Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Ashford and St. Peter's Hospitals NHS Foundation Trust	Evidence Review B	82	16	"To deliver High Flow, either Optiflow Junior or the Precision Flow (Vapotherm) system was used." This is quoted in the economic evaluation for the Hipster Study. What is not noted is that only 6 of 267 babies receiving High Flow were on the Precision Flow device, the other 261 babies were on Optiflow Junior (this is described in Table 3.2 of the Supplementary Appendix of the paper). Whilst this will not change the economic evaluation, it emphasises the point that, in the same way that not all ventilation and not all CPAP is the same, nor is it likely that all High Flow is the same.	Thank you for your comment. It has now been clarified in the text that the majority of babies were on Optiflow Junior, but the review did not differentiate between different types of Hi Flow and so the committee were unable to make recommendations relating to a specific type of Hi Flow. The committee acknowledged that there are different types of Hi Flow delivery systems. However, it was noted that there are no studies comparing different delivery systems of Hi Flow in the population of interest. Also, most studies did not differentiate between Hi Flow delivered from the Optiflow Junior or Precision Flow (Vapotherm) device. As a result, we did not assess the effectiveness of individual types of Hi Flow but grouped them into one comparison. The committee were also of a view that at the current state of research it was more important to assess the effectiveness of Hi Flow as a whole rather than assess the effectiveness of different systems used to deliver it. Looking back at the evidence for the outcome of BPD, only 1 small study used exclusively Optiflow to deliver Hi Flow (n=34), 2 studies Vapotherm (n=191), and the rest did not differentiate between different systems to deliver Hi Flow. Making

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					inferences on the effectiveness of Optiflow from such a small sample would have resulted in an extremely high uncertainty and would not have added any valuable information to the committee decision making. The committee discussion of the evidence section in the evidence review B includes committee considerations on the different systems used to deliver NIV, including Hi Flow. The discussion was expanded to make the above points clearer.
Ashford and St. Peter's Hospitals NHS Foundation Trust	General	General	General	The guideline appears to have omitted to describe the weaning of babies from respiratory care including the weaning of oxygen.	Thank you for your comment. The committee prioritised the aspects of ventilation that they agreed would have the greatest benefit in standardising practice, and agreed that primary mode of ventilation should be prioritised above weaning. The committee did not therefore review any evidence for weaning from respiratory support and so were unable to make recommendations.
Ashford and St. Peter's Hospitals NHS Foundation Trust	General	General	General	The guideline appears to have omitted to describe the investigation of babies with ongoing oxygen requirements (such as the use of saturation studies, the role of pH studies to assist with the diagnosis of the oxygen "dependent" baby, the evidence for any criteria to remain in oxygen and how to plan discharge and community follow-up for babies requiring low flow oxygen, including recommendations for frequency of weaning oxygen. Given that the committee used their expertise to make recommendations where the evidence was weak elsewhere in the guideline, it would seem reasonable that, even if the evidence is weak, then the committee should make recommendations which	Thank you for your comment. Following consultation on the scope, saturation studies, pH studies or community follow-up were not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for these areas and so were unable to make recommendations. The committee prioritised the aspects of ventilation that they agreed would have the greatest benefit in standardising practice, and

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				can then be submitted as a draft response for further consultation?	agreed that primary mode of ventilation should be prioritised above weaning. Planning for discharge is included in the guideline (see section 1.7) and recommendations have been made on this.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	4	4	The guideline states to "use continuous positive airways pressure (CPAP) where clinically appropriate". We have published a prospective study (in Archives of Disease in Childhood FNE) and a retrospective review (in Signa Vitae) of our experience of using the Vapotherm Precision High Flow system for pre-admission stabilisation. We do not know if all High Flow systems are able to stabilise babies successfully, but the guideline should acknowledge that there are NIV techniques that may be suitable for preterm respiratory stabilisation.	Thank you for your comment. The paper you have published, Reynolds 2016, was not included because it is not a comparative study and so did not meet our protocol inclusion criteria. The other paper, Reynolds 2017, was not included in the review because it is a retrospective cohort study and, as RCT evidence was available, did not meet our protocol inclusion criteria. Based on the RCT evidence from the review, CPAP was found to be the most effective form of non-invasive ventilation (NIV) in our population of preterm babies. The committee acknowledged that there are different types of Hi Flow delivery systems. However, it was noted that there are no studies comparing different delivery systems of Hi Flow in the population of interest. Also, most studies did not differentiate between Hi Flow delivered from the Optiflow Junior or Precision Flow (Vapotherm) device. As a result we did not assess the effectiveness of individual types of Hi Flow, but grouped them into one comparison. The committee were also of a view that at the current state of research it was more important to assess

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					the effectiveness of Hi Flow as a whole rather than assess the effectiveness of different systems used to deliver it. On looking back at the evidence we have identified that for the outcome of BPD, only 1 small study used exclusively Optiflow to deliver Hi Flow (n=34), 2 studies Vapotherm (n=191), and the rest did not differentiate between different systems to deliver Hi Flow. Making inferences on the effectiveness of HI Flow (Optiflow) from such a small sample would have resulted in an extremely high uncertainty and would not have added any valuable information to the committee decision making. The committee discussion of the evidence section in the evidence review B includes committee considerations on the different systems used to deliver NIV, including Hi Flow. The discussion has been expanded to make the above points clearer.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	4	4	The guideline states to "use continuous positive airways pressure (CPAP) where clinically appropriate". This implies that all CPAP is similar. There is published evidence that different CPAP, applied in different ways (prongs, mask) have different work of breathing and therefore the suitability for use, especially in the extremely preterm baby, may vary.	Thank you for your comment. The committee acknowledged that the trials assessing CPAP in the review used different modes of delivery. However, there was not sufficient evidence to compare the differences between ventilator driven and flow driver CPAP. As a result we did not assess the effectiveness of individual types of CPAP, but grouped them into one comparison.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	4	11	Why would it not be "feasible" to use a minimally invasive administration technique? The indications, evidence and training	Thank you for your comment. The recommendation has been clarified to explain that using a minimally invasive administration

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				for less invasive surfactant administration (LISA) are well described and the evidence is published as meta-analyses.	technique may not be feasible due to units not having the correct equipment or healthcare professionals who have been trained in this technique. The committee anticipated that over time more and more units would adopt this technique and use it wherever possible to avoid unnecessary intubation.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	4	14	"Choose between nasal cannula and incubator oxygen". Is the group implying that these are equally preferable. Our view would be that nasal cannula would give more stable oxygen delivery and can deliver oxygen that is humidified.	Thank you for your comment. From the review of the evidence, there was no indication to suggest that there was any difference in effectiveness or safety of nasal cannula compared to incubator. However, the committee acknowledged the small quantity of evidence upon which this was based and discussed in which groups of babies the different techniques should be used, and this is included in the rationale and impact. For example, incubators may be used for short-term use and assessment, while nasal cannula are preferable for longer-term use as they facilitate the handling of the baby and provides a more stable form of administration. As the committee agreed there was some uncertainty over the choice of methods, they removed 'depending on the age of the baby and their clinical stability.' from the recommendation. Evidence was sought that compared humidified to non-humidified oxygen delivery, but no relevant studies were found for this comparison. However, as the committee thought this was standard practice and of importance they made a

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					consensus recommendation to support best practice of humidifying oxygen when it is administered at higher flow rates, such as 2 litres per minute or more.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	10	8	No mention of whether atropine is useful as a premedication.	Thank you for your comment. The evidence in this review showed that there were no benefits to using atropine, so no recommendations including atropine were made.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	10	8	Does the committee think that morphine is as useful as fentanyl given their different pharmacokinetics – they appear to be given equal weighting?	Thank you for your comment. While morphine and fentanyl do have different pharmacokinetics, as you mentioned, there was no evidence favouring one over the other. The committee was therefore unwilling to make a recommendation that specified which one to use, so instead made the broader recommendation to use an opioid analgesic.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	26	21	"Babies born extremely preterm are less likely to manage successfully on nasal high-flow therapy as the primary mode of ventilation when compared to babies born less preterm." The risks of a generic description is that there is a failure to acknowledge that there might be differences between different High Flow systems. The trials done in Australia (Hipster and Hunter) for example, used the F&P Optiflow system for High Flow. The failure rates described in those studies are much higher than the failure rates we have described (presented at an international meeting last year and currently in press) using a different High Flow system. The combined criteria to allocate a description of failure are not standard. However we are concerned that, by taking a generic description, the committee is inferring that all CPAP and all High Flow systems produce equal clinical efficacy, and this is not a reasonable inference. The only published evidence to date on this for High Flow is an	Thank you for your comment. The committee acknowledged that there are different types of Hi Flow delivery systems. However, it was noted that there are no studies comparing different delivery systems of Hi Flow in the population of interest. Also, most studies did not differentiate between Hi Flow delivered from the Optiflow Junior or Precision Flow (Vapotherm) device. As a result we did not assess the effectiveness of individual types of Hi Flow, but grouped them into one comparison. The committee were also of a view that at the current state of research it was more important to assess the effectiveness of Hi Flow as a whole rather than assess the effectiveness of different systems used to deliver it. The committee's discussion of the evidence

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				underpowered pilot study comparing the two devices at up to 6L/min, which showed improved extubation success at 72hrs using the Precision Flow compared to the Optiflow device. (Miller SM, Dowd SA (2010) High-flow nasal cannula and extubation success in the premature infant: a comparison of two modalities. J Perinatol 30(12): 805-808.) More studies are obviously needed to answer this important question.	section in the evidence review B was has been expanded to make this point clearer. On looking back at the evidence we have identified that for the outcome of BPD, only 1 small study used exclusively Optiflow to deliver Hi Flow (n=34), 2 studies Vapotherm (n=191), and the rest did not differentiate between different systems to deliver Hi Flow. Making inferences on the effectiveness of Hi Flow (Optiflow) from such a small sample would have resulted in an extremely high uncertainty and would not have added any valuable information to the committee decision making. The HIPSTER trial (Roberts 2016) that you referenced was included in this review. The protocol for the HUNTER trial was published in 2017 and was picked up in the evidence search for this review (Manley. 2017). Though the trial has now been completed, the results have not yet been published beyond the conference (Pediatric Academic Societies Meeting, 5-8 May 2018, Toronto, Canada) proceedings that you referenced, and we have contacted the authors but they have not been able to supply the data, so we are unable to include this evidence in the review. However, we have now acknowledged the HUNTER trial in the 'Other factors the committee took into account' section.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					We will also notify the surveillance team at NICE that this may provide evidence necessitating a future update of this question. The committee acknowledged the lack of evidence in this area by making a research recommendation.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	26	21	"Using their clinical experience the committee agreed that CPAP would be a more suitable option for use in babies born more preterm." Please can you describe in your response what clinical experience the committee has with using which High Flow system in what context for what population in their daily practice, so that the clinical experience described can be quantified?	Thank you for your comment. The members of the committee had variable experience of using high flow, and they acknowledged that units may differ in the amount they use this technique. However, there was sufficient experience and expertise amongst the committee with high flow to allow a recommendation to be made.
Ashford and St. Peter's Hospitals NHS Foundation Trust	Short Guideline	30	12	Please can the committee now consider their recommendation in light of the publication of the recent paper (Shaffer, J Peds 2018) which showed greater survival without BPD and less deaths, but more intestinal perforation and late-onset sepsis, in a large trial of 982 preterm infants randomised to receiving prophylactic low dose hydrocortisone or placebo.	Thank you for your comment. Shaffer 2018 was not identified in our literature searches because it was published after our search cut-off date. We have now reviewed it and note that this paper is an individual patient data meta-analysis of 4 RCTs. Our analysis included these 4 RCTs along with 2 additional trials. One of these additional trials was not included by Shaffer 2018 because individual patient data were not available and the other because hydrocortisone was initiated after 7 post-natal days. The endpoint used by Shaffer was 'survival without BPD' – this is a composite outcome not included in our review protocol, which treated survival and BPD as separate outcomes. Because our review already included the Shaffer data but looked at different outcomes this may have led to the different findings.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Association of Paediatric Chartered Physiotherapists	General	General	General	No mention in the guidelines of airway clearance, including physiotherapy or not to include physiotherapy or about suctioning	Thank you for your comment. Following consultation on the scope, airway clearance, including physiotherapy, was not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for these areas and so were unable to make recommendations.
Association of Paediatric Chartered Physiotherapists	General	General	General	VAP (ventilation acquired pneumonia) bundles are not mentioned and should be as starting to become common practice on a neonatal unit.	Thank you for your comment. Following consultation on the scope, ventilation acquired pneumonia was not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for this and so were unable to make recommendations.
Association of Paediatric Chartered Physiotherapists	General	General	General	No mention of optimising humidification, which should be standardised practice for ventilated babies/Non-invasive ventilators.	Thank you for your comment. The committee did not make a recommendation on humidifying oxygen as, like you, they believed it was standard practice. However, to avoid confusion the committee have now included a recommendation on humidification, based on their expertise.
Association of Paediatric Chartered Physiotherapists	General	General	General	No mentioning about optimal positioning or frequency around position changes.	Thank you for your comment. Following consultation on the scope, positioning or position changes were not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for this and so were unable to make recommendations.
Association of Paediatric Chartered Physiotherapists	General	General	General	No mention of the value of a physiotherapy chest assessment, especially for surgical babies.	Thank you for your comment. Following consultation on the scope, physiotherapy chest assessment, was not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for this area and so were unable to make recommendations.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Association of Paediatric Chartered Physiotherapists	Short Guideline	5	6-8	It says if VTV not effective consider HFOV - is this only until babies are term?	Thank you for your comment. This guideline covers the care of preterm babies only and does not give guidance on term babies.
Association of Paediatric Chartered Physiotherapists	Short Guideline	9	9-13	With references to the carbon dioxide ranges, it says day 4 onwards accept PC02 up to 10 - when do we accept a high CO2 until? Are we assuming they have a chronic lung disease and therefore high CO2? Does it depend on specific patient groups, eg very premature, prolonged ventilation and therefore higher risk of CLD (Chronic lung disease) - if so I don't think this is clear enough. Do we accept it regardless of pH?	Thank you for your comment. The issues of pH and CO2 levels for specific patient subgroups were not prioritised for inclusion in the evidence review and as a result the committee were unable to make specific recommendations on these topics. The committee agreed that pH thresholds were a matter for local guidance and that the accepted duration of high CO2 is a matter of clinical judgement.
Association of Paediatric Chartered Physiotherapists	Short Guideline	11	9-11	We are concerned that NIDCAP has been included in the respiratory guidelines when it states it can help with cognitive development.	Thank you for your comment. The evidence review for this question looked at what different types of parent and carer involvement are effective at improving babies' outcomes in a specific population of preterm babies receiving respiratory support, and one of the outcomes considered was neurodevelopmental delay. Thus, although we appreciate that interventions such as NIDCAP can be used in a wider range of preterm babies, we found that in this specific population there was some evidence for improved cognitive development, and so made a recommendation for NIDCAP, for preterm babies less than 27 weeks, in whom it was cost-effective.
Association of Paediatric Chartered Physiotherapists	Short Guideline	11	13	Mentions skin to skin but not a time frame and prolonged stay in this position isn't recommended for respiratory care.	Thank you for your comment. There was no evidence to inform a recommendation on the optimal duration of skin-to-skin contact. Although the evidence for skin-to-skin contact did not show any benefit, there was no evidence of harm.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					The committee were also aware of other studies examining the mechanisms underlying skin-to-skin contact, for example, the positive effect of kangaroo care in reducing cortisol levels and raising oxytocin levels, which aided breastfeeding and improved babies' digestion. The committee identified that in their clinical experience the only risk from skin to skin care was the risk of accidently extubating a baby, but that this was extremely rare.
Association of Paediatric Chartered Physiotherapists	Short Guideline	17	12-18	Why mention follow-up using the bayleys III assessment when this does not marry up with the previous NICE guideline of Developmental follow-up of children and young people born preterm, where bayleys III was not mentioned.	Thank you for your comment. The mention of Bayley II is in the 'terms used in this guideline' section and does not form part of the recommendations. Choice of what scales to use to develop a composite neurodevelopmental outcome when assessing evidence was based on the scales that were reported in the clinical studies. Many of these studies we included in the evidence reviews used the Bayley II scale to assess neurodevelopmental outcomes, and therefore we used these as our outcome measure. Our guideline does not make any recommendations about neurodevelopmental follow-up or what scales to use to measure this, and, as you rightly point out, this is already covered in the existing NICE guideline on the Developmental follow-up of children and young people born preterm.
Association of Paediatric Chartered Physiotherapists	Short Guideline	39 40	25-28, 14-17	Why pick NIDCAP if stating costing implications and the question why would it improve parents' access? There are other neurodevelopmental care approaches and we do not consider	Thank you for your comment. The evidence review for this question looked for evidence for a wide range of developmental approaches and interventions that could increase parenteral

