

## Neonatal parenteral nutrition

### [A1] Predictors of enteral feeding success

*NICE guideline NG154*

*Evidence reviews*

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*These evidence reviews were developed by  
the National Guideline Alliance which is part of  
the Royal College of Obstetricians and  
Gynaecologists*



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# Indications for, and approaches to, starting parenteral nutrition: predictors for enteral feeding success

## Review question

What are the predictors for enteral feeding success?

## Introduction

Parenteral nutrition (PN) is central to the care of very preterm infants as gastrointestinal immaturity precludes early administration of milk volumes sufficient to support growth. Term infants who have surgery for gastrointestinal conditions or who are too sick to be fed enterally also benefit from PN. While PN is essential in these situations there are risks associated with it, including infection, liver impairment and central line related complications. The benefits of PN must be weighed against the risks and the establishment of enteral feeds should be a goal of nutritional management.

## Summary of the protocol

See Table 1 for a summary of the Population, Prognostic factors to be considered, and Outcome (PPO) characteristics of this review.

**Table 1: Summary of the protocol (PPO table)**

<b>Population</b>	<ul style="list-style-type: none"> <li>• Babies born at term, up to 28 days after their birth (term babies)</li> <li>• Moderately preterm babies (32-36 weeks' gestation)</li> <li>• Critically ill babies</li> </ul>
<b>Prognostic factors to be considered</b>	<ul style="list-style-type: none"> <li>• Birth weight,               <ul style="list-style-type: none"> <li>◦ May be considered as a continuous variable and categorical variable (low birth weight (&lt;1500g))</li> </ul> </li> <li>• Gestational age</li> <li>• Growth restriction</li> <li>• Critical illness (NEC, intestinal failure, short bowel syndrome, surgery/other therapy, congenital gastrointestinal defects, PPHN, HIE, Meconium aspiration, sepsis, and others as reported)</li> <li>• Age of mothers (aged 17 years of under)</li> <li>• Socioeconomic status of mothers</li> </ul>
<b>Outcomes</b>	<p><b>Critical</b></p> <ul style="list-style-type: none"> <li>• Proportion of neonates achieving enteral feeding success (volume based or kcal)               <ul style="list-style-type: none"> <li>◦ 100ml/kg/day by day 4</li> </ul> </li> <li>• Hypertriglyceridemia               <ul style="list-style-type: none"> <li>◦ Other PN associated liver disease</li> </ul> </li> <li>• Nitrogen balance</li> <li>• Metabolic acidosis</li> </ul> <p><b>Important</b></p> <ul style="list-style-type: none"> <li>• None</li> </ul>

*HIE: Hypoxic ischaemic encephalopathy; NEC: necrotising enterocolitis; PN: parenteral nutrition; PPHN: persistent pulmonary hypertension of the newborn.*

For further details see the review protocol in appendix A.

## **Clinical evidence**

### **Included studies**

A systematic review of the clinical literature was conducted but no studies were identified which were applicable to this review question.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

### **Excluded studies**

Studies not included in this review are listed, and reasons for their exclusions are provided in appendix K.

### **Summary of clinical studies included in the evidence review**

No studies were identified which were applicable to this review question (and so there are no evidence tables in Appendix D).

### **Quality assessment of clinical outcomes included in the evidence review**

No studies were identified which were applicable to this review.

## **Economic evidence**

### **Included studies**

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question. A single economic search was undertaken for all topics included in the scope of this guideline. Please see supplementary material D for details.

### **Excluded studies**

No studies were identified which were applicable to this review question.

### **Summary of studies included in the economic evidence review**

No economic evaluations were identified which were applicable to this review question.

### **Economic model**

This review question was prioritised for economic modelling. However, clinical data was insufficient to inform the economic model.

## **Evidence statements**

### **Clinical evidence statements**

No clinical evidence was identified which was applicable to this review question.

### **Economic evidence statements**

No economic evidence was identified which was applicable to this review question.

## **The committee's discussion of the evidence**

### **Interpreting the evidence**

#### ***The outcomes that matter most***

The committee prioritised the number of babies going on to successful enteral feeding (i.e. babies reaching 100ml/kg/day by day 4) as the most critical outcome. If babies do not start successful enteral nutrition (EN), then they must receive PN to ensure that they get the nutrition that they need. Although enteral feeding practice was not included in the scope of the guideline it is recognised that parenteral feeding practice is linked to enteral feeding success, that is if enteral feeding is not tolerated, PN must be initiated. Other critical outcomes included hypertriglyceridemia (and other PN related liver diseases), nitrogen balance and metabolic acidosis. These outcomes were considered critical by the committee as they are the most likely adverse consequences of rapid or excessive EN provision that is these may arise if the baby's digestive system is not adequately mature to take on EN. The committee did not prioritise any outcomes as important.

#### ***The quality of the evidence***

No clinical evidence was identified for this review.

### **Benefits and harms**

#### **Indications for neonatal parenteral nutrition**

No clinical evidence was identified for this review; therefore the committee made the recommendations using informal consensus, based on their experience and expertise. The committee agreed that there is a risk of significant deficits in nutrition, short-term and long-term adverse events if babies born at 30<sup>+6</sup> weeks or earlier are not supported by PN from birth. They therefore decided that a firm recommendation to provide PN to all babies less than 31<sup>+0</sup> weeks was justified. Babies less than 31<sup>+0</sup> weeks would usually be classified as very preterm, and the committee agreed that these babies would not be able to tolerate sufficient enteral feeding, for instance due to physiologic immaturity of the gastrointestinal tract, including decreased gastrointestinal motility and reduced intestinal enzyme activity. The committee discussed whether to make recommendations based on birth weight as well as gestational age. However, they agreed that these would be correlated, and if the recommendation included more than one parameter it may lead to uncertainty in deciding when to start PN, so they based the recommendation solely on age at birth. More mature growth restricted babies would be covered under the condition of poor feed tolerance as described below. In relation to weight the committee also discussed whether to specifically address small for gestational age babies or babies with intrauterine growth restrictions. However, they decided that this was not needed because those babies who need parenteral nutrition may not make sufficient progress with enteral feeds in the first 72 hours after birth and this situation is covered in another recommendation.

