously breathing infants on CPAP where adequate expertise is available.	High quality evidence, strongly recommended.
Every effort should be made to optimise training and build resource in delivering LISA in units caring for preterm infants. In situations where either the skills or equipment for safely performing LISA are not available, INSURE might be considered as an interim alternative to minimise mechanical ventilation.	

Early respiratory support in neonatal unit	
1. Non-invasive ventilation (Aim should be to avoid ventilation where possible):	
• CPAP or High Flow Nasal Therapy (HFNT) can be considered for primary or post- extubation respiratory support.	High quality evidence, strongly recommended.
No consensus exists on safe upper limits of pressure that can be used. Early evidence seems to suggest that higher starting CPAP pressures might be safe and more effective than lower pressures (<8 H ₂ 0 cm) to reduce extubation failure.	
In the more preterm population risk of treatment failure is higher with HFNT. Units choosing to use HFNT as primary respiratory support for lower gestational ages should be able to offer rescue CPAP to prevent intubation.	
 BiPAP devices are <i>not</i> superior to CPAP alone. However Synchronised and non-synchronised forms of Non-invasive positive pressure ventilation (S-NIPPV, NS-NIPPV) could be considered as the preferred mode of extubation <i>if local</i> <i>expertise and resource is available</i> to prevent reintubation. 	High quality evidence, recommended if resource and expertise available.

2. Mechanical Ventilation:	
• Volume targeted ventilation (VTV) should be the preferred mode of invasive ventilation when using conventional MV in the neonatal unit as a lung protective strategy. A volume range of 4-6ml/kg is the optimal operational range for the first 2 weeks. <i>Every effort should be made to maintain</i> <i>babies on this lung protective mode where possible.</i>	High quality evidence, strongly recommended.
• High frequency oscillatory ventilation (HFOV) can also be considered as an alternative initial mode of ventilation as a lung protective strategy, especially in extremely preterm infants. Use of volume targeting with HFOV (HFOV-VG) has been shown to reduce CO2 variability.	Low quality evidence, recommended when resource and experience is available.
3. Permissive hypercarbia does not reduce BPD and there is no consensus to safe upper limit which can be tolerated. A modest degree of hypercarbia might be tolerated to facilitate weaning of ventilation maintaining pH > 7.22.	Low quality evidence and weak recommendation.

	1. Early Breast Milk and nutrition	
	• Exclusive and early feeding with mother's own expressed breast milk (MBM) is strongly recommended.	High quality of evidence strongly recommended.
	 In absence of mother's own milk (MBM), donor breast milk (DBM) should be recommended as the alternative. 	Moderate to low quality evidence but strong recommendation in absence of MBM.
	 In absence of alternative evidence, recommended parenteral and enteral intakes of macronutrients, minerals and vitamins with early optimised parenteral nutrition should be targeted as per ESPGHAN 2022 guidance. 	Expert consensus, strongly recommended.
	2. Targeted approach to PDA management	
	• Routine attempts at PDA closure cannot be recommended.	Moderate quality evidence.
Optimising care of other organ systems	 However carefully selected infants, with echocardiographic and clinical evidence of hemodynamically significant duct, who are at risk of being mechanically ventilated beyond 10 days might benefit from early pharmacotherapy aimed at closure. Local expertise / resources for point of care functional assessment of PDA might help such decision making 	Low quality evidence.
	 Prolonged exposure to hemodynamically significant PDA might be associated with increased risk of pulmonary vascular disease associated with BPD. 	Moderate quality evidence.
	3. Prevention / Reduction of LONS	
	 Quality improvement measures aimed at prevention or reduction of late onset neonatal sepsis (LONS) can have positive impact of reduction of morbidities like BPD. 	Low quality evidence, strongly recommended practice.

	1. Caffeine	
	 Caffeine should be started early (within 72 hours), preferably within first 24 hours 	High quality of evidence, strongly recommended.
	 Post - natal corticosteroids (PCS): Consider the use of early low-dose prophylactic Hydrocortisone, when not associated with indomethacin, on preterm infants born below 28 weeks of gestation on day 1 of life. N.B: Data is limited in infants born below 24 weeks of gestation due to their underrepresentation in clinical trials. Consider the use of Dexamethasone in preterm infants who are 8 days or older and still need invasive ventilation, on a case-by-case basis, based on clinical assessment and level of 	High quality evidence, recommended.
Pharmacological interventions	respiratory support, after discussion with parents with a consideration to stop if there is no clinical response. Routine use of Dexamethasone is not recommended in every preterm infant who is requiring mechanical ventilation.	Moderate quality evidence, recommended based on risk analysis.
	There is insufficient evidence to suggest optimal dosing of PCS at present, especially for dexamethasone. However, the most commonly used dexamethasone regime in the UK is the DART regime	
	The hydrocortisone mentioned in the framework refers to the dosing regimen used in the PREMILOC clinical trial.	
	 3. Diuretics No high-quality evidence exists to indicate that routine use of diuretics reduces BPD. 	
	 Use in selected patient cohorts with radiological/ clinical evidence of pulmonary oedema can be considered for short- term improvements in pulmonary mechanics and reduction of oxygen requirement. 	Low quality evidence, not routinely recommended. Can be considered an option in selective scenarios

Multi-disciplinary team and parental	 Interdisciplinary care teams Early involvement of interdisciplinary care teams can potentially improve outcome and alleviate associated co- morbidities Neonatal Dietetic Support Support from specialist neonatal dietitian (if available) should be sought for collaborative nutritional management of all preterm infants Paediatric respiratory / ENT Teams Consideration should be given for early involvement of paediatric respiratory physicians or ENT if there are recurrent failed extubations (more than 2), added co-morbidities such as suspected airway problems, neuromuscular weakness involving respiratory drive or effort, Tracheo-oesophageal Fistula, congenital lung anomalies, or unexplained oxygen requirement. In those children who are planned for tracheostomy insertion, a review by respiratory paediatrics 	All these interventions are strongly recommended where the resources are available – Expert consensus.
involvement	 A. Neonatal physiotherapy Support from experienced neonatal physiotherapy team (if available) should be sought for collaborative management of the ventilated infant 5. Speech and Language Therapy Support from experienced Speech and Language therapy (SALT) team should be sought to assess and support feeding progression for babies on respiratory support 6. Parents Parents should be viewed as partners in care, and supported with accurate and individualised information throughout the neonatal stay, including in decision making around respiratory support, and BPD 	

Overview of the Improvement Journey

How to use this toolkit

This toolkit is not intended to be read as a guideline, which mandates a standard improvement journey for all units. Instead, it is a practical resource from which units who wish to reduce BPD rates for preterm babies can select the most suitable interventions for their context. The improvement solutions for each unit may be different. Individual units are encouraged to interrogate their own processes and outcomes in order to select QI interventions which are best suited to their context. The following steps are commonly taken on an improvement journey. Each step is discussed further in subsequent sections.

1.	Define the problem	Approach Identify magnitude of problem	Methods & Tools Fishbone diagram Case review Process mapping Pareto chart Learn from experts Driver diagram	Outcome Define problem, identify root cause and outline improvement
2.	Develop a shared purpose	Form a team of enthusiasts	Engaging a team and engaging stakeholders	Establish a shared objective and a culture for change
3.	Plan & implement changes	Formulate, prioritise and test solutions	Project Charter QI Methodology	Complete a formalised plan of proposed improvements
4.	Test and measure improvement	Test, review and retest improvements	PDSA Measurement Run chart Statistical Process Control Chart	Determine whether improvement has resulted in change
5.	Implement, sustain and embed	Implement widely and ensure sustainability	Education Communication Motivation Governance	Shared learning and embedding changes into practice

Figure 4: The improvement journey

Phase One: Define the problem

Where are we now? - Baseline and benchmarking data

It is important to understand your local data, and to benchmark where possible in the context of regional, national and international standards (NSQI 11,12) (10) observing any changes over recent years. To achieve this, your team should understand how to look at your local data, what questions to ask and where to access benchmarking data such as Badgernet National reports and comparison charts, the network data dashboards, <u>NNAP Online</u> as examples.

Being able to convey these data to the wider team clearly and concisely will facilitate a stronger commitment to the implementation of quality improvement interventions. It is recommended that those doing QI work should assess all their process and outcome measures through the lens of inequality, and to identify whether specific process or outcome measures are needed to specifically try and understand the impact of health inequality on BPD.

Not all measures are necessarily feasible to adopt for all units, the following are examples of measures which could be considered.

Process Measures

- 1. Proportion of infants delivered between 23-32 weeks who receive only non-invasive ventilation in 1st week of life.
- 2. Proportion of preterm infants who are invasively ventilated receiving volume targeted ventilation.
- 3. Proportion of preterm infants born below 30 weeks gestation who receive Caffeine within the first 24 hours.
- 4. Use of post-natal corticosteroids
- 5. Incidence of late onset neonatal sepsis and CLABSI

Outcome Measures

Direct measures

- 1. Percentage of infants born at < 32weeks who have a diagnosis of BPD at 36 weeks.
- Percentage of infants born at < 32weeks who have a diagnosis of severe BPD (s- BPD) (defined as requirement of invasive ventilation or NIPPV or CPAP or nasal cannula oxygen at >21/min) at 36 weeks.
- 3. Percentage of babies born at <32 weeks who are discharged on home oxygen support.

Indirect or surrogate markers

1. Compliance to saturation target range (91%-95%) in infants <32 weeks indicating what percentage of time the infant is spending within this or outside this range.

It may also be useful to ask:

- Are your data both accurate and complete? Do you have missing data?
- How has your data changed over time?
- How does your data compare with other units in your network and nationally?

How did we get here? Brainstorming barriers and enablers

In this section we describe some of the common barriers and enablers to reducing the incidence of BPD to help you get the discussion started within your team. We encourage you to consider these and add your own in order to find solutions which are appropriate for your local setting.