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				one should be listed over another and not in a respiratory guideline.	involvement in the care of preterm babies requiring respiratory support. For many of the interventions included in the review there was no evidence available for our specific population, but there was evidence that NIDCAP improved neurodevelopmental outcomes in this group of babies and so the committee recommended its use. We agree that saying it will improve parents' access to this developmental care is confusing and have reworded the sentence to make it clearer that it is the babies who will benefit from improved access to NIDCAP, but that it will lead to greater parenteral involvement in care.
Association of Paediatric Chartered Physiotherapists	Short Guideline	40	1-2	Family Integrated Care (FIC) is mentioned and that not enough evidence yet for improving respiratory outcomes. FIC is not purely for respiratory guidelines and this care is new to the UK - past 3 to 4 years.	Thank you for your comment. The evidence review for this question looked for evidence for a wide range of interventions that could increase parenteral involvement in the care of preterm babies requiring respiratory support. There was no evidence that Family Integrated Care (FIC) led to any benefits compared to standard care in this group of babies and therefore it could not be recommended. However, the committee made a research recommendation to determine if there are benefits with FIC, and if the evidence becomes available in the future, then the recommendations in a future guideline could be updated.
Association of Paediatric Chartered Physiotherapists	Short Guideline	41	5	The guideline recommends supporting babies being discharged on respiratory support, but do not clarify what this means, for example home oxygen or long term ventilation.	Thank you for your comment. Respiratory support would encompass all types of respiratory support – supplemental oxygen, non-invasive ventilation

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					or invasive ventilation – so the recommendations on discharge apply to all these babies
Bliss	Short Guideline	General	General	Bliss welcomes the focus of this guideline gives to the important of parental involvement in their baby's care.	Thank you for your comment. We agree that the guideline has a useful focus on the importance of parental involvement.
Bliss	Short Guideline	12	8	It is welcome that the need for psychological support for parents is recognised in this guideline. However, Bliss believes it should be strengthened to read 'trained mental health professionals' A recent Bliss survey showed 80 per cent of parents felt their mental health became worse after a neonatal experience. Additionally, many parents reported being diagnosed with a mental health condition such as anxiety, PTSD or post-natal depression in connection with their neonatal experience. Despite this, parents were more likely to receive support from their partners (80 per cent) and their family (72 per cent) than they were mental health professionals (13 per cent) while they were on the unit. Additionally it is well-evidenced that parents of babies who have a neonatal experience are more likely to experience mental health problems when compared to the general population. Early, targeted support from a trained mental health professional is imperative to ensure parents receive the support they need.	Thank you for your comment. We agree that parents need support during and after their neonatal experience. The recommendation for offering psychological support came from the studies stating that parents wanted to have access to counselling or mental health services. There was no evidence on who should deliver this support, the number of hours, sessions, or format. The committee discussed this at length and agreed that it was likely this person would be different in different units so instead used the wording of a "professional who is trained to deliver this type of help."
Bliss	Short Guideline	12	12	This recommendation is confusing. If parents are present on the unit, parents should be given information about their baby's treatment and progress face-to-face as updates become available. I'm not sure how another method could be preferable? If this recommendation is relating specifically to when parents are not on the unit then this should be stated to avoid confusion.	Thank you for your comment. Even if parents are present on the unit with their baby they may have preferences about the amount and detail of information they are given so this may apply to when parents are on or off the neonatal unit. However, the wording of this recommendation has been clarified to recommend that parents are specifically asked how they wish to be kept

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					informed, and how they wish to be contacted when they are away from the neonatal unit.
Bliss	Short Guideline	13	General	In addition to what is listed under 1.6.14, access to free overnight accommodation and access to/information about financial support to be made available. Distance is a significant barrier to parents being with, and caring for their baby. Additionally, a neonatal stay is costly for families – financially as well as emotionally – with parents responding to a Bliss survey spending on average £2,256 over their baby's neonatal stay on top of their usual expenses. For babies to have the best outcomes, including those born premature and requiring respiratory support it is vital that parents are able to take the lead in their baby's care. Service planners have an important role to ensure parents are supported to easily be with their baby.	Thank you for your comment. We agree that accommodation, travel issues and financial concerns may all pose problems for parents/carers of all preterm babies. However, our evidence review focussed specifically on issues that were important to parents/carers of preterm babies receiving respiratory support, and these topics were not identified in the themes from the qualitative review so we were unable to make recommendations on these areas. There is, however, a recommendation that parents should be able to have 24-hour access and be able to care for their baby overnight.
Bliss	Short Guideline	13	21	Suggest extending this recommendation to read 'foster positive and supportive relationships by providing parents and carers with 24-hour access to their baby, including during unit ward rounds and handover.'	Thank you for your comment. The committee agreed 24 hour access to the unit was important, and also recommended that parents and carers should participate in discussions about their baby during ward rounds, so the committee did not think it was necessary to amend this recommendation.
Bliss	Short Guideline	40	17	Unsure about what this line means – what is the benefit of parents having improved access to NIDCAP? I assume the benefit is improved confidence and greater ability to provide care to their own baby, if so this should be stated instead as it's not really parents who have access to NIDCAP, it's the babies themselves.	Thank you for your comment. We agree that it is the baby who benefits from NIDCAP, but that it allows the parents greater involvement in the care of their baby, and so have reworded this sentence.
British Association of Perinatal Medicine	Short Guideline	General	General	Overall, the document is weighted too heavily towards parental care/involvement, management of services, discharge on respiratory support (very uncommon). Whilst family involvement is to be encouraged, specific guidance on this seems out of place in	Thank you for your comment. During the scoping process, the involvement of parents and carers in the NICU and during discharge were identified as key areas due to the lack of guidance specific to

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				this document as it has little evidence base and the elements suggested are better discussed in documents such as the Bliss Baby Charter which are specifically related to this.	babies requiring respiratory support. Of the 4 reviews pertaining to this area, 1 was quantitative and assessed the effectiveness of parental involvement in the NICU and the other 3 were qualitative and assessed information and support needs whilst on the NICU and during discharge. The management of services emerged from the data in the relevant reviews as an area for which parents identified a need for support and information. We were aware of the Bliss Baby Charter and our recommendations reflect those made by Bliss, where the evidence was consistent with them.
British Association of Perinatal Medicine	Short Guideline	5	5-12	The two recommendations about VTV being preferred mode of ventilation (1.2.6) and avoiding synchronised pressure-limited ventilation (1.2.7) are confusing. True Volume controlled ventilation (VCV) is uncommonly used in the UK; the volume targeting is achieved by using Volume Guarantee (VG) or TTV as additional options on a primary mode of ventilation. Most studies of VTV have used synchronised modes of ventilation such as AC, SIMV or PSV as the primary mode. The wording of these recommendations seems to suggest that VTV should be used in conjunction with a non-synchronised mode of ventilation which would be incorrect. The 3 studies of SPLV and NSPLV included in this analysis are very old, have used ventilators with air pressure sensors which are suboptimal for triggering compared to airflow sensors and have methodological flaws. The analysis is dominated by the study by Baumer et al which had serious methodological issues	Thank you for your comment. We have clarified the recommendations on invasive ventilation to state that VTV should be used in combination with synchronised ventilation. In the full evidence review B it is explained that VTV includes Volume guarantee ventilation (VGV), Target tidal volume (TTV), Pressure regulated volume control (PRVC) ventilation (PRVCV), Volume limited ventilation (VLV), Volume-assured pressure support (VAPS), any synchronised pressure limited ventilation + volume guarantee, and SIMV + volume guarantee. AC/PTV/PSV + VG would be included in VTV i.e. any synchronised pressure limited ventilation + volume guarantee.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				including a very high mortality rate casting doubt on the overall neonatal care, use of sedation and often paralysis in the Triggered ventilation arm, use of a mix of ventilators with different characteristics etc. Whether results drawn from such studies of low quality and older equipment are applicable to modern neonatal; ventilators would be questionable. Apart from determining delivered tidal volume (and hence restricting volutrauma), other aspects ventilation remain similar between SPLV and SPLV with volume targeting. Whilst it is accepted that there are well conducted RCTs evaluating different modes of neonatal ventilation, casting aside Synchronised ventilation may not be appropriate. A recent international survey of respiratory management of extremely preterm infants (Beltempo M, Neonatology 2018;114:28-36) shows that synchronised ventilation (SIPPV/AC) with or without volume targeting is the most commonly used ventilatory mode in this patient group. Currently, provision of HFOV is considered complex intensive care and restricted to NICUs under the Neonatal Critical Care Service Specification (E08/S/a) in England. The recommendation of using HFOV as the only alternative ventilatory strategy for preterm infants if VTV is not feasible is very likely to require increased transfer of babies from LNUs into NICUs, and will have service delivery implications. The multitude of ventilatory strategies enable tailoring respiratory support for an individual baby based on the respiratory characteristics which are very dynamic in this population. Recommendations for a specific mode (other than VTV) in the	Also, the definitions of all ventilation modes were added to the 'terms used in this guideline' section. When making recommendations the committee took into account that the quality of evidence in these reviews was mostly of low quality and we acknowledged your concerns regarding the 3 studies of SPLV and NSPLV. However, the synthesis of RCTs using an NMA ensured that all evidence, whether direct or indirect, was used to produce coherent estimates of the relative effects of every ventilation mode compared to every other. However, because multiple sources of evidence were used, the final estimates are more robust than if only direct sources of evidence were included for the reasons you have outlined i.e. the results are less likely to be influenced by the 3 studies of SPLV and NSPLV included in this analysis. So for example, in comparing SPLV with NSPLV the NMA considered not only direct evidence but also indirect evidence, for example, trials comparing VTV with SPLV and also VTV with NSPLV, etc., which introduces a substantial additional evidence base on which to base recommendations. Also, a threshold analysis was undertaken to assess the robustness of the conclusions based on the NMA to potential biases in the included evidence. Study level threshold analysis found the findings to be sensitive only to one RCT (D'Angio 2005) which compared SIMV and VTV.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				absence of robust recent data using modern neonatal ventilator risks 'one size fits all' approach. **Suggest:** VTV should be recommended as the preferred ventilatory strategy for preterm infants requiring invasive respiratory support. HFOV should be recommended as suitable alternative support for those who can not be managed on VTV but the negative recommendation (1.2.7) about Synchronised pressure limited ventilation should be omitted. At least, the use of Volume targeting in conjunction with a synchronised ventilatory mode such as AC/PSV/SIMV should not be discarded. There should be a comment that using VTV may not be feasible where there is a large leak around the endotracheal tube.	Given rapid advancements in neonatal care, and the available clinical evidence there was evidence that VTV which also includes any synchronised pressure limited ventilation + volume guarantee was beneficial for mortality prior to discharge and BPD at 36 weeks PMA, and there was also evidence that volume targeted ventilation reduced the incidence of pneumothorax and days on invasive ventilation compared with SPLV, SIMV and NSPLV. As such the committee were of a view that there is fairly convincing evidence that volume targeting is preferred to any other invasive ventilation including SPLV. SPLV in our analysis was clearly inferior to other modes for mortality prior discharge, days on invasive ventilation, and pneumothorax and is in line with the committee clinical experience i.e. that preterm babies do not perform as well with SPLV as other invasive ventilation techniques for primary respiratory support. The committee acknowledged that not all neonatal units are trained to use HFOV appropriately, which could lead to hypocapnia, and also VTV may not be appropriate for all preterm babies, for example where there is an air leak. As a result, the committee have added a recommendation to consider the use of SIMV when VTV or HFOV could not be used. The fact that VTV may not be suitable when there is an air leak is explained in evidence review B,

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					'The committee's discussion of the evidence' and in the rationale and impact section of the guideline.
British Association of Perinatal Medicine	Short Guideline	6	2-6	**Corticosteroids:** 1. The recommendation about the use of postnatal steroids to prevent BPD should be reworded to 'For preterm babies who are 1-2 weeks old and still receiving invasive ventilation…' rather than 'Preterm…who are 8 days or older…'. The latter is likely to be interpreted as requiring use of steroids at 8 days of age and likely to inadvertently lead to increased use of postnatal steroids when the overall direction is for reducing their use. A range of 1-2 weeks is in keeping with the range used in the Cochrane Reviews and also enabling to defer the use of steroids given the uncertainty about the risk of adverse neurodevelopmental outcome. Suggest wording such as "Consider steroids after 8 days in those babies in whom there appears little prospect of extubation without this, Ideally following a trial of extubation. Should a dose of dexamethasone be suggested?	Thank you for your comment. The evidence reviewed identified that the benefits of corticosteroids were greater in babies 8 days or older so this is why we used that age cut-off in the recommendation. The recommendation should not be interpreted as requiring the use of steroids. We used 'consider' to reflect a recommendation for which the evidence of benefit is less certain, and would not expect steroids to be used in all cases for this group. We have also reworded the recommendation to make it clear that it applies to those who are 'still requiring invasive ventilation for respiratory disease'. There was insufficient evidence to recommend a specific dose of dexamethasone.
British Association of Perinatal Medicine	Short Guideline	8	5-6	**Caffeine:** Should the option of stopping 5 days after respiratory support has stopped be at least discussed as in the CAP study	Thank you for your comment. In the Methods section of the original CAP trial (Schmidt 2006), the authors recommended continuing caffeine until the baby had "tolerated at least five consecutive days without the use of positive airway pressure." However, this protocol was not supported by any evidence or references and was not discussed further in the trial so the committee were unable to make recommendations based on this.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Association of Perinatal Medicine	Short Guideline	8	15	The guideline does not address the role of targeted ibuprofen in management of PDA. Should it acknowledge the on-going, large UK based, multicentre RCT (Baby-OSCAR trial)?	Thank you for your comment. The guideline acknowledges the Baby-OSCAR trial that is ongoing in the 'Other factors the committee took into account' section for the review on the effectiveness of interventions for closing a PDA in evidence review C - Managing respiratory disorders.
British Association of Perinatal Medicine	Short Guideline	9	7-8	**Oxygen:** This recommendation is not evidence based and although maybe agreed by a consensus on the group is certainly contentious – recommend comments moved to explanation similarly to comments on low dose prophylactic hydrocortisone on which there is some evidence. ? recommend research in this area	Thank you for your comment. The committee were disappointed that there was not more recent evidence on the use of transcutaneous oxygen monitoring, but were aware that it can be a useful technique and is already used in many units and so did not think it would be contentious for a 'consider' recommendation to be made, and also made a research recommendation as you suggest. The comparison with the hydrocortisone is not quite straightforward as the committee knew there was already an ongoing study comparing hydrocortisone with placebo, and made an additional research recommendation to compare hydrocortisone with dexamethasone, whereas they were not aware of any similar ongoing studies with transcutaneous oxygen monitoring. In addition, the committee agreed that to make a recommendation to use a particular monitoring method was not likely to increase risks to babies, whereas recommending a pharmacological treatment such as hydrocortisone may lead to additional risks, as well as benefits.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Association of Perinatal Medicine	Short Guideline	9	9-16	**Carbon dioxide:** Should there be a recognition of the use of continuous end tidal CO2 if only as a research priority in explanation?	Thank you for your comment. As the committee only considered the levels of carbon dioxide and did not prioritise a review question looking at the method of monitoring CO2, it was not possible for the committee to make recommendations on the use of continuous end tidal CO2 monitoring, nor to make a research recommendation.
British Association of Perinatal Medicine	Short Guideline	10	5-10	**Premedication:** Should there be a recommendation of some sort sedation/analgesia for minimally invasive surfactant administration techniques? **Consider morphine if the baby is in pain, using a validated pain score** Suggest a comment that there is little evidence that there is benefit in routinely measuring pain scores	Thank you for your comment. This review did not assess the use of pre-meds specifically for minimally invasive surfactant administration and therefore the committee were unable to make specific recommendations on this topic. The committee agree with your comment that that there is little evidence for the benefit of routinely measuring pain scores and therefore we have amended the recommendation to state that pain should be assessed as defined by local guidelines.
British Association of Perinatal Medicine	Short Guideline	11	12	**Developmental care** It is reasonable to suggest that the baby's environment is considered and aspects of developmental care used to optimise this. The evidence that NIDCAP as a package is beneficial is controversial and training staff In this particular approach could reasonably be considered an unnecessary expense.	Thank you for your comment. The committee agreed that there would be some costs related to training for NIDCAP, but the recommendation was based on evidence that NIDCAP was cost-effective for preterm babies <27 weeks gestational age and prevented neurodevelopmental delay.
Chiesi Ltd.	Short Guideline	3	5 (Table 1)	We are concerned that 'treated with surfactant' is included as a risk factor for BPD. We appreciate that this is qualified with a footnote explaining that this could reflect the severity of the baby's condition but we feel that this could be misinterpreted and may discourage surfactant use in eligible babies who would benefit from surfactant administration. We would suggest that 'increasing	Thank you for your comment. The evidence for this review question identified that babies who had been treated with surfactant had a higher risk of BPD. As this is not exactly the same population as the group of babies who need 'increasing respiratory support including those requiring