The committee acknowledged that for babies over 31<sup>+0</sup> weeks enteral nutrition is usually commenced promptly and advanced faster than for less mature infants. It is outside the scope of this guideline to develop recommendations on enteral nutrition feeding; however, the committee agreed based on their experience and expertise that if the baby is not making sufficient progress on enteral nutrition by 72 hours then PN would need to be provided, to prevent nutritional deficits. The committee agreed on 72 hours to balance the benefits of pursuing an enteral feeding regimen with the harms of not receiving sufficient nutrition and agreed that a three day cut-off would provide a safety net for the baby by which a decision needs to be made either way (continuing on enteral or starting parenteral nutrition). The committee also discussed what would indicate good progress during the first 72 hours. The committee agreed that if by 72 hours of enteral nutrition feeding the baby is increasing intake



and has reached, or has almost reached 100ml/kg/day then it would usually be the case that PN would not be indicated. However, they decided, by informal consensus, not to include this in the recommendation because it would be a too prescriptive cut-off and sufficient progress depends on many different factors that cannot be easily defined. They therefore agreed, based on their experience and expertise, that the assessment of 'sufficient progress' would need to involve a degree of clinical judgement.

The committee also agreed that babies with a congenital gut disorder and critically ill preterm and term babies (with, for example, sepsis) should have their need for PN assessed. If it is thought that the likelihood of making progress on enteral feeding is low, PN should be started.

### **Starting neonatal parenteral nutrition if enteral feeds are stopped**

The committee considered the indications for PN if enteral feeding is stopped for any reason. Because preterm babies have limited stores and the potential for accumulating deficits, the committee agreed, based on their experience and expertise, that if enteral feeds were stopped and babies are unlikely to restart enteral feeds within 48 hours of stopping or babies who have stopped enteral feeds for 24 hours and there was no prospect of restarting and making adequate progress with enteral feeds in the next 48 hours (often that would be because of suspected necrotising enterocolitis or a critical illness such as sepsis), PN should be started.

In term babies, the committee based its recommendation on current practice and the more replete nutritional stores of a baby born at term. They therefore decided that PN is indicated if enteral feeds were stopped and babies are unlikely to restart enteral feeds within 72 hours of stopping or after a stoppage of 48 hours rather than 24 hours and if progress has not been made with enteral feeds in the following 48 hours. For term babies examples of reasons for why they would not be able to restart within a further 48 hours can be similar to those for preterm (for example sepsis or critical illness) but could also be related to a surgical procedure (for example a surgical gut disorder).

### **Cost effectiveness and resource use**

There was no existing economic evidence for this review question. The committee noted the lack of clinical evidence in this area. However, it was explained that the recommendations in this area reinforce current clinical practice and will not incur additional resources to the NHS. The recommendations relate to the care that directly impacts on the outcomes for these babies and the committee expressed the view that these recommendations are essential and justified on clinical grounds.

### **References**

No evidence was identified which was applicable to this review question.

# Appendices

## Appendix A – Review protocols

Review protocol for review question: What are the predictors for enteral feeding success?

**Table 2: Review protocol – predictors for enteral feeding success**

Field (based on PRISMA-P)	Content
Review question	What are the predictors for enteral feeding success?
Type of review question	Prognostic
Objective of the review	Indications for, and approaches to, starting parenteral nutrition in preterm and term infants.
Eligibility criteria – population/disease/condition/issue/domain	<ul style="list-style-type: none"> <li>• Babies born at term, up to 28 days after their birth (term babies)</li> <li>• Moderately preterm (32-36 weeks' gestation)</li> <li>• Critically ill babies</li> </ul>
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	<p><b>Factors to be considered</b></p> <ul style="list-style-type: none"> <li>• Birth weight, May be considered as a continuous variable and categorical variable (low birth weight (&lt;1500g))</li> <li>• Gestational age</li> <li>• Growth restriction</li> </ul> <p>Critical illness (NEC, intestinal failure, short bowel syndrome, surgery/other therapy, congenital gastrointestinal defects, PPHN, HIE, Meconium aspiration, sepsis, and others as reported)</p> <ul style="list-style-type: none"> <li>• Age of mothers (aged 17 years of under)</li> <li>• Socioeconomic status of mothers</li> </ul>
Eligibility criteria – comparator(s)/control or reference (gold) standard	Not applicable
Outcomes and prioritisation	<p><b>Critical:</b></p> <ul style="list-style-type: none"> <li>• Proportion of neonates achieving enteral feeding success (to be defined by the committee) – can allow 2 definitions e.g., volume based or kcal for example: 100ml/kg/day by day 4</li> <li>• Hypertriglyceridemia               <ul style="list-style-type: none"> <li>○ Other PN associated liver disease</li> </ul> </li> </ul>

Field (based on <u>PRISMA-P</u> )	Content
	<ul style="list-style-type: none"> <li>• Nitrogen balance</li> <li>• Metabolic acidosis</li> </ul>
Eligibility criteria – study design	<p>Only include published full text papers-</p> <ul style="list-style-type: none"> <li>• Systematic reviews/meta-analyses of cohort studies</li> <li>• Prospective population-based cohort studies</li> <li>• Prospective single centre or multicentre cohort studies</li> </ul> <p>No date restriction needed.</p> <p>Participant numbers (no restriction for observational studies).</p> <p>Exclude:</p> <ul style="list-style-type: none"> <li>• Conference abstracts</li> <li>• Follow-up of RCTs</li> </ul>
Other inclusion exclusion criteria	<p><b>Inclusion:</b></p> <p>Clinical settings that provide neonatal care or specialist paediatric care.  UK and non-UK studies (non-UK studies from middle and high income countries according to WHO/World Bank criteria).</p>
Proposed sensitivity/sub-group analysis, or meta-regression	<ul style="list-style-type: none"> <li>• Parents or carers whose first language is not English</li> <li>• Parents or carers who have learning difficulties or disabilities</li> </ul> <p>There are inequalities that have been identified relating to how information is provided to them and the type of support they need.</p> <ul style="list-style-type: none"> <li>• It is known that being a young woman (aged 17 years or under) or a woman with a low socioeconomic status increases the risk of giving birth to a baby preterm. These groups could require particular support and specific recommendations may be required to address their particular needs.</li> </ul> <p><b>Stratified analysis:</b></p> <ul style="list-style-type: none"> <li>• Babies born at term, up to 28 days after their birth (term babies).</li> </ul>