Table 2: Barriers and enablers for core strategies

Core element	Barriers	Enablers
Perinatal Optimisation: Antenatal interventions, delivery room management	 Cultural barriers. Lack of education and training of staff. Individual interventions and lack of bundle approach. 	 Education and Simulation based training. Strong perinatal culture. Please refer to the BAPM Toolkit on Building Successful Perinatal Teams. Parental stories and lessons from high performers. Using quality resources like the BAPM Antenatal Optimisation Toolkit.
Delivery Room Practices and Early Respiratory Support: Ventilation modes, non-invasive ventilation strategies	 Confusion among staff regarding names given to modalities in different ventilator models (eg: PC AC, SIPPV, etc). Lack of experience with volume targeted ventilation and lack of awareness around it. Lack of conviction and support to provide non-invasive transition (CPAP) in DR to preterm infants. Insufficient training in LISA. 	 Training and education based on physiological principle using terms like – "supporting all breaths, supporting only set number of breaths". Education and training on volume targeting Simulation based training on DR CPAP. delivery. Senior staff support and presence Workshops on LISA.
Optimising care of other organ systems	 Lack of robust evidence to provide guidance on consensus management of PDA in preterm infants. Suboptimal hand hygiene and aseptic practices. 	 Regional guidelines Development of local expertise in point of care scan(POCUS) to adopt targeted management based on functional assessment of PDA. ANTT training, infection prevention bundles like central line bundle, VAP (ventilator associated pneumonia) bundle

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Pharmacological interventions: Oxygen	 Lack of awareness of saturation target range based on gestation age. Inconsistent upper and lower limits set for alarm, often turning choosing too wide a range to avoid alarm fatigue. Manual titration of oxygen – has consistently been linked to time spent outside range being significant. 	 Education in setting oxygen saturation alarm limits. Prescription of oxygen with identification of appropriate saturation threshold. Consider use of histogram analysis to understand temporal trends and automated oxygen control. <i>Although current evidence does not suggest these reduce BPD</i>, but can improve time spent in target zone (91%- 95%).
Caffeine citrate	 Oversight during prescribing. Possible lack of awareness of its impact on BPD. 	 Staff education regarding impact of early caffeine beyond apneoa of prematurity. Use of a preterm passport/ bundle (eg PERIPrem/ PERIPrem Cymru) might lead to less missed instances.
Postnatal corticosteroids Hydrocortisone Dexamethasone	 Limitations in currently available BPD prediction tools. Anxiety around long-term developmental effects of post-natal corticosteroids Lack of staff awareness of the importance of timely targeted treatment Lack of resources for empowering parents in shared clinical decision making 	 Education of the recent evidence of postnatal corticosteroids use Provision of information leaflets on BPD Prioritize regular multi-disciplinary discussions on the infant's progress including respiratory outcomes
Diuretics/ Other pharmacological adjuncts	 Lack of robust data from clinical trials Established local practice of using them despite sufficient evidence 	 Careful selection of patient groups trying to identify who can benefit from these interventions

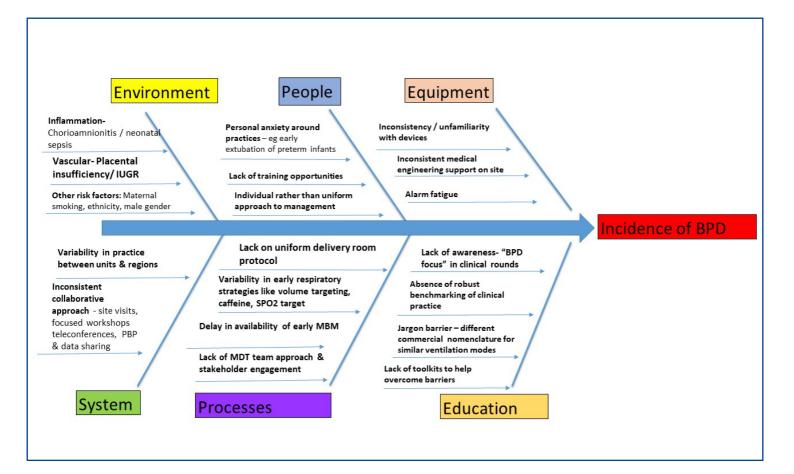
Multi-disciplinary team and parental involvement.		 Specific lactation support for mothers Education for staff on the importance of meeting nutritional targets . Funding sources for AHP staff support Involvement of MDT members in clinical rounds and decision making.
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How did we get here?

QI tools

There are many tools to help your team understand your current practice and identify how to improve. You do not need to use all these tools but should explore which of these tools works best for your team. All of these tools are explained further and templates available in the BAPM QI Made Easy pages. (11)

Figure 5. An example of a fishbone diagram analysing incidence of BPD



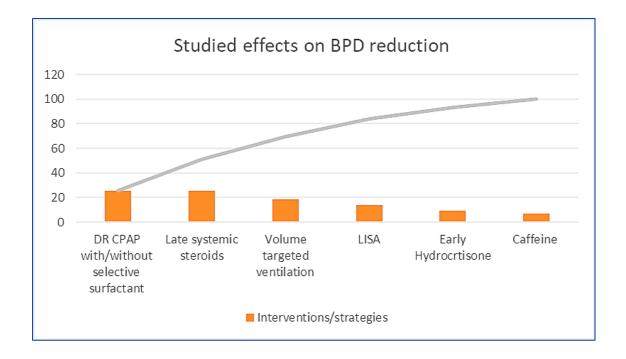
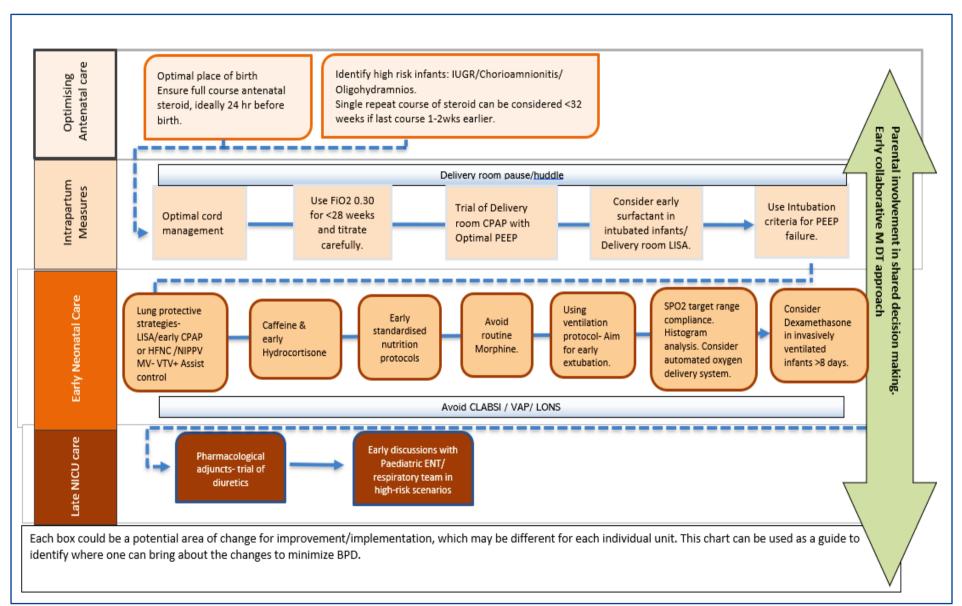


Figure 6. Example of a Pareto analysis chart for key interventions aimed at minimising BPD

Figure 7. Process mapping for best practice interventions



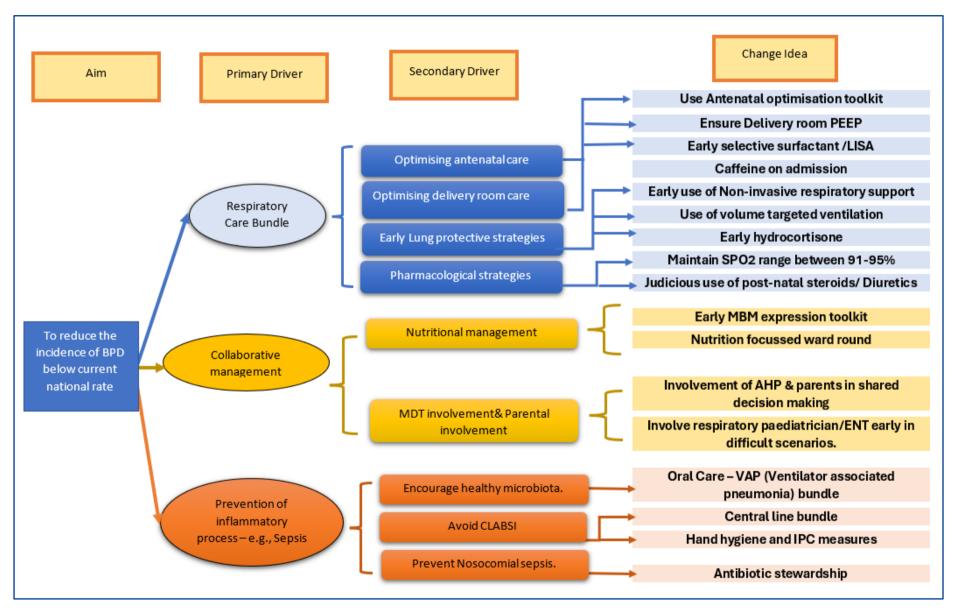


Figure 8: Driver diagram on preventing/minimising incidence of BPD

Learning from others

It can also be helpful to speak to other units about how they have reduced their BPD rates. High performing units and those who have made significant improvements over time can be identified from NNAP online. Some teams have shared examples below.

Project PEEP: Introduction of a Preterm Respiratory Care Bundle on NICU

Shared by: Lucy Bradley; Dr Teim Eyo, Jo Jones, Zara Grandison, Yvonne Huskins, Dr Nitesh Singh from Neonatal Intensive Care Unit, University Hospitals Coventry and Warwickshire NHS Trust.

Project aim: To reduce oxygen dependency at 28 days through strategy comprising 4 cycles-

- Cycle 1 involved training staff in using LISA
- Cycle 2 implemented this technique
- Cycle 3 introduced delivery room nasal CPAP (DRCPAP)
- Cycle 4 focused on staff training in using video-laryngoscopy

Results: Reduction in delivery room intubation in 27-32 weeks' gestation from 70% to 0% over 4 cycle period. Between 25-27 weeks (about 6 months) rates of delivery room intubation reduced by approximately 30-40%.

Reduction in oxygen dependency at 28 days by 50% in infants between 27-32 weeks gestation Top tips:

- 1. Inclusion of all members of the interdisciplinary team has helped significantly with adoption of practices.
- 2. Stepwise approach to application of the practice changes per gestational age might be more effective.

BPD improvement project from the Trevor Mann Baby Unit, Brighton

Shared by: Ramon Fernandez, Bettina Reulecke, Nikolay Drenchev, Heike Rabe and Cassie Lawn.

Background and aim: 10 years ago, the BPD rate was>40% and established practice was prophylactic intubation, surfactant and ventilation. Unfortunately translating this knowledge into successful practice was not easy as structured guidance including resuscitation algorithms and training had not systematically been widely developed, yet.

Project aim: Development of a preterm respiratory care pathway, primarily focusing on reducing early intubation and surfactant administration through early "aggressive" NCPAP support.

Improvement Plan:

- 1. To review the literature for a wide range of different NCPAP practices and devise a structured algorithm. The algorithm has been shared with the wider neonatal community in Infant Journal (1).
- 2. Introduce regular intensive staff training on the early use of bubble NCPAP as the chosen modality
- 3. Measure improvement using the local database and Badgernet data to identify annual rates of babies intubated, receiving surfactant and ventilated after birth.
- 4. Adjust practice based on additional individual staff feedback, e.g. NCPAP interface care for the prevention of mid-face injuries.

Outcomes

Overall, there was a marked increase in NCPAP days with a reduction of intubation, surfactant and ventilation. The BPD rate dropped to approx. 32% and is currently just below 30% according to VON data. Improvements in BPD rates as a result of our practice were presented and published at the ESPR 2013 (2). The care pathway harmonised our practice, promoting a standardised approach at medical and nursing level.

Top tips for implementation

Unlike mechanical ventilation, successful NCPAP care is highly dependent on the training and expertise of the nursing staff. Inclusion of nurses at all seniority levels is key in providing a high level NCPAP care.