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				respiratory support including those requiring surfactant' would be more suitable and would still capture the same cohort being referred to	surfactant' (but who may or may not have received it) we have not been able to make this change to the wording. However, in order to make this clearer and to ensure surfactant is not omitted, we have also included this important caveat in the recommendation.
Chiesi Ltd.	Short Guideline	3	5 (Table 1)	Invasive ventilation is listed as a risk factor for BPD for babies < 28 weeks, however we feel this would be more appropriate for all preterm babies[1,2,3], with the additional consideration that the severity of BPD can often correlate with lower gestational age[1,2,3] [1]Zhonghua et al. Chin J Pediatr, 2011,49(09):655-662 [2] Trembath et al. Clin Perinatol. 2012,39(3):585-601 [3]Brener Dik et al. Arch Argent Pediatr, 2017,115(5):476-482	Thank you for your comment. We have rechecked the evidence report and it shows that invasive ventilation at <24 hours of age is a risk factor for bronchopulmonary dysplasia in those babies born at less than 32 weeks so we have amended this in Table 1. Thank you for citing these additional references We have checked whether these should be included: Trembath 2012 was not included as it was an expert review and so did not meet the review protocol criteria. Zhonghua 2011 and Brener Dik 2017 would not have been included as they are from non-OECD countries and so did not meet the review protocol criteria.
Chiesi Ltd.	Short Guideline	4	7-8	We are concerned that the term 'for stabilisation' may cause confusion and might be interpreted differently amongst clinicians – we would suggest removing this and making the statement simply 'All babies requiring intubation and ventilation should be given surfactant'	Thank you for your comment. The words 'for stabilisation' were used to indicate that this was during the early hours of life, but appreciate this may not be clear as babies may need stabilisation at other times, so have added the words 'in the early postnatal period' to clarify this.
Chiesi Ltd.	Short Guideline	4	9-10	We acknowledge that not all surfactants are licenced for less invasive surfactant administration, and that this is noted in a	Thank you for your comment. The non-licensed status of medicines in NICE guidance is always

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				footnote, however we would suggest that this is also clarified in the main body of the text to make this clear to the reader	included in a footnote and so we are unable to make the change you have suggested.
Chiesi Ltd.	Short Guideline	4	9-10	We feel that this section would benefit from some additional information on how to identify and manage infants who need surfactant but do not require invasive ventilation, as at present we feel that the guidance lacks this information, which may therefore limit clinicians' confidence in use of surfactant in this context. We would suggest rewording the first sentence to the following: 'Surfactant may be required for infants who do not need invasive ventilation. These may be identified within the first few hours of life by worsening respiratory effort, increasing need for non-invasive ventilation, increasing oxygen requirement[1] (fractional inspired oxygen concentration >0.3[1,2]). When giving surfactant to these babies, a minimally invasive technique should be used[1].' [1]Banerjee S et al, Surfactant replacement therapy for respiratory distress syndrome in preterm infants: UK national consensus. Pediatr Res 2019. Feb 19 doi: 10.1038/s41390-019-0344-5. [Epub ahead of print]. [2]Dargaville et al. Neonatology, 2013,104:8-14	Thank you for your comment. The committee agreed that the use of surfactant in preterm babies was part of mainstream clinical practice and therefore did not require a detailed evidence review. Instead, the aim of this recommendation is to reduce the use of intubation solely for the purpose of administering surfactant, and instead encourage the use of non-invasive administration techniques, or intubation followed by early extubation and there was evidence for benefit with both these techniques. The evidence review therefore focused on the most effective administration techniques and dosing regimens in those preterm babies receiving surfactant. As it is established clinical practice in the UK to give surfactant to preterm babies needing invasive ventilation in the early post-natal period, the committee made a consensus recommendation that reinforces this. Thank you for citing these 2 studies. We have checked these and confirm they were not included in the evidence review for the following reasons: 1. Banerjee S et al was 'Academic in confidence' and so could not be included without the author's permission. 2. Dargaville 2013 this is a non-randomised study and so did not meet the protocol criteria.
Chiesi Ltd.	Short Guideline	8	3-4	We feel that this recommendation may be too restrictive and would suggest that this be amended to include all babies <32	Thank you for your comment. This recommendation for babies < 30 weeks is based

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				weeks. Most studies on the efficacy of caffeine citrate include babies of a gestational age between <30 and <34 weeks, with the majority being <32 weeks[1]. [1]Abdel-Hady et al. World J Clin Pediatr, 2015,4(4):81-93	on the clinical evidence for benefit at <31 weeks, and the fact that 1.25 kg (the inclusion criteria of the CAP study) is the 50th centile for weight at 30 weeks, on the UK low birthweight growth chart. There will be some babies who are <1.25 kg at 31 or 32 weeks who would qualify for caffeine on a weight criteria, and there are some babies at 30 weeks who weigh 1.8 kg, but in general gestation is more important than weight for complications of prematurity. Apnoeas of prematurity generally cease to be a problem after 34 weeks. The cited publication, Abdel-Hady 2015, was not included because it is an expert review paper and not a primary research study.
Chiesi Ltd.	Short Guideline	8	5-6	We feel that this information might benefit from being more closely aligned to that which appears in the SmPC for caffeine citrate, where it is recommended to stop caffeine at 37 weeks post-gestational age, after a period of 5-7 days has passed without a significant apnoeic attack	Thank you for your comment. This recommendation was based on evidence from the included studies that this was an appropriate time at which to stop the administration of caffeine.
Chiesi Ltd.	Short Guideline	16	18	We would suggest that this sentence is reworded to 'Administration of surfactant through a thin endotracheal catheter without insertion of an endotracheal tube or invasive ventilation' as this is consistent with the description in the SmPC for LISA using Curosurf	Thank you for your comment. We have made this change of wording as you suggested.
Chiesi Ltd.	Short Guideline	18	21	We feel that there is sufficient evidence to indicate that LISA is at least comparable to INSURE as a minimally invasive surfactant administration technique, in terms of a number of significant neonatal outcomes such as need for mechanical ventilation and risk of BPD[1-5].	Thank you for your comment. The committee thought there was sufficient evidence meeting our review protocol criteria to compare minimally invasive techniques (such as LISA) with early extubation techniques (such as INSURE), and

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Having reviewed the evidence that was considered in compiling this draft guidance, we are concerned that a number of key clinical trials were omitted from this review process which, if included, would support a statement justifying the use of LISA as a minimally invasive technique for surfactant administration[6-14] [1]Banerjee S et al, Surfactant replacement therapy for respiratory distress syndrome in preterm infants: UK national consensus. Pediatr Res 2019. Feb 19 doi: 10.1038/s41390-019-0344-5. [Epub ahead of print]. [2]Isayama et al. JAMA, 2016, 316:611-624 [3]Aldana-Aguiree et al. Arch Dis Child Fetal Neonatal Ed 2016, 0:F1-F7 [4]Rigo et al, Eur J Paediatr, 2016 [5]Wu et al, Pediatr Pulmonol, 2017, 52(6):844-854 [6]Klebermass et al. Neonatology, 2013,103:252-8 [7] Mirnia et al. Medical Journal of Islamic World Academy of Sciences, 2013,21:143-148 [8] Aguar et al, Acta Paediatrica, 2014,103:e229-33 [9] Gopel et al, Acta Paediatrica, 2015,104:241-6 [10] Krajewski et al, J Matern Fetal Neonatal Med, 2015,28(10):1161-4 [11]Mohammadizadeh et al, J Res Pharm Pract, 2015,4:31-6 [12]Bao et al, Pediatrics, 2015,15:21 [13]Teig et al, Z Geburtsh Neonatol, 2015,219:266-273 [14] Ramos-Navarro et al, Clinics, 2016,71(3),128-134	that is why the committee recommended minimally invasive administration. The papers listed were not included because they did not meet our review protocol criteria for the following reasons: Non-randomised study design: Gopel 2015, Krajewski 2015, Aguar 2014, Teig 2015, Klebermass 2013, Ramos-Navarro 2016. Randomised trial from a non-OECD member country: Bao 2015, Mohammadizadeh 2015, Mirnia 2013. Systematic reviews – these were checked for any relevant trials but not included themselves (as not all the papers would necessarily have et the protocol criteria for our review and our own meta-analysis was conducted): Rigo 2016; Isayama. 2016, Wu 2017. Papers which were not in the public domain could not be included as evidence without the author's permission: Banerjee. S, et al. Conference abstract: Aldana-Aguiree 2016 - this conference abstract was not identified in our search but the later full publication of the Aldana-Aguiree (2017) systematic review was checked for relevant RCTs.
Chiesi Ltd.	Short Guideline	19	20-21	Having reviewed the evidence that was considered in compiling this draft guidance, we are concerned that a further series of	Thank you for your comment. There was insufficient evidence from randomised trials to

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				studies pertaining to the optimal dose of surfactant to improve neonatal outcomes were omitted from review. We feel that, if included, these studies would be sufficient to support a statement indicating that a 200mg/kg initial dose of surfactant is superior to 100mg/kg in terms of improvement in neonatal outcomes (reduced need for redosing, mortality prior to hospital discharge, death or oxygen requirement at 36 weeks postmenstrual age[1-6]) [1] Sweet et al, Neonatology, 2017,111:107-125 [2] Cogo et al, Pediatrics, 2009,124:e950-e957 [3] Ramanathan, Am J Perinatol, 2004,21:109-119 [4] Cloete et al, South African Journal of Child Health, 2013,7(4): 148-152 [5] Dizdar, Amer J Perinatol, 2012,29(02):95-100 [6] Singh et al, Cochrane Database of Systematic Reviews, 2015,12	support recommendations on surfactant dosing regimens. The cited studies were excluded for the following reasons: Publication not an RCT: Sweet 2017, Cogo 2009. Comparison not of interest for review: one surfactant versus another and not regimen or dosing: Ramanathan 2004, Dizdar 2012, Singh 2015. Retrospective review: Cloete2013.
Gloucestershire Royal Hospital	General	General	General	The guideline essentially does not give any useful recommendations and some of the statements are misleading. The way it currently stands, does it add any value to our current respiratory care practice? It gives decent recommendations on supporting parents and the general care of babies. i.e., it goes beyond the 'immediate respiratory care' of the preterm newborn, but does not make any recommendation on home oxygen, what pulse oximetry thresholds to use etc.	Thank you for your comment. We hope that the guideline will confirm and standardise best practice. We are pleased you think the recommendations on supporting parents and general care of babies are useful, and the committee agreed this was an important aspect of respiratory care of preterm babies. Following consultation on the scope, home oxygen was not identified as priority for inclusion in this guideline. The committee did not therefore review any evidence for home oxygen therapy and so were unable to make recommendations on this. However, a recommendation on target saturation levels is included in section 1.4.
Gloucestershire Royal Hospital	Short Guideline	3	Table 1	As rightly acknowledged in the rationale/impact link, surfactant and treatment for PDA are unlikely to be causal, and including	Thank you for your comment. The committee realised that this could be an unintended

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				them as risk factors may have the unintended effect of reducing their use.	consequence of the information in Table 1 and included a footnote stating that 'treated with surfactant' and 'treated for a patent ductus arteriosus (PDA)' is likely to reflect the severity of the baby's condition. Surfactant should be used, and a PDA should be treated, where clinically appropriate. However, in order to make this even clearer, we have also included this important caveat in the recommendation.
Gloucestershire Royal Hospital	Short Guideline	4	3	Suggest early CPAP rather than 'where clinically appropriate'	Thank you for your comment. The committee agreed that it was not appropriate to recommend CPAP for all preterm babies - for example if the baby is not breathing, or is very preterm and does not have the necessary respiratory drive - and therefore used the term 'where clinically appropriate'.
Gloucestershire Royal Hospital	Short Guideline	4	9	Suggest when to give surfactant and how much; effectively, the draft recommendation is saying 'if you think it's needed, do it' – I would imagine most neonatologists would do what they think is necessary, so the recommendation has no added value.	Thank you for your comment. Administration of surfactant to preterm babies who show signs of respiratory distress syndrome is standard practice so the committee did not carry out a review of the evidence on when to give surfactant. The committee did look for evidence to compare different doses of surfactant but did not find any. The aim of this recommendation is to reduce the use of intubation solely for the purpose of administering surfactant, and instead encourage the use of non-invasive administration techniques, or intubation followed by early extubation.
Gloucestershire Royal Hospital	Short Guideline	4	14	That's obvious and what is being done all units; why doesn't the guideline rather comment on saturation targets, for which there is evidence?	Thank you for your comment. The guideline does comment on saturation targets, in section 1.4.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					Recommendation 1.4.2 advises an oxygen saturation target of 91-95% in preterm babies.
Gloucestershire Royal Hospital	Short Guideline	5	6	Does anyone use these terms? Most neonatal ventilators use some form of pressure limited, time cycled ventilation, with volume targeting/volume guarantee. Why can't the guideline suggest using IMV with volume guarantee rather than what they shouldn't be? You have used a lot of terms that people are not familiar with and omitted the ones they are most likely to understand.	Thank you for your comment. The committee acknowledge that the ventilation terms can be confusing, and that often different terminology is used for the same technique. To assist readers we have now included a table in the 'Terms used in this guideline' section that shows how the different types of ventilation were grouped together. We have also included a new recommendation to clarify that SIMV can be used when VTV or HFOV are not suitable.
Gloucestershire Royal Hospital	Short Guideline	6	10	Is perforation the only risk of using corticosteroids in babies under 8 days? At least that's what this implies.	Thank you for your comment. There was also evidence that indicated a risk of hypertension in this group. This is addressed by the recommendation to monitor the blood pressure of babies who receive dexamethasone, because of the risk of hypertension.
Gloucestershire Royal Hospital	Short Guideline	6	14	What about blood sugar?	Thank you for your comment. The committee agreed that blood sugar monitoring should be standard practice and would be carried out routinely on most preterm babies receiving respiratory support. For this reason, following consultation on the scope, blood sugar monitoring was not identified as a priority for inclusion in this guideline.
Gloucestershire Royal Hospital	Short Guideline	8	1	Doesn't the committee even have a consensus on diuretics?	Thank you for your comment. The committee were disappointed that there was no evidence on the use of diuretics to prevent or treat bronchopulmonary dysplasia, and were unable to reach a consensus. However, the committee

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					made 2 research recommendations relating to the use of diuretics in this population.
Helen and Douglas House	Short Guideline	General	General	May we suggest that the Guideline includes a link to NG61 (End of life care for infants, children and young people with life limiting conditions). This is relevant for those babies for whom 'death is a possible or likely outcome' particularly if any ceiling or limitation is considered to their treatment.	Thank you for your comment. The committee discussed at length whether or not it was appropriate to include a link to the End of life guideline but agreed that the requirement to move to end of life care was very rare in the population of preterm babies considered by this guideline, and that it was not therefore appropriate to include this link.
Helen and Douglas House	Short Guideline	General	General	The guideline could be more prescriptive about the need for planning for discharge in babies requiring continued respiratory support at home (looking at Brompton Hospital to Home guideline and/or at local long term ventilation policies), particularly highlighting the need for early referrals for assessments for care packages.	Thank you for your comment. The guideline contains a section on discharge planning (section 1.7) which includes a recommendation to 'consider early referral to, and regular contact with, community and continuing healthcare teams' and the committee agreed this would include assessment for care packages.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	General	General	General	Guideline focuses mainly on early respiratory care. The guideline does not differentiate between early respiratory care and on-going long term respiratory care. This would be important as the thresholds for intervention are different. We feel this should be included in this guideline.	Thank you for your comment. Following consultation on the scope, long term respiratory care after discharge from the neonatal unit was not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for this and so were unable to make recommendations.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	General	General	General	The guideline mentions early respiratory care and discharge planning. It does not provide any guidance about weaning from non-invasive modes of ventilation. What evidence is available for weaning non-invasive ventilation? This is important as this practice varies widely across various neonatal units in the country. If there is no evidence then this could be a research recommendation.	Thank you for your comment. The committee prioritised the aspects of ventilation that they agreed would have the greatest benefit in standardising practice, and agreed that primary mode of ventilation should be prioritised above weaning.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					Therefore no evidence was sought on weaning from non-invasive ventilation, and so it was not possible to make a research recommendation made for this topic.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	General	General	General	There is no mention of thermoregulation which would be important part of early respiratory care.	Thank you for your comment. Following consultation on the scope, thermoregulation was not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for thermoregulation and so were unable to make any recommendations. In addition, the committee were aware that thermoregulation is an NNAP target and that standards therefore already exist on this.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	3	Table	In table 1 consider changing wording to say 'RDS needing treatment with surfactant' and 'symptomatic PDA needing treatment' rather than phrases used as it implies that surfactant increases the risk for BPD.	Thank you for your comment. The evidence for this review question identified that babies who had been treated with surfactant and who had treatment for their patent ductus arteriosus (PDA) had a higher risk of BPD. As this is not exactly the same population as the group of babies who had respiratory distress syndrome needing surfactant (but who may or may not have received it) or babies who had a symptomatic PDA needing treatment (but who may or may not have received it) we have not been able to make this change to the wording. However, in order to make this clearer and to ensure surfactant is not omitted or PDAs not treated, we have also included this important caveat in the recommendation.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	4	3	Point 1.2.1 is very vague and would not be applicable as a general rule to neonates born at all the gestations.	Thank you for your comment. The committee made the recommendation for the use of CPAP rather than invasive ventilation, where clinically appropriate, so as to limit the risks associated