Field (based on <u>PRISMA-P</u> )	Content
	<ul style="list-style-type: none"> <li>• Moderately preterm babies (32-36 weeks' gestation)</li> <li>• Babies who are critically ill or need surgery</li> </ul> <p><b>Confounding factors:</b></p> <ul style="list-style-type: none"> <li>• Age of baby</li> <li>• Birth weight: low birth weight (&lt;2500g); very low birth weight (&lt;1500g) and extremely low birth weight (&lt;1000g)</li> <li>• Sex of baby</li> <li>• Gestation</li> <li>• Neurodevelopmental outcomes: <ul style="list-style-type: none"> <li>○ Biological (sex, small for gestational age, ethnicity)</li> <li>○ Neonatal (PVL, IVH, infarct, sepsis, ROP, NEC, antenatal/postnatal steroids, BPD at 36 weeks)</li> <li>○ Social (SES, substance abuse, alcohol abuse, multiple pregnancy, chorioamnionitis, neglect, maternal age, maternal mental health disorder)</li> <li>○ Postnatal (epilepsy, age of establishing feeding)</li> </ul> </li> </ul>
Selection process – duplicate screening/selection/analysis	<p>Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer.</p> <p>A random sample of the references identified in the search will be sifted by a second reviewer. This sample size will be 10% of the total, or 100 studies if the search identifies fewer than 1000 studies. All disagreements in study inclusion will be discussed and resolved between the two reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers.</p>
Data management (software)	<p>Pairwise meta-analyses, if possible, will be performed using Cochrane Review Manager (RevMan5). 'GRADEpro' will be used to assess the quality of evidence for each outcome. Low income countries will be downgraded for indirectness.</p> <p>NGA STAR software will be used for generating bibliographies/citations, study sifting, data extraction and recording quality assessment using checklists (ROBIS (systematic reviews); ROBINS-I (Cochrane risk of bias tool for Non-randomised studies));</p>
Information sources – databases and dates	<p>Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase.</p> <p>Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix B for full strategies.</p>

Field (based on <u>PRISMA-P</u> )	Content
Identify if an update	This is a new topic for the guideline and is not an update.
Author contacts	Developer: The National Guideline Alliance <a href="https://www.nice.org.uk/guidance/indevelopment/gid-ng10037">https://www.nice.org.uk/guidance/indevelopment/gid-ng10037</a>
Highlight if amendment to previous protocol	For details please see section 4.5 of <a href="#">Developing NICE guidelines: the manual 2014</a> .
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see appendix B.
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of <a href="#">Developing NICE guidelines: the manual 2014</a> . The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the ‘Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox’ developed by the international GRADE working group <a href="http://www.gradeworkinggroup.org/">http://www.gradeworkinggroup.org/</a>
Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of <a href="#">Developing NICE guidelines: the manual 2014</a> .
Methods for analysis – combining studies and exploring (in)consistency	For details of the methods please see supplementary material C.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of <a href="#">Developing NICE guidelines: the manual 2014</a> . If sufficient relevant RCTs evidence is available, publication bias will be explored using RevMan software to examine funnel plots.  Trial registries will be examined to identify missing evidence: Clinical trials.gov, NIHR Clinical Trials Gateway.
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of <a href="#">Developing NICE guidelines: the manual 2014</a> .
Rationale/context – Current management	For details please see the introduction to the evidence review.

Field (based on <u>PRISMA-P</u> )	Content
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Joe Fawke (Consultant Neonatologist and Honorary Senior Lecturer, University Hospitals Leicester NHS Trust) in line with section 3 of <a href="#">Developing NICE guidelines: the manual 2014</a> . Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details of the methods please see supplementary material C.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.
PROSPERO registration number	Not registered with PROSPERO.

*BPD: bronchopulmonary dysplasia; CCTR: Cochrane controlled trials register; CDSR: Cochrane database of systematic reviews; DARE: database of abstracts of reviews of effects; GRADE: grading of recommendations assessment, development and evaluation; HIE: Hypoxic ischaemic encephalopathy; HTA: health technology assessment; IVH: intraventricular haemorrhage; MID: minimally important difference; NEC: necrotising enterocolitis; NGA: National Guidelines Alliance; NHS: national health service; NICE: National Institute for Health and Care Excellence; NIHR: national institute for health research; PN: parenteral nutrition; PPHN: persistent pulmonary hypertension of the newborn; PROSPERO: International prospective register of systematic reviews; PVL: periventricular leukomalacia; RCT: randomised controlled trial; RoB: risk of bias; ROBINS-I: risk of bias in non-randomised studies of interventions; ROBIS: risk of bias in systematic reviews; ROP: retinopathy of prematurity; SD: standard deviation; WHO: World Health Organisation.*

## Appendix B – Literature search strategies

### Literature search strategies for review question: What are the predictors for enteral feeding success?

#### Databases: Medline; Medline Epub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	INFANT, NEWBORN/
2	(neonat\$ or newborn\$ or new-born\$ or baby or babies).ti,ab.
3	or/1-2
4	PARENTERAL NUTRITION/
5	PARENTERAL NUTRITION, TOTAL/
6	PARENTERAL NUTRITION SOLUTIONS/
7	ADMINISTRATION, INTRAVENOUS/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
8	INFUSIONS, INTRAVENOUS/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
9	CATHETERIZATION, CENTRAL VENOUS/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
10	exp CATHETERIZATION, PERIPHERAL/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
11	((parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
12	((peripheral\$ or central\$) adj3 line? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
13	(catheter\$ adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
14	(drip? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
15	or/4-14
16	ENTERAL NUTRITION/
17	INTUBATION, GASTROINTESTINAL/
18	GASTROSTOMY/
19	JEJUNOSTOMY/
20	((enteral\$ or tube? or oral\$ or sip) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
21	((Nasogastric\$ or gastrointestinal\$) adj3 (tube? or intubate\$ or nutrition\$ or feed\$ or fed\$)).ti,ab.
22	Gastrostom\$.ti,ab.
23	Jejunostom\$.ti,ab.
24	or/16-23
25	ENERGY INTAKE/
26	NUTRITIONAL STATUS/
27	MALNUTRITION/
28	((energy or volume? or kcal or kilocalorie? or nutrition\$) adj3 (goal? or target\$)).ti,ab.
29	((optimi\$ or success\$) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
30	((ml? or milliliter?) adj3 (kg? or kilogram?) adj3 (d or day)).ti,ab.
31	(feed\$ adj3 (tolera\$ or intolera\$)).ti,ab.
32	(malnutrition or malnourish\$).ti,ab.
33	early nutrition\$.ti,ab.
34	nutrition\$ support\$.ti,ab.
35	or/25-34
36	((Initiat\$ or Start\$ or Introduc\$ or Earl\$ or Advanc\$ or Achiev\$ or Establish\$ or Tolera\$ or Success\$ or Full\$) adj3 (enteral\$ or tube? or oral\$ or sip) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
37	((Initiat\$ or Start\$ or Begin\$ or Introduc\$ or Earl\$ or Establish\$ or Predict\$ or Indicat\$ or Need\$) adj5 (parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
38	((Initiat\$ or Start\$ or Begin\$ or Introduc\$ or Earl\$ or Establish\$ or Predict\$ or Indicat\$ or Need\$) adj5 (PN or SPN or IPN or TPN or STD-PN or IND-PN)).ti,ab.
39	or/37-38
40	((preterm\$ or pre-term\$ or prematur\$ or pre-matur\$ or pre#mie? or premie or premies or (low adj3 birth adj3 weigh\$) or (low adj3 birthweigh\$) or LBW or VLBW or (small adj3 gestation\$ adj3 age?) or SGA or (grow\$ adj3 (restrict\$ or retard\$)) or IUGR or (critical\$ adj3 ill\$) or (necroti\$ adj3 enterocolit\$) or NEC or (intestin\$ adj3 fail\$) or short bowel? syndrome? or surgery or (surgical adj3 procedure?) or postoperati\$ or ((post or follow\$ or after) adj3 operati\$) or ((digest\$ or gastrointestinal) adj3 (defect\$ or abnormal\$ or anomal\$)) or (persistent adj3 (pulmonary hypertens\$ or fetal circulat\$)) or PPHN or (hypoxi\$ adj3 ischemi\$ adj3 encephalopath\$) or HIE or (meconium adj3 aspirat\$ or inhal\$) or sepsis or septic?emi\$ or ((septic or endotoxic or toxic) adj3 shock) or ((intensive or critical) adj3 care) or NICU?) adj5 (parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
41	ADEPT.ti,ab.
42	SIFT.ti,ab.
43	or/41-42
44	3 and 15 and 24 and 35
45	3 and 15 and 36
46	3 and 24 and 39
47	3 and 24 and 40
48	3 and 15 and 43