Patience with practice changes, seeing it through, carefully monitoring performance at different levels and adjusting practice in a PDSA style is key to:

- 1. Establish whether a practice change has "truly" led to the desired improvements.
- 2. Establish what needs to be modified to achieve continuous improvement through gradual changes of practice, e.g. introduction of high-flow therapy alongside bNCPAP without radical unjustified changes.

Phase Two: Develop a Shared Purpose

Developing a shared purpose across team or organisational boundaries can be challenging. One of the key components to a successful project is having an implementation team that has representation from all relevant teams and from both hospital and community settings to ensure commonality of language and a philosophy of working toward shared goals.

Engaging your multidisciplinary team

A team that is engaged, resilient, enthusiastic and committed to working together will create the right culture for change.

Teams should ideally be around 6-10 members and include:

- A Project lead (could be from any part of the multidisciplinary team).
- Multidisciplinary representation including a perinatal team, paediatricians, neonatal nurses including pharmacists, physiotherapist, infant feeding team, speech and language therapists, specialist dietitians, occupational therapists.
- Tertiary specialists- Paediatric respiratory team, ENT.
- People with expertise in QI and data analysis.

When forming your team consider:

- Who are the most influential people within the perinatal multi-disciplinary team? these may not be the most senior staff members. Consider inviting those who are unsure or oppositional to understand perspective and secure buy in from the outset. See BAPM Perinatal Teams Toolkit
- What is the culture like amongst members of the perinatal multidisciplinary team? Are maternity and neonatal teams equally invested in the goal of your BPD QI work?
- Where are the areas likely to be affected by any changes do you need to engage staff from outside of your unit team, for example parent advisory groups?
- Why should people want to be involved in your project share your vision and think how you are going to engage people and maintain their commitment?
- What is your expectation of team members what will they be required to do in terms of time and effort?
- How often will you meet?
- When are people available and are your time commitments realistic?
- What else is going on? Are there existing workstreams with overlapping agendas that could be pulled together to prevent duplication. Are there other QI projects which may have to take priority?

Stakeholder engagement

These groups need to be:

1. Prioritised- in terms of the power they have to make your project succeed or fail.

2. Understood- how are they likely to feel or react to the proposed changes?

3. **Informed**- devise a communication plan to sustain interest and win over doubters. This plan should include modalities of communication (e.g. presentations, emails, newsletters), frequency (monthly, weekly, daily) and key messages you want to deliver.

Context

It is a worthwhile activity at this stage to review the context in which you wish to implement your changes. Although the changes you wish to implement have been successful elsewhere, differences in the culture and the context between units may result in variable results.

Phase Three: Plan and Implement Changes

Project Charter

It can be useful to construct a Project Charter at the start of this phase to detail your proposed improvement, including the resources required and the potential benefits to patients. <u>NHS</u> <u>Improvement(12)</u> and <u>NHS Education for Scotland(13)</u> have examples.

Formulate, prioritise and test solutions

There are a number of methodologies that can be adopted to implement a quality improvement strategy. No single quality improvement method is better than others; what matters more is having a consistent approach that you are familiar with and skilled in applying. The Model for Improvement is a widely recognised approach within healthcare and is frequently associated with positive outcomes for improvement and will be used here as an illustration.

The Model for Improvement

Ask yourself:

- What is it you want to achieve?
- How will you know that a change is an improvement?
- What changes can you test that will result in an improvement?

For each change idea, a PDSA cycle can be used:

Plan

- Which intervention(s) to try first? This may be the intervention most likely to make an impact, the easiest to implement or the one that will best address the need felt by the team.
- How will this intervention be introduced into clinical practice?
- Who and what will be required to make this happen?
- Predict what you think the change might be?

Do

 When and how will this plan be carried out? A timescale is useful. Document problems and unexpected observations.

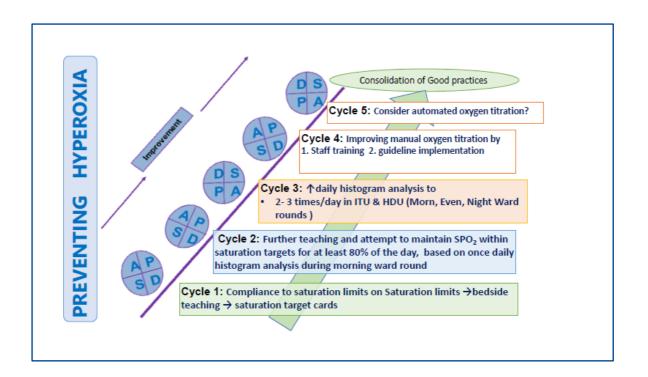
Study

• Use established tools to analyse your data (see Phase 4). Has your change idea resulted in improvement? Is this a real improvement? Does your data suggest your change idea needs modified? Why might this be so? Compare your data to your predictions.

Act

Identify and carry out any modifications needed to this change idea to make it more effective, using further PDSA cycles as needed i.e., Adapt, Adopt or Abandon.

Figure 9. Example PDSA Model



PDSA cycle can be adopted for individual idea changes, or each bundle of intervention adopted by units. The following is a hypothetical example of a PDSA cycle aimed at improving compliance to oxygen saturation targeting.

Phase Four: Test and measure improvement

In this phase, improvements are tested, reviewed and re-tested through a series of PDSA cycles to decide what works and what does not i.e. is the intervention producing the impact that we expected it would?

Data collection

Measuring for improvement is different to the data collected for research or to prove whether clinical interventions work or not. This type of measurement asks the questions 'how do we make it work in our context?' and 'how do we know that a change is an improvement?' It is important that you collect the right data for your project (NSQI 15). In terms of actual metrics, any QI work aimed at reducing incidence of BPD ought to focus on:

- a) Patient outcome measures: reflect the impact on the patient e.g. incidence of BPD in the unit, percentage of infants discharged home on oxygen support. These are the most meaningful of measures and add 'value' to the patient/family as well as the healthcare professional, the organisation and society at large. These, however, generally take time to show effect and require patience and sustained efforts.
- b) Process measures: the way systems and processes work to deliver the desired outcome. These focus on some aspect of the improvement process and could be used for a change idea or primary or secondary driver e.g. percentage of preterm infants who received nooninvasive ventilation in the first week of life, percentage of eligible infants who received LISA. These are useful to make sure that interventions planned as part of the QI efforts are happening to plan (compliance with your change ideas). These are also much easier to measure and usually show an effect much earlier compared to the real outcome measures. If process measures are suggesting improvement, our confidence in a positive patient outcome increase.
- c) Balancing measures: this is what may be happening elsewhere in the system as a result of the change. These focus on the unintended consequences of a QI intervention e.g. rates of extubation failure or incidence of nasal injury might increase with use of more early noninvasive ventilation. These will need to be addressed with locally acceptable interventions to maintain a balance.

Prior to the commencement of any QI work, it is vital to determine how the measures above can be collected. It would be prudent to consider if the measure required is already routinely recorded as part of clinical care within the local unit's electronic patient record system. If so, these data could be extracted directly from the electronic system, avoiding duplication of work.

Data analysis and display

How will any change be measured, assessed and displayed?

Common tools to present and analyse your data include *run charts, statistical process control charts(SPC)*. All require a level of knowledge and skill to collate and interpret correctly. Important measurement should not be a 'before and after' audit which is unreliable in measuring true change, but a continuous process over time during which your interventions/changes are evaluated and modified as appropriate. The information obtained from our measurement processes should be packaged in different ways and communicated in the most appropriate way to parents, nursing and

medical neonatal teams, midwives, maternity support workers, managers, commissioners and so on.

There is growing evidence to highlight that visual display of data within working spaces and discussion about measurements using "huddles" and similar processes is more effective than traditional meetings. All of the options for analysis detailed below are explained in the <u>BAPM QI Made Easy(11)</u> pages ('Interpreting your Data'). For in-depth understanding of run charts and SPC charts please see the <u>NHS Improvement website(14)</u>.

It is important to highlight the value of SPC charts (Figure 10) as a critical tool to 'measure' improvement. It serves well to engage frontline teams in this specific QI work and display it to the relevant teams 'in their face' as this can be very effective in generating meaningful actions and sustained improvement.

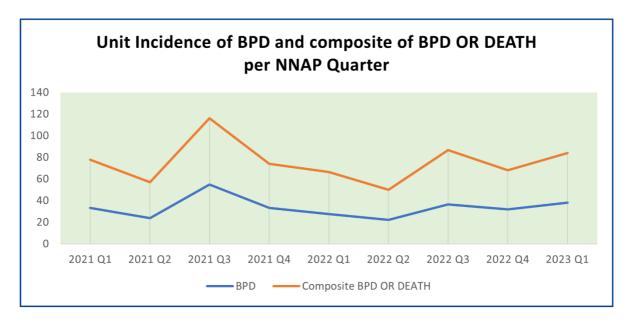


Figure 10: Example of a Run Chart

Phase Five: Implement, Embed and Sustain

This phase involves the wider implementation of improvements such that change becomes embedded in routine practice throughout the system and is sustained with governance arrangements.

Spread

This can involve formal methods such as *dissemination* that includes presentations, publications, leaflets, posters, learning boards, social media, some of which may have limited reach within your department and may be better disseminated via network/LMS meetings and GIRFT benchmarking mechanisms; or informal methods of *diffusion* where word of mouth, champions and opinion leaders can accelerate your message. Consider carefully what is required for the embedding of changes within your service.

Sustainability

The ability of a service to implement and sustain change is dependent on various strengths and weaknesses of any one project. A useful tool to do so is the NHS Sustainability Model (<u>NHS</u> <u>Improvement: Sustainability Model and Guide</u>).

Barriers to sustained improvement

It is not unusual to find the size of a previous improvement lessen over time. It is important to understand why so that solutions can be tailored to the problem. Different approaches will be effective for different people and different situations. The following activities may be useful: talk to key individuals, observe clinical practice in action, use a questionnaire to survey staff, brainstorm with a focus group, use 'improvement huddles'. Education is a key element of overcoming barriers particularly within an interactive forum; using experts to influence others within your staffing structure; reminder systems to prompt clinicians; and ensuring feedback of data to staff in a format that they find useful; all these can help to reinvigorate and embed your changes for improvement (NSQI 2, NSQI 18).

Parental Feedback

Never underestimate the power of patient stories to motivate and reinvigorate a team to implement change. Examples are shown here (with thanks to the parent representatives of this working group).

Emma, mum of identical twins born at 27+4 weeks

"It would really help families if BPD was explained to them - I think the first time we ever realised our babies had BPD was when we saw it on their discharge summaries! & we were like 'what on earth is that?!' It would have been good to understand more about what BPD is, what can cause it, how it can be treated, what short & long-term effects it could have on your baby, etc. Also, I was never 100% sure if BPD & CLD were the same thing, so it would be good to have consistency in the way BPD is talked about.

Thinking about optimum care in regards to BPD, it would also help families if a clear explanation was given as to why certain treatments are given/not given, e.g. surfactant & it would have been useful to understand whether BPD is something that a baby will always have, or whether it's something they can grow out of (I still don't know the answer to this actually!).

