Neonatal parenteral nutrition

Consultation on draft scope
Stakeholder comments table

27 April 2017– 25 May 2017

Organisation	Page no.	Line no.	Comments	Developer's response
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	1	1	Addressing need for a guideline: *Why the guideline is needed* We suggest changing to ***Why another guideline is needed*** OR ***Why a new guideline is needed***	Thank you for your comment. This is a standard NICE scope template and the section provides the rationale for 'why the guideline is needed' even if there are other guidelines that are already published on the topic.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	10	3	*Parent or carer health-related quality of life* seems to be rather outlying outcome measure and we do not believe that it has potential for improvement of management of parenteral nutrition. It is quite predictable that parents would feel better if their child did not need PN but they would like their child to have optimal nutrition at the same time. Although we recognize that this kind of outcome is trendy **we would suggest removing this point from the outcome measures**.	Thank you for your comment. We would like to keep this outcome because parent views may be highly relevant to specific areas of the guideline particularly to approaches to prescribing and providing PN and especially information and support.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	2	19	Addressing need for a guideline: On p.2.l.12 the draft states *There is wide variation across the UK in neonatal parenteral nutrition.* Further on p.2. a summary of suboptimal management prior to 2010 is given on lines 14-19. We suggest adding the following facts behind 2.19: 2.19.+ ***There is evidence of suboptimal management of parental nutrition in the UK prior to 2010 despite European Guidelines having been in place.*** 2.19.++ ***Reasons for non-compliance with existing guidelines prior to 2010 is poorly understood.*** 2.19.+++ ***There is no new evidence about management of parenteral nutrition in the UK after 2010 or after new UK guidelines have been published (BAPM 2016).***	Thank you for your comment. This sections is aimed to convey why a guideline for this topic is needed. We cannot comment on other guideline that have been previously published. We will not be looking at reasons for non-compliance, but there will be an implementation process once the guideline has been published. Even though there may not be new evidence the guideline will be developed according to NICE methodology and will also include health economic considerations and analysis which was not carried out for other guidance, such as the BAPM, 2016 document.
Aberdeen Maternity	3	13 - 15	Addressing possible bias towards standard PN bags: Current formulation: *The use of standardised, rather than*	Thank you for your comment. This section is intended as a general background to the topic rather than pre-empting what

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Hospital (NHS Grampian, Scotland)			*individualised, parenteral nutrition is established practice in some countries, and in some neonatal operational delivery networks in the UK.* We suggest changing to ***The option of using standardised PN formulations has been utilised more frequently in some parts of the UK.***	the evidence or recommendations will or should say. We have also reworded this section to read: 'The use of standardised and individualised parenteral nutrition regimens, including consideration of their clinical and cost effectiveness, and safety, are therefore important'. We have also removed the final sentence of this section because we agreed that this seemed to imply that this was the only reason why the guideline was needed. An evidence review will be conducted on this topic (please see review question 3.8 in section 3.5) and the Committee can then draft recommendations.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	4	1 - 3	Addressing possible bias towards standard PN bags: In the draft: *A guideline is needed to explore the evidence behind standardised concentrated parenteral nutrition regimes to see if safety, quality and cost can 3 be improved.* The formulation does not seem to fit the heading of the segment – *Current practice*. Also, the *need for exploring evidence* would be better addressed by a literature review or a study than a guideline. Obviously, literature review is a part of the process but it could also lead to not-covering this particular aspect in the guideline. In line with the heading, we suggest changing to ***The balance of advantages and disadvantages of using either individualized or standard PN formulation is currently addressed on the level of individual patients and individual neonatal units.***	Thank you for your comment. We have reworded this section to read: 'The use of standardised and individualised parenteral nutrition regimens, including consideration of their clinical and cost effectiveness, and safety, are therefore important'. We have also removed the final sentence of this section because we agreed that this seemed to imply that this was the only reason why the guideline was needed.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	6	8	In the current version: [Those who] *need surgery* We do not see a general need for surgery especially important for PN. Hernia repair or ventriculo-peritoneal shunt placement or closure of meningomyelocele or many other examples of surgery would not change nutritional needs. The group specified in 6.7 (*critically ill*) would arguably cover the relevant surgical patients more specifically than the	Thank you for your comment. This guideline is intended for those who may need parenteral nutrition and so implicitly it would not be relevant to babies undergoing surgery but able to deal with enteral feeds.

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			general *need* [for] *surgery*. Besides, the <u>*need*</u> for surgery (e.g. need for a surgical procedure later on) would not mean anything at all for management of nutrition. **We suggest omitting 6.8**	
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	7	10	Why would *individual vitamins and trace elements* not be covered? It could actually be included in the *Current practice* part that *individual vitamins and trace elements* are usually provided in PN but they are dosed in a combined formulation. At least iron seems to be covered by the guideline according to the suggested questions (9.3). **We would be very much interested in a guideline that covers vitamins and trace elements provided in PN either individually or as a composite formula**.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making regarding the constituents in PN. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Trace element and vitamin administration were not considered such areas. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	7	11	The intention seems to be not to cover *fluid volume and electrolyte quantity needs.* We assume that substances such as NaCl, KCl, Na-Acetate, K-Acetate would be covered by the term *electrolytes*. These substances dissociate into the actual electrolytes – cations and anions – K+, Na+, Cl- and C2H3O2-. Apart from maintaining volume of different compartments electrolytes also play various roles in metabolism. **We would prefer covering electrolytes in the guideline but we appreciate the intention not to.** We see a discrepancy with the declared intention anyway as some anionic electrolytes are included in the guideline (9.4).	Thank you for your comment. There is an increased risk of metabolic acidosis due to excess chloride administration particularly in preterm babies and in those receiving intravenous electrolytes in parenteral nutrition. The acetate - chloride balance is important in reducing this risk. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Electrolyte quantity was not considered such an area. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.

