National Institute for Health and Care Excellence

Final

Neonatal parenteral nutrition

[D1] Glucose

NICE guideline NG154

Evidence reviews

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Final

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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Contents

Optimal target dose and approach for carbohydrates

Review questions

This evidence report contains information on two questions conducted as one review relating to the individual constituents (carbohydrates) in parenteral nutrition for preterm and term babies.

- D1a. What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?
- D1b. What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

Introduction

Carbohydrate, in the form of glucose, is an essential constituent in parenteral nutrition (PN). It provides an important source of energy, and is essential for normal metabolism.

Hyperglycaemia is associated with increased mortality and increased morbidity in very preterm infants. Balancing the need for optimal energy intake against the potential risks of hyperglycaemia and/or its treatment is a key and area of nutritional strategy in very preterm infants. Determining a safe minimum and maintenance total intravenous glucose intake and a regimen to achieve this dose is therefore the objective of this review. An incremental rather than a sudden increase in glucose intake could be beneficial by reducing the risk of very early hyperglycaemia. Unlike other nutrients, glucose is the base constituent of most other (non-PN) fluids. This means total fluid intake and other infusions (e.g. drugs) will also affect total intravenous glucose intake. It is important to recognise this when determining an appropriate intravenous glucose (carbohydrate) dosage to aim for in preterm and term infants.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	• Babies born preterm, up to 28 days after their due birth date (preterm babies) • Babies born at term, up to 28 days after their birth (term babies)
Intervention	Optimal target dose • Any amount of carbohydrate (g/kg/d) Optimal way to achieve this • Starting dose • Rate of Increase in carbohydrates
Comparison	Optimal target dose • Each other Optimal way to achieve this • Different starting doses • Different increases • Different regimens

Outcomes	Critical • Neurodevelopmental outcomes (general cognitive abilities at two years corrected age as measured by a validated scale) • Adverse effects of IV carbohydrates: ○ Infection including sepsis ○ Hyperglycaemia (surrogate outcome - use of insulin) ○ Hypoglycaemia ○ PN associated liver disease **Important** • Mortality • Body composition (measured as Lean mass, fat-free mass, fat mass, adipose tissue, nitrogen accretion) • Growth/Anthropometric measures: ○ Weight gain (g/kg/d) ○ Linear growth ○ Head circumference (mm) • Duration of hospital stay • Nutritional intake (g/kg/d) (defined as proportion of prescribed carbohydrates actually received)

IV: intravenous; PN: parenteral nutrition

For full details see the review protocol in appendix A.

Clinical evidence

Included studies

As limited RCT evidence was available, we also included observational studies. Three studies were identified for this review (Forsyth 1995, Morgan 2014, Pineault 1988).

Optimal target dose

One randomised controlled trial ((RCT); Morgan 2014), one cross-over RCT (Forsyth 1995) and one observational study (Pineault 1988) compared higher versus lower glucose intake.

How to achieve target dose

All of the included studies kept glucose intake consistent across the study periods. No studies were identified that compared different starting doses or rates of increase.

The included study is summarised in Table 2.

See the literature search strategy in appendix B, study selection flow chart in appendix C, study evidence tables in appendix D, and GRADE tables in appendix F.