I think just ensuring that everything is explained in simple terms, so that we can understand what is happening & how the equipment is supporting our baby, is really helpful. The main thing is having the opportunity to ask questions if we need to & to get clear, simple, timely answers."



Sarah, mum of Summer Davis, born at 25+6 weeks. 110 days in NICU

"We had never heard of BPD until months after Summer was discharged from NICU, we had heard the term chronic lung disease when it was discussed that she needed DART to be extubated regardless of her PJRT (Permanent Junctional Reciprocating Tachycardia) as she had been on the ventilator for such a long time. I was unsure if BPD and chronic lung disease were the same thing. Knowing what we know now would have changed the way we, as parents would have dealt with many aspects of Summers 110 days in NICU.

I wish so much that I had been given some information/advice on what breast pumps are out there. There are so many more options available than I knew at the time. Another point to note is the mention of the psychological effect of BPD on parents. This was not something I had ever considered, however over the last few months it has become clear that there has been an impact on my mental health, which is heightened each time we are admitted for another respiratory issue. Since leaving NICU Summer came home on oxygen and has been admitted multiple times for respiratory viruses including RSV, adenovirus, para influenza, rhinovirus, bronchiolitis etc. An understanding of the psychological impact of BPD on parents prior to leaving NICU may better prepare them for potential issues in the future.

A good time to be given guidance on the lasting effects of BPD would be on leaving NICU. The different methods for oxygen delivery, medications, and anything which can be done at home could assist us with how we manage her BPD.

Finally, from my perspective the main change which would have helped us, and maybe even improved Summer's outcome is knowledge and education. The understanding of terminology, meds, treatments, guidelines and the other information contained in the BAPM document would have armed us with the tools to best advocate for our premature baby. Use of leaflets/posters etc which can be accessed by parents when they are ready, will equip them to work with the healthcare professionals to care for their child."

Special considerations, emerging strategies, and variation in approaches

The current understanding of BPD is continuously evolving due to newer models of pathophysiological process being explored focusing on perinatal inflammation, pulmonary vascular development, and role of oxygen species (15), and with this evolving knowledge there are dynamic changes to clinical practice. This section focuses on certain strategies and care pathways which are not yet based on high quality evidence but have generated discussion and could be potentially considered to be areas of future research and clinical relevance.

Automated Oxygen delivery systems

The principle of using automated or closed loop oxygen delivery (A-FiO2) is based on continuous SpO2 monitoring using pulse oximeter, regular feedback to the machine and changes in FiO2 delivery based on this feedback. A recent survey conducted among 192 UK neonatal unit showed that around 19 neonatal units (9.9%) units used A-FiO2(16). The only definitive conclusion that has been drawn from initial studies is that A-FiO2 maintains a higher percentage of time in the target SPO2 range as compared to manual control, and can reduce time spent in severe hypoxemia, but no high-quality evidence is available on improvement in clinical outcomes(17), (18). When considering the use of automated oxygen delivery systems, careful consideration needs to be taken on what cumulative frequency oxygen saturation curves result (the percentage of time spent at the range of different saturations). Better understanding and or regulation of both oxygen saturation algorithms and automatic oxygen control algorithms based on research is ultimately needed to make them safe.

Early respiratory management of the infants born between 22–23-weeks

In the UK, after publication of the BAPM framework on management of extreme preterm infants (19), infants born between 22-23 weeks gestation are being increasingly offered active survival focused care. There is paucity of high-quality data behind management principles of these infants. However, consensus opinion from clinical experience shared by units with good outcome tends to indicate certain differences could exist in approach to their cardiorespiratory management as compared with other preterm infants born at higher gestational ages (20–22).

- Development of trained dedicated resuscitation team with the most experienced and skilled members leading delivery room management.
- Early intubation due to high incidence of CPAP failure in this age group.
- Adopting a highly lung protective strategy with volume targeting from the very beginning.
- Adopting a more cautious approach towards early extubation to avoid extubation failures.

Use of predictive toolkits for BPD

The interest in an optimal prediction toolkit for BPD risk assessment is not new. It is perhaps important and clinically relevant as an accurate or near-accurate prediction of development of BPD in a preterm infant might help adopt strategies aimed at prevention and help in parental consultations. These prediction tools, such as the web-based BPD estimator developed by the National Institute of Child Health and Human Development (NICHD) (23), may have the potential to identify infants at high risk of BPD who may benefit from targeted treatments such as postnatal dexamethasone. However, these tools have limitations in their analysis and lack external validation in a contemporary, sufficiently large UK cohort of premature infants, predisposing them to bias and

limiting their use in clinical practice (24,25). *Hence, there is insufficient evidence to support the use of any BPD prediction tools in clinical practice at present without further good quality studies to externally validate the BPD prediction tools*.

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Appendix 1. Helpful resources

QI Resources

BAPM Quality Webpages

Specific BAPM resources at <u>www.bapm.org/pages/2-quality</u> Other QI resources at BAPM QI Signpost: <u>www.bapm.org/resources/category/Quality%20Resources</u>

Institute for Healthcare Improvement

http://www.ihi.org/resources/Pages/default.aspx

Maternity and Neonatal Health Safety Collaborative

https://improvement.nhs.uk/resources/maternal-and-neonatal-safety-collaborative/

https://www.england.nhs.uk/wp-content/uploads/2020/08/20190308_Optimisation_v2.1.pdf

BPD resources

Several QI resources aimed at compiling best practice interventions to reduce BPD have been published by regional neonatal organisations/bodies and neonatal centres. Some notable recent publications/ resources are listed below for reference:

- 1. Guideline for the Prevention of Bronchopulmonary Dysplasia and Assessment of Evolving Bronchopulmonary Dysplasia - Toronto center for neonatal neonatal health. https://torontocentreforneonatalhealth.com/respiratory/(26)
- 2. SPSP-MCQIC resources for BPD toolkit. (27)
- 3. AAP –NICHD Prevention of Bronchopulmonary Dysplasia: A Summary of Evidence-Based Strategies. Erik Jansen. Neoreviews (2019). (28)

Appendix 2: Organisational Drivers

1. **National Neonatal Audit Programme** (NNAP) Since 2013 the NNAP has reported on the proportion of babies with gestation at birth less than 32 weeks who are receiving any oxygen or respiratory support at 36 weeks post menstrual age. Since 2015, NNAP has reported on a composite of BPD and death as outcome in addition to BPD as an isolated outcome.

- a. Annual rates of BPD as reported by NNAP have shown an increasing trend as depicted above in Graph 1.
- b. There exists a wide variation between neonatal networks and units for this outcome (33.5% 46%) probably indicating unwanted variations in practice or lack of standardisation and optimisation of care. Analysis taking baseline maternal and baby characteristics into account suggests that being cared for in certain neonatal units might result in a chance of being diagnosed with BPD of approximately 10% higher or lower than their chance of being diagnosed with BPD had they been cared for elsewhere.(29)

2. **NICE** has published a guideline for "Specialist neonatal respiratory care for babies born preterm (NG124) (30) "highlighting risk factors for BPD and providing recommendations around the early respiratory care strategies.

3. **GIRFT (Getting It Right First Time**)- The GIRFT national report for neonatology(31) has, as one its key recommendations, to implement NICE guidelines outlined above for respiratory care in preterm infants. As specific action plans GIRFT recommends:

a) Developing local guidance for preterm infant respiratory support in delivery suites to minimise use of mechanical ventilation.

b) Providing guidance and training in use of minimally invasive techniques for administering surfactant.

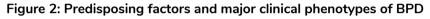
c) Provide guidance and training on use of synchronised volume-targeted ventilation and supporting units to make a business care for procuring ventilation devices which can deliver synchronised volume targeted ventilation.

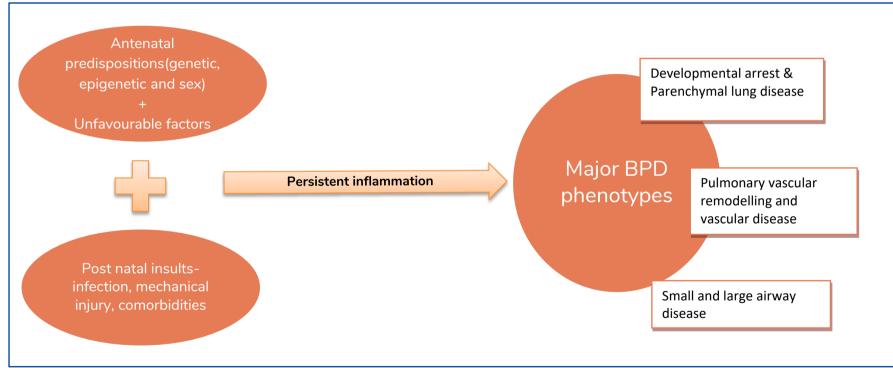
4. The **European Consensus Guidelines on the Management of Respiratory Distress Syndrome** has been updated in 2022 with key recommendations and evidence grading on strategies around optimisation of preterm respiratory support. (32)

5. Scottish Patient Safety Program Maternity and Children Quality Improvement Collaborative (SPSP-MCQIC) (33) has embedded optimal measures for early preterm management in the Preterm Perinatal Wellbeing Package (PPWP)

Appendix 3 - Pathogenesis and risk factors for BPD

The pathobiology of BPD is complex and influenced by various pre and post -natal factors. While inflammation is considered to be the final common pathway, BPD is the clinical expression of developmental plasticity, and a constant process of lung injury and repair (34). A detailed discussion regarding pathogenesis of BPD is beyond the scope of this toolkit, but fig 2 provides a simplistic visual summary of the proposed mechanisms leading to the disease process and its clinical expressions based on current understanding.