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Aberdeen Maternity Hospital (NHS Grampian, Scotland)	7	3 - 7	The formulation about licensed medicines is rather strong. While the preference for licensed use of medicines may be clear and universal, in the context of neonatal medicine including PN, medicines licensed for specific neonatal indication are in minority. We believe that this fact has been already discussed at the first scoping meeting and a recommendation was made to acknowledge this specific situation in neonatal medicine in the document. **We support softening the formulation and reflecting the reality of prevalent need for medicines outside the licence in the neonatal medicine including PN.**	Thank you for your comment. The text that is referred to in your comment is standard text about licensed medicines within NICE guideline. It does not preclude recommendations for off license use to be drafted for parenteral nutrition in neonates. In cases where the use of medicines is outside the license and the Committee want to recommend its use, it can be done and a further different type of footnote is added to explain this.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	8	16	*Indications for ... parenteral nutrition* Our understanding is that PN should provide optimal nutrition where delivering optimal nutrition enterally is not possible. We would like to include the following questions: **What patients could safely sustain period of malnutrition / iatrogenic catabolism?** **What is a safe period of malnutrition / iatrogenic catabolism in preterm or term infants?** Even if the answer is that there is no evidence that any period of malnutrition in any group of patients is safe, we believe that the suggested questions would provide stronger basis for compliance with recommendations than any questions formulated so far (e.g. who profits most from PN...). On this occasion we would also like to note that non-compliance was the principal reason for sub-optimal management of PN in the past, not absence of guidelines.	Thank you for your comment. We do agree that the aim is to provide optimal nutrition and consequently the use of PN to avoid malnutrition will be a key priority. The evidence review protocols necessary to inform recommendations on the provision of optimal PN will be developed in discussion with the Guideline Committee.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	9	3	*What quantity of intravenous iron should be provided?* It could be argued that iron is not a trace element as the quantity required is significantly higher compared to other trace elements, however, the prevalent opinion is to include iron in trace elements. According to 7.10, trace elements were not supposed to be covered by this guideline.	Thank you for your comment. We note your view on the terminology regarding trace elements although the scope does not state that iron should or should not be regarded as such. With regards to trace elements and vitamins the scope of this guideline does not attempt to cover evidence reviews on all

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			We would prefer if trace elements and vitamins were covered but if the scope of the guideline should exclude trace elements, including iron does not seem congruent.	aspects of decision making regarding the constituents in PN. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Trace element and vitamin administration were not considered such areas. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	9	4	*What is the most effective balance between intravenous chloride and acetate?* As we mentioned above, we would prefer including electrolytes in the guideline in general. Picking only chloride and acetate seems random and unreasonable concerning comparative importance of for example potassium and sodium compared to chloride and relatively infrequently used acetate. We suggest either **including all electrolytes (Na, K, Cl, Acetate) or omitting 9.4**	Thank you for your comment. There is an increased risk of metabolic acidosis due to excess chloride administration particularly in preterm babies and in those receiving intravenous electrolytes in parenteral nutrition. The acetate - chloride balance is important in reducing this risk. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Electrolyte quantity was not considered such an area. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based on Committee consensus.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	General	General	Need for a guideline: Despite various guidelines had been in place, parenteral nutrition (PN) was not managed optimally (at least prior to 2010). Since the NCEPOD review the practice has significantly improved according to our experience. Admittedly, there may not be evidence of improved practice after 2010 but the same lack of evidence would apply for the justification of a new guideline responding to the 7 years old report.	Thank you for your comment. The issue of competing guidelines is not restricted to the topic of PN. For many topics covered by NICE other guidance is often available from related stakeholder organisations. Compared to other guidance (such as BAPM or ESPGHAN) NICE guidelines include health economic analysis and therefore the guideline will not only address clinical but also cost-effectiveness of the key areas in the scope. It will therefore provide important

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			Need for a new guideline implicates an assumption that the existing guidelines are in some ways deficient and that PN is still being mismanaged. **Development of new guideline should include analysis of failure of existing guidelines in order to avoid repeating running in to the same problems**: 1) the new guideline may not be followed just the same way; 2) development of the guideline may be wrongly timed – the process may be late – situation has changed and/or meanwhile the field has been satisfactorily covered by a guideline developed by a different agency (BAPM). One argument for a new NICE guideline could be a stronger jurisdiction, provided we could demonstrate non-compliance with UK guideline recently issued by a different agency. Another argument could be different formulation of certain questions that would prevent non-compliance. We strongly believe that non-compliance with guidelines was the principal reason of sub-optimal management of PN, not absence of guidelines. The general comments above translate into suggested changes:	additional information. We also believe that compliance may be improved if there is consistent guidance from different sources to reinforce the message with the proviso that we cannot pre-empt whether or how consistent our guidance will be with others that are already published. Unfortunately the comment seems to end abruptly and we are not able to locate your suggested changes.
Aberdeen Maternity Hospital (NHS Grampian, Scotland)	General	General	Possible bias towards standard PN bags: Standard bags have been in use in the UK for at least the last decade and although they might not have been utilized everywhere to the same degree, standard PN formulations were available to anyone. The emphasis on standard bags in the document seems unnecessary at certain places. A new range of standard bags is being strongly pushed to the market at present (Numeta, Baxter). To avoid any suspicion from bias, certain formulations should be reviewed. The coincidence of late arrival of this guideline and new product on the market may be susceptible for corporate influences.	Thank you for your comment. We will review this topic in the guideline (please see draft review question 3.8) and the Committee will review the clinical and health economic evidence and will draft recommendations based on this and the expertise in the group. We cannot pre-empt whether the use of standardised bags will be recommended or not.
Baxter Healthcare Ltd	General		When developing the guidelines, as well as clinical considerations for neonatal parenteral nutrition, the	Thank you for your comment. Although this aspect is important, it was not considered a priority for evidence review.

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			complexity and requirement for aseptic preparation of the prescribed parenteral nutrition solution should also be taken in to account. This should include but not be limited to the support of the MHRA position on the preferred use of licenced products over special manufactured solutions where available.	NICE guidelines do not attempt to cover every aspect of a subject area but focus mainly on those in which there is variation in clinical practice. Even though outside the current scope we may be able to comment on this in our reviews on 'What approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?' or 'What is the efficacy and safety of standardised parenteral nutrition bags compared with individualised bags?' (see draft question 7 and 3.8 in section 3.5 of the scope). We cannot pre-empt what the details of the questions will include or what will be recommended based on them. This will be decided during guideline development, but we can raise the issue when these topics are discussed.
Baxter Healthcare Ltd	General		Any recommendation for the use of standardised solutions should take in to account the availability and provision of terminally sterilised formulations of neonatal parenteral nutrition.	Thank you for your comment. An evidence review will be undertaken on standardised compared to individualised PN administration (please see section 3.5). Recommendations will be drafted by the Committee during guideline development. We are therefore unable to pre-empt this issue.
Baxter Healthcare Ltd	General		None of the risks associated with neonatal parenteral nutrition preparation must be overlooked. Any recommendations should take in to account the associated risks of complex prescriptions and the administration of separate components at the baby's bedside.	Thank you for your comment. The details of each review questions will be discussed with the Committee. We believe that issues such as risks associated with complex prescription could feature in our topic 'What approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?' in section 3.5 of the scope.
Baxter Healthcare Ltd	General		Any recommendations should not adversely affect the compounding capacity available within, and to, the NHS by placing additional demand for complex aseptic production on the system.	Thank you for your comment. Although this aspect is important, it was not considered a priority for evidence review. NICE guidelines do not attempt to cover every aspect of a subject area but focus mainly on those in which there is variation in clinical practice. Even though outside the current scope we may be able to comment on this in our reviews on 'What approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?' or 'What is the efficacy