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

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes	Comments
Forsyth 1995 Crossover RCT UK	N = 20 Mean GA 30.9 weeks (SE 0.4) Mean BW 1314g (SE 65)	High glucose regimen (n=20) 12 g/kg/day (8.3mg/kg/minute) of glucose	Low glucose regimen (n=20) 8 g/kg/day (5.5mg/kg/minute) of glucose	• Nutritional intake	After 24 hours, infants were changed to the alternative regimen which was continued again for 24 hours. Therefore babies served as their own controls.
Morgan 2014 RCT UK	N=150 Preterm babies born at <29 weeks GA and birthweight <1200g Mean GA 26.7 weeks (SD 1.3) Mean BW 892g (SD 170.5)	SCAMP (n=66) 15.6 g/kg/day glucose plus 3.8 g/kg/day protein/lipid	Control (n=69) 13.5 g/kg/day glucose plus 2.8 g/kg/day protein/lipid	• Late onset sepsis • Mortality • Weight change • Head circumference	Dosage of proteins and lipids also differed between groups. Study was not powered to assess differences in major complications. PN was initiated at median of 3 hours after birth.
Pineault 1988 Observational study with cross-over component Canada	N = 16 Appropriate-for-gestational-age babies with unchanging clinical conditions Mean GA 35 weeks (SE 1.0) Mean BW 2150g (SE 158)	High glucose regimen (n=16) 60 kcal/kg^{-1}/d^{-1}: 11 g/kg/-1/day-1 glucose; 1g/kg-1/d-1 lipids 80 kcal/kg^{-1}/d^{-1}: 17g/kg-1/day^{-1} glucose; 1 g/kg-1/day^{-1} lipids	Low glucose regimen (n=16) 60 kcal/kg^{-1}/d^{-1}: 5 g/kg/-1/day-1 glucose; 3g/kg-1/d-1 lipids 80 kcal/kg^{-1}/d^{-1}: 11g/kg-1/day^{-1} glucose; 3 g/kg-1/day^{-1} lipids	• Nitrogen balance • Nitrogen retention • Nutritional intake	Dosage of lipids also differed between groups. Babies were assigned to groups based on calorie intake and completed two nutrition phases (high glucose [low fat] and low glucose [high fat]). Therefore, babies served as their own controls.

BW: birthweight; GA: gestational age; IV: intravenous; PN: parenteral nutrition; SCAMP: standardised, concentrated with added macronutrients parenteral; SD: standard deviation; SE: standard error.

See appendix D for full evidence tables.

Quality assessment of clinical outcomes included in the evidence review

GRADE was conducted to assess the quality of outcomes. Evidence was identified for critical and important outcomes. The clinical evidence profiles can be found in appendix F.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to these review questions. 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 these review questions.

Summary of studies included in the economic evidence review

No economic evaluations were identified which were applicable to these review questions.

Economic model

No economic modelling was undertaken for these reviews because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

Clinical evidence statements

Higher versus lower glucose intake

Infection (including sepsis) at 28 days and 36 weeks' corrected gestational age (CGA)

- Moderate quality evidence from 1 RCT (n=150) showed a clinically important difference in rate of infection at 28 days in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake, with more babies with infection associated with lower glucose intake. However, there was uncertainty around the effect: Relative risk (RR) 0.74 (95% CI 0.47 to 1.18).
- Low quality evidence from 1 RCT (n=127) showed no clinically important difference in rate of infection at 36 weeks' CGA in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake. However, there was high uncertainty around the effect: RR 0.94 (95% CI 0.63 to 1.41).

Mortality at 28 days and 36 weeks' CGA

- Low quality evidence from 1 RCT showed no clinically important difference in rate of mortality at 28 days (RR 1.17 [95% CI 0.45 to 3.07]; n=150) or 36 weeks' CGA (RR 0.93 [95% CI 0.44 to 1.95]; n=127) in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake. However, there was high uncertainty around the effects.

Nitrogen accretion

Evidence statements for nitrogen balance and retention are divided into two isocalorific comparisons (babies receiving 60kcal/kg/day containing different dosages of glucose; babies receiving 80kcal/kg/day containing different dosages of glucose)

Nitrogen balance (mg/kg/day)

- Very low quality evidence from 1 observational study (n=8) showed no clinically important difference in nitrogen balance in babies who received 60kcal/kg/day and higher (11g/kg/day) compared with lower (5g/kg/day) glucose intake. However, there was high uncertainty around the effect: Mean difference (MD) -8.00mg/kg/day (95% CI -30.49 to 14.49).
- Very low quality evidence from 1 observational study (n=8) showed a clinically important difference in nitrogen balance in babies who received 80kcal/kg/day and higher (17g/kg/day) compared with lower (11g/kg/day) glucose intake, with greater nitrogen balance associated with the group of babies receiving higher glucose intake. However, there was uncertainty around the effect: MD 5.00mg/kg/day (95% CI -3.87 to 13.87).