The "timeline" in Figure 3 indicates variables that might impact on the process of lung development from preconception through the neonatal course

Figure 3: Respiratory journey in a preterm infant

Conception	Preterm birth Stage of RDS	Stage of evolving lung disease
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Management principle	Perinatal optimi	sation	Minimising lung injury and optimising manag	ement of other organ systems
Positive impact	 Female sex Ethnicity 	 Antenatal steroids(ANS) Appropriate place of birth Optimal delivery room practices Early surfactant for intubated/symptomatic infants 	 Early hydrocortisone Early Caffeine Early CPAP/NIV LISA Volume targeted ventilation Early extubation Exclusive MBM and early enteral nutrition 	 Open lung strategy (keeping lung optimally recruited with appropriate PEEP) Optimal nutritional and metabolic bone status
Negative impact (not necessarily causal)	 Maternal smoking Fetal growth restriction (IUGR) Chorioamnionitis Ethnicity Genetic predisposition 	 Place of birth Incomplete course/ No ANS Hypothermia 	 Sepsis, Ventilator Associated Pneumonia (V. Barotrauma, volutrauma, atelectotrauma a (inflammation generated due mechanical strewall from ventilation) Persistent hemodynamically significant shue Delayed enteral nutrition, poor growth 	nd biotrauma ss at the alveolo-capillary
Modifiable factors which can have positive impact	Using/Adopting optimisation be practices		 Early respiratory practices Early MBM MDT involvement in collaborative management Extubation protocol Expertise/ resource for point of care assessment of PDA 	 PEEP focus MDT involvement in collaborative management, discussion with respiratory team Role of pharmacotherapy- steroids/ diuretics

Appendix 4. Reference and evidence for Core Element 1

Core Element 1. Perinatal Optimisation: Antenatal interventions, delivery room management

Intervention	Evidence summary	Evidence sources
1. Delivery in the optimum location (NICU for <27/40)- with network systems to support and audit of compliance Including ex- utero transfer	 Delivering the preterm infant at an optimal place (Neonatal intensive care unit for GA <27weeks) has not been causally linked to reduction of BPD, but has been reported to have strong positive impact on outcome of survival and major co-morbidities: Reduced risk of death of extreme preterm infants if birth occurs in a high volume, neonatal intensive care setting (35-38) 1 more infant surviving for every 13-20 infants born in tertiary hospital rather than non-tertiary hospital (Helenius et al, 36) Reduction in major morbidities of extreme preterm infants if born in a tertiary centre -2-3 x higher risk of s- IVH/PVH (Helenius et al, 36) 	References: (35)Lasswell et al, 2010 (36) Helenius et al, 2019 (37) Watson et al, 2014 (38) Shah et al, 2020 (39)Foglia et al (40) Boland et al, 2017 (41)Mohamed et al, 2017 (42) Sasaki et al, 2019 (43) Redpath et al, 2017 (43) Redpath et al, 2020 Professional Recommendations: (19) Perinatal Management of Extreme Preterm Birth Before 27 weeks of Gestation (2019). A BAPM Framework for practice- Infants before 27 weeks, less than 28 weeks if multiples, and if estimated fetal weight <800grams should be born in Maternity centre with a co located

 -1.3x higher risk of death (39) 	in Scotland: Scottish Government; 2017 [Available from: https://www.gov.scot/publications/best-start-five-year-forward-plan- maternity-neonatal-care-scotland Recommendation 45: ensure that clear agreements are in place to treat the highest risk preterm babies and the sickest term babies in need of complex care in fewer centres
 Being born in a non-NICU setting +/- transfer is associated with increased risks of mortality, IVH and severe brain injury in extreme preterm infants (<i>36, 40-41</i>) 	 (32)European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update- Mothers at high risk of preterm birth <28–30 weeks of gestation should be transferred to perinatal centres with experience in management of RDS (B1). Standards and Quality Improvement Initiatives: (46)NNAP - 85% of babies born < 27weeks should be born in a maternity service on the same site as a NICU
	(47)European Standards of Care for Newborn Health: Maternal transfer for specialist care: EFCNI, Cetin I, Schlembach D et al; 2018 [Available from: https://newborn-health-standards.org/maternal-transfer/ - Transfer of pregnant women for specialist care (for mother and/or newborn infant) is an essential component of perinatal care and is carried out in a timely, safe and efficient manner
	 (48)Maternity and Neonatal Safety Improvement Program (49)Neonatal Critical Care Quality Dashboard: NHS England; 2019/20 [Available from: https://www.england.nhs.uk/wp- content/uploads/2019/03/nicu-metric-definitions-19-20.pdf. (27)SPSP Maternity and Children Quality Improvement Collaborative (MCQIC) (50)PERIPrem Care Bundle: West of England Academic Health Sciences Network 2020 [Available from: https://www.weahsn.net/our- work/transforming-services-and-systems/periprem/periprem-project/.

2. Antenatal steroids: All women giving birth before 34 weeks of gestation, should receive a full course of antenatal steroids no longer than 7 days prior to birth, and ideally within 24-48 hours.	 There exists strong evidence that ANS accelerates fetal lung maturation and is currently considered a key performance indicator for preterm optimisation in the UK. There is moderate certainty of evidence that treatment with ANS is associated with a reduction in neonatal and perinatal death, RDS (average RR 0.66, 95% CI 0.56 to 0.77) and need for mechanical ventilation (RR 0.68, 95% CI 0.56 to 0.84), no obvious clinical benefit has been demonstrated in reduction of BPD (<i>51-53</i>) 	 References: (51)McGoldrick et at , 2020. (52)Park et al, 2016 (53) Deshmukh et al, 2017 (54)WHO recommendations on interventions to improve preterm birth outcomes France: World Health Organisation; 2015 [Available from: https://apps.who.int/iris/bitstream/handle/10665/183037/9789241508988 _eng.pdf;jsessionid=966E028B4E46B3A246043A64E83F85EC?sequence=1. (55)Preterm Labour and Birth: National Institute for Clinical Excellence; 2019 [Available from: https://www.nice.org.uk/guidance/ng25. (56)Care of Women Presenting with Suspected Preterm Prelabour Rupture of Membranes from 24+0 Weeks of Gestation (Green-top Guideline No. 73): Royal College of Obstetricians & Gynaecologists; 2019 [Available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg73/. (32)European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update Professional Recommendations: WHO, NICE and RCOG: Offer antenatal steroids to women at risk of preterm birth within the next 7d: from 24-33+6w ref 4-6 European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update (32) Offer a single course of prenatal corticosteroids to all women at risk of preterm delivery, from when pregnancy is considered viable up to 34 weeks of gestation. Discuss the use of ANS: NICE: between 23+0-23+6w
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		BAPM: <i>from 22 weeks where active resuscitation is planned</i> European Consensus Guideline on the Management of Respiratory Distress Syndrome, 2022: <i>from when infant is considered viable</i>
		Standards and Quality Improvement Initiatives: (1)NNAP: At least 85% of mothers who give birth 23-33+6w should receive at least one dose of steroids prior to birth (48)MatNeoSIP (49)NHS England Neonatal Critical Care Quality Dashboard (33)MCQIC-SPSP in Scotland. Preterm Perinatal Wellbeing package ref (50)PERIPrem care bundle of the West of England AHSN
management by deferring min clamping by 1 minute red out but sign larg ren	elaying of clamping the cord after birth by 1 hin has been strongly associated with eduction in mortality and the composite utcome of neurological injury or mortality ut has not been shown to have any gnificant effect on comorbidities like BPD in arge cohorts (<i>Lodha et al, 57</i>). This however emains a standard of practice and a strong ecommendation	References: (57)Lodha et al, 2019 Professional Recommendations: (32)European Consensus Guideline on the Management of Respiratory Distress Syndrome, update 2022 (58)European Standards of Care for Newborn Health: Prevention of Bronchopulmonary Dysplasia (BPD)

4.Optimising thermoregulation during delivery room stabilisation and admission	 Maintaining normothermia (36.5-37.5) during preterm stabilisation and admission remains a standard of care. Admission hypothermia is associated with an increased risk of bronchopulmonary dysplasia (59,60) An admission temp of 35-35.9 increased BPD by OR 1.26, and temp of < 35.0 increased risk of BPD by OR 1.81(59,60) 	References: (59) Lee at al, 2019 (60)Costeloe et al, 2000 Professional recommendations: (61)Wyckoff MH, et al. Neonatal life support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. <i>Circulation</i> . 2020- Maintenance of normal temperature is a key initial step in stabilisation of the newborn at birth. (62) Madar J, et al, European Resuscitation Council Guidelines 2021: Newborn resuscitation and support of transition of infants at birth, European Resuscitation Council Guidelines 2021: Newborn resuscitation and support of transition of infants at birth (cprguidelines.eu) The temperature of newborn infants should be maintained between 36.5 ° C and 37.5 ° C. (32) European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update
		Distress Syndrome: 2022 Update Maintain body temperature between 36.5°C and 37.5°C at all times. (48) Maternity and Neonatal Safety Improvement Programme: NHS Improvement; [Available from: NHS England » Maternity and Neonatal Safety Improvement Programme] (49) Neonatal Critical Care Quality Dashboard: NHS England; 2019/20 [Available from: https://www.england.nhs.uk/wp-

		content/uploads/2019/03/nicu-metric-definitions-19-20.pdf. (33) Preterm Perinatal Wellbeing Package: Maternity and Children Quality Improvement Collaborative, Scottish Patient Safety Programme. Health Improvement Scotland; [Available from: https://ihub.scot/media/5311/20180808-preterm-web.pdf] (50)PERIPrem Care Bundle: West of England Academic Health Sciences Network 2020 [Available from: https://www.weahsn.net/our- work/transforming-services-and-systems/periprem/periprem-project/.
5.Use of delivery room CPAP to aid non-invasive respiratory transition (where appropriate) rather than endotracheal intubation)	 Recent Cochrane meta-analysis (Subramaniam et al, 68) – prophylactic or very early CPAP reduced incidence of BPD at 36 weeks as compared to mechanical ventilation (RR 0.89, 95% CI 0.8 to 0.99; RD -0.04, 95% CI -0.08 to 0.00; 3 studies, 2150 infants; moderate certainty evidence); and death or BPD (RR 0.89, 95% CI 0.81 to 0.97; RD -0.05, 95% CI -0.09 to 0.01; 3 studies, 2358 infants; moderate certainty evidence). One additional infant could survive to 36 weeks without bronchopulmonary dysplasia for every 20-35 babies treated with CPAP in the delivery room rather than being intubated (Schmolzer et al, 67). 	References:(63)Morley CJ, et al COIN trial group(64) Finer NN, et al, SUPPORT study group(65) Dunn MS, et al, VON DRM study group(66) Fischer HS et al, 2013(67) Schmolzer M, et al, 2014(68) Subramaniam P, et al, Cochrane Rev. 2016;(69)Bamat et al, Cochrane rev 2021(39) Foglia E.E, Jensen E.A, Kirpalani H, State of the Art Review: Delivery room interventions to prevent bronchopulmonary dysplasia in extremely preterm infants, Perinatol. 2017 November ; 37(11): 1171–1179. doi:10.1038/jp.2017.74.(30) NICE Guideline [NG124]-Specialist neonatal respiratory care for babies born preterm- https://www.nice.org.uk/guidance/ng124/resources/specialist-neonatal- respiratory-care-for-babies-born-preterm-pdf-66141658884805(32) Sweet D.G, Carnielli V.P, Greisen G, European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update (70) Ng EH, Shah V. Guidelines for surfactant replacement therapy in neonates. Paediatr Child Health. 2021