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				and safety of standardised parenteral nutrition bags compared with individualised bags?' (see draft question 7 and 3.8 in section 3.5 of the scope). We cannot pre-empt what the details of the questions will include or what will be recommended based on them. This will be decided during guideline development, but we can raise this issue when these topics are discussed.
British Association of Perinatal Medicine	General	General	Very important topic - BAPM applauds NICE tackling this guideline	Thank you for your comment.
British Association of Perinatal Medicine	General	General	No mention of neurodevelopmental outcome	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
British Association of Perinatal Medicine	General	General	"Neonate" does not apply to all preterm babies until 28 days past their due date	Thank you for your comment. We have defined the population in section 2.1 (Who is the focus?) without using the term neonate. This includes clear definitions of the limits to the days that we are talking about. This is included in the title only to indicate that this is a guideline for clinicians working in settings where neonates are cared for.
British Specialist Nutrition Association	General	General	As well as clinical considerations when developing the guidelines any recommendation should take into account the requirement for aseptic preparation. As much as possible aseptic preparations should be standardised in numbers of formulations. This should include but not be limited to the support of the MHRA position on the preferred use of licen**s**ed products. Any recommendation for the use of standardised solutions in conjunction with clinical suitability should take into account the availability and provision of terminally sterilised formulations. The recommendations should take into account the associated risks of complex prescriptions and administration	Thank you for your comment. Aseptic preparation was not directly included in the scope because this is a requirement throughout PN. Even though outside the current scope we may be able to comment on this in our reviews on 'What approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?' or 'What is the efficacy and safety of standardised parenteral nutrition bags compared with individualised bags?' (see draft question 7 and 3.8 in section 3.5 of the scope). We cannot pre-empt what the details of the questions will include or what will be recommended based on them. This will be decided during guideline development.

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			of separate components. The risks associated with neonatal parenteral nutrition preparation must not be overlooked.	
Imperial college healthcare NHS trust	2	10	PN also contains important non nutritional components eg buffer such as acetate – add to list of components?	Thank you for your comment. These are examples of components and this list is not meant to be exhaustive. The whole section is be a brief description of the background and is not meant to be comprehensive. The issue of chloride and acetate balance is covered in our key areas in section 3.3 of the scope.
Imperial college healthcare NHS trust	3	10	add in babies whose feeds are withheld because of septic ileus	Thank you for your comment. Babies with ileus due to sepsis would be included under the category of 'critically ill'.
Imperial college healthcare NHS trust	3	15	add that standard PN is suitable for the majority of stable preterm babies but that surgical and critically ill babies may need individualised bags	Thank you for your comment. This section is intended as a general background to the topic rather than pre-empting what the evidence or recommendations will or should say. We have also reworded this section to read: 'The use of standardised and individualised parenteral nutrition regimens, including consideration of their clinical and cost effectiveness, and safety, are therefore important'. We have also removed the final sentence of this section because we agreed that this seemed to imply that this was the only reason why the guideline was needed. An evidence review will be conducted on this topic (please see review question 3.8 in section 3.5) and the Committee can then draft recommendations.
Imperial college healthcare NHS trust	7	9	Although the composition and delivery of enteral feeds cannot be covered it might be useful to acknowledge that PN in neonates is usually accompanied by enteral feeds. Also that different approaches to enteral feeding in different units can profoundly affect a babies overall nutritional intake.	Thank you for your comment. We will cover the matter of enteral nutrition administration in the review question on strategies to facilitate discontinuation of PN (question 6 in section 3.5). As you say this will not focus on the composition of enteral feeds, but on their delivery.
Neonatal Critical Care Clinical	1	18 - 19	What is the evidence for 'inadequate nutrition increasing the need for assisted ventilation? AS far as we are aware, this does not exist.	Thank you for your comment. We have removed this example from the sentence.

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Reference Group				
Neonatal Critical Care Clinical Reference Group	1	24 - 25	Parenteral nutrition is a standard of care – this should be stated here	Thank you for your comment. We have revised this to read 'widely used' rather than 'increasingly used'.
Neonatal Critical Care Clinical Reference Group	2	24 - 25	Is there evidence for this weight and gestational age cut-off? In our opinion, this is speculative	Thank you for your comment. We have now revised the gestational age to 31 weeks and 1,500g as this is more widely accepted. This is meant to be a general background section and as indicated in the scope we will look at 'indications for and approaches to PN' as one of our key areas.
Neonatal Critical Care Clinical Reference Group	2	29	We suggest that the emphasis here should be on the prevention of growth failure rather than reversing it.	Thank you for your comment. We have rewritten the relevant sentence to emphasise prevention rather than reversal of growth failure.
Neonatal Critical Care Clinical Reference Group	6	24	This should include trace elements also.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making regarding the constituents in PN. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Trace elements were not considered such an area. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Neonatal Critical Care Clinical Reference Group	6	25	It may be better to state: 'all electrolytes, including chloride and acetate'	Thank you for your comment. There is an increased risk of metabolic acidosis due to excess chloride administration particularly in preterm babies and in those receiving intravenous electrolytes in parenteral nutrition. The acetate - chloride balance is important in reducing this risk. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic

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				is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Electrolyte quantity was not considered such an area. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based on Committee consensus.
Neonatal Critical Care Clinical Reference Group	6	28	It may be better to state 'Weaning down and stopping parenteral nutrition in preterm and term babies'	Thank you for your comment. The key area is referring to 'stopping'. However, our review question 6 in section 3.5 provides more detail on how we are planning to review this. The question we posed is 'what strategies are best for stopping parenteral nutrition'. We believe that weaning would fall into the category 'strategies for stopping'.
Neonatal Critical Care Clinical Reference Group	7	9	We agree that a comprehensive guideline on enteral feeding should be outside of this guideline, but it is impossible to omit some guidance on enteral feeding with respect to the total macronutrient intake and weaning and stopping parenteral nutrition. Therefore, some guidance on the enteral feeding regimen should be included in this guideline.	Thank you for your comment. We will cover the matter of enteral nutrition administration in the review question on strategies to facilitate discontinuation of PN (question 6 in section 3.5). This will not focus on the composition of enteral feeds, but on their delivery. The guideline Committee will consider how the administration of enteral feeds might appropriately alter their approach to PN composition.
Neonatal Critical Care Clinical Reference Group	9	12	As in comment 7 above, it may be better to state: 'Weaning down and stopping parenteral nutrition'	Thank you for your comment. The key area is referring to 'stopping'. However our review question 6 in section 3.5 provides more detail on how we are planning to review this. The question we posed is 'what strategies are best for stopping parenteral nutrition'. We believe that weaning would fall into the category 'strategies for stopping'.
Neonatal Critical Care Clinical Reference Group	9	19	The main outcomes for searching and assessing evidence should include neurodevelopmental assessment and body composition. Also, future trials are likely to include cardiovascular and metabolic outcomes as well as neurodevelopmental outcomes.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.