#	Searches
49	or/44-48
50	limit 49 to english language
51	LETTER/
52	EDITORIAL/
53	NEWS/
54	exp HISTORICAL ARTICLE/
55	ANECDOTES AS TOPIC/
56	COMMENT/
57	CASE REPORT/
58	(letter or comment*).ti.
59	or/51-58
60	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
61	59 not 60
62	ANIMALS/ not HUMANS/
63	exp ANIMALS, LABORATORY/
64	exp ANIMAL EXPERIMENTATION/
65	exp MODELS, ANIMAL/
66	exp RODENTIA/
67	(rat or rats or mouse or mice).ti.
68	or/61-67
69	50 not 68

### Databases: Embase; and Embase Classic

#	Searches
1	NEWBORN/
2	(neonat\$ or newborn\$ or new-born\$ or baby or babies).ti,ab.
3	or/1-2
4	PARENTERAL NUTRITION/
5	TOTAL PARENTERAL NUTRITION/
6	PERIPHERAL PARENTERAL NUTRITION/
7	PARENTERAL SOLUTIONS/
8	INTRAVENOUS FEEDING/
9	INTRAVENOUS DRUG ADMINISTRATION/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
10	exp INTRAVENOUS CATHETER/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
11	((parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
12	((peripheral\$ or central\$) adj3 line? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
13	(catheter\$ adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
14	(drip? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
15	or/4-14
16	ENTERIC FEEDING/
17	exp DIGESTIVE TRACT INTUBATION/
18	GASTROSTOMY/
19	JEJUNOSTOMY/
20	((enteral\$ or tube? or oral\$ or sip) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
21	((Nasogastric\$ or gastrointestinal\$) adj3 (tube? or intubate\$ or nutrition\$ or feed\$ or fed\$)).ti,ab.
22	Gastrostom\$.ti,ab.
23	Jejunostom\$.ti,ab.
24	or/16-23
25	CALORIC INTAKE/
26	NUTRITIONAL STATUS/
27	MALNUTRITION/
28	((energy or volume? or kcal or kilocalorie? or nutrition\$) adj3 (goal? or target\$)).ti,ab.
29	((optimi\$ or success\$) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
30	((ml? or milliliter?) adj3 (kg? or kilogram?) adj3 (d or day)).ti,ab.
31	(feed\$ adj3 (tolera\$ or intolera\$)).ti,ab.
32	(malnutrition or malnourish\$).ti,ab.
33	early nutrition\$.ti,ab.
34	nutrition\$ support\$.ti,ab.
35	or/25-34
36	((Initiat\$ or Start\$ or Introduc\$ or Earl\$ or Advanc\$ or Achiev\$ or Establish\$ or Tolera\$ or Success\$ or Full\$) adj3 (enteral\$ or tube? or oral\$ or sip) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
37	((Initiat\$ or Start\$ or Begin\$ or Introduc\$ or Earl\$ or Establish\$ or Predict\$ or Indicat\$ or Need\$) adj5 (parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
38	((Initiat\$ or Start\$ or Begin\$ or Introduc\$ or Earl\$ or Establish\$ or Predict\$ or Indicat\$ or Need\$) adj5 (PN or SPN or IPN or TPN or STD-PN or IND-PN)).ti,ab.
39	or/37-38
40	((preterm\$ or pre-term\$ or prematur\$ or pre-matur\$ or pre#mie? or premie or premies or (low adj3 birth adj3 weigh\$) or (low adj3 birthweigh\$) or LBW or VLBW or (small adj3 gestation\$ adj3 age?) or SGA or (grow\$ adj3 (restrict\$ or retard\$) or IUGR or (critical\$ adj3 ill\$) or (necroti\$ adj3 enterocolit\$) or NEC or (intestin\$ adj3 fail\$) or short bowel? syndrome? or surgery or (surgical adj3 procedure?) or postoperati\$ or ((post or follow\$ or after) adj3 operati\$) or



#	Searches
	((digest\$ or gastrointestinal) adj3 (defect\$ or abnormal\$ or anomal\$)) or (persistent adj3 (pulmonary hypertens\$ or fetal circulat\$)) or PPHN or (hypoxi\$ adj3 ischemi\$ adj3 encephalopath\$) or HIE or (meconium adj3 (aspirat\$ or inhal\$)) or sepsis or septic?emi\$ or ((septic or endotoxic or toxic) adj3 shock) or ((intensive or critical) adj3 care) or NICU?) adj5 (parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$).ti,ab.
41	ADEPT.ti,ab.
42	SIFT.ti,ab.
43	or/41-42
44	3 and 15 and 24 and 35
45	3 and 15 and 36
46	3 and 24 and 39
47	3 and 24 and 40
48	3 and 15 and 43
49	or/44-48
50	limit 49 to english language
51	letter.pt. or LETTER/
52	note.pt.
53	editorial.pt.
54	CASE REPORT/ or CASE STUDY/
55	(letter or comment*).ti.
56	or/51-55
57	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
58	56 not 57
59	ANIMAL/ not HUMAN/
60	NONHUMAN/
61	exp ANIMAL EXPERIMENT/
62	exp EXPERIMENTAL ANIMAL/
63	ANIMAL MODEL/
64	exp RODENT/
65	(rat or rats or mouse or mice).ti.
66	or/58-65
67	50 not 66