 There is insufficient data as of now to guide the safe range of PEEP that can be used for delivery room CPAP. A recent Cochrane review (Bamat et al, 2021) did not find a difference between "low (< or equal to 5 cmH2O) vs moderate-high (>5 cm H2O) in the outcome of death or BPD (Bamat et al, 69). 	 (71)COMMITTEE ON FETUS AND NEWBORN. Respiratory support in preterm infants at birth. Pediatrics. 2014; 133:171–4. [PubMed: 24379228] (33) MCQIC BPD Webinar (ihub.scot) (72) Kaempf J, et al, 2020 Professional Recommendations: (30)NICE Guideline [NG124]-Specialist neonatal respiratory care for babies born preterm: When stabilising preterm babies who need respiratory support soon after birth and before admission to the neonatal unit, use continuous positive airways pressure (CPAP) where clinically appropriate, rather than invasive ventilation. (32)European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update Spontaneously breathing preterm infants should be stabilised using CPAP (A1). Intubation should be reserved for babies not responding to positive pressure ventilation via face mask or nasal prongs (A1) (71) Using CPAP immediately after birth with subsequent selective surfactant administration may be considered as an alternative to routine intubation with prophylactic or early surfactant administration in preterm infants (Level of Evidence: 1, Strong Recommendation) (70)Canadian Paediatric Society Position statement: Guidelines for surfactant replacement therapy in neonates: Non-invasive respiratory support (e.g., CPAP) should be provided to preterm infants with RDS from

		birth. (Grade B) Standards and Quality Improvement Initiatives: (30) NICE Guideline [NG124]-Specialist neonatal respiratory care for babies born preterm. Quality standard [QS193] <i>Quality statement 1: Respiratory support soon after birth after birth-</i> <i>Preterm babies having respiratory support soon after birth and before</i> <i>admission to the neonatal unit are given continuous positive airways</i> <i>pressure (CPAP), if clinically appropriate, rather than invasive ventilation.</i>
		(33)Scottish MCQIC BPD standards (MCQIC BPD Webinar (ihub.scot))
LISA (where appropriate)	Please see below	

Appendix 5. Reference and evidence for Core Element 2

Core element 2. Early Respiratory Support: Ventilation modes, non-invasive ventilation strategies

Intervention	Evidence summary	Evidence Source
Early surfactant administration (LISA vs Insure vs LMA vs old school)	 Meta-analyses show reduced rates of BPD where LISA is used compared to Nasal CPAP or other modes of surfactant administration (Isayama et al, 73). Though there has been 17 trials comparing LISA to other modes of surfactant administration, only 2 included infants < 25 weeks. (Kakkilaya et al, 75). A recent Cochrane review (Abdel-Latif et al, 76) concluded that compared to ETT surfactant, LISA decreased death or BPD (RR 0.59, 95% CI 0.48–0.73), BPD (RR 0.57, 95% CI 0.45–0.74, number need to treat for benefit [NNTB] 13, 95% CI 9–24) and the need for MV within 72 HOL (RR 0.63, 95% CI 0.54– 0.74, NNTB 8, 95% CI 6–12). LISA also decreased mortality and severe intracranial hemorrhage (RR 0.63, 95% CI 0.42–0.96, NNTB 22, 95% 	References:(73)Isayama et al 2016(39)Foglia et al(74)Aldana-Aguirre et al-2015(75)Kakkilaya et al, 2022(76)Abdel-Latif et al, 2021(32)Sweet D.G, Carnielli V.P, Greisen G, European Consensus Guidelines on theManagement of Respiratory Distress Syndrome: 2022 Update (karger.com)(77)Cummins et al, 2020(30)NICE Guideline [NG124]-Specialist neonatal respiratory care for babiesborn preterm- https://www.nice.org.uk/guidance/ng124/resources/specialist-neonatal-respiratory-care-for-babies-born-preterm-pdf-66141658884805(70) Ng EH, Shah V. Guidelines for surfactant replacement therapy in neonates.Paediatr Child Health. 2021 Feb 1;26(1):35-49. doi: 10.1093/pch/pxaa116.PMID: 33552321; PMCID: PMC7850281.(71)COMMITTEE ON FETUS AND NEWBORN. Respiratory support in preterminfants at birth. Pediatrics. 2014; 133:171-4. [PubMed: 24379228](30) NICE: Specialist neonatal respiratory care for babies born pretermQuality standard [QS193] Quality statement 2-Quality statement 2: Minimallyinvasive administration of surfactant Specialist neonatal respiratory care forbabies born preterm Quality standards NICE(33)MCQIC BPD Webinar (ihub.scot)Professional Recommendations AND Quality Improvement Standards:(32)European RDS Guidelines update- LISA is the preferred method of

(RR 95% 74) 3.Ea	arly rescue surfactant treatment	surfactant administration for spontaneously breathing babies on CPAP (30)NICE Guideline [NG124]- When giving surfactant to a preterm baby who does not need invasive ventilation, use a minimally invasive administration technique.
dec	hours of age) in infants with RDS creases the risk of mortality, air k, and chronic lung disease in eterm infants NNT 16 <i>(Foglia et al,</i>)	(70)Canadian Paediatric Society Position statement: Guidelines for surfactant replacement therapy in neonates: For spontaneously breathing infants on CPAP with RDS, non-invasive methods of surfactant administration, such as LISA or MIST, are preferable
the (37) pre of t con (Ka 5.A mad (Cu larg	ISA compared with INSURE reduced e risk of BPD/death with NNTB 12 ?), however only 1 trial included eterm infants <25 weeks and none the trials were powered for a mposite outcome of death or BPD <i>akkilaya et al, 75</i>) werosolised surfactant delivery has ade a resurgence in recent years. Immins et al, 80 reported the gest RCT of 457 preterm and term ants comparing aerosolised	American Academy of Pediatrics Committee on Fetus and Newborn subsequently policy statement 2014 - Respiratory Support in Preterm Infants at Birth: Surfactant replacement, given as prophylaxis or rescue treatment, reduces the incidence of RDS, air leaks, and mortality in preterm infants with RDS (level of evidence [LOE] 1) Early rescue surfactant treatment (<2 hours of age) in infants with RDS decreases the risk of mortality, air leak, and chronic lung disease in preterm infants (LOE 1). Standards and Quality Improvement Initiatives: (30)NICE Specialist neonatal respiratory care for babies born preterm-Quality
calf rep at 4 0.4	factant with CPAP alone and ported a reduction in intubation rate 4 days of life (RR: 0.51 (90% CI: 1–0.63)). Other feasibility studies ve been reported.	 Standard statement 2: Preterm babies who need surfactant are given it using a minimally invasive technique if they do not need invasive ventilation (47) The European Standards of Care for Newborn Health ref 9: Prevention of Bronchopulmonary Dysplasia (BPD) Surfactant is administered via a thin intra-tracheal catheter if FiO2 is >0.30 or using INSURE (intubation surfactant and extubation).

		(33)Scottish MCQIC BPD standard (MCQIC BPD Webinar (ihub.scot))
Volume targeted ventilation as the preferred mode of ventilation if invasive ventilation is required	Volume targeted ventilation as opposed to pressure limited ventilation reduces death or bronchopulmonary dysplasia by 27%, NNT 8 and Intraventricular haemorrhage (grades 3–4) by 47%, NNT 11 compared with pressure- limited ventilation. <i>(78-79)</i>	References: (78)Klingenberg et al, Cochrane Rev 2017 (79)Peng et al, 2014 (32) European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 (58) Poets et al, European Standards of Care for Newborn Health: Prevention of Bronchopulmonary Dysplasia (BPD (50)PERIPrem Care Bundle: West of England Academic Health Sciences Network 2020 [Available from: https://www.weahsn.net/our- work/transforming-services-and-systems/periprem/periprem-project/. (33)MCQIC BPD Webinar (ihub.scot) Professional Recommendations And Quality Improvement Initiatives: (30)NICE Guideline [NG124]-Specialist neonatal respiratory care for babies born preterm: For preterm babies who need invasive ventilation, use volume-targeted ventilation (VTV) in combination with synchronised ventilation as the primary mode of respiratory support. (32)European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update: DOI: 10.1159/000528914 Lung-protective modes such as VTV or high-frequency oscillation ventilation should be the first choice for babies with RDS who require MV Standards and Quality Improvement Initiatives: (47)The European Standards of Care for Newborn Health: Volume targeted ventilation (at 5-7 ml/kg) is used plus adequate PEEP level, if intubation cannot be avoided.

		 (30) NICE Guideline [NG124]-Specialist neonatal respiratory care for babies born preterm -Quality Standard statement 3: <i>Preterm babies having invasive ventilation are given volume-targeted</i> <i>ventilation (VTV) in combination with synchronised ventilation.</i> (50)PERIPrem care bundle of the West of England AHSN (33)Scottish MCQIC BPD standards (MCQIC BPD Webinar (ihub.scot))
Use of HFOV as primary mode of respiratory support in preterm infants	 High frequency ventilation applied with an open lung strategy as primary respiratory support is being increasingly used, especially in the infants born between 22-24 weeks(<i>Norman et al</i>, 80) Cochrane review reported a significant decrease in chronic lung disease among survivors at 36-37 weeks (RR 0.86, 95% CI 0.78 to 0.96; summary RD - 0.05, 95% CI -0.08 to -0.02; NNTB 20, 95% CI 12 to 50). But there was significant heterogeneity and using random effects model the benefit was borderline significant (<i>Cools et al</i>, 81) Use of Volume targeting with 	References: (80)Norman et al, 2022 (81)Cools et al, Cochrane Rev 2015 (82)Tuzun et al, 2020 (83)Iscan et al 2015

	HFO has been studied in small crossover RCTs and observational and feasibility studies. The only benefit that can be inferred from these is a possible tighter control of PCO2 and avoidance of fluctuations in CO2. This physiological principle might be considered beneficial for extreme preterm infants (82- 83)	
Use of non-invasive modalities as primary mode of respiratory support OR post-extubation support in preterm infants with RDS (NCPAP/HFNC, NS-NIPPV, S- NIPPV, NHFOV, NAVA)	certainty evidence CochraneDistress Syndro2021(Subramaniam et al, 68)(47) Preventior	al, 2020 al, 2021 et al, 2001 al Consensus Guidelines on the Management of Respiratory ome: 2022 Update of Bronchopulmonary Dysplasia (BPD) - EFCNI - European are for Newborn Health (newborn-health-standards.org) 2019
	pressures of <8 cmH20 (Kidman et al, 88) (CPAP or (s)NIPH	. 2022 ecommendations: Consensus Guidelines on the Management of Respiratory ndrome: 2022 Update PV should be started from birth in all babies at risk of RDS, such eeks of gestation who do not need intubation for stabilisation