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Neonatal Critical Care Clinical Reference Group	9	8	This section should include addressing the use of filters (separate aqueous and lipid filters) and light protection as this may affect the consumables costs of delivering parenteral nutrition considerably, whilst the evidence base is relatively small.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Filters and light protection were not considered such areas. The administration and prescription of PN would need to take account of the use of filters and light protection for the individual bags and administration of PN. There are clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Nottingham University Hospitals	2	10	'situations' rather than 'settings'?	Thank you for your comment. We have revised this accordingly.
Nottingham University Hospitals	2	8	Is formulas better than formulae?	Thank you for your comment. The NICE style guide specifies the use of formulas rather than formulae (please see NICE style guide).
Nottingham University Hospitals	3	9	Add in 'where the gut is unable to provide full nutrition'?	Thank you for your comment. The focus of this bullet point is that critically ill babies commonly need PN for a variety of reasons. We would therefore like to keep this as it is.
Nottingham University Hospitals	4	1 - 3	Is this why a guideline is needed?	Thank you for your comment. We have reworded an earlier section to read: 'The use of standardised and individualised parenteral nutrition regimens, including consideration of their clinical and cost effectiveness, and safety, are therefore important'. We have also removed the final sentence of this section because we agreed that this seemed to imply that this was the only reason why the guideline was needed.
Nottingham University Hospitals	7	11	Fluid volume allowed has a major impact on nutritional intake, so is essential to consider when designing PN regimens	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Fluid administration was not considered such an area. This matter is not specific to neonates requiring PN. The administration of PN would need

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				to take account of the fluid requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide fluid administration and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Nottingham University Hospitals	8	26	Is there any evidence to suggest quantity of individual amino acids in order to recommend one specific amino acid mixture over another?	Thank you for your comment. This section is to outline draft review questions. We cannot pre-empt how much evidence there will be and what it will say. However, we believe that it is an important question to pose for this topic.
Nottingham University Hospitals	9	10 - 11	Presumably this will differentiate between early days of stabilisation and later stable infants?	Thank you for your comment. This section broadly outlines the draft review questions but is not meant to supply a detailed description of how the review may be carried out. The specifics of this review will be decided with the Guideline Committee, but we can highlight your comment at the time when this will be discussed.
Nottingham University Hospitals	9	6 - 7	This will clearly be dependent on whether nutritional profile is appropriate	Thank you for your comment. We cannot at this stage pre-empt what the evidence will show and what will be recommended. This will be discussed when the topics is reviewed and results are presented to the Guideline Committee.
Royal College Of General Practitioners	General		• Most of these patients have never been in the community. There may be some commissioning issues e.g. Cost of length of stay relevant to primary care but this is well out of the range of conditions managed by GPS and we are not able to comment as it is beyond our expertise and not in our remit • Who is responsible for prescribing in the community – the paediatrician or GP if it is a prescription for parenteral nutrition? • Will this guidance cover feeding through a naso-gastric tube or Mic-Key button? These babies are being discharged into the community so any guidance should include weaning off specialist solutions onto breast milk or other milks. Guidance	Thank you for your comment. We agree that babies in need of parenteral nutrition will usually be managed in hospital setting and not in the community. Some of the topics that you are referring to will be covered but not for community settings, for instance 'strategies for stopping parenteral nutrition' would include weaning and 'approaches to prescribing and providing parenteral nutrition' would most likely cover the relevant responsibilities of team members. Patterns of growth after hospital discharge most likely will not be covered and would be outside the remit of the guideline (possibly more related to the upcoming postnatal care guideline update). Critically ill babies and those that need surgery are in the scope and therefore considerations will have to be made about associated benefits and risk of providing PN in these groups

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			tailored for community paediatric nurses and GPs with a sliding scale to allow for growth. • Infants receiving this nutrition often have other problems as well so guidance on interaction with other medications and the use/benefit/risks of antibiotics could be added with consideration for a frequently asked FAQs section • Will Storage/ procedures/risks/benefits will be in the guideline or excluded?	(which may include interactions with other medications). The details of each review question will be debated and signed-off by the Committee during guideline development and we will raise these issues when we get to this topic. The guideline will not review evidence on topics such as the devices and techniques used for enteral tube feeding.
Royal College of Nursing	General	General	The Royal College of Nursing welcomes proposals to develop this guideline.	Thank you for your comment.
Royal College of Nursing	General	General	The draft scope seems comprehensive and we do not have specific comments to make at this stage. We welcome and agree with the rationale of the need for a guideline.	Thank you for your comment.
Royal College of Paediatrics and Child Health	1	18 - 19	The comment on increased need for assisted ventilation because of 'inadequate nutrition' needs qualifying. What is the evidence for this?	Thank you for your comment. We have removed this example from the sentence.
Royal College of Paediatrics and Child Health	1	18 - 19	The comment on increased need for assisted ventilation because of 'inadequate nutrition' needs qualifying. What is the evidence for this?	Thank you for your comment. We have removed this example from the sentence.
Royal College of Paediatrics and Child Health	1	20 - 22	The term 'inappropriate nutritional management' is vague. Again, needs qualifying / defining	Thank you for your comment. This section provides a concise background to the topic and a rationale for why the guideline is needed. As such we worded this intentionally vague since it could refer to many ways of 'inappropriate' nutritional management. Without a much longer description it would otherwise not be possible to be more precise. We would therefore like to keep this as it is.
Royal College of Paediatrics	1	20 - 22	The term 'inappropriate nutritional management' is vague. Again, needs qualifying / defining	Thank you for your comment. This section provides a concise background to the topic and a rationale for why the guideline is needed. As such we worded this intentionally vague since it

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and Child Health				could refer to many ways of 'inappropriate' nutritional management. Without a much longer description it would otherwise not be possible to be more precise. We would therefore like to keep this as it is.
Royal College of Paediatrics and Child Health	1	23	Number of babies needing neonatal care should be referenced to NNAP (National Neonatal Audit Programme based at RCPCH) and NNRD (National Neonatal Research Database at Imperial)	Thank you for your comment. We have now made reference to the National Neonatal Audit Programme rather than Bliss. The numbers from the National Neonatal Research Database at Imperial were slightly different. We therefore decided to reference only one rather than both since the Audit Programme is more widely used in clinical practice.
Royal College of Paediatrics and Child Health	1	24 - 25	It would be more accurate to say that 'Parenteral nutrition is a standard of care' rather than being 'increasingly used'.	Thank you for your comment. We have revised this to read 'widely used' rather than 'increasingly used'.
Royal College of Paediatrics and Child Health	1	24 - 25	It would be more accurate to say that 'Parenteral nutrition is a standard of care' rather than being 'increasingly used'.	Thank you for your comment. We have revised this to read 'widely used' rather than 'increasingly used'.
Royal College of Paediatrics and Child Health	10	3	What is meant by 'parent or carer health-related quality of life' this needs to be expanded to ensure the meaning of the outcome is clear. Does this include mental health outcomes?	Thank you for your comment. We would like to keep this outcome because parent views may be highly relevant to specific areas of the guideline particularly to approaches to prescribing and providing PN and especially information and support.
Royal College of Paediatrics and Child Health	11	1	All comments above relevant to the diagram.	Thank you for your comment. The pathway at this stage is very draft version and is mainly included for illustrative purposes. However, it was updated in according to revisions to the scope that were made to address stakeholder responses.
Royal College of Paediatrics and Child Health	11	1	All comments above relevant to the diagram.	Thank you for your comment. The pathway at this stage is very draft version and is mainly included for illustrative purposes. However, it was updated in according to revisions to the scope that were made to address stakeholder responses.
Royal College of Paediatrics	2	24	Is there a source for this comment? Suggest < 31 weeks may be more accurate.	Thank you for your comment. We have now revised this to 31 weeks as suggested. This is meant to be a general