### Databases: Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; and Health Technology Assessment

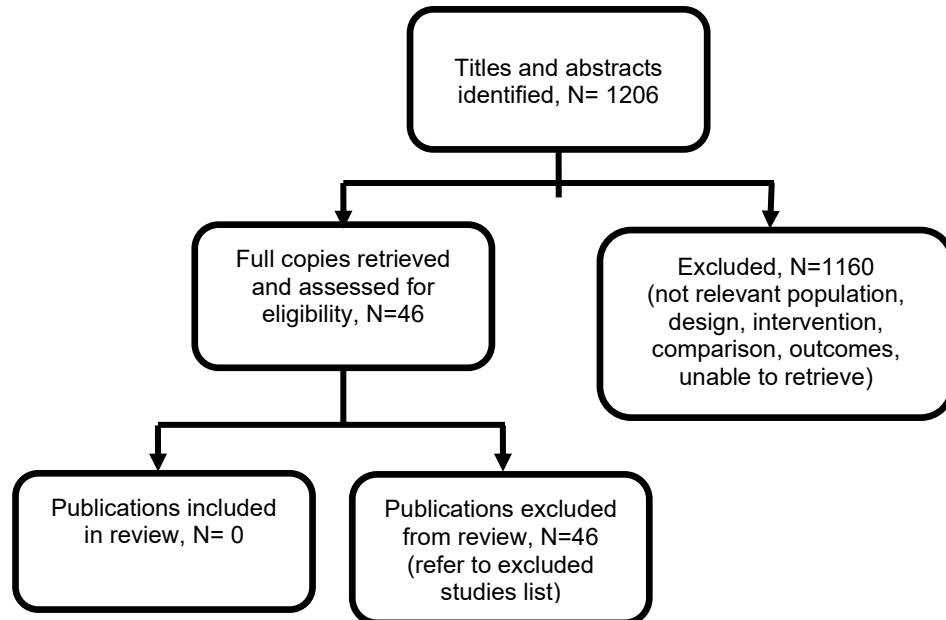
#	Searches
1	MeSH descriptor: [INFANT, NEWBORN] this term only
2	(neonat* or newborn* or new-born* or baby or babies):ti,ab
3	#1 or #2
4	MeSH descriptor: [PARENTERAL NUTRITION] this term only
5	MeSH descriptor: [PARENTERAL NUTRITION, TOTAL] this term only
6	MeSH descriptor: [PARENTERAL NUTRITION SOLUTIONS] this term only
7	MeSH descriptor: [ADMINISTRATION, INTRAVENOUS] this term only
8	MeSH descriptor: [INFUSIONS, INTRAVENOUS] this term only
9	MeSH descriptor: [CATHETERIZATION, CENTRAL VENOUS] this term only
10	MeSH descriptor: [CATHETERIZATION, PERIPHERAL] explode all trees
11	#7 or #8 or #9 or #10
12	(nutrition* or feed* or fed*):ti,ab
13	#11 and #12
14	((parenteral* or intravenous* or intra-venous* or IV or venous* or infusion?) near/3 (nutrition* or feed* or fed*)):ti,ab
15	((peripheral* or central*) near/3 line? near/3 (nutrition* or feed* or fed*)):ti,ab
16	(catheter* near/3 (nutrition* or feed* or fed*)):ti,ab
17	(drip? near/3 (nutrition* or feed* or fed*)):ti,ab
18	#4 or #5 or #6 or #13 or #14 or #15 or #16 or #17
19	MeSH descriptor: [ENTERAL NUTRITION] this term only
20	MeSH descriptor: [INTUBATION, GASTROINTESTINAL] this term only
21	MeSH descriptor: [GASTROSTOMY] this term only
22	MeSH descriptor: [JEJUNOSTOMY] this term only
23	((enteral* or tube? or oral* or sip) near/3 (nutrition* or feed* or fed*)):ti,ab
24	((Nasogastric* or gastrointestinal*) near/3 (tube? or intubate* or nutrition* or feed* or fed*)):ti,ab
25	Gastrostom*:ti,ab
26	Jejunostom*:ti,ab
27	#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
28	MeSH descriptor: [ENERGY INTAKE] this term only
29	MeSH descriptor: [NUTRITIONAL STATUS] this term only
30	MeSH descriptor: [MALNUTRITION] this term only
31	((energy or volume? or kcal or kilocalorie? or nutrition*) near/3 (goal? or target*)):ti,ab
32	((optimi* or success*) near/3 (nutrition* or feed* or fed*)):ti,ab

#	Searches
33	((ml? or milliliter?) near/3 (kg? or kilogram?) near/3 (d or day)):ti,ab
34	(feed* near/3 (tolera* or intolera*)):ti,ab
35	(malnutrition or malnourish*):ti,ab
36	early nutrition*:ti,ab
37	nutrition* support*:ti,ab
38	#28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37
39	((Initiat* or Start* or Introduc* or Earl* or Advanc* or Achiev* or Establish* or Tolera* or Success* or Full*) near/3 (enteral* or tube? or oral* or sip) near/3 (nutrition* or feed* or fed*)):ti,ab
40	((Initiat* or Start* or Begin* or Introduc* or Earl* or Establish* or Predict* or Indicat* or Need*) near/5 (parenteral* or intravenous* or intra-venous* or IV or venous* or infusion?) near/3 (nutrition* or feed* or fed*)):ti,ab
41	((Initiat* or Start* or Begin* or Introduc* or Earl* or Establish* or Predict* or Indicat* or Need*) near/5 (PN or SPN or IPN or TPN or STD-PN or IND-PN)):ti,ab
42	#40 or #41
43	((preterm* or pre-term* or prematur* or pre-matur* or premie or premies or (low near/3 birth near/3 weigh*) or (low near/3 birthweigh*) or LBW or VLBW or (small near/3 gestation* near/3 age?) or SGA or (grow* near/3 (restrict* or retard*)) or IUGR or (critical* near/3 ill*) or (necroti* near/3 enterocolit*) or NEC or (intestin* near/3 fail*) or short bowel? syndrome? or surgery or (surgical near/3 procedure?) or postoperati* or ((post or follow* or after) near/3 operati*) or ((digest* or gastrointestinal) near/3 (defect* or abnormal* or anomal*)) or (persistent near/3 (pulmonary hypertens* or fetal circulat*)) or PPHN or (hypoxi* near/3 ischemi* near/3 encephalopath*) or HIE or (meconium near/3 aspirat* or inhal*) or sepsis or septic?emi* or ((septic or endotoxic or toxic) near/3 shock) or ((intensive or critical) near/3 care) or NICU?) near/5 (parenteral* or intravenous* or intra-venous* or IV or venous* or infusion?) near/3 (nutrition* or feed* or fed*)):ti,ab
44	ADEPT:ti,ab
45	SIFT:ti,ab
46	#44 or #45
47	#3 and #18 and #27 and #38
48	#3 and #18 and #39
49	#3 and #27 and #42
50	#3 and #27 and #43
51	#3 and #18 and #46
52	#47 or #48 or #49 or #50 or #51