(HFNT) is non-inferior to CPAP in prevention of reintubation and incidence of BPD and can be considered as an alternative to CPAP for primary or post- extubation respiratory support and may lead to a reduction in nasal trauma (Ramaswamy et al, 85)	 (A1) Ability to escalate to NIPPV will reduce the need for invasive MV in some infants (A1). Standards and Quality Improvement Initiatives: 2. The European Standards of Care for Newborn Health: Infants on n-CPAP are switched to synchronised nasal ventilation if respiratory distress visible while on CPAP
 The use of NIPPV(synchronised or non synchronised) for primary respiratory support compared to NCPAP has been shown to reduce BPD in one SR-MA (Solevag et al, 86) but included RCTs targeted GA 28- 34weeks only and level of evidence was moderate to low. 	
 5. When compared to Variable flow CPAP, synchronised and non-synchronised NIPPV reduces reintubation rates significantly (RR] [95% CrI]: 0.22[0.12, 0.35] and 0.44 [0.27, 0.67] respectively) with s-NIPPV being superior. (Ramaswamy et al, 85) 6. NIPPV as an intervention can 	

	reduce extubation failures by 30% when compared to CPAP, NNT -8 <i>(Ferguson et al, 84)</i>
	7. NIV-NAVA and NHFOV are interesting new modes of non invasive ventilation and might be superior as post extubation support but only preliminary clinical data are available and these modalities are still not widely adopted across UK(89,90,91).
	1. Permissive hypercapnia as a ventilatory strategy has been practiced for a long time but has not been validated in literature, nor has the safe upper limit of PCO2 been References: (92)Carlo et al, 2022 (93)Thome et al, 2015 (93)Thome et al, 2015 (93)Thome et al, 2022 (95)Thome et al, 2017 (95)Thome et al, 2017
Acceptance of permissive	defined. (30) NICE Guideline [NG124]-Specialist neonatal respiratory care for babies
hypercarbia	2. A recent multicentre randomised trial comparing higher permissive hypercapnia (max PCO2 10 kpa) to moderate hypercarbia max PCO2 8 Kpa) did not find anyborn preterm (32) European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update (72)Kaempf et al, 2021 (96)Ambalavan et al
	difference between incidence Professional Recommendations: of BPD in these groups (Thome
	et al, 93) (32)European Consensus Guidelines on the Management of Respiratory
	3. Follow up of the same patient Distress Syndrome: 2022 Update:
	cohort concluded that a higher <i>Permissive hypercapnia will potentially allow reduced tidal volumes and</i>

	 mortality, IVH and BPD with permissive hypercapnia (Wong et al, 94) 5. Secondary exploratory data analysis of Surfactant, Positive Pressure, and Oxygenation Randomised Trial (SUPPORT) reported higher PCO2 to be 	
	 independently associated with adverse outcomes of IVH, BPD and mortality. (Ambalavan et al 96). 6. Given the evidence a modest degree of hypercarbia can be used at clinicians' discretion to aid extubation but higher limits of PCO2 cannot be nowing hypercarbia degree of an and be used at clinicians' discretion to aid extubation but higher limits of PCO2 cannot be nowing hypercarbia degree of a section and be now the adverse of adverse of adverse of adverse of a section and be now the adverse of adve	
Use of extubation criteria to aid weaning and early extubation	routinely recommended Minimising time on mechanical ventilation partly through use of strict	References: (97)Levesque et al, 2011
weaning and early extubation in mechanically ventilated infants	extubation partly through use of strict extubation criteria has been shown to reduce BPD in a range of studies, also when included in quality improvement	(72)Kaempf et al, 2021

initatives has helped reduce BPD. (97,72)	4. Vermont Oxford Network (VON) neonatal intensive care units (NICUs) (the POD) Ref
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Appendix 6. Reference and evidence for Core Element 3

Core Element 3. Optimisation of other organ systems

Nutrition

There is a large body of literature describing the role of growth and nutrition in the prevention of BPD, including several recent reviews, however there are few RCT's specifically looking at nutrition and BPD as an outcome. Nutritional requirements during the process of evolving lung disease in a preterm infant is complicated by many factors including increased work of breathing, hypermetabolic states and inflammation, leading to a catabolic state. This is often worsened by use of diuretics and steroids. Therefore, there is a very strong basis for recommending that established recommended nutrient intakes are met for all infants.

We recommend (in the absence of evidence to the contrary) that:

1. Recommended intakes of macronutrients, minerals and vitamins are met

2. Strong efforts are made to optimise intakes of maternal expressed breastmilk to support lung growth, development, function, and repair.

There is no evidence from RCTs that provision of nutritional support for infants at risk of developing BPD fundamentally differs from those without lung disease. The aim therefore would be to meet recommended energy and protein requirements in the first few weeks after birth as early nutritional deficiencies may be associated with adverse outcomes.

Assessment of nutrition should include review of anthropometric and biochemical data, clinical status, medication exposure and estimated nutritional requirements. Individualised nutritional support with close monitoring should be considered at least weekly, ideally with a dietitian familiar with this population embedded within the wider MDT.

Intervention/strategy	Evidence	Evidence sources
Adopting an early Nutrition focus during clinical rounds	 Aim to meet recommended parenteral and enteral intakes of macronutrients, minerals and vitamins with early optimised parenteral nutrition and early 	Neonatal parenteral nutrition NICE guideline Published: 26 February 2020 www.nice.org.uk/guidance/ng154

 feeding with human milk (preferably fortified). Calorie and protein intake- The optimal calorie and 	(98) 2022 Enteral Nutrition In Preterm Infants:
· · ·	
protein intake for infants at risk of BPD is yet to be	ESPGHAN Position Paper
definitively defined. Adequate protein intake is	
needed for the promotion of linear growth, lung	(99) Miller et al, 2023
growth, and for the repair of damaged tissue. We	
recommend enteral intake within the range of 115-	(100)Rocha et al, 2021
160 kcal/kg/d and protein intakes 3.5 to 4g/kg/day as	
per ESPGHAN 2022 guidelines.	(101)Karatza et al, 2022
3. Recommended daily requirements should be met.	
There is little data to suggest giving higher intakes	(102)Fang et al, 2021
(above recommended) is beneficial.	
4. Vitamin A- vitamin A is crucial for respiratory	(103)Jiang et al, 2022
epithelial cells, cellular differentiation and surfactant	
production and vitamin A levels have been found to	(104)Phattraprayoon et al, 2022
be lower in subjects developing BPD (Hustead et al).	
However, based on the current available evidence	(72)Kaempf et al, 2021
routine enteral or intramuscular Vitamin A	
supplementation in high doses cannot be	
recommended to reduce incidence of BPD.	
5. Monitoring of growth via anthropometric	
measurements should include weight, head	
circumference and length for assessment of linear	
growth.	

Early introduction of exclusive Breast milk	 Exclusive feeding of maternal expressed breast milk (EBM) has been shown to reduce incidence of BPD (105)BAPM MBM toolkit
	and should be strongly encouraged and recommended (105,106, 107)(106)Villamor- Martinez et al, 2019
	2. In absence of mother's own milk (MOM), donor breast milk (DBM) has been shown to reduce(107)Kim et al, 2019
	incidence of BPD and days on mechanical ventilation (108) Villamor-Martinez et al, 2018 when compared to preterm formula and should be
	recommended as the alternative to MOM (<i>Villamor-</i> (109)Arslanoglu et al, 2019 Martinez et al, 108)
	 Fortification of breast milk is recommended unless contraindicated as MOM or DBM does not provide sufficient nutrition for the very low birth weight (110) Hendrickson K et al, 2017
	(VLBW) infant when fed at the usual feeding volumes leading to slow growth with the risk of (32)European Consensus Guidelines on the
	bronchopulmonary dysplasia (<i>Arslanoglu et al,</i> 109) 4. Preterm formula should only be considered when Update
	MOM is unavailable and DBM has been declined. But Enteral feeding with mother's milk should be started
	caution is advised, especially among ELBW infants, due to concern for increased risks of NEC, increased duration of TPN, and increased rates of sepsis in infants receiving preterm formulas as their sole or primary enteral feeding. (Hendrickson et al, 110)from the first day if the baby is hemodynamically stable (B2).

Monitoring of bone health in infants on full enteral nutrition	Bronchopulmonary dysplasia (BPD) infants present an increased risk and incidence of metabolic bone disease (MBD).	(111)ESPGHAN/ESPEN/ESPR/CSPEN guidelines on paediatric parenteral nutrition: (112)Bozzetti et al, 2009
	Aim to meet recommended intakes for minerals including calcium, PO4 and also vitamin D and macronutrients to optimise management and reduce risk of BPD. The typical biochemical picture of MBD includes normal serum calcium, low serum phosphorus, and high serum alkaline phosphatase and high Parathyroid hormone concentrations.	(113)Chinoy et al, 2019

Cardiovascular and fluid management principles

Fluid management- Liberal vs restricted fluid approach debate

Early studies by Bell et al (1998) had reported a non-significant trend in reduction of BPD with a restricted fluid approach in early preterm life. However, this approach has often been empirically adopted with the aim of reducing the incidence of BPD, often the rationality being extrapolated from use of diuretics in later life. This practice does not appear to be based on strong evidence.

There exists a controversy regarding risk-benefit analysis of early targeted management of the hemodynamically significant PDA. Although observational cohort studies have independently reported causal relationship between PDA and BPD, this has not been evidenced by any RCT till date. A detailed discussion of this area is not in the scope of this toolkit.

Intervention/strategy	Evidence	Evidence sources
Monitoring fluid balance and titration according to electrolyte status and weight	 There is no high-quality evidence to suggest fluid restriction as an intervention for early preterm management or established BPD. 1. Empirical fluid restriction in the preterm infants can lead to nutritional restriction, reduction in systemic blood flow and early renal compromise and CANNOT be recommended (115,116) 2. Recent evidence from single centre studies indicates that rather than absolute volume of fluid administered, the cumulative fluid balance (CFB) after 1 week of life might have some bearing on respiratory outcome with positive balance being possibly associated with adverse outcome. (Sharma et al, 116) 3. Allowing for 6-15% weight loss and maintaining a sodium level in the lower end of normal range can be 	(114)Barrington et al, 2017 (115)Abbas et al, 2019 (116)Sharma et al, 2021
	considered (Sharma et al, 116)	

	Based	on current evidence:	
	1.	Routine management of PDA CANNOT be	
Management principles of PDA		recommended for reducing BPD.	(117)Clyman et al, 2022
	2.	Early targeted approach towards the	
		hemodynamically significant PDA (defined by	(118)Giesinger et al, 2023
		predefined echocardiographic criteria and clinical	
		factors) specially in gestational ages lower than 26	(119) Mirza et al, 2019
		weeks might be pragmatic (Giesinger et al, 120,	
		Liebowitz et al, 122)	(120)Clyman et al, 2020
		➢ No RCT till date has demonstrated significant	
		causal association with PDA and BPD as an outcome.	(121)Clyman et al, 2021 (secondary analysis of
		Observational studies have reported higher incidence of BPD in preterm infants who have been	PDA-TOLERATE)
		exposed to moderate-large shunts of PDA over a	
		prolonged period of time. (Clyman et al , 117, 120)	(122)Liebowitz et al, 2019
		BPD might be higher in population with prolonged	
		exposure to a significant shunt for a period >11-14	(123)Villamor et al, 2023
		days along with mechanical ventilation for a period of	
		>10 days (Clyman et al, 121)	
	3.	There is moderate certainty of evidence that	
		prolonged exposure to a hemodynamically signifcant	
		PDA might be associated with an increased risk of	
		pulmnary vascular disease in extremely premature	
		infants (Villamor et al, 123).	

Late onset neonatal sepsis as a risk factor of BPD

Inflammation as a final common pathway for BPD has been well established. It has recently been understood that post-natal sepsis, specifically culture positive sepsis increases odds of incidence of BPD in preterm infants significantly.