Nitrogen retention (%)

- Very low quality evidence from 1 observational study (n=8) showed a clinically important difference in nitrogen retention in babies who received 60kcal/kg/day and higher (11g/kg/day) compared with lower (5g/kg/day) glucose intake. However, there was high uncertainty around the effect, with increased nitrogen retention associated with babies receiving lower glucose intake: MD -2.30% (95% CI -7.26 to 2.66).
- Very low quality evidence from 1 observational study (n=8) showed a clinically important difference in nitrogen retention in babies who received 80kcal/kg/day and higher (17g/kg/day) compared with lower (11g/kg/day) glucose intake, with increased nitrogen retention associated with babies receiving higher glucose intake. However, there was uncertainty around the effect: MD 1.20% (95% CI 0.81 to 3.21).

Weight change at day 7, 14, 21 and 28, and 36 weeks' CGA

- High quality evidence from 1 RCT (n=135) showed no clinically important difference in weight gain at 7 days in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake: MD 20.00g (95% CI -16.88 to 56.88).
- Moderate quality evidence from 1 RCT showed no clinically important difference in weight gain at 14 days (MD 44.00g [95% CI 5.27 to 82.73]; n=135), 21 days (MD 64.00g [95% CI 20.72 to 107.28]; n=135), 28 days (MD 46.00g [95% CI -5.91 to 97.91]; n=135) or 36 weeks' CGA (MD 95.00g [95% CI 15.54 to 174.46]; n=124) in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake. However, there was uncertainty around the effects.

Head circumference gain at day 7, 14, 21 and 28, and 36 weeks' CGA

- High quality evidence from 1 RCT (n=135) showed no clinically important difference in head circumference gain at 7 days in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake: MD 1.00cm (95% CI -2.05 to 4.05).
- Moderate quality evidence from 1 RCT showed no clinically important difference in head circumference gain at 14 days (MD 2.00cm [95% CI -1.05 to 5.05]; n=135), 21 days (MD 4.00cm [95% CI 0.62 to 7.38]; n=135) or 36 weeks' CGA (MD 5.00cm [95% CI 1.68 to 8.32]; n=126) in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake. However, there was uncertainty around the effects.
- Moderate quality evidence from 1 RCT (n=135) showed a clinically important difference in head circumference gain at 28 days in babies who received higher (15.6g/kg/day) compared with lower (13.5g/kg/day) glucose intake, with greater head circumference in

the group of babies receiving higher glucose intake. However, there was uncertainty around the effect: MD 6.00cm (95% CI 2.32 to 9.68).

Nutritional intake (g/kg/day)

- Low quality evidence from 1 observational study (n=8) showed a clinically important difference in glucose intake in babies who received 60kcal/kg/day and higher (11g/kg/day) compared with lower (5g/kg/day) glucose intake, with greater glucose intake associated with babies receiving higher glucose intake: MD 5.50g/kg/day (95% CI 5.25 to 5.75).
- Low quality evidence from 1 observational study (n=8) showed a clinically important difference in glucose intake in babies who received 80kcal/kg/day and higher (17g/kg/day) compared with lower (11g/kg/day) glucose intake, with greater glucose intake associated with babies receiving higher glucose intake: MD 4.40g/kg/day (95% 4.15 to 4.65).
- Moderate quality evidence from 1 RCT (n=20) showed a clinically important difference in glucose intake in babies who receive higher (12g/kg/day) compared with lower (8g/kg/day) glucose intake, with greater glucose intake associated with babies receiving higher glucose intake: MD 3.90g/kg/day (95% CI 3.70 to 4.10).