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and Child Health				background section and as indicated in the scope we will look at 'indications for and approaches to PN' as one of our key areas.
Royal College of Paediatrics and Child Health	2	24	What is the source of this comment? More accurate to say below 31 weeks. This is backed up by data from the NNRD.	Thank you for your comment. We have now revised this to 31 weeks as suggested. This is meant to be a general background section and as indicated in the scope we will look at 'indications for and approaches to PN' as one of our key areas.
Royal College of Paediatrics and Child Health	2	29	It is incorrect / confusing to state that postnatal growth failure is a 'potentially reversible risk factor for neurocognitive impairment'. While it is recognised that poor growth is associated with worse neurodevelopmental outcomes, no study has shown that improved growth leads to better neurodevelopmental outcomes. Improved nutrition may well lead to better neurodevelopmental outcomes but the evidence for this is yet to be shown. 'Reversing' growth failure could be interpreted to mean aiming for 'catch-up growth' with all its attendant risks. It would be preferable to prevent growth failure than aiming to 'reverse' it.	Thank you for your comment. We have revised this sentence to emphasise the importance of preventing growth failure if possible rather than reversing it. It states that growth failure may be prevented and that growth failure is a risk factor for neurocognitive impairment.
Royal College of Paediatrics and Child Health	2	29	It is incorrect / confusing to state that postnatal growth failure is a 'potentially reversible risk factor for neurocognitive impairment'. While it is recognised that poor growth is associated with worse neurodevelopmental outcomes, no study has shown that improved growth leads to better neurodevelopmental outcomes. Improved nutrition may well lead to better neurodevelopmental outcomes but the evidence for this is yet to be shown. 'Reversing' growth failure could be interpreted to mean aiming for 'catch-up growth' with all its attendant risks. It would be preferable to prevent growth failure than aiming to 'reverse' it.	Thank you for your comment. We have revised this sentence to emphasise the importance of preventing growth failure if possible rather than reversing it. It states that growth failure may be prevented and that growth failure is a risk factor for neurocognitive impairment.
Royal College of Paediatrics and Child Health	3	20	Do parenteral nutrition services also include pharmacy? Does this need to be included more explicitly?	Thank you for your comment. The aim of this section is to briefly outline the rationale for why this guideline is needed. It is not meant to be comprehensive. However, one of our key areas in section 3.3 is 'service design' and one of the draft review questions in section 3.5 of the scope is 'What

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				approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?' Most likely pharmacy will feature in this topic.
Royal College of Paediatrics and Child Health	3	22	Here and elsewhere, 'regime' should be replaced by 'regimen'!	Thank you for your comment. We have revised this replacing regime with regimen for consistency.
Royal College of Paediatrics and Child Health	3	22	Here and elsewhere, 'regime' should be replaced by 'regimen'!	Thank you for your comment. We have revised this replacing regime with regimen for consistency.
Royal College of Paediatrics and Child Health	3	5	More accurate to say 'Preterm babies in the immediate postnatal period who are establishing enteral feeds' rather than 'who have not yet established an adequate intake of enteral milk'.	Thank you for your comment. We have revised this accordingly.
Royal College of Paediatrics and Child Health	3	5	More accurate to say 'Preterm babies in the immediate postnatal period who are establishing enteral feeds' rather than 'who have not yet established an adequate intake of enteral milk'.	Thank you for your comment. We have revised this accordingly.
Royal College of Paediatrics and Child Health	4	24-8	Concentrated solutions are useful for all babies, not just the smallest. Some of the sickest babies are full term, and arte often fluid restricted. As fluid is given on mL/kg basis, all are affected equally.	Thank you for your comment. This sentence has now been removed.
Royal College of Paediatrics and Child Health	5	14	Change to 'parents and carers of babies' to be more lay friendly, and to acknowledge that parents will be referring to guideline in reference to their own baby or babies, rather than the whole neonate population.	Thank you for your comment. We have revised this as suggested.
Royal College of Paediatrics and Child Health	5	15	Need to include in the people planning neonatal care: Neonatal Critical Care Clinical Reference Group, Neonatal Operational Delivery Networks	Thank you for your comment. These are implicitly included in the categories listed in the first two bullets. The examples are not meant to be exhaustive.
Royal College of Paediatrics	5	2	Change "People" to Babies or Infants using "neonatal" services	Thank you for your comment. We have rephrased this sentence to highlight parents or carers of newborn babies.

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and Child Health				
Royal College of Paediatrics and Child Health	6	14	Aspect of parenteral nutrition not included here is individualised versus standardised approaches.	Thank you for your comment. We have included this topic already. Please see review question 3.8 in section 3.5.
Royal College of Paediatrics and Child Health	6	14	Aspect of parenteral nutrition not included here is individualised versus standardised approaches.	Thank you for your comment. We have included this topic already. Please see review question 3.8 in section 3.5.
Royal College of Paediatrics and Child Health	6	24	Should state 'minerals, iron and trace elements'. Though appreciate that detailed guidance on individual trace elements probably outside the scope.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making regarding the constituents in PN. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Trace elements were not considered such an area. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Royal College of Paediatrics and Child Health	6	24	Should state 'minerals, iron and trace elements'.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making regarding the constituents in PN. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Trace element were not considered such an area. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Royal College of Paediatrics and Child Health	6	25	Better to refer to electrolytes in general. Why the focus on 'chloride and acetate' balance?	Thank you for your comment. There is an increased risk of metabolic acidosis due to excess chloride administration particularly in preterm babies and in those receiving intravenous electrolytes in parenteral nutrition. The acetate - chloride balance is important in reducing this risk.