Late onset neonatal sepsis	 There was 1.5 - 3 times increased odds of BPD associated with post-natal sepsis as reported in a large cohort of infants between 25-28 weeks gestation in the Korean neonatal network (124)Kim S et al, 2020 	
	 Occurrence of BPD was 2.6 times more likely increased with presence of Coagulase negative sepsis (CoNS) and 1.7 times more likely with sepsis (125)Liljedahl M et al, 2004 	
	 Interventions aimed at reducing in the incidence of nosocomial infections led to reduction in incidence of BPD (126)Lapcharoensap W et al, 2017 	

Appendix 7. Reference and evidence for Core Element 4

Core element 4. Pharmacological adjuncts

Intervention/strategy	Evidence	Evidence sources
Target oxygen saturation target 91-95	 Target oxygen saturation, which is recommended for preterm infants requiring supplemental oxygen beyond the stabilisation period is between 91 - 95%. The lower oxygen saturation target of 85% - 89% was associated with a 17% higher risk of death and 33% higher risk of severe necrotising enterocolitis (than the higher saturation target of 91 - 95% as reported in the NeoPROM meta-analysis. 	(32)European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update (127) Askie et al, 2018
Early use of Caffeine citrate	Babies born at or below 30 weeks of gestational age should receive caffeine citrate as early as possible and ideally before 3 days of age. Caffeine citrate reduced the incidence of BPD (a OR 0.63(0.52-0.76), cerebral palsy at 18 to 21 months' follow up.	(128) Schmidt et al, 2006
Use of Postnatal corticosteroids	For the purposes of this section we shall consider hydrocortisone and Dexamethasone – as they are the most commonly used steroid preparations for prevention of BPD.	
	<u>Consider</u> the use of early low-dose prophylactic hydrocortisone, when not associated with indomethacin and systemic steroids, on preterm infants born below 28 weeks of gestation on day 1 of	

	life.	
Early Hydrocortisone	 Early hydrocortisone reduces the risk of combined outcome of mortality and BPD by 10% (95% Cl 1% - 18%) and increases the odds of survival without BPD by 45% (95% Cl 11% - 90%) (Doyle et al, Cochrane,2021), (130). Early hydrocortisone has no effect on cerebral palsy (Risk ratio (RR) 1.05, 95% Cl 0.66 - 1.66). (Doyle et al, 2021 (130)) Early hydrocortisone increases the risk of gastrointestinal perforation by two times (RR 2.05, 95% Cl 1.21 - 3.47) (130), especially when given in association with indomethacin exposure with 2.5 times increase in the odds of gastrointestinal 	(129)Lemyre et al, 2020
	 perforation (OR 2.50, 95% CI 1.33-4.69) (Shaffer et al, 131) 4. The commonest used regime for early hydrocortisone is based on the PREMILOC trial (Baud et al, 133) 	(130) Doyle et al, 2021
Dexamethasone use after 1 st week of life	NB: The effectiveness of Hct in reducing BPD among the most premature of infants has not been adequately tested. The mean GA for the meta-analysis (Shaffer et al) in the Hydrocortisone group was 26.1 weeks and the largest RCT included in that (PREMILOC) did not include infants <24 weeks.	(131)Shaffer et al, 2019

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	<u>Consider</u> the use of dexamethasone, when not associated with non-steroidal anti-inflammatory drugs, in preterm infants at high risk of BPD who are 8 days or older and still need invasive ventilation. Routine use of dexamethasone is not recommended.	(132)Doyle et al 2021
	 Dexamethasone use from 7 days old probably reduces the risk of combined outcome of mortality or BPD by 25% (95% Cl 16% - 33%). (Doyle et al, Cochrane rev 2021, (130)). Dexamethasone use from 7 days old has not been shown to increase risk of cerebral palsy (RR 1.17, 95% Cl 0.84 - 1.61). NB: It is 	(133)Baud et al, 2016
	anticipated that cerebral palsy affects 135 infants who received dexamethasone (95% Cl 95 to 193) per 1,000 infants.	(30)NICE 2019 ⁶
Late use of Inhaled corticosteroids	 3. Moderately early-initiated (8-14 days), medium cumulative dose (2-4mg/kg) dexamethasone, moderately early-initiated (8-14 days), high cumulative dose (>4mg/kg) dexamethasone and late-initiated (15-27 days), high cumulative dose (>4mg/kg) dexamethasone were the top three most beneficial intervention in reducing the risk of BPD and death (RR ranging 0.61 - 0.70) (Ramaswamy et al, (134) 	(https://www.nice.org.uk/guidance/NG12), (129)Lemyre et al2020
	Based on currently available evidence use of late (>7days) inhaled corticosteroids cannot be routinely recommended. Very low quality evidence exists possibly indicating that late use of inhaled corticosteroids MIGHT reduce use of systemic steroids and reduce extubation failure rate (RR 0.51, 95% CI	(134)Ramaswamy et al, 2021

	0.26 to 1.00; RD –0.22, 95% CI –0.42 to –0.02; NNTB 5) (Onland et al, 135)	(135)Onland et al, 2022
Prudent trial of Diuretics	 Routine use of Diuretics cannot be recommended for prevention of BPD as there is no data from RCTs or systematic reviews to suggest any benefit. Very low-grade evidence suggests that use of diuretics in selected patient cohorts with radiological/ clinical evidence of pulmonary oedema can be considered for short-term improvements in pulmonary mechanics. Short term decrease in airway resistance and increase in airway compliance with furosemide in infants with BPD. May improve respiratory scores, lung mechanics, and decrease fraction of inspired oxygen. 	(136)Stewart et al, Cochrane Database Rev 2011 (137)Michael et al 2018 (138)Iyengar et al, 2015

Appendix 8. Reference and evidence for Core Element 5

Core element 5. Multi-disciplinary team input

Intervention	Evidence	Evidence sources
Early involvement and continued collaboration of interdisciplinary care teams	 The early involvement and collaboration of key professions in the care plan/management plan enhances clinical effectiveness, impacts on length of stay, enhances therapeutic interventions, helps avoid complications and improves longer term neurodevelopmental outcomes. Interdisciplinary care teams have the potential to alleviate many of the issues associated with BPD, and improve outcomes for these infants 	References:(139)NHS England, Implementing the Recommendations of the Neonatal Critical Care Transformation Review(31)Neonatal GRIFT Programme national speciality report: https://future.nhs.uk/system/login?nextURL=%2 Fconnect%2Eti%2FGIRFTNational%2Fview%3Fobj ectId%3D130557829(140)Abman SH, et al. 2017Professional Recommendations:
		Standards and Quality Improvement Initiatives: 5. https://www.bapm.org/resources/service-

		 and-quality-standards-for-provision-of- neonatal-care-in-the-uk British Dietetic Association (BDA) dietetic staffing recommendations for neonatal units; <u>https://www.bda.uk.com/uploads/assets/ab</u> <u>614d3e-e095-4e4f-</u> <u>96ae1458204e8810/391a27be-69a0-4b43-</u> <u>a52d54a731da7f01/BDA-Formatted-Staffing- Recc.pdf</u>
Weekly nutrition focused ward rounds supported by a dietitian	Nutrition focused ward rounds and required titrations in nutrition should be considered at least weekly in concert with a dietitian familiar with this population.	 (72)Kaempf J, 2017 (141)British Dietetic Association (BDA) dietetic staffing recommendations for neonatal units (endorsed by BAPM) Standards and Quality Improvement Initiatives: Vermont Oxford Network (VON) neonatal intensive care units (NICUs) (the POD)
Support from experienced neonatal physiotherapy team (if available) should be sought for collaborative management of the ventilated infant	Neonatal chest physiotherapy is a highly specialised area of respiratory care. Whilst there is some evidence for the use of certain physiotherapy interventions (such as positioning -ref Hough et al 2014 and Loi et al 2022), this should be undertaken only by those with requisite experience, knowledge and competence. Till date the only clinical outcome that has been shown to have significantly improved with physiotherapy is post- extubation atelectasis (PEA). Support from experienced physiotherapists for infants struggling to wean from	 (142)APCP (Association of Paediatric Chartered Physiotherapists) Guidance for Good Practice for Physiotherapists Working in Neonatal Care (143)Gardner, D. et al (144)Gonçalves, R et al (145)Hough, J.et al

ventilation may standardise and optimise the collaborative weaning process. Interventions which might have some improvement impact outcomes on pathologies like atelectasis and retained secretions include:	(146)Loi, B.et al (147)Luca, D. D. <i>et al.</i> (148)Morrow, B. M. et al
 Positioning (145,146) Optimising humidification Ensure best practice suction techniques (143,144,148). Percussion and/or vibrations – these are avoided in infants <1500 grams in first week to minimise risk of IVH. When used, percussions should be of moderated vigour and maintaining physiological stability should be paramount. Mucoactives (N acetyl cysteine, DNAse) (Luca et al, 147) 	 Professional Recommendations: TOOLKIT FOR HIGH-QUALITY NEONATAL SERVICES 2013: All units caring for babies requiring intensive care and providing a chest clearance service have access to a paediatric respiratory physiotherapist with experience in assessing and treating premature and sick newborn babies.
N.B: Very little evidence supports the use of physiotherapy techniques, therefore detailed understanding of the literature and professional consensus is required in order to apply treatment techniques judiciously and safely to preterm infants, which differ in vulnerability and physiology from their term counterparts. The Physiotherapist is referred to the APCP Guidance for Good Practice for further information.	

Support from experienced Speech and Language therapy (SALT) team should be sought for risk assessment for oral feeding on respiratory support.	Consideration should be given for use of risk assessment for oral feeding on respiratory support/HHFNC prior to commencing oral feeding on respiratory support.	(149)Murphy et al. (150)Hanin et al. 2015 Neonatal-care-position-paper-2023.pdf (rcslt.org)
Parents should be involved as partners in care, supported and provided adequate information while their preterm baby is on respiratory support	 7. NICE quality statement on involving parents and carers while their preterm baby is on respiratory support: Parents should be supported, informed and involved and carers while their preterm baby is on respiratory support, and during the discharge process for safe discharge planning. 8. Surveys have demonstrated that respiratory heath and overall medical fragility was a key priority for parents second only to developmental concerns (Jaworski et al, 151) Reduced risk of BPD has been reported by involving parents early in their infants' care and/or by applying NIDCAP. Caring for preterm infants in infant-parent rooms supporting continuous parental presence has been shown to reduce odds of BPD (aOR 0.72; 95% CI 0.61, 0.86) in an international survey and linked cohort study (Lehtonen et al, 152) 	 (30)NICE guideline (NG 124) (151) Jaworski M, et al 2022 (47) Prevention of Bronchopulmonary Dysplasia (BPD) - EFCNI - European Standards of Care for Newborn Health (newborn-health-standards.org) (152)Lehtonen et al,2020 Professional Recommendations: NICE Guideline [NG124]-Specialist neonatal respiratory care for babies born preterm: Recommendation 1.6 - Involving parents and carers while their preterm baby is on respiratory support. Supporting and informing parents and carers while their preterm baby is on respiratory support Recommendation 1.7- Planning safe discharge from the neonatal unit for preterm babies on respiratory support

 Standards and Quality Improvement Initiatives: 2. The European Standards of Care for Newborn Health: Reduced risk of BPD by involving parents early in their infants' care.
3. NICE Guideline [NG124]Quality Standard statement 5: Parents and carers of preterm babies who are having respiratory support are helped to care for their baby.
9. NNAP Standards: Parental consultation/presence on ward round nnap_summary_report_on_2021_data.pdf (rcpch.ac.uk) 7



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