## Appendix C – Clinical evidence study selection

**Clinical study selection for: What are the predictors for enteral feeding success?**

**Figure 1: PRISMA flow chart for clinical article selection for review question, what are the predictors of enteral feeding success?**



## **Appendix D – Clinical evidence tables**

### **Clinical evidence tables for review question: What are the predictors for enteral feeding success?**

No evidence was identified which was applicable to this review question.

## **Appendix E – Forest plots**

### **Forest plots for review question: What are the predictors for enteral feeding success?**

No evidence was identified which was applicable to this review question.

## **Appendix F – GRADE tables**

### **GRADE tables for review question: What are the predictors for enteral feeding success?**

No evidence was identified which was applicable to this review question.

## **Appendix G – Economic evidence study selection**

### **Economic evidence study selection for review question: What are the predictors for enteral feeding success?**

One global search was conducted for all review questions. See supplementary material D for further information.

## **Appendix H – Economic evidence tables**

### **Economic evidence tables for review question: What are the predictors for enteral feeding success?**

No evidence was identified which was applicable to this review question.



## **Appendix I – Economic evidence profiles**

### **Economic evidence profiles for review question: What are the predictors for enteral feeding success?**

No evidence was identified which was applicable to this review question.

## **Appendix J – Economic analysis**

### **Economic evidence analysis for review question: What are the predictors for enteral feeding success?**

No economic analysis was conducted for this review question.

## Appendix K – Excluded studies

### Excluded clinical and economic studies for review question: What are the predictors for enteral feeding success?

#### Clinical studies

**Table 3: Excluded studies and reasons for their exclusion**

Study	Reason for Exclusion
Abbott, J., Berrington, J., Bowler, U., Boyle, E., Dorling, J., Embleton, N., Juszcak, E., Leaf, A., Linsell, L., Johnson, S., McCormick, K., McGuire, W., Roberts, T., Stenson, B., The Speed of Increasing milk Feeds: a randomised controlled trial, <i>BMC Pediatrics</i> , 17, 39, 2017	Protocol paper.
Agostoni, C., Francescato, G., Agosti, M., Nutrition in the critically ILL: Enteral and parenteral nutrition in the newborn, <i>Archives of Disease in Childhood</i> , 97, A65, 2012	Conference abstract.
Agostoni, C., Mosca, F., Optimising enteral nutrition in the premature infant, <i>Archives of Disease in Childhood</i> , 99, A2, 2014	Conference abstract.
Armstrong, Lindsey B., Ariagno, Katelyn, Smallwood, Craig D., Hong, Charles, Arbuthnot, Mary, Mehta, Nilesh M., Nutrition Delivery During Pediatric Extracorporeal Membrane Oxygenation Therapy, <i>JPEN. Journal of parenteral and enteral nutrition</i> , 42, 1133-1138, 2018	Study does not meet protocol eligibility criteria - not predictors of enteral feeding success; outcomes not reported separately for eligible population (median age range 0 to 16.4 months).
Atanasova, V., Veskov, L., Enteral nutrition of extremely low birth weight infants, <i>Journal of Maternal-Fetal and Neonatal Medicine</i> , 29, 288, 2016	Conference abstract.
Ayede, A. I., Achieving optimal feeds for preterm babies, recommendations and realities in practice: nigerian perspective, <i>Annals of Ibadan postgraduate medicine</i> , 9, 1-7, 2011	Commentary paper.
Bajaj, N., Preterm nutrition and neurodevelopment: An overview, <i>Perinatology</i> , 17, 153-162, 2017	Commentary paper.
Belfort, Mandy Brown, Ehrenkranz, Richard A., Neurodevelopmental outcomes and nutritional strategies in very low birth weight infants, <i>Seminars in fetal &amp; neonatal medicine</i> , 22, 42-48, 2017	Non-systematic review.
Belling-Dierks, F., Glaser, K., Wirbelauer, J., Rucker, V., Frieauff, E., Does rapid enteral feeding increase intestinal morbidity in very low birth weight infants? A retrospective analysis, <i>Journal of Maternal-Fetal and Neonatal Medicine</i> , 30, 2690-2696, 2017	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported.
Butler, T. J., Szekely, L. J., Grow, J. L., A standardized nutrition approach for very low birth weight neonates improves outcomes, reduces cost and is not associated with increased rates of necrotizing enterocolitis,	Outcome of interest does not fit the inclusion criteria; Proportion of neonates achieving EN feeding success not reported as an outcome.