Economic evidence statements

No economic evidence was identified which was applicable to these review questions.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee prioritised neurodevelopmental outcomes and the following adverse effects of IV carbohydrates as critical outcomes: infection including sepsis, hyperglycaemia, hypoglycaemia and PN associated liver disease as these can be directly linked to glucose load (for example optimal glucose intake has an impact on energy to support growth of all functions including neurodevelopment as well as supporting the immune system to prevent infections).

Mortality, body composition, growth, duration of hospital stay and nutritional intake were selected as important outcomes. Adequate glucose as an energy substrate is pivotal to growth which can impact on duration of hospital stay. However, lean growth should not be compromised; and therefore a balance to achieve good growth and a normal body composition is the aim.

The quality of the evidence

The quality of the evidence for this review was assessed using GRADE methodology. The evidence was considered very low to high quality according to GRADE criteria. Evidence was downgraded due to imprecision around the effect estimate and study design (for example, the observational study with a cross-over component).

The committee noted that it is difficult to disentangle the effects of varying amounts of glucose from other constituents (lipids and amino acids) of PN as more than one constituent varied across study arms for two of the included studies. The committee noted that this confounded the evidence and made it difficult to draw clear conclusions related to amounts of glucose on their own.

Benefits and harms

There was no difference in mortality or weight gain based on glucose intake. The evidence for sepsis, head circumference and nitrogen accretion was inconsistent. There was evidence

that actual glucose intake was higher when target intake was higher, demonstrating that it is feasible to achieve a higher glucose intake.

Due to the concurrent variation of dosages in other constituents of PN, the committee noted that the evidence was only indirectly able to support a recommendation for an optimal glucose maintenance dose required in preterm infants. They also noted that it provided no evidence in term infants or how to achieve the maintenance dose. Therefore, the committee decided to make a recommendation based on informal consensus, usingtheir experience and expertise, and decided to make one recommendation applicable to both preterm and term babies.

Starting carbohydrates

In their discussion the committee agreed that a range of starting dosages should be provided to allow some clinical judgement about each babies' particular circumstances. The committee considered what the minimum recommended starting glucose intake should be. Low intakes of glucose (a main energy source) may impair amino acid utilisation and growth. In the absence of studies designed to investigate this, the committee considered the minimum glucose dosage in a range of other neonatal PN studies. They agreed that a minimum starting dosage of 6 g/kg/day of glucose would be sufficient for a baby that had already larger energy stores (such as late preterm and term babies). Based on their knowledge and experience the committee decided that a maximum starting dosage of 9 g/kg/day would be safe for babies in need of higher energy intakes (such as very preterm babies). Therefore the committee decided to recommend, based on informal consent, a higher dosage of up to 9 g/kg/day to address the energy needs of babies not on enteral feeds.

Maintaining carbohydrates

The committee also discussed what the appropriate maintenance range of carbohydrates should be. Again the committee agreed that this needs clinical judgement based on each individual baby. Those on a lower starting range are likely to only require the minimum maintenance range (9 g/kg/day) as compared to those who start on a higher dosage. Based on their knowledge, the committee noted that hyperglycaemia (caused by too much glucose) is associated with increased mortality and morbidity in preterm infants although it is possible that this is a marker of organ immaturity. Hyperglycaemia also increases the complexity of acute fluid and electrolyte management. The treatment threshold for hyperglycaemia varies considerably between UK neonatal services. Hyperglycaemia treatment comprises two options: glucose reduction or insulin therapy. Glucose reduction results in large interpatient variations in energy intake and poor growth. Insulin therapy is complex, risks hypoglycaemia and has potentially other long term adverse outcomes. However, this is outside the scope of this guideline, and therefore there are no recommendations on this. Taking these considerations into account the committee agreed by informal consensus that a dosage of 16 g/kg/day would be a safe maximum recommendation.