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				The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Electrolyte quantity was not considered such an area. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based on Committee consensus.
Royal College of Paediatrics and Child Health	6	25	Better to refer to electrolytes in general. Why the focus on 'chloride and acetate' balance?	Thank you for your comment. There is an increased risk of metabolic acidosis due to excess chloride administration particularly in preterm babies and in those receiving intravenous electrolytes in parenteral nutrition. The acetate - chloride balance is important in reducing this risk. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Electrolyte quantity, apart from the chloride acetate balance, was not considered such an area. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based on Committee consensus.
Royal College of Paediatrics	6	28	Suggest 'weaning and stopping' parenteral nutrition, rather than just stopping.	Thank you for your comment. The key area is referring to 'stopping'. However our review question 6 in section 3.5 provides more detail on how we are planning to review this.

Organisation	Page no.	Line no.	Comments	Developer's response
and Child Health				The question we posed is 'what strategies are best for stopping parenteral nutrition'. We believe that weaning would fall into the category 'strategies for stopping'.
Royal College of Paediatrics and Child Health	6	28	Suggest 'weaning and stopping' parenteral nutrition, rather than just stopping.	The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Electrolytes administration, apart from the chloride acetate balance, was not considered such an area. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Royal College of Paediatrics and Child Health	6	3-4	Would suggest this is reworded as it currently could be interpreted that babies born up to 28 days after their due date are preterm. Would suggest: 'babies born premature (before 37 weeks gestation) receiving parenteral nutrition up to 28 days after their expected due date.'	Thank you very much. We believe that readers of this document would know the gestation that preterm is referring to. Since we do have a topic on indications for receiving parenteral nutrition we would not like to add 'receiving parenteral nutrition' because those not yet receiving it are not excluded from the scope.
Royal College of Paediatrics and Child Health	6	5	Should be 'babies born at term up to 28 days after birth' not 'due birth date'. Else can be confusing for eg: a baby born at 42 weeks is also 'term'.	Thank you for your comment. We had used due birth date because it would be more inclusive for those born between 37 and 40 weeks gestation (i.e. slightly longer follow-up). However, we agree that those born at 42 weeks are then theoretically disadvantaged. Given the definition of neonate as 28 weeks post birth we thought it reasonable to adopt your suggested wording. Clinical judgment can of course be applied in extrapolating from any recommendations made.
Royal College of Paediatrics	6	5	Should be 'babies born at term up to 28 days after birth' not 'due birth date'. Else can be confusing for eg: a baby born at 42 weeks is also 'term'.	Thank you for your comment. We had used due birth date because it would be more inclusive for those born between 37 and 40 weeks gestation (i.e. slightly longer follow-up).

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and Child Health				However, we agree that those born at 42 weeks are then theoretically disadvantaged. Given the definition of neonate as 28 weeks post birth we thought it reasonable to adopt your suggested wording. Clinical judgment can of course be applied in extrapolating from any recommendations made.
Royal College of Paediatrics and Child Health	7	1	Service design – needs to be defined more ie does this include pharmacy	Thank you for your comment. The draft review question to 'service design' in section 3.5 of the scope is 'What approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?' Most likely pharmacy will feature in this topic. However, the detailed plan of this review (the protocol) will be discussed with the Guideline Committee during the development of this guideline.
Royal College of Paediatrics and Child Health	7	14	To include NICE Quality Standard for Neonatal Care (2010)	Thank you for your comment. We have added this Quality Standard to a new subsection of 4.1 entitled 'NICE quality standards that may need to be revised or updated when this guideline is published'.
Royal College of Paediatrics and Child Health	7	22	The specialist neonatal Care guideline in development is now called the " Specialist Neonatal Respiratory care for babies born preterm Guideline"	Thank you for your comment. We have revised this accordingly.
Royal College of Paediatrics and Child Health	7	9	While it is reasonable to exclude enteral feeding regimens from this guideline it is important to recognise that while making recommendations on intakes of macronutrients in parenteral nutrition one has to consider how much macronutrient intakes enteral feeds provide. This is also relevant when weaning and stopping parenteral nutrition.	Thank you for your comment. We will cover the matter of enteral nutrition administration in the review question on strategies to facilitate discontinuation of PN (question 6 in section 3.5). This will not focus on the composition of enteral feeds, but on their delivery. The guideline Committee will consider how the administration of enteral feeds might appropriately alter their approach to PN composition.
Royal College of Paediatrics and Child Health	7	9	While it is reasonable to exclude enteral feeding regimens from this guideline it is important to recognise that while making recommendations on intakes of macronutrients in parenteral nutrition one has to consider how much macronutrient intakes enteral feeds provide. This is also relevant when weaning and stopping parenteral nutrition.	Thank you for your comment. We will cover the matter of enteral nutrition administration in the review question on strategies to facilitate discontinuation of PN (question 6 in section 3.5). This will not focus on the composition of enteral feeds, but on their delivery. The guideline Committee will consider how the administration of enteral feeds might appropriately alter their approach to PN composition.

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Royal College of Paediatrics and Child Health	7	9, 11, 14	Fluid Volume is a key factor in providing appropriate amounts of amino acids, carbohydrates and lipids.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Fluid administration was not considered such an area. This matter is not specific to neonates requiring PN. The administration of PN would need to take account of the fluid requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide fluid administration and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Royal College of Paediatrics and Child Health	8	18	Although it may be implied by this statement, is it worth explicitly defining babies where it is not beneficial to provide PN. (e.g. those expected to be on iv fluids only for a short time)	Thank you for your comment. One of our key areas is 'indications for and approaches to, starting parenteral nutrition' with the associated question (in section 3.5) 'Which preterm and term babies benefit most from parenteral nutrition?' We believe that the outcome of this review would also determine who may not benefit from PN.
Royal College of Paediatrics and Child Health	9		Although electrolytes are excluded – perhaps this should include guidance about phosphate and calcium to prevent bone disease of prematurity	Thank you for your comment. Please see section 3.5 (key issues and questions) where the review question '3.5 What quantity of intravenous minerals (calcium, phosphorus and magnesium) should be provided?' is proposed to cover this topic.
Royal College of Paediatrics and Child Health	9		As protein in strongly associated with brain development would it be worth considering neurodevelopmental outcome although we accept there are a lot of confounding factors that may make this difficult to assess	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	13	Should include weaning as well as stopping parenteral nutrition	Thank you for your comment. The key area is referring to 'stopping'. However our review question 6 in section 3.5 provides more detail on how we are planning to review this. The question we posed is 'what strategies are best for stopping parenteral nutrition'. We believe that weaning would fall into the category 'strategies for stopping'.