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				It is also important to highlight early identification of failure of non-invasive ventilation to ensure timely intervention. Criteria for failed non-invasive ventilation during early neonatal period would be useful. Threshold for intervention at this early stage would be different to threshold when the baby is a few weeks old. This needs to be highlighted.	with invasive ventilation. The committee agreed that it was not appropriate to recommend CPAP for all preterm babies - for example if the baby is not breathing, or is very preterm and does not have the necessary respiratory drive - and therefore used the term 'where clinically appropriate'. Criteria for failed non-invasive ventilation, or when to transfer to invasive ventilation were not looked at as part of the evidence review, and would vary depending on the age of the baby.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	4	3	Local factors e.g. distance from labour ward to NNU, method of moving a baby e.g. resuscitaire, transport incubator will also influence early care. The guideline should acknowledge this in either a rationale & impact or interpreting the evidence section.	Thank you for your comment. The committee recognised that local factors such as place of birth, or distance from the labour ward to the neonatal unit would influence early care. As you suggest, we have added a section to the committee's discussion of the evidence to state that the committee noted these factors.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	4	9	The guideline does not address, which preterm babies receiving non-invasive ventilation should be given surfactant. The guideline recommends use of minimally invasive techniques while administering surfactant in non-ventilated babies but acknowledges that the evidence is weak. We question whether the recommendation is worded more strongly than the evidence justifies due to the high intubation rate (nearly 75%) in babies receiving MIST in the Kribs trial. We also note the lack of evidence regarding the best minimally invasive technique and surfactant dose regimen.	Thank you for your comment. Administration of surfactant to preterm babies who show signs of respiratory distress syndrome is standard practice so the committee did not carry out a review of the evidence on which preterm babies should receive surfactant. The aim of this recommendation is to reduce the use of intubation solely for the purpose of administering surfactant, and instead encourage the use of non-invasive administration techniques, or intubation followed by early extubation, and there was evidence for benefit with both these

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				The meta-analysis conducted by More K et al 2014 was not included in the evidence review, please can you clarify why. The recommendation for using minimally invasive techniques would need significant change in practice in units that do not routinely use this when there is only limited evidence of clinical benefit.	techniques. There was evidence that minimally invasive surfactant techniques reduced the incidence of BPD, pneumothorax and days on ventilation compared to invasive administration, so the evidence for this comparison was not weak. The committee agreed that the mechanical ventilation rate in Kribs (2015) was high, although these results were consistent with the two other trials of minimally invasive surfactant administration techniques versus endotracheal administration of surfactant. The committee were also disappointed with the lack of evidence for the best overall technique and the best dosage regimen, as you have noted, and hence made research recommendations to address both of these issues. The Moore 2014 systematic review was checked for relevant randomised trials, but not included itself, as the systematic review process used often means that not all the papers in a systematic review would meet the protocol inclusion criteria. The committee were aware that minimally invasive surfactant administration requires training and this is discussed in the rationale and impact section. In this section they acknowledged that not all neonatal units have the facilities to carry out minimally invasive surfactant

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					administration techniques, and not all healthcare professionals have been trained to use them. The committee agreed that in these circumstances, endotracheal surfactant administration followed by early extubation should be used, because there was evidence that it reduces the incidence of BPD compared with conventional administration of surfactant with continued ventilation. The committee worded the recommendation to encourage the use of minimally invasive surfactant administration techniques where available, in order to avoid intubation.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	5	6	Can you please clarify where do you see the role of SIMV, which is one of the most commonly used modes of neonatal ventilation, when VTV cannot be achieved.	Thank you for your comment. The evidence showed an increase in BPD at 36 weeks PMA with SIMV compared with VTV and HFV, however, the committee agreed that since there was no evidence to suggest a difference between SIMV compared with NSPV and SPLV for the outcomes assessed that it should remain a treatment option in preterm babies where VTV and HFOV are not clinically suitable. The committee therefore made a new recommendation stating that SIMV could be used in these circumstances.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	5	6	Special care and local neonatal units are commissioned to provide short term ventilation only. Consequently preterm neonates in these units are either ventilated for a short time only or require a mode of ventilation compatible with being transported to another neonatal unit. Does the guideline need to acknowledge this?	Thank you for your comment. The committee recognised that local factors such as place of birth, or proximity to the neonatal unit would influence early care. As you suggest, we have added a section to the committee's discussion of

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					the evidence in evidence review B to state that the committee noted these factors.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	5	6	Transport: most transport services do not have ventilators that provide volume-targeted or High Frequency Oscillation ventilation (HFOV). Is it important to acknowledge that it might be difficult to achieve the strongly worded recommendation in a neonatal transport setting?	Thank you for your comment. Following consultation on the scope, respiratory care during neonatal transport was not identified as a priority for inclusion in this guideline The committee did not therefore review any evidence for respiratory support during transportation and so were unable to make any recommendations on this.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	8	16	The guideline mentions treatment of Patent Ductus Arteriosus (PDA) when it causes a significant clinical problem. As this is slightly vague did the committee consider echocardiographic measurements of PDA and cardiac assessment to inform the decision to treat?	Thank you for your comment. Our review for this question looked at the effectiveness of different interventions to close the patent ductus arteriosus and was not designed to identify ways to measure and assess PDA, including echocardiographic measurements or cardiac assessment, so the committee could not comment on this in the recommendations.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	9	6	The only saturation targets mentioned in the guideline are 91-95%. It should specify that this is after the transition to ex-utero life. It is normal to have saturations of less than 91% in the first few minutes of life and in most babies these saturations improve over a few minutes without oxygen. Not clearly mentioning this may cause confusion and misinterpretation, resulting in administration of supplemental oxygen to preterm neonates when not truly indicated.	Thank you for your comment. We have amended the wording to make it clear that this target is after initial stabilisation of the baby following birth.
Leicester Neonatal Services, University Hospitals Leicester NHS Trust	Short Guideline	9	10	The guideline deals with oxygen monitoring but does not mention pCO2 monitoring. Given that transcutaneous pO2 monitoring should be considered did the committee consider transcutaneous pCO2 monitoring or end-tidal CO2 measurements for those invasively ventilated? If not could this be a possible research recommendation?	Thank you for your comment. As the committee only considered the levels of carbon dioxide and did not prioritise a review question looking at the method of monitoring CO2, it was not possible for the committee to make recommendations on the use of transcutaneous CO2 monitoring or end tidal CO2 monitoring As we did not look for this

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					evidence for these methods of monitoring the committee were not able to make research recommendation.
Neonatal & Paediatric Pharmacists Group	Evidence Review C	60	General	Question 3.6: we agree that the evidence supports the recommendation to use higher doses of caffeine citrate.	Thank you for your comment and agreement.
Neonatal & Paediatric Pharmacists Group	Short Guideline	General	General	In order to avoid dosing errors due to caffeine base/citrate confusion, we would recommend that caffeine is consistently referred to throughout the guideline as caffeine citrate as per the MHRA safe practice advice from 2013 and the BNF for Children. Both terms are currently used.	Thank you for your comment. We have corrected this and now refer to caffeine citrate throughout the guideline and evidence report C.
Neonatal & Paediatric Pharmacists Group	Short Guideline	8	11-13	If the guideline is to recommend checking plasma-caffeine levels in babies who receive more than 20mg/kg, has consideration been given to what 'safe' levels are? BNF for Children caffeine citrate monograph (https://doi.org/10.18578/BNFC.539203955) highlights that signs of toxicity only normally occur at concentrations >50mg/L (260 micromol/L). It also states that therapeutic range for plasma-caffeine concentration is usually 10–20 mg/L (50–100 micromol/L), but a concentration of 25–35 mg/L (130–180 micromol/L) may be required. Evelina London Paediatric Formulary caffeine citrate monograph states (http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80/content/10149776-b327-415a-96bd-5003e0a4a10b) Therapeutic range: 8-30mg/L. Toxicity: >50mg/L. So what do the guideline committee consider to be a 'safe' level?	Thank you for your comment. The committee expected that only a small number of babies would require higher doses of caffeine. We have added a footnote to the recommendation to specify that when measuring plasma levels, prescribers should use the local laboratory's reference ranges. The British National Formulary for Children's entry on caffeine citrate was also added as a footnote, as this provides more detailed guidance on therapeutic levels.
Neonatal & Paediatric Pharmacists Group	Short Guideline	33	3-8	This rationale states that the recommendation will have a minimal impact on current practice. However, if all units move to a higher maintenance dose it will at least double the costs of caffeine citrate therapy. If more units now need to monitor levels this will also be associated with additional costs and workload.	Thank you for your comment. In most cases, oral caffeine is used which has a low acquisition cost, although the committee acknowledged that the intravenous formulation is associated with substantially higher acquisition cost. However, we were aware that irrespective of dose a single vial will be required and as such increasing the dose

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					will not increase the costs. Also, the number of babies requiring intravenous solution is small. The committee agreed that not many babies would require very high doses and there will be therefore only be a small increase in the number of levels that are monitored, and therefore only a small increase in costs and workload. This has been clarified in the rationale and impact section.
Neonatal CRG	Short Guideline	General	General	The guideline has no guidance on support for babies with severe long term lung disease who are unlikely to be able to go home on low flow oxygen. These situations are relatively infrequent but require expertise of specialist paediatric respiratory / long term ventilation teams. Guidance on appropriate transition to paediatric services, when this should be considered and when modes of respiratory support frequently used in smaller, younger babies, including high flow nasal cannula oxygen, nasal CPAP and nasal PPV should be replaced by consideration for tracheostomy and paediatric devices, would be useful.	Thank you for your comment. Following consultation on the scope, long-term management of chronic lung disease after discharge from the neonatal unit was not identified as a priority for inclusion in this guideline. The committee did not therefore review any evidence for these areas and so were unable to make recommendations. However, the guideline does include planning for discharge on respiratory support.
Neonatal CRG	Short Guideline	General	General	The guideline has little or no mention of the importance of good nutrition and facilitation of good growth and monitoring and treatment of metabolic bone disease.	Thank you for your comment. Following consultation on the scope, nutrition, growth or metabolic bone disease were not identified as priorities for inclusion in this guideline. The committee did not therefore review any evidence for these areas and so were unable to make recommendations. However, the committee were also aware that a NICE guideline on neonatal parenteral nutrition is currently in development.
Neonatal CRG	Short Guideline	5	9-12	It is unclear whether the guideline recommends not using various trigger modes of ventilation with VTV (AC, SIPPV, PTV) as well as with PLTC ventilation. We are concerned that this recommendation implies that various trigger modes should not be	Thank you for your comment. The recommendation on invasive ventilation has been clarified to state that volume-targeted ventilation should be used in combination with synchronised ventilation and we have also added a new

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				used with VTV. Clarification of this part of the text would be useful.	recommendation to clarify that SIMV can be used when VTV or HFOV are not suitable. In the full evidence review B there is a more detailed explanation of the modes of ventilation included in this review. (Finally, the definitions of all modes were added to the 'Terms used in this guideline' section. We hope these changes make the guideline easier to understand.
Neonatal CRG	Short Guideline	9	11-15	PCO_2 and PO_2 should be used rather than pCO_2 and pO_2 (i.e. upper case P, rather than lower case P) – see: Negri M, Cascio CL. Use of lower case "p" or uppercase "P" to express Blood gas data: Does it make a difference? Clin Chem 2006; 52: 1614 The rationale sections use upper case P, so this is confusing.	Thank you for your comment. pCO2 and pO2 have been changed to PCO2 and PO2 throughout the guideline as you suggest for consistency.
Neonatal Network NI	Short Guideline	General	General	The guideline is over prescriptive and dogmatic.	Thank you for your comment. We hope the guideline provides clear evidence-based recommendations and that it will form a useful basis for local implementation.
Neonatal Network NI	Short Guideline	5	2	The new evidence presented by Hunter et al at the PAS in October 2018 clearly demonstrates that nasal Hi-Flow therapy is inferior to nasal CPAP and therefore shouldn't be recommended as an equal option for first line therapy and need to ensure recommendation to "consider" is not viewed in this way.	Thank you for your comment. We believe this is a reference to the HUNTER trial, with lead author Brett Manley (a multi-centre RCT comparing nasal high flow with nasal CPAP as primary support for newborn babies with early RDS). The protocol for the HUNTER trial was published in 2017 and was picked up in the evidence search for this review (Manley 2017), Though the trial has now been completed, the results have not yet been published beyond the conference proceedings (Pediatric Academic Societies Meeting, 5-8 May 2018, Toronto, Canada) that you referenced, so we were unable to include this evidence in the review. We have contacted the author but we are unable to obtain this data until it

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					is published. However, we have now acknowledged this trial in the 'Other factors the committee took into account' section of our evidence report. We will also notify the surveillance team at NICE that this may provide evidence necessitating a future update of this question. We also amended the recommendation to remove the statement "Base the decision on the age of the baby and their prematurity," as the committee recognised that the choice between CPAP and nasal high-flow is a complex clinical decision and should be made for babies on an individual basis.
Neonatal Network NI	Short Guideline	5	9	Wording "Do not use" is unhelpful. As it stands, it could imply that it is OK to use non-synchronised ventilation modes. There is no mention of SIMV as a mode, which is the most commonly used mode of ventilation in Northern Ireland. We would suggest that it would be better to state that synchronised modes of ventilation should be used with Volume Guarantee.	Thank you for your comment. As you suggest, the recommendation on which mode of invasive ventilation should be used has been clarified to state the volume-targeted ventilation should be used in combination with synchronised ventilation. When making the recommendations the committee acknowledged that there was no difference between VTV and SIMV for mortality prior to discharge. However, the evidence showed an increase in the incidence of BPD at 36 weeks PMA with SIMV when compared with VTV and HFOV. The committee agreed that there was no evidence to suggest a difference between SIMV and NSPLV, and SPLV for the outcomes assessed and that it should remain only a treatment option in preterm babies where VTV and HFOV are not clinically suitable. Therefore

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					we have added a new recommendation to clarify that SIMV can be used when VTV or HFOV are not suitable.
Newborn Services, Manchester University NHS Foundation Trust	Evidence Review B	76	22	We raise a concern over the data analysis in Table 15 and believe that the finding that VTV is so much more probable *to be the best ventilation technique* may be due to low numbers in that group, with possible positive reporting bias leading to an error in interpretation. It is noted that here SIMV is the second "best" ventilation, with HFOV being third.	Thank you for your comment. The committee made an a priori assumption that there would need to be at least 100 babies randomised to a treatment across all included trials in the NMA for them to make a recommendation with confidence. There were 396 and 319 randomised to mortality prior to discharge and BPD at 36 weeks in the NMAs, respectively. The possible positive reporting bias could equally been expected for other ventilation modes and not only VTV. However, to look for unpublished RCTs was beyond the scope of this analysis. The committee also agreed that there is clinical plausibility behind better respiratory outcomes with VTV, given that volutrauma induced by excessive volume and atelectrauma induced by inadequate volume with other invasive ventilation techniques can lead to chronic lung disease. The committee acknowledged that there was no difference between SIMV and VTV or HFOV for mortality prior to discharge outcome. However, there was evidence that SIMV was worse when compared with VTV and HFOV for BPD at 36 weeks PMA, and also there was a clinically significant increase in the neurodevelopmental outcome of cerebral palsy with SIMV compared with HFV. Overall, the committee was of a view that since there was no evidence for a difference

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					between VTV and HFOV, HFOV is preferred over SIMV.
Newborn Services, Manchester University NHS Foundation Trust	Evidence Review B	80	13	We note also that the validity of Table 16 is in doubt due to the documented bias and the lack of good fit for the model.	Thank you for your comment. The recommendations in this area are based on the best available evidence. Although, when making recommendations, the committee acknowledged the limitations associated with the available evidence. The lack of good fit for the models is likely to be the consequence of poorly conducted primary research in this area i.e. the ability to violate the protocol and switch from one mode to the other with the same equipment, heterogeneous population of preterm babies included in the studies, with gestational ages crossing pre-specified stratification set in protocol, the age at which ventilation was started also crossed pre-specified stratifications or was not stipulated in the inclusion criteria, etc. Even though Table 16 is in doubt due to the documented bias and the lack of good fit for the model, the results are in line with the clinical practice i.e. the committee highlighted that VTV is widely used in clinical practice and that there is clinical plausibility behind better respiratory outcomes with VTV, given that volutrauma and atelectrauma induced by excessive volume and inadequate volume respectively of other invasive ventilation techniques can lead to chronic lung disease. Also, the findings for SPLV is in line with