Other considerations

The committee noted that in practice, glucose is given as a default component in many other intravenous infusions as well as the PN solution. The total glucose intake must take into account all these sources when interpreting the maximum recommended glucose intake. Furthermore, total carbohydrate intake will only be equivalent to glucose intake when infants are receiving no enteral feeds. The committee acknowledged that the maximum recommended glucose intake should be reduced with increasing enteral carbohydrate intake, but due to a lack of evidence did not directly make a recommendation on this. The committee acknowledged that the evidence did not clearly demonstrate how carbohydrates should be increased; based on experience the committee agreed that PN should be increased gradually to reach the maintenance dose, this is to reduce the potential risk of adverse

events such as hyperglycaemia. The committee suggested 4 days as an example as this would be in line with both amino acid and lipid increments.

No evidence was found on babies who do not start PN from birth. The committeeagreed by informal consensus, based on their knowledge and experience, that babies starting PN after the first 4 days of life should start PN based on the recommended maintenance range. Babies starting PN after this time point may have already made progress with incrementing up to the maintenance levels of macronutrients required for growth from their enteral nutrition. If that enteral nutrition has to be stopped (for example, due to development of necrotising enterocolitis) and PN started the committee felt that returning to starting doses of macronutrients would likely lead to nutritional deficit. Alternatively, babies may be starting PN after this time point as they have not made sufficient progress with enteral fees within the first 72 hours after birth. However, the committee agreed, based on their expertise, that the quantity of macronutrients that can be tolerated is closely linked to the postnatal age of the baby, with older babies able to tolerate greater nutritional intake. Therefore, the committee agreed starting on the maintenance range would be appropriate even if progress has not been made with enteral feeds. The committee agreed to use the same approach for other constituents whenever there is an absence of evidence.

Cost effectiveness and resource use

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

The committee explained that recommendations pertaining to an optimal target dosage of carbohydrate in preterm and term babies who are receiving PN or neonatal care and the optimal way of achieving this target dosage would not incur extra resource implications to the health care system.

The committee noted that getting the optimal amount of carbohydrate for neonatal PN may result in avoiding additional costs associated with adverse effects to the NHS (i.e. incorrect amounts of carbohydrates can result in adverse events which may require resource-intensive management).

The committee explained that recommendations in this area reflect practice across many units and as such cost savings to the NHS, if any, are likely to be negligible.

References

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Mesotten, D., Joosten, K., van Kempen, A., Verbruggen, S., ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates, Clinical Nutrition, 37, 2337-2343, 2018

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Morgan, C., McGowan, P., Herwitker, S., Hart, A. E., Turner, M. A., Postnatal head growth in preterm infants: a randomized controlled parenteral nutrition study, Pediatrics, 133, e120-8, 2014

Pineault 1988

Pineault, M., Chessex, P., Bisaillon, S., Brisson, G., Total parenteral nutrition in the newborn: impact of the quality of infused energy on nitrogen metabolism, American Journal of Clinical Nutrition, 47, 298-304, 1988

Appendices

Appendix A – Review protocols

Review protocol for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

Table 3: Review protocol for carbohydrates

Field (based on PRISMA-P)	Content
Review question	D1a. What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care? D1b. What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?
Type of review question	Intervention review
Objective of the review	The objective of this review is to identify evidence to determine the optimal target dose of carbohydrates (glucose) required by preterm and term babies. In addition, this question will aim to identify what the starting dosage of carbohydrates should be to reach the optimal target dose required.
Eligibility criteria – population/disease/condition/issue/domain	• Babies born preterm, up to 28 days after their due birth date (preterm babies) • Babies born at term, up to 28 days after their birth (term babies).
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	D1a. • Any amount of carbohydrate (g/kg/d) D1b. • Starting dose; Rate of Increase in carbohydrates
Eligibility criteria – comparator(s)/control or reference (gold) standard	D1a. • Each other