Study	Reason for Exclusion
sepsis or mortality, <i>Journal of Perinatology</i> , 33, 851-7, 2013	
Cagle, Judith, Armentrout, Debra, Huseby, Valerie, Halbardier, Brenda, Garcia, Jose, Sparks, John W., Moya, Fernando R., Randomized, controlled trial of slow versus rapid feeding volume advancement in preterm infants, <i>Pediatrics</i> , 114, 1597-600, 2004	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Carlson, S. J., Ziegler, E. E., Nutrient intakes and growth of very low birth weight infants, <i>Journal of perinatology : official journal of the California Perinatal Association</i> , 18, 252-8, 1998	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Chellis, M. J., Sanders, S. V., Webster, H., Dean, J. M., Jackson, D., Early enteral feeding in the pediatric intensive care unit, <i>JPEN. Journal of parenteral and enteral nutrition</i> , 20, 71-3, 1996	Participants do not fit the inclusion criteria; mean age 5.8 years.
Chessex, P., Enteral and parenteral feeding of the low-birthweight infant, <i>Annales Nestle</i> , 46, 82-93, 1988	Commentary paper.
Christmann, V., Visser, R., Engelkes, M., de Grauw, A. M., van Goudoever, J. B., van Heijst, A. F. J., The enigma to achieve normal postnatal growth in preterm infants--using parenteral or enteral nutrition?, <i>Acta paediatrica (Oslo, Norway : 1992)</i> , 102, 471-9, 2013	Intervention does not fit the inclusion criteria; study altered AA and energy of PN.
Cormack, B. E., Bloomfield, F. H., Audit of feeding practices in babies <1200 g or 30 weeks' gestation during the first month of life, <i>Journal of Paediatrics and Child Health</i> , 42, 458-463, 2006	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Cowan, M. J., Hyperemesis gravidarum: implications for home care and infusion therapies, <i>Journal of intravenous nursing : the official publication of the Intravenous Nurses Society</i> , 19, 46-58, 1996	Commentary paper.
Dama, M., Rao, U., Bulsara, M., Rao, S., Delayed commencement of enteral feeds in gastroschisis results in delay in achieving full enteral feeds: A systematic review and meta regression, <i>Journal of Paediatrics and Child Health</i> , 52, 50, 2016	Conference abstract.
Dama, Madhuri, Rao, Uday, Gollow, Ian, Bulsara, Max, Rao, Shripada, Early Commencement of Enteral Feeds in Gastroschisis: A Systematic Review of Literature, <i>European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery ... [et al] = Zeitschrift fur Kinderchirurgie</i> , 27, 503-515, 2017	Study outcomes do not meet protocol eligibility criteria - not predictors of successful enteral feed; time to full enteral feed reported only.
De Nisi, G., Berti, M., De Nisi, M., Bertino, E., Early enteral feeding with human milk for VLBW infants, <i>Journal of biological regulators and homeostatic agents</i> , 26, 69-73, 2012	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.

Study	Reason for Exclusion
Dinerstein, A., Nieto, R. M., Solana, C. L., Perez, G. P., Otheguy, L. E., Largaia, A. M., Early and aggressive nutritional strategy (parenteral and enteral) decreases postnatal growth failure in very low birth weight infants, <i>Journal of Perinatology</i> , 26, 436-42, 2006	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Dunn, L., Hulman, S., Weiner, J., Kliegman, R., Beneficial effects of early hypocaloric enteral feeding on neonatal gastrointestinal function: preliminary report of a randomized trial, <i>The Journal of pediatrics</i> , 112, 622-9, 1988	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Ergenekon, E., Hirfanoglu, I., Soysal, S., Gucuyener, K., Bas, V., Turan, O., Beken, S., Kazanci, E., Onal, E., Turkyilmaz, C., Koc, E., Atalay, Y., Short and longterm effects of individualized enteral protein supplementation in preterm newborns, <i>Journal of Maternal-Fetal and Neonatal Medicine</i> , 25, 135, 2012	Conference abstract.
Ergenekon, Ebru, Soysal, Sebnem, Hirfanoglu, Ibrahim, Bas, Veysel, Gucuyener, Kivilcim, Turan, Ozden, Beken, Serdar, Kazanci, Ebru, Turkyilmaz, Canan, Onal, Esra, Koc, Esin, Atalay, Yildiz, Short- and long-term effects of individualized enteral protein supplementation in preterm newborns, <i>The Turkish journal of pediatrics</i> , 55, 365-70, 2013	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Fouad, D., Early enteral feeding and the risk of necrotising enterocolitis, <i>Colorectal Disease</i> , 12, 33, 2010	Conference abstract.
Fouad, D., Hansen, R., Boraei, A. S., Sherlock, R., Does early enteral feeding increase the risk of necrotising enterocolitis in neonates?, <i>International Journal of Gynecology and Obstetrics</i> , 119, S350, 2012	Conference abstract.
Hamilton, Emily, Massey, Cynthia, Ross, Julie, Taylor, Sarah, Early enteral feeding in very low birth weight infants, <i>Early Human Development</i> , 90, 227-30, 2014	Outcome of interest does not meet the inclusion criteria; EN feeding success not reported as an outcome.
Hock, Alison Maria, Chen, Yong, Miyake, Hiromu, Koike, Yuhki, Seo, Shogo, Pierro, Agostino, Initiation of Enteral Feeding After Necrotizing Enterocolitis, <i>European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery ... [et al] = Zeitschrift fur Kinderchirurgie</i> , 28, 44-50, 2018	Study does not meet protocol eligibility criteria - systematic review of 2 retrospective studies comparing early vs late EN.
Joffe, Ari, Anton, Natalie, Lequier, Laurance, Vandermeer, Ben, Tjosvold, Lisa, Larsen, Bodil, Hartling, Lisa, Nutritional support for critically ill children, <i>Cochrane Database of Systematic Reviews</i> , 2016	Participants do not meet the inclusion criteria, children aged over 1 year.
Khan, Z., Morris, N., Unterrainer, H., Haiden, N., Holasek, S. J., Urlesberger, B., Effect of standardized feeding protocol on nutrient supply and postnatal growth of preterm infants: A prospective study, <i>Journal of Neonatal-Perinatal MedicineJ Neonatal Perinatal Med</i> , 11, 11-19, 2018	Study does not meet protocol eligibility criteria - multivariate analysis for relevant outcomes not performed.