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					their general clinical experience i.e. that preterm babies do not perform as well with SPLV as other invasive ventilation techniques for primary respiratory support. This was based on committee clinical experience that the synchronisation of every single breath in SPLV can result in less favourable outcomes for the preterm baby in comparison with other invasive modes. So, irrespective of the doubts due to the documented bias and the lack of good fit for the model, the findings are in line with the committee experiences of clinical practice.
Newborn Services, Manchester University NHS Foundation Trust	Short Guideline	5	6	We would be concerned that the suggestion to use HFOV for babies who do not respond to VTV may result in other effective modes being bypassed, and possibly result in more complications for babies who may have responded well to (for example) PC-SIMV. Some babies do not clinically respond to VTV for many reasons, while some ventilators are better than others at delivering it - assuming no leak on the endotracheal tube. Some smaller units (where preterms may be delivered by chance) may not be familiar enough with HFOV to implement its use safely, and to minimise risk of pneumothoraces and over-ventilation.	Thank you for your comment. The committee agreed that there was convincing evidence favouring invasive ventilation with volume guarantee (which includes synchronised modes with VG) for mortality prior to discharge and BPD at 36 weeks, and there was evidence that HFOV should be considered as the next best alternative. However, the committee did recognise that there may be circumstances where VTV is not suitable and there are no trained staff in the use of HFOV, and therefore the committee have now added an additional recommendation stating that SIMV could be used in these circumstances. . The aim of the recommendations is to encourage the best practice and the committee agreed that neonatal units should be able to deliver techniques of VTV and HFOV.
Newborn Services, Manchester University NHS Foundation Trust	Short Guideline	5	9	Whilst we agree that there is some evidence to support using VTV as a first-line ventilation mode, and that HFOV should be	Thank you for your comment. When making the recommendations the committee acknowledged

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				considered, we would argue that SIMV is an appropriate alternative. We note that SIMV is not specifically listed in this paragraph prohibiting several modes of ventilation, and presume therefore that this remains an acceptable choice. We also note the associated data in Evidence review B, table 14, which does not show that mortality is greater with SIMV compared with Volume Targeted Ventilation. 1.02 (0.57-1.84).	that there was no difference between VTV and SIMV for mortality prior to discharge. However, the evidence showed an increase in the incidence of BPD at 36 weeks PMA with SIMV when compared with VTV and HFOV. The committee agreed that there was no evidence to suggest a difference between SIMV and NSPLV, and SPLV for the outcomes assessed and that it should remain only a treatment option in preterm babies where VTV and HFOV are not clinically suitable. Therefore we have added a new recommendation to clarify that SIMV can be used when VTV or HFOV are not suitable.
Newborn Services, Manchester University NHS Foundation Trust	Short Guideline	5	14	There may be occasion (for clinical reasons) to trial a preterm baby short-term on Nitric Oxide for severe SDLD with PPHN. Whilst we agree that NO should not be a standard practice for preterms, we would suggest against complete prohibition.	Thank you for your comment. We have updated the wording of this recommendation to read: "Do not routinely use inhaled nitric oxide for preterm babies who need respiratory support for respiratory distress syndrome (RDS), unless there are other indications such as pulmonary hypoplasia or pulmonary hypertension."
Newborn Services, Manchester University NHS Foundation Trust	Short Guideline	13	22	24-hour access to babies is not feasible in every unit, for reasons of space or confidentiality for example whilst ward-rounds are ongoing. We agree however that parents should be invited to attend the ward-round for their own baby.	Thank you for your comment. The committee agreed that 24 hour access is ideal and that parents should always be involved in discussions about their own baby during ward rounds, as we have recommended.
NHS Greater Glasgow and Clyde	Short Guideline	17	13	*"severe (score of more than 2 standard deviation [SD] below normal on 12 validated assessment scales, or a score of less than 70 on the Bayley scale of 13 infant development mental developmental index [MDI] or psychomotor 14 developmental index [PDI]"*	Thank you for your comment. You are correct that the Bayley III scale does not use the terms MDI and PDI. However, the mention of Bayley II is in the 'terms used in this guideline' section and does not form part of the recommendations. The choice of what scales to use to develop a composite neurodevelopmental outcome when assessing

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				This is a reference to Bayley II but Bayley III does **not use the terms MDI and PDI**, Bayley III assessment is divided into 5 domains Cognitive/Expressive communication, Receptive communication/ fine motor and gross motor Composite score <70 for Cognitive/Language/or Motor, is considered severe (as mentioned above) **Thank you for excellent clear to follow guideline**	evidence was based on the scales that were reported in the clinical studies. Many of these studies used the Bayley II mental developmental index or psychomotor developmental index to assess neurodevelopmental outcomes and therefore we used these as our outcome measure. Our guideline does not make any recommendations about neurodevelopmental follow-up or what scales to use.
Oxford University Hospitals NHS Foundation Trust	Short Guideline	General	General	Great work from the GDG. Well done.	Thank you for your comment.
Oxford University Hospitals NHS Foundation Trust	Short Guideline	9	9	**Carbon dioxide**. Given the advice at line 7 on consideration of transcutaneous oxygen monitoring for preterm babies on invasive ventilation who are clinically unstable, would the GDG perhaps consider adding a similar comment for transcutaneous carbon dioxide monitoring. 'For preterm babies on invasive ventilation who are clinically unstable, consider transcutaneous carbon dioxide monitoring.' The two are often combined on a single sensor. Users would argue that TcCO2 monitoring is very useful and provides a particular safeguard for babies on HFOV, in whom iatrogenic hypocarbia can readily occur in non-volume guarantee mode. The baby with TcO2 monitoring is likely to also be on a saturation monitor.	Thank you for your comment. As the committee only considered the levels of carbon dioxide and did not prioritise a review question looking at the method of monitoring CO2, it was not possible for the committee to make recommendations on the use of transcutaneous CO2 monitoring.
Oxford University Hospitals NHS Foundation Trust	Short Guideline	9	10	The GDG sensibly favours more permissive pCO2 ranges and argues that fewer adjustments in ventilator settings will be necessary than the former practice of adhering to narrower ranges. This implies that fewer blood gases will be needed and I would argue that the comment above (Comment 1) making the case for transcutaneous carbon dioxide monitoring is all the more relevant. TcCO2 monitoring used well reduces the number of blood gases required.	Thank you for your comment. As the committee only considered the levels of carbon dioxide and did not prioritise a review question looking at the method of monitoring CO2, it was not possible for the committee to make recommendations on the use of transcutaneous CO2 monitoring.
Raigmore Hospital – NHS Highland	Short Guideline	5	6	Our concerns from Inverness, a local neonatal unit is about the paragraph on Volume targeted ventilation (1.2.6/ 1.2.7):	Thank for your comment. The committee agreed that there was convincing evidence favouring

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				'For preterm babies who need invasive ventilation, use volume-targeted 6 ventilation (VTV) as the primary mode of respiratory support. If VTV is not 7 effective, consider high-frequency oscillatory ventilation (HFOV). 8 *1.2.7 Do not use synchronised pressure-limited ventilation such as assist'* We feel the wording is too strong here. We agree that Volume targeted ventilation is ideal and of course available always in larger centres. There needs to be some mention of ' in smaller units after initial stabilisation' that this should be aimed for. It is not realistic yet here to ventilate everyone with that mode, it requires time to train people as we all have all been brought up with pressure limited ventilation (which of course most of us also in larger centres use on initial stabilisation in the delivery room). On 1.2.9. We need to be aware that in local neonatal units NO is not available, so maybe in this sentence one could add 'if available'. Of course we aim that babies at an increased risk of pul hypoplasia are born in a centre who does have NO facilities.	invasive ventilation with volume guarantee (which includes synchronised modes with VG) for mortality prior to discharge and BPD at 36 weeks. There was also evidence that SPLV was inferior to other invasive ventilation modes for mortality prior to discharge, days on invasive ventilation and pneumothorax and as a result, this mode should not be used as a primary ventilation mode in preterm babies requiring respiratory care. Based on this evidence the committee therefore agreed it was appropriate to make strong recommendations. However, the committee did recognise that there may be circumstances where VTV is not suitable and there are no trained staff in the use of HFOV, and therefore the committee have now added an additional recommendation stating that SIMV could be used in these circumstances. The aim of the recommendations is to encourage the best practice and the committee agreed that neonatal units should be able to deliver techniques of VTV and HFOV. In relation to your comment on nitric oxide, the recommendation suggests that it should not be routinely used for preterm babies with respiratory distress syndrome but may be appropriate in babies with pulmonary hypoplasia or pulmonary hypertension. As you suggest, these babies would therefore need to be treated in a unit that is able to provide NO therapy.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Resuscitation Council UK	Algorithm	General	General	The guideline and evidence reviews do not offer evidence or recommendations on respiratory support beyond selection and continuance of the primary mode of support. The algorithm section on 'Assisted ventilation' does not accurately reflect the guideline content.	Thank you for your comment. The mode of primary respiratory support was prioritised by the committee for the network meta-analysis used for this evidence review. The algorithm is intended to provide an overview of the guideline content and includes all the topics on which recommendations were made, but we have adjusted the assisted ventilation section to indicate that the recommendations only cover the primary mode of ventilation.
Resuscitation Council UK	Evidence review A	24	13	Typographical error "bais".	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review A	25	14-15	Typographical error "invasively ventilation" in both sentences.	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review A	27	3	Correction to text required for "**Error! Reference source not found".**	Thank you for your comment. This error message has been corrected.
Resuscitation Council UK	Evidence review A	27	4	Typographical error in legend b "arterioususa".	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review A	27	4	We are concerned that elements of Table 19 may cause confusion for some readers. 'Footnote a' does to some extent acknowledge that there may be gaps in the evidence informing the risk factors for BPD table. This could be strengthened and clarified further by indicating in the legend that the stated risk factors were identified through a strict review protocol that may have excluded evidence from smaller or single centre studies. The listed risk factors have been identified as 'independent risk factors for BPD'; this could be stated in the table title. This would further help to clarify why there may be other risk factors not listed for every intended reader.	Thank you for your comment. The footnote has been amended as you suggest to include the fact that the evidence was identified from large prospective cohort studies. It is not usual NICE style to include details of the method of analysis (such as 'independent') in the title of the table, as this detail is already included in the impact and rationale.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Resuscitation Council UK	Evidence review A	27	13-14	This rationale states that "There was no evidence of a link between antenatal steroids, chorioamnionitis, intrauterine growth restriction, ethnicity or race, or postnatal steroid use, and BPD". This may be misinterpreted as implying that the review has found evidence of no association; rather than there being insufficient evidence on which to draw conclusions. As detailed in pages 28-32 of Evidence Review A. Association and causality differ which is not clearly addressed in the current review.	Thank you for your comment. To make it clear that no evidence was found we have amended the wording of the rationale to state 'No evidence was found to link antenatal steroids, chorioamnionitis, intrauterine growth restriction, ethnicity or race, or postnatal steroid use, and BPD'.
Resuscitation Council UK	Evidence review A	31	30	Typographical error "includein the the".	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review B	General	General	The Ciuffini 2014 and Lavizzari 2016 studies include the same study population as explained https://jamanetwork.com/journals/jamapediatrics/article-abstract/2580306 Citation: Lavizzari A, Colnaghi M, Ciuffini F, et al. Notice of Duplicate Publication: Heated, Humidified High-Flow Nasal Cannula vs Nasal Continuous Positive Airway Pressure for Respiratory Distress Syndrome of Prematurity: A Randomized Clinical Noninferiority Trial (*JAMA Pediatr*. doi:10.1001/jamapediatrics.2016.1243). *JAMA Pediatr.* 2016;170(12):1228. doi:10.1001/jamapediatrics.2016.3743 The single death reported in each study may therefore be a duplicate (see Table 74 page 553). This critical point may also have impacted on the data regarding BPD at 36 weeks PMA (see Table 75 page 553) and other analyses within the NMA for non-invasive ventilation.	Thank you for your comment. Thank you for bringing the dual reporting to our attention, Ciuffini 2014 has since been excluded due to dual reporting in Ciuffini 2014 and Lavizarri 2016. The NMA and pairwise analyses were re-run with the new data with no change in the results or conclusions.
Resuscitation Council UK	Evidence review B	12	1	The review protocol for question 1.1 specifically excludes resuscitation but this was not an exclusion criterion within the	Thank you for your comment. As resuscitation was excluded in the protocol, the term was not

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				search strategy. The distinction between resuscitation and stabilisation can be unclear, especially for preterm babies; it would be helpful if the guideline could briefly explain how this was dealt with.	included in the search strategy. The exclusion filter that was used is a generalised one that is used in all guidelines to exclude very low level study types, such as editorials, animal studies, etc. Resuscitation was not listed as a specific exclusion criteria, as you suggest it should have been, because of the risk that the search strategy would then exclude relevant studies that happened to mention resuscitation in the abstract but would otherwise be relevant. We have updated the Methods chapter so that this process is outlined more transparently.
Resuscitation Council UK	Evidence review B	13	24	In this table summarising the protocol the critical outcome definition used for BPD differs to that used in evidence review A. Differing definitions also occur across PICO tables in other Evidence reviews. Secondly, use of the classification "or 28 days of age' would infer that the traditional Classic BPD definition is being accepted rather than the 'New BPD' clinical definition established by the NICHD (2000). The latter uses duration of requirement as 'for 28 days' to differentiate true oxygen dependency. It is unclear if this is a typographical error; as included studies were required to have been conducted post 1990. As currently written the definition for BPD used in Evidence Review B differs from the definition used for the national NNAP audit measure. A statement about choice of definition would clarify this and help to resolve any concerns that may arise when reviewing clinical practice both in relation to this guideline and reported NNAP audit results for any specific neonatal unit. Please note that the definition used for the review protocols in 'Evidence Review B' is consistent across the five review questions as	Thank you for your comment. All of the reviews that included BPD as an outcome measured BPD at both commonly used time points - 28 days of age (traditional) or 36 weeks postmenstrual age (new). These timepoints were specified in the protocols. We acknowledge that BPD at 36 weeks PMA is the definition used for the national NNAP audit measure, but both definitions were used so that the searches and reviews captured all of the available evidence. Analyses were performed via subgroup analyses, i.e. outcomes reported as BPD at 36 weeks PMA were not pooled with outcomes reported at 28 days of age. However, for the review on risk factors for BPD, the committee chose only to consider babies who required oxygen at 36 weeks PMA, as this was the more appropriate definition for this review.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				detailed in appendix B; Table 1 has been used as an illustrative example.	
Resuscitation Council UK	Evidence Review B	23	18-21	There is some inconsistency between lines 18-21 on page 23 and lines 17-18 on page 22. This review looks at balancing the benefits and risks of different approaches. No evidence is presented showing an absence of negative consequences related to CPAP; just that evidence supports it as a preferred option. Minor rewording would clarify this. Please note typographical errors: "the t potential" and "negativeconsequence" .	Thank you for your comment. We have corrected the typographical errors. We have edited the 'Benefits and harms' section so that it is clearer that we are stating that the review is balancing the benefits and harms of the different interventions and that evidence that favours CPAP does not in itself demonstrate a lack of negative consequences.
Resuscitation Council UK	Evidence Review B	23	22	The statement "…..not breathing adequately after 10 minutes of support…" is included in the illustrative example of indications for invasive ventilation in the delivery room. Was this committee consensus or evidence based? This could be interpreted as "a preterm infant who is breathing ineffectively should receive mask ventilation for 10 minutes before intubation is considered?".	Thank you for your comment. This particular statement was based on committee consensus, but is not a recommendation. We have amended this statement in the committee's discussion of the evidence section so that it is clear that if babies are not breathing after a period of time, this would be an indication for invasive ventilation. The initial wording of 'after 10 minutes of support' has been replaced with 'a period of support' as the suggestion of 10 minutes was not evidence-based. A sentence was also added to suggest that in the minutes after birth, the Newborn Life Support guidelines should be followed.
Resuscitation Council UK	Evidence review B	25	27	Typographical error, there is a discrepancy in the full text and acronym for MIST; Minimally Invasive Surfactant Therapy rather than Administration.	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review B	37	26	Typographical error "thereforethe".	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review B	37	31-35	We welcome that the review has highlighted the paucity of evidence for use of laryngeal masks; and the related research recommendation.	Thank you for your comment.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Resuscitation Council UK	Evidence review B	48	47	Typographical error "y".	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Evidence review B	103	9	We are aware of the ongoing and current clinical use of a Sensormedics HFOV device in a NICU; as well as this device being in clinical use in PICU settings. Currently this sentence is inaccurate.	Thank you for your comment. The committee agreed that this equipment is not widely used, cannot be repaired and is obsolete, and its use does not represent the standard clinical practice.
Resuscitation Council UK	Evidence review B	553	7	Table 74 appears to include numerical errors for denominators examples identified: - Ciuffini CPAP 93 and Hi Flow 86 total 179 (the trial actually included 177 infants CPAP 92 and HF 85) - Lavizzari CPAP 159 and HF 159 (the published trial actually included 316 infants , 158 in each arm) - Wood CPAP 61 and SiPAP 61 (the trial actually included a total of 120 infants, 60 in each arm) It can be noted that these denominators are correct in table 75. The denominator for Salvo 2015 also differs between table 74 and 75. Additionally, for the Roberts 2016 trial both table 74 and 75 detail the denominators as CPAP 294 and HF 289 but this includes the 19 exclusions that were made prior to intention to treat analysis. These possible errors raise concern over accuracy of the NMA conducted on the topic of mortality.	Thank you for your comment. In the dataset for mortality, several studies reported zero events of interest in some arms (that is, the number of babies dead prior to discharge was zero). Combining such data can be problematic: when zero events occur in some arms of a study, the log-OR becomes undefined (as does the variance), which causes problems in the analysis and precludes the estimation of relative effects. As a result, continuity corrections are needed. Using a continuity correction for studies with zero counts allows the log-OR to be estimated, and hence allows synthesis via standard NMA methods. There are many possible continuity correction methods. In the present study, a continuity correction of 0.5 was added to both the number of events and the number of non-events across all study arms, in studies in which one or more (but not all) arms had zero events. This has now been clarified in the text. Generally, continuity correction is not needed in large networks with a small number of arms with 0 events. However, the network for mortality outcome was small with a large number of arms with zero events. As a result, in this particular NMA continuity correction was applied.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					Ciuffini 2014 has been excluded from the review because it dual-reported babies that were reported in Lavizzarri 2016, but this did not make any difference to the results or the conclusions. Lavizzari 2016 - the denominators are different due to the continuity correction in the mortality NMA. This was clarified in the text and table. Wood 2013 and Salvo 2015 - the denominators are different due to the continuity correction in the mortality NMA. This was clarified in the text and table. Roberts 2016 - thank you for spotting this. These figures were corrected. All analyses including NMAs and pairwise were re-run using the corrected data. The results and conclusions were unchanged.
Resuscitation Council UK	Evidence Review D	50	8	The review protocol, in particular the defined comparator blood pressure target levels, resulted in exclusions. RCTs were identified but did not meet the inclusion criteria for the review. This is different to there being no evidence. It would help the broader readership to be provided with more information about the comparators used for BP targets and why these were defined as such.	Thank you for your comment. The comparator blood pressure target levels were chosen on the basis of current clinical practice as accepted levels for preterm babies, and based on the committee's expertise. The review protocol has been updated to make this clear. No studies were excluded for using different target levels.
Resuscitation Council UK	Evidence Review E	31	39	Typographical error – missing word "showed a clinically decrease"	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Methods	6	11	The guideline and evidence reviews do not offer evidence or recommendations on respiratory support beyond selection and	Thank you for your comment. The wording 'as the primary mode of respiratory support' is included in