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Royal College of Paediatrics and Child Health	9	13	Should include weaning as well as stopping parenteral nutrition	Thank you for your comment. The key area is referring to 'stopping'. However our review question 6 in section 3.5 provides more detail on how we are planning to review this. The question we posed is 'what strategies are best for stopping parenteral nutrition'. We believe that weaning would fall into the category 'strategies for stopping'.
Royal College of Paediatrics and Child Health	9	16	Would suggest rephrasing and adding an additional question to ensure that parental or carer involvement is represented: 8.1 ''What information and support do parents and carers value and need when their baby or babies are receiving parenteral nutrition?' 8.2 ''What involvement in their baby or babies care do parents and carers value when they are receiving parenteral nutrition?''	Thank you for your comment. We believe that support would also encapsulate a level of involvement. In the context of PN it is difficult to focus on the involvement of care because PN is complex and a lot of the decisions will have to be made by the clinicians on short notice. We would therefor like to keep this as it is.
Royal College of Paediatrics and Child Health	9	19	This should include neurodevelopmental outcomes, as discussed in the stakeholder's meeting. This is a cardinal functional outcome of neonatal care. This receives prominence in the introduction section of this document as a justification for the guideline so it seems odd not to include this when searching for evidence. There are indeed RCTs looking at neurodevelopmental outcomes of parenteral nutrition interventions, so to exclude this would be a major flaw.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	19	Body composition is a far better outcome measure of nutritional intervention than growth and should be included in the search. Growth is a very poor outcome measure of nutritional intervention. While it is recognised that gold standard methods of assessment, including that to measure body composition may not be accessible in the routine clinical setting, research that demonstrates a favourable outcome using gold standard assessment tools carries more weight that that using less robust means. Any search of the evidence should include all relevant outcomes.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.

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Royal College of Paediatrics and Child Health	9	19	Several studies have used labelled isotope and nitrogen retention studies as short term outcomes of parenteral nutrition interventions. This should be included in any search else the search risks not being comprehensive enough and potentially excluding vital evidence. See point above.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	19	A key and increasingly reported complication of parenteral nutrition in neonates is the 're-feeding syndrome' and this should be included. This is particularly relevant to mineral intakes in relation to amino acids.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	19	This should include neurodevelopmental outcomes, as discussed in the stakeholder's meeting. This is a cardinal functional outcome of neonatal care. This receives prominence in the introduction section of this document as a justification for the guideline so it seems odd not to include this when searching for evidence. There are indeed RCTs looking at neurodevelopmental outcomes of parenteral nutrition interventions, so to exclude this would be a major flaw.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	19	Body composition is a far better outcome measure of nutritional intervention than growth and should be included in the search. Growth is a very poor outcome measure of nutritional intervention. While it is recognised that gold standard methods of assessment, including that to measure body composition may not be accessible in the routine clinical setting, research that demonstrates a favourable outcome using gold standard assessment tools carries more weight that that using less robust means. Any search of the evidence should include all relevant outcomes.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	19	Several studies have used labelled isotope and nitrogen retention studies as short term outcomes of parenteral nutrition interventions. This should be included in any search else the search risks not being comprehensive enough and potentially excluding vital evidence. See point above.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.

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Royal College of Paediatrics and Child Health	9	19	A key and increasingly reported complication of parenteral nutrition in neonates is the 're-feeding syndrome' and this should be included. This is particularly relevant to mineral intakes in relation to amino acids.	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.
Royal College of Paediatrics and Child Health	9	28	Central venous catheter complications are not a complication of parenteral nutrition per se. While this is a risk it is incorrect to state it as a complication of PN.	Thank you for your comment. The problem of CVC related complications was thought to be of central importance to the process of PN administration, although we do acknowledge that they can arise in other contexts.
Royal College of Paediatrics and Child Health	9	28	Central venous catheter complications are not a complication of parenteral nutrition per se. While this is a risk it is incorrect to state it as a complication of PN.	Thank you for your comment. The problem of CVC related complications was thought to be of central importance to the process of PN administration, although we do acknowledge that they can arise in other contexts.
Royal College of Paediatrics and Child Health	9	8	Whether PN can safely be started as soon as umbilical lines are inserted (without need for X-ray) – "golden hour" measures	Thank you for your comment. The evidence regarding the positioning of parenteral nutrition venous lines will be reviewed and the Guideline Committee will consider appropriate recommendations.
Royal College of Paediatrics and Child Health	general		This is a massive topic and will take considerable time. As such we feel it will not be possible to produce comprehensive guidelines without adequate resources – this means that NICE should provide appropriate funding for the time taken for members of the WG to review the literature and produce recommendations. It is also quite likely that consensus will be hard to achieve. Providing a guideline/recommendations with wide ranges (of intakes) might be needed, but these may not help individuals so we suggest trying to provide both 'acceptable ranges' (evidence based) and 'targets' - perhaps where less robust evidence, but based on expert opinion. For example, many clinicians are happy to follow 'expert' opinion, so rather than simply providing a range e.g. protein 2.7-3.8g it might help units to also know what the expert groups recommends e.g. 'targeting' 3g or 3.5g was considered appropriate.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making regarding PN. As noted by you, the topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. It is a massive topic as you say and a selective approach focussing on areas of most uncertainty around management strategies or costs was taken in this scope. Whether or not a formal consensus method will need to be used will be decided during guideline development in conjunction with the Committee. NICE guidelines use the wording of recommendations to reflect the strength of the evidence (including consensus) please see 'making decisions using NICE guidelines'.

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			The danger of a range is that some will always aim at lower intake and some at high – and that is not necessarily the way guidelines were intended to be interpreted. ESPEN/ESPGHAN joint guidelines on PN in children and adults has taken >2 years to produce, using around 30+ 'experts' with 10 chapters each containing 10-20 recommendations. On many it was difficult to reach 'agreement' so for this NICE ratified guideline, presentation of 'recommendations' needs to somehow reflect the level of agreement/consensus - or not – that was achieved using a Delphi type process.	
Royal College of Paediatrics and Child Health	General		Very timely piece on back of BAPM framework, it will be great to have additional guidance.	Thank you for your comment.
Royal College of Paediatrics and Child Health	General		Would be really helpful if you were able to make recommendations on e-prescribing as PN prescribing is a significant source of errors and a NICE standard would provide weight to argue a case at Trust level.	Thank you for your comment. Possible errors related to e-prescribing are not restricted to PN and are therefore outside the remit of this guideline.
Royal College of Paediatrics and Child Health	General	24-27	We hope you will address the points raised about fluid balance; what is strength of evidence that higher total fluid volumes in first week are detrimental to outcomes? In order to achieve BAPM amino acid quantities you have to give larger volumes of PN even with the most concentrated of solution, and this can be 100-110 ml/kg/day on day one for those babies with multiple infusions. Guidance on this area will be key to ensuring doctors commit to providing optimal nutrition rather than reducing PN to keep to historical daily fluid volumes.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Fluid administration was not considered such an area. This matter is not specific to neonates requiring PN. The administration of PN would need to take account of the fluid requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide fluid administration and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Royal College of Paediatrics	General	General	Where vitamins should be – e.g. administered with lipid, rather than aqueous solution.	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of