Study	Reason for Exclusion
Lap, Chiara C. M. M., Brizot, Maria L., Pistorius, Lourens R., Kramer, William L. M., Teeuwen, Ivo B., Eijkemans, Marinus J., Brouwers, Hens A. A., Pajkrt, Eva, van Kaam, Anton H., van Scheltema, Phebe N. Adama, Eggink, Alex J., van Heijst, Arno F., Haak, Monique C., van Weissenbruch, Mirjam M., Sleeboom, Christien, Willekes, Christine, van der Hoeven, Mark A., van Heurn, Ernst L., Bilardo, Catherina M., Dijk, Peter H., van Baren, Robertine, Francisco, Rossana P. V., Tannuri, Ana C. A., Visser, Gerard H. A., Manten, Gwendolyn T. R., Outcome of isolated gastroschisis; an international study, systematic review and meta-analysis, <i>Early Human Development</i> , 103, 209-218, 2016	Study design and outcomes do not meet protocol eligibility criteria - retrospective study and systematic review assessing time to full enteral feed; not predictors of successful enteral feeding.
Leaf, Alison, Dorling, Jon, Kempley, Stephen, McCormick, Kenny, Mannix, Paul, Linsell, Louise, Juszczak, Edmund, Brocklehurst, Peter, Abnormal Doppler Enteral Prescription Trial Collaborative, Group, Brocklehurst P, Dorling J. Kempley S. Leaf A. Mannix P. McCormick K. Cooke R. Newell S. Puntis J. Yu L. Alfirevic Z. Brocklehurst P. Deans M. Ewer A. Fellows P. Khan K. Leaf A. Ayers S. Bowler U. Hoddell B. Juszczak E. Kennedy A. King A. Linsell L. Logan M. Saroglou L. Murdoch E. Staines J. Wickham T. Manikonda R. Chatfield S. Newby E. Eason J. Barnard I. Wagstaff M. Grain L. Cruwys M. Coombs R. McCormick K. Bilolihar H. Hubbard M. Thirumurugan A. Katumba J. Twomey A. Gopinathan V. Clarke P. Thompson F. Mannix P. Dorling J. Babiker S. McEwan P. Scorer T. Rubin S. Manzoor A. Wardle S. Farrier M. Boden G. Del Rio A. Yadav M. Kumar Y. Lewis V. Sen S. Menon G. Kempley S. Craig S. Gupta R. Rabe H. Jones S. Embleton N. Kumararatne B. Brown N. Leaf A. Luyt K. Stalker D. Satodia P. Harikumar C. Jones R. Bowden L. Millman G., Early or delayed enteral feeding for preterm growth-restricted infants: a randomized trial, <i>Pediatrics</i> , 129, e1260-8, 2012	Outcome of interest does not fit the inclusion criteria; EN feeding success not reported as an outcome.
Manea, A., Boia, M., Iacob, D., Dima, M., Iacob, R. E., Benefits of early enteral nutrition in extremely low birth weight infants, <i>Singapore Medical Journal</i> , 57, 616-618, 2016	Outcome of interest does not meet the inclusion criteria; EN feeding success not reported as an outcome.
McClure, R. J., Newell, S. J., Randomised controlled trial of trophic feeding and gut motility, <i>Archives of disease in childhood. Fetal and neonatal edition</i> , 80, F54-8, 1999	Intervention does not fit the inclusion criteria: Parenteral nutrition versus trophic feeding.
Morgan, Jessie, Young, Lauren, McGuire, William, Delayed introduction of progressive enteral feeds to prevent necrotising enterocolitis in very low birth weight infants, <i>Cochrane Database of Systematic Reviews</i> , 2014	Outcome of interest does not meet the inclusion criteria; EN feeding success not reported as an outcome.
Mosqueda, E., Sapiegiene, L., Glynn, L., Wilson-Costello, D., Weiss, M., The early use of minimal enteral nutrition in extremely low birth weight	Outcome of interest does not meet the inclusion criteria; EN feeding success not reported as an outcome.

Study	Reason for Exclusion
newborns, <i>Journal of Perinatology</i> , 28, 264-269, 2008	
Nangia, S., Bishnoi, A., Goel, A., Manda, P., Tiwari, S., Saili, A., Early total enteral feeding in stable very low birth weight infants: A before and after study, <i>Journal of Tropical Pediatrics</i> , 64, 24-30, 2018	Study outcomes do not meet protocol eligibility criteria - days to achieve full enteral feeding; multivariate analysis not conducted.
Ng, D. V. Y., Unger, S., Asbury, M., Kiss, A., Bishara, R., Bando, N., Tomlinson, C., Gibbins, S., O'Connor, D. L., Neonatal Morbidity Count Is Associated With a Reduced Likelihood of Achieving Recommendations for Protein, Lipid, and Energy in Very Low Birth Weight Infants: A Prospective Cohort Study, <i>Journal of Parenteral and Enteral Nutrition</i> , 42, 623-632, 2018	Study outcomes do not meet protocol eligibility criteria - days to achieve full EN; achieving recommended energy levels.
Ng, D. V., Brennan-Donnan, J., Unger, S., Bando, N., Gibbins, S., Nash, A., Kiss, A., O'Connor, D. L., How Close Are We to Achieving Energy and Nutrient Goals for Very Low Birth Weight Infants in the First Week?, <i>Jpen: Journal of Parenteral &amp; Enteral Nutrition</i> , 41, 500-506, 2017	Study outcomes do not meet protocol eligibility criteria - association between energy, macronutrients and likelihood of reaching full enteral feeds.
Raturi, S., Zheng, Q., Daniel, L. M., Shi, L., Rajadurai, V. S., Agarwal, P. K., Nutritional intake and growth velocity in preterm extremely low-birthweight infants in Asia: Are we doing enough?, <i>Journal of Paediatrics and Child Health.</i> , 2017	Study outcomes do not meet protocol eligibility criteria - age or day of reaching full feeds; number receiving fully fortified feeds.
Terrin, Gianluca, Passariello, Annalisa, Canani, Roberto Berni, Manguso, Francesco, Paludetto, Roberto, Cascioli, Concetta, Minimal enteral feeding reduces the risk of sepsis in feed-intolerant very low birth weight newborns, <i>Acta paediatrica (Oslo, Norway : 1992)</i> , 98, 31-5, 2009	Outcome of interest does not meet the inclusion criteria; EN feeding success not reported as an outcome.
Tyson, J. E., Kennedy, K. A., Minimal enteral nutrition for promoting feeding tolerance and preventing morbidity in parenterally fed infants, <i>The Cochrane database of systematic reviews</i> , CD000504, 2000	Systematic review protocol.
Tyson, J. E., Kennedy, K. A., Lucke, J. F., Pedroza, C., Dilemmas Initiating Enteral Feedings in High Risk Infants: How Can They Be Resolved?, <i>Seminars in Perinatology</i> , 31, 61-73, 2007	Commentary paper.
Wang, L. Y., Hung, H. Y., Hsu, C. H., Kao, H. A., Huang, F. Y., Clinical experience with early enteral feeding in very-low-birth-weight infants, <i>Chung-Hua Min Kuo Hsiao Erh Ko i Hsueh Hui Tsa Chih</i> , 38, 282-7, 1997	Outcomes of interest does not meet the inclusion criteria.
Williams, A. F., Early enteral feeding of the preterm infant, <i>Archives of Disease in Childhood: Fetal and Neonatal Edition</i> , 83, F219-F220, 2000	Commentary paper.
Wilson, D. C., McClure, G., Energy requirements in sick preterm babies, <i>Acta paediatrica (Oslo, Norway : 1992). Supplement</i> , 405, 60-4, 1994	Commentary paper.

## **Economic studies**

No economic evidence was identified for this review. See supplementary material D for further information.



## **Appendix L – Research recommendations**

### **Research recommendations for review question: What are the predictors for enteral feeding success?**

No research recommendations were made for this review question.