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				continuance of the primary mode of support. This list should indicate exclusions including: post-extubation respiratory support and weaning modalities. This also appears in the draft guideline on page 45.	the recommendation itself and therefore we have not included it in the lists in the methods chapter or context section of the guideline as these are only summaries of the guideline content.
Resuscitation Council UK	Short Guideline	1	7	"**This guideline covers…..**" implies that this includes all aspects of respiratory care within the hospital setting. As post-extubation respiratory support and weaning modalities have not been reviewed this statement should be revised to more accurately reflect the guideline content.	Thank you for your comment. This sentence has been amended to make it clearer what topics are coved in the guideline.
Resuscitation Council UK	Short Guideline	3	5	We are concerned that some elements of Table 1 may cause confusion for some readers. 'Footnote a' does to some extent acknowledge that there may be gaps in the evidence informing the risk factors for BPD table. This could be strengthened and clarified further by indicating in the legend that the stated risk factors were identified through a strict review protocol that may have excluded evidence from smaller or single centre studies. The listed risk factors have been identified as 'independent risk factors for BPD'; this could be stated in the table title. This would further help to clarify why there may be other risk factors not listed for every intended reader.	Thank you for your comment. The footnote has been amended as you suggest to include the fact that the evidence was identified from large prospective cohort studies. The word independent has not been included in the title of the table as this would not necessarily show that there may be other risk factors that are not listed.
Resuscitation Council UK	Short Guideline	5	6	To avoid misinterpretation of points 1.2.6 and 1.2.7 it should be clarified that the recommendations concern primary respiratory support and not post-extubation or weaning strategies. Consider amending the recommendation headings.	Thank you for your comment. The wording 'as the primary mode of respiratory support' is included in the recommendation itself and therefore we have not included it in the already rather long sub-heading.
Resuscitation Council UK	Short Guideline	9	6	This guideline suggests saturation targets of 91-95%; we think it should specify that this is after the transition to ex-utero life. As we know it is normal to be born blue and have saturations <91% initially and	Thank you for your comment. We have amended the wording to make it clear that this target is after initial stabilisation of the baby following birth.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				these saturations normally improve over the first few minutes of life.	
Royal College of Nursing, CYP Specialist Care Forum	Short Guideline	4	2	*We are concerned that the subheading *'Respiratory support before admission to the neonatal unit'* suggests that the standard 1.2.1 reducing the use of invasion of ventilation where clinically appropriate is only applicable prior to admission to neonatal unit and not an on-going standard for care. *We suggest inserting the following: *When stabilising and* ***managing on-going care of*** *preterm babies needing*	Thank you for your comment. The evidence review for this question only considered preterm babies prior to their admission to the neonatal unit so we have only been able to make recommendations for babies in this timeframe. However, we agree that non-invasive ventilation should be used where possible in the neonatal unit and this is covered by recommendation 1.2.6.
Resuscitation Council UK	Short Guideline	10	Footer	Text is missing from reference 7; ends with an incomplete sentence.	Thank you for your comment. This has been corrected.
Resuscitation Council UK	Short Guideline	19	25	Automated oxygen titration systems may be useful, and we support the research recommendation to explore this.	Thank you for your comment. The committee agree that automated titration systems require further research.
Resuscitation Council UK	Short Guideline	22	3-4	This rationale states that "There was no evidence of a link between antenatal steroids, chorioamnionitis, intrauterine growth restriction, ethnicity or race, or postnatal steroid use, and BPD". This may be misinterpreted as implying that the review has found evidence showing no association; rather than there being insufficient evidence on which to draw conclusions. As detailed in pages 28-32 of evidence review A. Association and causality differ which is not clearly addressed in the current review.	Thank you for your comment. The rationale section has been amended to make it clear that no evidence was found, rather than there being evidence of no difference.
Resuscitation Council UK	Short Guideline	23	14	Consider revising this very long sentence to improve readability.	Thank you for your comment. This sentence has been split into smaller sentences to make it easier to read.
Resuscitation Council UK	Short Guideline	24	1	The recommendation and rationale for respiratory support before admission to the neonatal unit are sound. However, there may be	Thank you for your comment. We acknowledge that there are different ways of delivering CPAP

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				challenges for implementation into practice that will need to be overcome including: staff, training and equipment/consumables. The review has not explored the patient interface and equipment required for delivering CPAP prior to admission to the neonatal unit. Many studies used short single/binasal prongs and specific CPAP devices; others did not report the specific interface (e.g. nasal prongs or face mask) used to provide CPAP from resuscitation devices (e.g. T-piece). Current practice regarding 'intubation cut-offs' as stated may reflect challenges around delivery of effective CPAP whilst in transit from the delivery room. Distance and logistics around this will vary centre to centre; method of moving a baby e.g. resuscitaire, transport incubator will also influence early care. Specific acknowledgement of these issues is important within such a guideline. It would be helpful for the evidence review to consider effectiveness of CPAP delivery, equipment and logistics as part of this recommendation and/or if insufficient evidence is found to suggest a research recommendation.	and a variety of factors that may influence the choice of different CPAP techniques. However, during protocol development, the committee agreed that all methods of administering CPAP could be grouped together, so subgroup analyses by delivery type were not prospectively planned for this review. The committee recognised that local factors such as place of birth, or distance from the labour ward to the neonatal unit would influence early care and this has now been noted in the committee's discussion of the evidence.
Resuscitation Council UK	Short Guideline	26	16	The rationale includes the following sentence: "The evidence showed that nasal high-flow therapy had the highest probability of being the best technique for reducing mortality before discharge, compared with other non-invasive ventilation techniques." We are concerned that this statement may be based on insufficient data as for the included trials this was often a secondary analysis outcome that rarely occurred. For high flow specifically; two of the three trials providing mortality data into the NMA analysis did not complete planned recruitment (Ciuffini 2014 / Roberts 2016). It is important to note that the Roberts trial ceased recruitment on the basis that independent data safety	Thank you for your comment. Ciuffini 2014 has been excluded from the review because it dual-reported babies that were reported in Lavizzarri 2016. Thank you for noticing that some of the numbers for Roberts 2016 were incorrect, but after correcting these and re-running the NMA, we found that the results and risk ratios remained the same. Regarding the numerical inaccuracies in the

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				monitoring identified a significant difference in the primary outcome (treatment failure). Acknowledgement of this should be made in the rationale. There were also numerical inaccuracies in the Summary tables included in the NMA as outlined below (see comment for page 553 line 7). This may have impacted on the results found.	Summary tables, some denominators in the non-invasive NMAs are different due to the fact that there were 0 events in the studies. If there are 0's the model does not run. As a result, a continuity correction is applied i.e. 0.5 is added to each arm of the study in question. Hence, the denominators are slightly different. This was explained in the text and relevant tables, and does not impact on the results.
Resuscitation Council UK	Short Guideline	27	10	Whilst it is clear for the non-invasive techniques that the review focusses on primary modes of respiratory support this does not come across as clearly for the invasive techniques described. Amending the section headings or content to promote this message is required.	Thank you for your comment. We have now amended the wording in the rationale for invasive ventilation to make it clear that the recommendations only refer to invasive ventilation used as the primary mode of respiratory support.
Resuscitation Council UK	Short Guideline	27	26	It is likely across a range of networks that SCBUs who may provide short-term and infrequent ventilation will tend to use pressure limited modes of ventilation. In our experience flow sensors are not always available for use due to costs, infrequency of use and training considerations. Equipment limitations for ventilation modes also exist within neonatal transport systems. If VTV modes that necessitate flow sensor use are being recommended; consideration that this may not be achievable or feasible in all settings should be acknowledged. The commentary on rationale could be expanded to include more detail as outlined in the associated evidence review about modes that may be needed in different clinical settings (e.g. SCBU / transport) and phases of respiratory care (e.g. weaning).	Thank you for your comment. There was convincing evidence that SPLV should be avoided as the evidence showed an increase in the incidence of mortality prior to discharge, compared with NSPLV, HFOV and VTV. The evidence also showed an increase in days on invasive ventilation and pneumothorax, compared to VTV. The committee was of a view that neonatal units should aspire to adopt best practice by using techniques of VTV and. The committee noted that that flow sensors required for volume targeted ventilation are expensive and this has been acknowledged in the rationale and impact and the committee discussion of the evidence sections. The committee prioritised the aspects of

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					ventilation that they agreed would have the greatest benefit in standardising practice, and agreed that primary mode of ventilation should be prioritised above weaning and use during transportation. The committee did not therefore review any evidence for weaning from respiratory support and transportation and so were unable to make recommendations. However, the recommendations on invasive ventilation have now been clarified, including a new recommendation on SIMV as an option when VTV and HFOV cannot be used and this may be suitable for situations such as weaning and transportation.
Resuscitation Council UK	Short Guideline	27	27	Many, but not all, neonatal units use some form of volume limited ventilation, but not every unit commonly uses HFOV as a primary / early secondary mode of ventilation. This comment may reflect the local experience of committee members in their units rather than all of UK current practice.	Thank you for your comment. The committee acknowledged that not all neonatal units are trained to use HFOV, but wished to encourage the use of this mode and agreed that neonatal units should be trained in safe practice techniques of HFOV. However, the committee have now included a new recommendation on SIMV as an option when VTV and HFOV cannot be used.
Resuscitation Council UK	Short Guideline	27	27	Acknowledgement that it is not feasible to give VTV or HFOV modes of ventilation prior to admission to a neonatal unit (e.g. on transit from delivery suite) should be included to avoid misinterpretation.	Thank you for your comment. There are separate recommendations on the preferred mode of ventilation to be used prior to admission to the neonatal unit and this section is about ventilation techniques on the neonatal unit so the committee did not think it was necessary to make this addition.
Royal College of Nursing, CYP Specialist Care Forum	Short Guideline	4	9	May we make this point: in relation to giving surfactant 1.2.3 we have noted on page 24(line 26) that there is **limited evidence** to	Thank you for your comment. The evidence was limited only for a comparison of different minimally

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				make recommendations and highlighted limited expertise in administration techniques as well as a lack of understanding of dose requirements or potential of multiple doses. Therefore this raises issues in relation to cost implications and disparity of care.	invasive techniques (compared to each other), or on different dosing regimens. There was evidence that minimally invasive surfactant techniques reduced the incidence of BPD, pneumothorax and days on ventilation compared to invasive administration, so the evidence for this comparison allowed recommendations to be made. The committee were aware that minimally invasive surfactant administration requires training and this is discussed in the rationale and impact section. In this section they acknowledged that not all neonatal units have the facilities to carry out minimally invasive surfactant administration techniques, and not all healthcare professionals have been trained to use them. The committee agreed that in these circumstances, endotracheal surfactant administration followed by early extubation should be used, because there was evidence that it reduces the incidence of BPD compared with conventional administration of surfactant with continued ventilation. In the absence of evidence about surfactant dosage the committee could not conduct a formal cost- effectiveness analysis. However, the committee noted that minimally invasive surfactant administration techniques have lower intervention costs when compared with other administration techniques including conventional

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					endotracheal administration as it does not require the use of a ventilator, ventilator tubing or such high intensity nursing. There may be short-term cost implications for some neonatal units where minimally invasive techniques are not current practice but the committee discussed that minimally invasive techniques may be associated with lower costs and better outcomes in the long term.
Royal College of Nursing, CYP Specialist Care Forum	Short Guideline	4	14	Please note, based on expertise and clinical contact, we feel it is important to highlight that the neonate should receive humidified oxygen where possible to prevent skin trauma. Giving that there is no supporting evidence (p26, line 4) in relation to humidified or non-humidified oxygen use we are concerned that this recommendation opposes best clinical practice of the need for humidifying oxygen. We are aware of historical concerns regarding growth of bacteria in stagnant water – however practice of frequent circuit changing eliminates this risk.	Thank you for your comment. There was no evidence for humidified versus non-humidified oxygen, but upon discussion of this comment, the committee agreed to make a consensus recommendation to support best practice of humidifying oxygen when it is administered at higher flow rates, such as 2 litres per minute or more. The committee acknowledged the concerns regarding bacterial growth in stagnant water and we have updated the Benefits and Harms section in evidence review B to acknowledge this risk and highlight that current best practice of regularly changing circuits eliminates this risk.
Royal College of Paediatrics and Child Health	Evidence Review E	23	General	This review of evidence is in part based on the incorrect assumption that propofol can be used as a single agent for premedication prior to intubation	Thank you for your comment. The committee agreed that intubation, while an uncomfortable procedure, is not known to be painful, and thus did not require an analgesic as part of the pre-medication.
Royal College of Paediatrics and Child Health	Short Guideline	General	General	1 national cohort, 1 single centre and 1 network meta-analysis study including many small studies not referenced (e.g. DETECT trial) suggest that early targeted treatment might reduce mortality	Thank you for your comment. Our review for this question looked at the effectiveness of different interventions to close the patent ductus arteriosus

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				and improve outcome. Current best practice in many large centres around the world is to have an early targeted approach. There are two ongoing large randomized controlled trials (OSCAR and BENEDUCTUS) that are trying to answer this question more reliably. The statement does not reflect what is considered current best practice and therefore should be changed to account for this. JAMA. 2015 Jun 23-30;313(24):2441-8. Sellmer A, et al. Arch Dis Child Fetal Neonatal Ed 2013;98:F505–F510 Am J Perinatol. 2015 Sep;32(11):1087-94. doi: 10.1055/s-0035-1548727. Epub 2015 Mar 31	and did not identify how treatments could be targeted. The committee agreed that current best practice is not well established but in the committee's discussion of the evidence, the committee acknowledged the ongoing study called Baby-OSCAR (Outcome after Selective Early Treatment for Closure of Patent Ductus Arteriosus in Pre-term Babies), which was comparing the use of ibuprofen to placebo to close large PDAs in preterm babies and following them up for 2 years. The results of this study will provide further guidance on the use of pharmacologic treatment to close a PDA. The committee has now also acknowledged the ongoing BeNeDuctus Trial that is comparing early treatment to expectant management and will provide further evidence to guide the use of PDA closure. We have flagged both these studies to the surveillance team at NICE as they may necessitate an update of this review. Thank you for providing the following references: Isayama 2015 PDA outcomes in Japan and Canada Rozé et al. 2015 Association between early screening for patent ductus arteriosus and in-hospital mortality Sellmer et al. 2013 Morbidity and mortality in preterm neonates with patent ductus arteriosus on day 3