Organisation	Page no.	Line no.	Comments	Developer's response
and Child Health			And what constitutes sufficient vitamin K supplementation not to require additional doses for prophylaxis at 7 or 28 days (if a baby has not received IM vitamin K at birth).	decision making regarding the constituents in PN. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Vitamin administration was not considered such an area. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Royal College of Paediatrics and Child Health	General	General	When to stop lipid – e.g. at 120mL/kg/day, or at full feeds	Thank you for your comment. The key area is referring to 'stopping'. The question we posed is 'what strategies are best for stopping parenteral nutrition'. Recommendations will be drafted based on a review of clinical and health economic evidence. The details of the review strategies will be decided in collaboration with the Committee. We cannot pre-empt what the conclusion from the evidence will be and what recommendations may be drafted based on this.
Royal College of Paediatrics and Child Health	General	General	When to stop PN? E.g. at full feeds, or at a certain minimum rate per hour/day	Thank you for your comment. The key area is referring to 'stopping'. The question we posed is 'what strategies are best for stopping parenteral nutrition'. Recommendations will be drafted based on a review of clinical and health economic evidence. The details of the review strategies will be decided in collaboration with the Committee. We cannot pre-empt what the conclusion from the evidence will be and what recommendations may be drafted based on this.
Royal College of Paediatrics and Child Health	General	General	The scope seems to cover main issues including choice of lipid and issues around electrolytes, especially calcium and phosphate balance.	Thank you for your comment.
Royal College of Paediatrics and Child Health	General	General	Additionally the 'hang time' for bags to see if 48 hour run times (as opposed to 48 hour out of fridge) are biochemically stable and microbiologically safe. This could have considerable cost savings.	Thank you for your comment. This area was not prioritised in the scope. Even though it could impact on costs it was felt that the other topics would address greater variation in practice. NICE guidelines do not address every aspect of decision making and this is a complex and big topic. We therefore had to be selective in what would be included.

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Royal College of Paediatrics and Child Health	General	General	Please refer to this research by Dr C. Morgan: G169 Preventing Early Postnatal Head Growth Failure in Very Preterm Infants: The Randomised Controlled SCAMP Nutrition Study	Thank you for your comment. The scope covers the key issues that will be addressed by the guideline. The reviews of the evidence will then look for relevant trials during guideline development. At this point in time we cannot pre-empt what will be included.
Royal College of Speech and Language Therapists	5	6	The RCSLT suggest adding speech and language therapists after dietitians in the relevant healthcare professionals. They often are very aware of these infants, and will be looking at early oral reflexes, non–nutritive interventions, as well as focusing on very basic parent–infant interaction, etc., and once parenteral feeding transitions to enteral feeds, speech and language therapists will be discussing appropriate times to begin oral feeding with the team.	Thank you for your comment. We have now added speech and language therapists to this section.
Royal College of Speech and Language Therapists	6	28	We suggest being more specific, in that when you stop parenteral feeding, you move onto enteral and then other methods of nutritional intake; therefore you will cover the expected pathway the infant will be expected to take.	Thank you for your comment. The key area is referring to 'stopping'. However our review question 6 in section 3.5 provides more detail on how we are planning to review this. The question we posed is 'what strategies are best for stopping parenteral nutrition'. We believe that the specific details of moving from parenteral to enteral feeding would fall into the category strategies for stopping. However, the scope document does not go into the exact details of every review topic. The specifics of how the evidence review will be carried out will be planned in the review protocol with the Committee when the guideline is being developed.
Royal College of Speech and Language Therapists	9	19	Re: main outcomes: We think it would be useful to have number of days on parenteral feeding, followed by number of days on enteral feeding, with days to achieving full oral feeding. This will help provide important variations in patterns of feeding development that different infants experience. For example, we know that very low birth weight infants, experience longer periods of parenteral feeds, and also infants who have enteral feeds delayed due to NEC – and	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.

Organisation	Page no.	Line no.	Comments	Developer's response
			identification of patterns to expect would be helpful for healthcare practitioners.	
Royal College of Speech and Language Therapists	9	8	We believe something on positioning generally, when infants are receiving parenteral feeds would be important to specify.	Thank you for your comment. NICE guidelines focus on areas where there is important variation in clinical practice. We believe that positioning when infants receive parenteral nutrition is not such an area.
Staffordshire, Shropshire & Black Country Newborn and Maternity Network	6		Section 3.3 - We feel that dealing with transfer and transport of PN between units is also a big issue and would benefit from being covered	Thank you for your comment. In section 3.3 one of our key areas is 'service design' with the associated review question '7 What approaches to prescribing and providing parenteral nutrition in preterm and term babies (for example, nutrition care teams) are effective and safe?'. We cannot provide the details of how this question will be approached in the evidence review at this stage (it is decided jointly with the Committee), but it is possible that safe transfer or transport may feature in this topic. We will highlight this point when the detailed approach to the question is planned.
Staffordshire, Shropshire & Black Country Newborn and Maternity Network	6		Section 3.3 - Fluid and electrolyte quantities are an essential component of PN management. A literature review of this component of PN management would be very helpful	Thank you for your comment. The scope of this guideline does not attempt to cover evidence reviews on all aspects of decision making. The topic is complex and very extensive and the intention has been to prioritise areas where there is important variation in practice. Fluid and electrolyte administration were not considered such areas. These are matters that are not specific to neonates requiring PN. The administration of PN would need to take account of the fluid and electrolyte requirements and restrictions for the individual baby. There are physiological, pathophysiological and clinical principles that guide the administration of these constituents and during the development of the guideline we may be able to highlight such principles based and on Committee consensus.
Staffordshire, Shropshire & Black Country Newborn and	6	8	Section 3.1 - Should this also include babies who are unable to meet nutritional needs through enteral feeds?	Thank you for your comment. The population would be all babies and 'indications for, and approaches to, parenteral nutrition' is one of the 'key areas' covered in section 3.3. We believe that 'unable to meet nutritional needs through enteral feeds' would be an indication for parenteral nutrition.

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Maternity Network				
Staffordshire, Shropshire & Black Country Newborn and Maternity Network	8		Section 3.5 - In addition to the indications, contraindications would be helpful. Including contraindications (or indeed lack of contraindications) for lipid infusions, to ensure clarity and consistency	Thank you for your comment. The details of each review questions will be discussed with the Committee. We believe that contraindications could be covered by adverse outcomes in relation to the administration of lipid infusions.
Staffordshire, Shropshire & Black Country Newborn and Maternity Network	9		Section 3.6 - Should ROP be included as a potential adverse outcome?	Thank you for your comment. For each evidence review consideration will be given to the particular outcomes that are relevant to the intervention. The main outcomes listed in 3.6 will generally be considered but specific outcomes may be required on a case by case basis.

**None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*