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					Unfortunately, none of these studies met inclusion criteria for this review as the intervention - early versus delayed screening - was not included in our review protocol.
Royal College of Paediatrics and Child Health	Short Guideline	3	3	Statement about effect of formula feeding on BPD risk is incorrect. Evidence for increased BPD risk is only shown for exclusive formula feeding since birth; the effect of mixed feeding cannot be quantified reliably to make such a statement, "Exclusive breastmilk feeding was associated with lower growth rates and a reduced risk of BPD as well as NEC and ROP," J Pediatr 2016;169:76-80. The statement should be rephrased to: exclusive formula feeding from birth	Thank you for your comment. The cited publication (Spiegler 2016) was included in the evidence review and showed an increased risk of BPD with mixed feeding compared to exclusive breast milk feeding. Mixed feeding was classified as infants who received any donor milk or mother's own milk as well as formula. It is true the risk of BPD was even higher with exclusive formula feeding compared to exclusive breast milk feeding, however it is still true to say that mixed feeding was associated with an increased risk of BPD, hence the terminology used in Table 1 of 'feeding with formula milk (exclusively or in addition to breast milk).'
Royal College of Paediatrics and Child Health	Short Guideline	3	5	The wording "treated with surfactant" and "treated for a patent ductus arteriosus" be changed to "Respiratory distress syndrome requiring surfactant treatment" and "Patent Ductus arteriosus requiring treatment". The addendum in the table is noted but this wording would obviate the need for an addendum.	Thank you for your comment. The evidence for this review question identified that babies who had been treated with surfactant and who had treatment for their patent ductus arteriosus (PDA) had a higher risk of BPD. As this is not exactly the same population as the group of babies who had respiratory distress syndrome requiring surfactant (but who may or may not have received it) or babies who had a PDA which required treatment (but who may or may not have received it) we have not been able to make this wording change. However, in order to make this clearer we have

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					also included this important caveat in the recommendation.
Royal College of Paediatrics and Child Health	Short Guideline	4	1	Volume targeted ventilation includes Volume Guarantee, Volume-Controlled and Volume Limited Ventilation. Many Ventilators use hybrid VT modes of ventilation along with SIMV/PSV/AC. The wording of the recommendation therefore needs to be clear as section 1.2.7 suggest that you should not use AC/PTV/PSV – however these can be used in VG modes. Unless the recommendation is that you shouldn't use hybrid modes of ventilation with VG? (Which is not supported by an evidence base)	Thank you for your comment. In the full evidence review B it is explained that VTV includes Volume guarantee ventilation (VGV), Target tidal volume (TTV), Pressure regulated volume control (PRVC) ventilation (PRVCV), Volume limited ventilation (VLV), Volume-assured pressure support (VAPS), any synchronised pressure limited ventilation + volume guarantee, and Synchronised intermittent mandatory ventilation (SIMV) + volume guarantee. AC/PTV/PSV + VG would therefore be included in VTV i.e. any synchronised pressure limited ventilation + volume guarantee. We have therefore clarified the recommendations on invasive ventilation to state that volume-targeted ventilation should be used in combination with synchronised ventilation. Also, we have added the definitions of all ventilation modes to the 'terms used in this guideline' section to help readers understand how the ventilation types were grouped together.
Royal College of Paediatrics and Child Health	Short Guideline	5	5	This guideline can be easily misread regarding the rejection of synchronised ventilation modes. Some may read that it only rejects pressure limited synchronised modalities, while other read that it has rejected synchronised volume targeted ventilation. The statement regarding HFOV could be misinterpreted as too strict as there is no evidence to support the primary use of HFOV.	Thank you for your comment. The relevant recommendation has been clarified i.e. VTV includes any ventilation with volume guarantee. The committee acknowledged that there was evidence that SPLV was worse when compared with HFOV for mortality prior to discharge and SIMV was worse when compared with HFOV for

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					BPD at 36 weeks PMA. Also, given that there was no evidence to suggest a difference between VTV and HFOV for any of the outcomes reported the committee agreed since VTV may not be appropriate for all preterm babies, for example where there is an air leak, HFOV is the second best method of invasive ventilation given the currently available evidence base. Also, the definitions of all ventilation modes were added to the 'Terms used in this guideline'.
Royal College of Paediatrics and Child Health	Short Guideline	5	5	Both statements are too strict with regard to the use of HFOV as exclusive second choice and the rejection of synchronised ventilation modes. The conclusion of the Cochrane review by Cools (2015) is not reflected correctly. It states: "There is evidence that the use of elective HFOV compared with CV results in a small reduction in the risk of CLD, but the evidence is weakened by the inconsistency of this effect across trials. Probably many factors, both related to the intervention itself as well as to the individual patient, interact in complex ways. In addition, the benefit could be counteracted by an increased risk of acute air leak. Adverse effects on short-term neurological outcomes have been observed in some studies but these effects are not significant overall. Most trials reporting long-term outcome have not identified any difference." Cools F, Offringa M, Askie LM. Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants. *Cochrane Database of Systematic Reviews* 2015, Issue 3. Art. No.: CD000104. A review by Poets points out further that evidence with regard to HFOV is comparing old, mainly non-synchronised modes and therefore this might not truly reflect current practice. Poets CF,	Thank you for your comment. The review by Cools 2015 is a traditional pairwise meta-analysis of RCTs which synthesized the results of different trials comparing the same pair of treatments, to obtain an overall estimate of the effect of one treatment relative to another. Our Network meta-analysis (NMA) has advantages over the standard pairwise meta-analysis in that it produced consistent estimates of the relative effects of all invasive ventilation modes including HFOV compared with every other invasive ventilation mode in a single analysis using both direct and indirect evidence. In situations where more than 2 interventions are being considered, synthesis of RCTs using NMA ensures that all relevant evidence, whether direct or indirect, is used to produce coherent estimates of the relative effects of every intervention compared with every other. This is the preferred method because multiple sources of evidence are

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Lorenz L. Arch Dis Child Fetal Neonatal Ed 2018;**103**:F285–F291. doi:10.1136/archdischild-2017-314264. At best a recent study has shown superiority of HFOV over SIMV + PSV. Respir Care 2014;59(2):159 –169.	used, and the final estimates of effect are more robust than if only direct sources of evidence were included. The use of the NMA deals with the problem that Poet 2018 refers to in that the NMA incorporated evidence on HFOV from all available trials and not only where HFOV is compared with old ventilation modes i.e. NSPLV.
Royal College of Paediatrics and Child Health	Short Guideline	5	14	General comment. There is no evidence supporting the 'prophylactic use' of iNO to prevent BPD in preterm infants. This is different to its use as a rescue treatment in babies with established RDS. **Recommendation: include a statement to the effect that iNo therapy should not be used in preterm infants to prevent BPD**	Thank you for your comment. The review was conducted to assess the use of inhaled nitric oxide in babies with respiratory distress syndrome, not the prophylactic use of inhaled nitric oxide for prevention of BPD, and thus we were unable to make a specific recommendation about its use in a prophylactic context.
Royal College of Paediatrics and Child Health	Short Guideline	5	14	This statement is agreed with, however, could it be stated slightly differently i.e. *Do not use inhaled nitric oxide routinely for preterm babies who need respiratory support for respiratory distress syndrome (RDS).* There is some evidence that iNO is effective in preterm infants with hypoxaemic respiratory failure associated with echo-confirmed PPHN physiology [Baczynski ADC 2017]. In babies with PPHN physiology, there is no alternative, superior, better studied, vasodilator. Issuing a statement that doesn't acknowledge this indication means that clinicians who elect to use iNO in this setting might well be unfairly criticised. Although there is no clear evidence of efficacy in preterm neonates, equally there is no definitive evidence of harm. Furthermore, there are	Thank you for your comment. We agree with your comment that inhaled nitric oxide (iNO) is beneficial for preterm babies with PPHN so we have updated the wording of this recommendation to read: "Do not routinely use inhaled nitric oxide for preterm babies who need respiratory support for respiratory distress syndrome (RDS), unless there are other indications such as pulmonary hypoplasia or pulmonary hypertension." The recommendation discourages the use of iNO for preterm babies with respiratory distress syndrome as iNO is expensive and had no evidence of benefit, but now does not prevent clinicians from using iNO for preterm babies with PPHN (or pulmonary hypoplasia).

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				also no concerning safety signals arising from term/near-term infant data. **Recommendation: change wording of this statement to include the word 'routinely'.**	
Royal College of Paediatrics and Child Health	Short Guideline	5	16	General comment. iNO is a relatively infrequently used drug with dubious efficacy and unproven safety in the preterm population. The evidence base for recommending use in specific sub-groups is lacking. Future RCTs to answer outstanding research questions are likely to be difficult to design and conduct. Retrospective cohort studies do not provide the level of detail to be informative. Prospective clinical registries have been recommended by international networks, and specifically relating to iNO use [Kinsella, J Peds 2016]. The ELSO registry is based on similar foundations and is considered mandatory for those using ECMO in neonates. **Recommendation: include a statement to the effect that information from preterm babies treated with iNO should be entered prospectively into available national/international registries.** **DOI. I chair the European inhaled nitric oxide registry which contains data on over 1900 neonates.** **https://www.medscinet.net/ino/default.aspx**	Thank you for your comment. Thank you for referencing the recommendations in Kinsella 2016. We have updated the wording of this recommendation to read: "Do not routinely use inhaled nitric oxide for preterm babies who need respiratory support for respiratory distress syndrome (RDS), unless there are other indications such as pulmonary hypoplasia or pulmonary hypertension." While we agree that it is good practice to enter babies into national/international registries, it was not within the remit of the guideline to recommend this. No research recommendations were made because the committee agreed that the evidence for the use of iNO in RDS (which was the aim of the evidence review) was sufficient for them to make a recommendation.
Royal College of Paediatrics and Child Health	Short Guideline	5	16	Another indication for NO is PPHN in preterm babies	Thank you for your comment. We have updated the wording of this recommendation to read: "Do not routinely use inhaled nitric oxide for preterm babies who need respiratory support for respiratory distress syndrome (RDS), unless there

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					are other indications such as pulmonary hypoplasia or pulmonary hypertension."
Royal College of Paediatrics and Child Health	Short Guideline	5	16	It is agreed that iNO should be considered in this population. The diagnosis of pulmonary hypoplasia is subjective. Most studies that have been done to date have included babies with PPROM, rather than pulmonary hypoplasia. The paper by Ellsworth [JAMA Pediatrics 2018] is an exception but should be included in the evidence review. **Recommendation: replace 'pulmonary hypoplasia' with 'hypoxaemic respiratory failure associated with prolonged rupture of membranes and oligohydramnios'.**	Thank you for your comment. The evidence review for this question looked at the use of inhaled nitric oxide in babies with respiratory distress syndrome, and hence the paper you have mentioned (Ellsworth 2018) was not included in the review. However, the committee were aware that pulmonary hypoplasia was one area in which there may be benefits for inhaled nitric oxide and have updated the recommendation to read: "Do not routinely use inhaled nitric oxide for preterm babies who need respiratory support for respiratory distress syndrome (RDS), unless there are other indications such as pulmonary hypoplasia or pulmonary hypertension. The committee acknowledged that the diagnosis of pulmonary hypoplasia is subjective, but have not replaced the term with ''hypoxaemic respiratory failure associated with prolonged rupture of membranes and oligohydramnios" as the intention is to mean pulmonary hypoplasia due to any reason.
Royal College of Paediatrics and Child Health	Short Guideline	6	10	Dexamethasone < 8 life increases also the risk for CP, "This review of trials revealed that the benefits of giving systemic corticosteroids to infants starting up to seven days after birth may not outweigh the known adverse effects. However, a particular corticosteroid called hydrocortisone shows promise in improving short-term outcomes without adversely affecting long-term	Thank you for your comment. Evidence for increased risk of cerebral palsy (CP) was inconsistent: 1 trial showed increased risk with dexamethasone and 3 showed no difference. Due to this we used a random effects meta-analysis which did not show an overall increased risk of

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				neurodevelopment. Beneficial effects of systemic corticosteroids overall included shorter time on the ventilator and less bronchopulmonary dysplasia, but adverse effects included higher blood pressure, bleeding from the stomach or bowel, perforation of the bowel, excessive glucose in the bloodstream, and **increased risk of cerebral palsy at follow-up, particularly in those treated with dexamethasone** - another type of corticosteroid. Early use of corticosteroids, especially dexamethasone, to treat or prevent bronchopulmonary dysplasia should be curtailed until additional research has been performed." Doyle LW, Cheong JL, Ehrenkranz RA, Halliday HL. Early (< 8 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD001146.	CP. The cited Doyle 2017 Cochrane review included 3 additional trials that did not meet our inclusion criteria (1 from a non-OECD country; 2 used a duration of corticosteroid dose that did not meet our criteria as 2 doses were given). Doyle 2017 also used a fixed meta-analysis model despite moderate heterogeneity of individual study effects (I^2=34%) - when a random effects model is used with their data there is no statistically significant increased risk of CP. The committee were aware of an ongoing hydrocortisone trial and mentioned this in their discussion of the evidence but this could not be included as it was not yet published. However, we will flag this to the NICE surveillance team as it may be appropriate to update these recommendations when the hydrocortisone data are available.
Royal College of Paediatrics and Child Health	Short Guideline	10	14	Propofol is an anaesthetic with no analgesic effect i.e. administration results in deep sedation BUT no analgesia. It is therefore inappropriate to recommend this as a sole premedication agent prior to intubation especially as it is often used in low dose to ensure the baby continues to breath during minimally invasive surfactant administration. Sedation does not abolish pain. See: JAMA. 2018 May 1;319(17):1790-1801.	Thank you for your comment. The committee agreed that intubation, while an uncomfortable procedure, is not known to be painful, and thus did not require an analgesic as part of the pre-medication. Thank you for the references you mentioned. We have reviewed these. You referenced Durrmeyer 2018 as the RCT that used propofol as a single agent in the review, as well as a Comment from Drs Fideler and Grasshoff and a response from Durrmeyer. Drs Fideler and Grasshoff raised

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				doi: 10.1001/jama.2018.3708 JAMA. 2018;320(11):1199. doi:10.1001/jama.2018.10014 JAMA. 2018;320(11):1199-1200. doi:10.1001/jama.2018.10025	concerns regarding the potential neurotoxicity of anaesthetics and analgesics on neurodevelopment and IVH. In their reply, Durrmeyer argued that 'a single, brief exposure to a general anaesthetic, as used in our study, was not within the scope of the FDA warning." Additionally, they highlighted that "epidemiological studies that found an association with neurodevelopmental impairment could not disentangle the respective roles of anaesthetics, surgery, pain, or the underlying condition Intubation, while an uncomfortable procedure, is not known to be painful and so does not require analgesia as part of the premedication regimen." Regarding IVH, Durrmeyer acknowledged that a relative imbalance between groups in sex and weight, which may have decreased risk factors for intraventricular hemorrhage in the atropine-propofol group, but speculated that a major neurotoxic effect of propofol was unlikely considering the results. We therefore think these references support the conclusion that propofol can be used as a premedication in preterm babies before intubation.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Royal College of Speech and Language Therapists	Short Guideline	11	4	Please specify that non-nutritive sucking can help parents identify oral readiness signs, oral secretion management, can enable professionals to check for oral reflex maturation, and reduce the risk or oral aversions (Harding et al, 2014).	Thank you for your comment. There was good evidence that non-nutritive sucking reduced length of hospital stay, however this was the only outcome relevant to our review that was reported in the included randomised trials. The committee also agreed that it may help soothe the baby between feeds, based on their experience. Thank you for citing the Harding 2014 paper: this is an expert review of studies which did not meet the inclusion criteria for our review.
Royal College of Speech and Language Therapists	Short Guideline	11	4	Parents can be encouraged to trial small amounts of oral intake according to an infant's need. The evidence for feeding infants on nCPAP and HFNC is varied, i.e. Evidence comparing infant development of full oral feeding when on nCPAP compared with HFNC is variable, with no significant differences between groups of infants reported in large randomized controlled trials (Campbell et al, 2006; Collins et al, 2013; Kugelman et al, 2015). Glackin et al's (2017) findings support this view, although a small sample size was investigated (22 infants in each group). Yoon et al (2011) compared 17 infants receiving nCPAP with 34 infants on HFNC and in contrast to the previously mentioned studies; found that days to develop full oral feeding tolerance and to regain birth weight took longer for HFNC infants compared with infants on nCPAP. Ferrara et al (2017) investigated infants bottle feeding whilst both on and off nCPAP. Results showed that the incidence of deep penetration and aspiration decreased significantly when infants were off nCPAP, although mild penetration and nasopharyngeal reflux remained the same under both conditions. Success with developing oral feeding skills for infants on HFNC have been reported in other	Thank you for your comment. Your comments pertain to review 6.1 What parent and carer involvement is effective in the care of preterm babies who are receiving respiratory support? The review compared the effect of different forms of parent/carer involvement on outcomes including days in hospital, BPD and neurodevelopmental outcomes. The studies that you referenced compared preterm babies on nCPAP to HFNC, and looked at outcomes including development of full oral feeding and thus did not meet the intervention/comparison or outcome requirements for this review. However, many of the studies that you referenced were assessed for inclusion in review 3.2 Effectiveness and safety of assisted ventilation techniques. Kugelman 2015 was included in our review. Several studies were excluded for the following reasons:

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				studies. Hanin et al, (2015) compared two groups of infants receiving nCPAP. One group received some oral feeds, while on nCPAP in contrast with a second group of infants receiving only gavage feeds. Infants receiving oral feeds developed earlier acquisition of feeding skills, but there were no clinically significant incidences of aspiration pneumonia between the two groups. Shetty et al, (2016) evaluated 116 infants, with infants receiving HFNC achieving oral feeding significantly earlier compared to those on nCPAP. The evidence base remains small, but some authors advocate that a cautious approach to introducing oral feeding for infants on all forms of respiratory support can have long term benefits, specifically in reducing oral aversions (Jadcherla et al, 2016; Shetty et al, 2016). ****We need to mention oral feeding to reduce future risks of oral aversions, but with caution, and with an individualised programme for each infant.*	• Campbell 2006 - study was only relevant to the Network Meta-Analysis (NMA) and did not include the outcomes of interest for the NMA • Collins 2013 and Glackin 2017 - covered post-extubation weaning • Jadcherla 2016 - the outcomes were not relevant Yoon 2011, Ferrara 2017, Hanin 2015 and Shetty 2016 were not identified in the search, but upon reviewing these references, they would not have been included in the review because: • Yoon 2011 and Shetty 2016 - retrospective cohort studies and our protocol specified that cohort studies would only be included if no RCT evidence was available, which was not the case • Ferrara 2017 - not comparative and only included 7 babies so it did not meet protocol inclusion criteria (> 15 babies in each arm) • Hanin 2015 - not relevant because both study arms received nCPAP and the intervention (type of feeding) was not relevant
Royal College of Speech and Language Therapists	Short Guideline	3	5	The RCSLT feel it would be useful to highlight in this table, that infants born before 32 weeks have increased risk of oral feeding problems (Uhm et al, 2013). Specifically, infants with respiratory difficulties are at risk of developing persistent oral feeding aversions and problems (Hawdon et al, 2000).	Thank you for your comment. The evidence review for this question only looked for evidence of risk factors for BPD. The Uhm 2013 paper is about dysphagia in babies and did not include BPD, so this paper would not have met our protocol criteria.
Royal College of Speech and Language Therapists	Short Guideline	18	General	Research suggestions:	Thank you for your comment. The guideline did not look for evidence on safe feeding for infants

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Further large randomised controlled trials which investigate a safe oral feeding protocol for infants on nCPAP and HFNC.	on nCPAP and HFNC, so we do not know whether there is evidence in this area or not. We are therefore unable to make the research recommendation that you have suggested.
Royal College of Speech and Language Therapists	Short Guideline	41	24	We also believe that information about early communication needs to be highlighted clearly here, as: Hearing begins to develop at 25 -26 weeks gestational age, with the development of cochlear hair cells which process sounds. At 26 – 28 weeks gestational age, infants can demonstrate responsiveness to voice (Kisilevsky et al, 2009). Around 30 weeks gestational age, active listening is developing and attunement to maternal voice occurs (Smith et al, 2007). At this stage, infants are reflexive in their responses, becoming reactive to events and people, and as they become familiar with their environments, they become anticipatory (Coupe & Golbart, 1986). These reactions become more differentiated as infants begin to perceive consistencies in their routines and develop specific preferences. Carers tend to interpret infant behaviours as meaningful. They are likely to act in ways that are nurturing and contingent (Tomassello &Todd 1983; Tomassello & Ferrar, 1986). Preterm birth is a risk factor for a range of difficulties, including language development (Aylward, 2002). The recent NICE guidelines for Developmental Follow up of children and Young People born preterm highlight that infants born prematurely are at risk of speech, language and communication problems (NICE guideline NG72 ; 2017). Significant increases in the risk of mild or moderate language impairment in early preterm children (<27 weeks) in comparison	Thank you for your comment. Review 6.1 'Assessing what parent involvement is effective in the care of preterm babies receiving respiratory support' included verbal interaction (including reading, singing to babies and talking to babies) and severe hearing impairment as interventions and outcomes of interest, respectively. However, no evidence for verbal interaction was identified in this review, thus no recommendations for this intervention were made. However, the committee have now acknowledged the importance of early communication with the baby in the committee's discussion of the evidence for review 6.1 in Chapter F.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				to term infants at 2.5 years of age was identified in one study (Serenius et al, 2013). Another study found that there were significantly increased risks of developmental speech and/or language delay between the ages of 3 and 5 years in preterm children (34-36+6 weeks) compared to those born at term (Rabie et al, 2015). In addition to potential speech, language and communication difficulties, the NICE guidelines for Developmental Follow up of children and Young People born preterm also identify other factors which can impact on communication development, and which children born prematurely are at risk of (NICE guideline NG72 ; 2017). These problems are: an increased risk of autistic spectrum conditions; an increased risk of learning and executive function problems in school, attention and listening difficulties, an increased risk of learning disabilities (and therefore having special educational needs), and increased risks of visual and /or hearing problems. ****we believe strongly that we add that parents need appropriately skilled professionals (speech and language therapists) advising and supporting their early interaction on discharge home.*	
Royal Free London NHS Foundation Trust	Evidence Review B	101	1-14	SIMV – not excluded in list of synchronised pressure limited ventilation, evidence review B indicates the panel recommend SIMV as an alternative mode where VTV/HFOV are not suitable – should this be stated more clearly in the guideline?	Thank you for your comment. A new recommendation has been added to the guideline stating that SIMV could be considered as an option when VTV and HFOV are not appropriate.
Royal Free London NHS Foundation Trust	Short Guideline	4	9-12	Intubation /surfactant -- Could the guideline include some acknowledgement /caveats for situations/units eg level 1 units, where a significant number of preterm babies will be transferred out and will likely require intubation for transport? And therefore thresholds for intubation/surfactant for stabilising for transfer may be less.	Thank you for your comment. The aim of this recommendation is to reduce the use of intubation solely for the purpose of administering surfactant, and instead encourage the use of non-invasive administration techniques, or intubation followed by early extubation and there was evidence for

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					benefit with both these techniques. However, the committee recognise that babies may need to be intubated for transport. However, following consultation on the scope, respiratory support during transport was not identified as a priority for inclusion in the guideline and so the committee were unable to make any recommendations relating to this.
Royal Free London NHS Foundation Trust	Short Guideline	5	9-12	We are reading this as an experienced team of paediatric and neonatal consultants and struggling to make sense/ understand this guidance Will there be more guidance on VTV ie using a synchronised mode, any evidence on preferable modes.	Thank you for your comment. The recommendation on invasive ventilation has been clarified to state that volume-targeted ventilation should be used in combination with synchronised ventilation and we have also added a new recommendation to clarify that SIMV can be used when VTV or HFOV are not suitable. In the full evidence review B there is a more detailed explanation of the modes of ventilation included in this review. Finally, the definitions of all modes have been added to the 'Terms used in this guideline' section. We hope these changes make the guideline easier to understand.
SenTecAG	General	General	General	We are concerned that this recommendation does not covers current clinical practice. The committee recommends an optimal target range for the CO2 level. Maintaining normal PaCO2 ranges in neonates is important as abnormal PaCO2 values may have detrimental effects on neonates' brain and lungs. Failure to keep a baby's O2, CO2, and pH levels normal can cause conditions such as retinopathy of prematurity (ROP), hypoxic-ischemic encephalopathy (HIE), cerebral palsy and periventricular leukomalacia (PVL). Neonates in critical care units often have fluctuations of PaCO2[1]. Therefore, very close monitoring of a	Thank you for your comment and information on CO2 monitoring. Although the committee agree that CO2 monitoring is important, the question of the most effective technique for this was not prioritised by the committee for an evidence review in this guideline. Instead the review question on CO2 monitoring looked at randomised trials comparing different target ranges for partial pressure of carbon dioxide. The publications you have cited were

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				baby's O2, CO2, and pH must occur, especially if the baby is premature. However, you did mentioned neither the possibility nor the importance of continuous monitoring of the CO2 level. There are several techniques, for monitoring the CO2 level available, such as arterial blood gas sampling, end-tidal monitoring and transcutaneous monitoring. However, not all techniques are appropriate for neonates, especially in cases of RDS and BPD, where in most cases ventilation/perfusion mismatch is relevant and therefore end-tidal monitoring is unreliable. End-tidal CO2 (etCO2) monitoring is sometimes also inefficient in patients with small tidal volumes[2] and inapplicable in certain ventilation modes such as HFO[3]. Arterial blood gas sampling provides only a snapshot every few hours and bears the risk of invasiveness, especially in neonatal patients[4], and is painful if no arterial line is available. Furthermore, frequent blood gas sampling can increase the need for blood transfusion with its related risks and costs. Furthermore, in non-invasive ventilation in particular, it is not possible to evaluate the ventilation status based on the tidal volume of the patient. Transcutaneous monitoring of CO2 and O2 provide a continuous and accurate measurement, supporting healthcare professionals to monitor ventilation and oxygenation in preterm babies and neonates. Due to the continuous nature of the transcutaneous measurement, CO2 as well as Intermittent blood sampling and analysis seems inadequate because potentially dangerous changes of CO2 might be missed or treated late.	therefore not included as evidence in the guideline because they were not randomised trials comparing target ranges.

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				The accuracy, safety and feasibility of the SenTec tcPCO2 sensor has been studied and validated in several clinical studies and publications. In a 2018 study[5], Van Weteringen et al. demonstrated that tcPCO2 measured with the SenTec Digital Monitoring System was in good agreement with conventional blood gas analysis. A total of 238 blood samples were analyzed from 69 infants with a gestational age of 25 2/7 to 27 4/7 weeks. The mean difference (Bias) of tcPCO2 compared to arterial PaCO2 has been reported at 1.8 mmHg, LoA (-19.1 – 22,7) (0.24 kPa, LoA (-2.3 – 3.0)) in the "no sepsis group". In a 2017 study[6], Aly et al. demonstrated that tcPCO2 monitoring using a temperature of 41°C is feasible and reliable in VLBW infants. TcPCO2 was monitored for 12 hours in Very Low Birth Weight (VLBW) Infants (inclusion criteria: BW < 1,500 g and gestational age (GA) ≤ 34 weeks). No skin complications were reported. Furthermore, the study showed that continuous CO2 monitoring is feasible and reliable in that population (preterms, GA 28.1 +-2.4 weeks) and allows real-time respiratory management of premature infants without the need to wait for the results of blood gases and therefore is expected to allow a more proactive weaning from mechanical ventilation. In a 2009 publication[7], Bolivar, J. et al. demonstrated that tcPCO2 monitoring is a reliable and safe way to monitor CO2 levels continuously. TcPCO2 has stronger correlation with PaCO2 values than etCO2 in neonates with congenital heart disease. In a 2008 publication[8], Rowley, D. et al. mentioned, that "the SenTec Digital Monitor yielded an excellent correlation when compared to ABG PaCO2 measurements and it may be used as	

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				a surrogate for ABG PaCO2 determination during neonatal HFOV." Nevertheless, you mentioned in chapter 1.4 "Monitoring" to consider transcutaneous oxygen monitoring for preterm babies on invasive ventilation who are clinically instable and to use continuously oxygen saturation supplemented by arterial blood sampling. However, transcutaneous PO2 monitoring is the only continuous measurement technique available, which is able to detect Hyperoxemia. As Hyeroxemia may have negative impact on the cerebral blood flow as well as increases the risk for Retinopathy of prematurity (ROP), tcPO2 monitoring is indicated for all ventilated preterm babies, supplemented with oxygen. As already mentioned, failure to keep a baby's O2, CO2, and pH levels normal may cause detrimental effects on neonates' brain and lungs, such as ROP, HIE or PVL. When underlying conditions are not properly diagnosed and treated, it is negligence. When conditions like hypoxic-ischemic encephalopathy and PVL result from this negligence, it constitutes medical malpractice. In case of a legal case, transcutaneous monitoring of CO2 and PO2 may help to prove that there was no negligence or medical malpractice present. Based on the clinical benefits of a noninvasive and continuous transcutaneous CO2 and O2 monitoring as well as the demonstrated safety and correlation with the PaCO2 value, we kindly ask you to consider the need of transcutaneous CO2 and O2 monitoring for ventilated babies born preterm. List of mentioned publications: 1) Wyatt, J.S., Edwards, A.D., Cope, M., Delpy, D.T., McCormick, D.C., Potter, A., Reynolds, E.O.	

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Response of cerebral blood volume to changes in arterial carbon dioxide tension in preterm and term infants, Pediatr Res., 1991, Jun 29(6): 553-7. 2) Brouillette, R. T., Waxman, D.H. Evaluation of the newborn's blood gas status, 1997, Clinical Chemistry 43:1, 215-221. 3) Berkenbosch, J. W., Tobias, J. Transcutaneous carbon dioxide monitoring during high frequency oscillatory ventilation in infants and children, Crit Care Med, 2002, Vol. 30, No. 5, 1024-1027. 4) Mukhopadhyay, S., Maurer, R., Puopolo, K. M. Neonatal Transcutaneous Carbon Dioxide Monitoring - Effect on Clinical Management and Outcomes, Respiratory Care, 2016, 61(1), 90–97. 5) Van Weteringen, W., Goos, T.G., van Essen, T., Gangaram-Panday, N.H., de Jonge, R.C.J., Reiss, I.K.M. Validation of a transcutaneous tcPO2/tcPCO2 sensor with an optical oxygen measurement in preterm neonates, Poster presentation at 14th European conference on pediatric and neonatal mechanical ventilation, Montreux 2018. 6) Aly, S., El-Dib, M., Mohamed, M., Aly, H. Transcutaneous Carbon Dioxide Monitoring with Reduced-Temperature Probes in Very Low Birth Weight Infants is feasible and reliable, Amer J Perinatol 2017; 34(05): 480-48. 7) Bolivar, J., Plato, A., Dobrolet, N., Katz, J., Soler, M., Rossi, A.	

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Transcutaneous Carbon Dioxide (TC-CO2) Monitoring in Neonates With Congenital Heart Disease. Poster presentation in Hot Topics in Neonatology Conference, Washington 2009. 8) Rowley, D.D., Glass, J., Hicks, T., Wheeler, T., Caruso, F. Evaluation of a Digital Transcutaneous PCO2 Sensor and its Correlation to Arterial Blood Gas PCO2 Measurements During Neonatal High Frequency Oscillatory Ventilation, Poster presentation at American Association for Respiratory Care (AARC), Annual Meeting 2008.	
The Royal College of General Practitioners	Short Guideline	General	General	This condition can have devasting and lifelong effects on a couple and their family. This was probably first publicly highlighted by the death of Patrick Kennedy on August 9th 1963, son to the US president and first lady. The guideline is well written and contains clear advice. However there appears to little reference to the prevention of this condition, the care of parents during this treatment and palliative care.	Thank you for your comment. The committee discussed your comment and is pleased that standards of neonatal care have improved greatly since 1963, mortality has decreased, and the availability of surfactant has made a great difference to the treatment of respiratory distress syndrome and subsequently bronchopulmonary dysplasia. The guideline covers both the use of surfactant for the prevention of bronchopulmonary dysplasia (section 1.2) and the care of parents (section 1.6). Although there may be some babies with respiratory disorders who do not survive and need palliative care this is very rare, and therefore it was not a priority to include palliative care within this guideline.
The Royal College of General Practitioners	Short Guideline	General	General	The European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2016 Update appears to focus more on use of non-invasive respiratory support to prevent lung damage and maintaining temperature control and nutritional support Neonatology 2017;111:107–125 DOI: 10.1159/000448985 https://www.karger.com/Article/Pdf/448985	Thank you for your comment. The guideline includes a recommendation to use non-invasive ventilation (recommendation 1.2.6) in babies who do not need invasive ventilation. Following consultation on the scope, nutritional support and thermoregulation were not identified as priorities for inclusion in this guideline. The

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					committee did not therefore review any evidence for this and so were unable to make recommendations. In addition, the committee were aware that thermoregulation is an NNAP target and that standards therefore already exist on this, and also that a NICE guideline on neonatal parenteral nutrition is currently in development.
The Royal College of General Practitioners	Short Guideline	11	2-20	There is no reference to continuity of care or providing any written or recorded information as well as offering video calls to allow parents more flexibility. What about translational services for parents who first language is not English and making reasonable adjustments for parents with a learning disability? Book without words may be a useful tool. How is any updated information communicated to their GP as the child will not yet be registered?	Thank you for your comment. The section on discharge planning (1.7) includes the recommendation to 'consider early referral to, and regular contact with, community and continuing healthcare teams' and this would include GPs. The baby would be registered with their GP, or the mother's GP would be contacted, in the same way as a baby not born preterm would be registered or the mother's GP contacted. It is likely the GP will already be aware of the birth having, in most cases, been involved in the antenatal care of the mother. The section on providing information (recommendations 1.6.9 to 1.6.13) states that the information should be '…appropriate to the parents' and carers' needs and preferences' and this would include the options you suggest (video calls, translated materials, adjustments for parents with learning disabilities). There is also a cross-reference to the NICE guideline on patient experience in adult NHS services which provides

Specialist neonatal respiratory care for babies born preterm

Consultation on draft guideline - Stakeholder comments table
12/10/2018 to 23/11/2018

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					further guidance on appropriate communication and information.

Registered stakeholders