Field (based on PRISMA-P)	Content
	D1b. • Different starting doses; Different increases; Different regimens

Outcomes and prioritisation	**Critical**
	• Neurodevelopmental outcomes (general cognitive abilities at two years corrected age as measured by a validated scale)
	• Adverse effects of IV carbohydrates:
	  ○ Infection including sepsis
	  ○ Hyperglycaemia (surrogate outcome – use of insulin)
	  ○ Hypoglycaemia
	  ○ Other PN associated liver disease
	Important
	• Mortality
	• Body composition (measured as Lean mass, fat-free mass, fat mass, adipose tissue, nitrogen accretion)
	• Growth/Anthropometric measures:
	  ○ Weight gain (g/kg/d)
	  ○ Linear growth
	  ○ Head circumference (mm)
	• Duration of hospital stay
	• Nutritional intake (g/kg/d) (defined as proportion of prescribed glucose actually received)

Eligibility criteria – study design	Only published full text papers- • Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) Participant numbers (no restriction for observational studies). For neurodevelopmental outcomes, studies with sample size of minimum 50 participants will be considered.) Conference abstracts of RCTs will only be considered if no evidence is available from full published RCTs (if no evidence from RCTs or comparative cohort studies available and are recent i.e., in the last 2 years-authors will be contacted for further information)
Other inclusion exclusion criteria	No date restriction
Proposed sensitivity/sub-group analysis, or meta-regression	Stratified analysis: • Babies born preterm, up to 28 days after their due birth date (preterm babies)

Field (based on PRISMA-P)	Content
	• Babies born at term, up to 28 days after their birth (term babies). Subgroup analysis: The following groups will be considered for subgroup analysis: Population subgroups: • Age of baby (first 2 weeks vs later) • Preterm (extremely preterm <28 weeks GA; very preterm: 28-31 weeks GA; moderately preterm: 32-36 weeks GA) • Birthweight: Low birth weight (< 2500g); very low birth weight (< 1500g) and extremely low birth weight (< 1000g) • Critically ill babies or those requiring surgery (for example, inotropic support, therapeutic hypothermia or fluid restriction) Setting subgroups: • Specialist care versus standard neonate care Important confounders (when comparative observational studies are included for interventional reviews): • Age of baby (first 2 weeks vs later) • Preterm (Very early <28 weeks' GA; 28-31 weeks' GA; 32-36 weeks' GA) • Birthweight: Low birth weight (< 2500g); very low birth weight (< 1500g) and extremely low birth weight (< 1000g) • Actual dose received • Sex of baby • Hyperglycaemia • Gestation (preterm versus term) • For neurodevelopmental outcomes: ○ Biological (sex, small for gestational age, ethnicity) ○ Neonatal (PVL, IVH, infarct, sepsis, ROP, NEC, antenatal/postnatal steroids, BPD at 36 weeks) ○ Social (SES, substance abuse, alcohol abuse, multiple pregnancy, chorioamnionitis, neglect, maternal age, maternal mental health disorder) ○ Postnatal (epilepsy, age of establishing feeding)
Selection process – duplicate screening/selection/analysis	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 identified fewer than 1000 studies. All disagreements

Field (based on PRISMA-P)	Content
	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.
Data management (software)	STAR was used to sift through the references identified by the search, and for data extraction Pairwise meta-analyses and production of forest plots was done using Cochrane Review Manager (RevMan5). 'GRADEpro' was used to assess the quality of evidence for each outcome. Clinical effectiveness For dichotomous outcomes, minimal important differences will be considered using thresholds of RR >0.80 and <1.25. For continuous outcomes, minimal important differences will be considered 0.5 times the SD of the control group
Information sources – databases and dates	Database(s): Embase 1974 to Present, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; Cochrane Library; WEB OF SCIENCE
Identify if an update	This is not an update.
Author contacts	Developer: The National Guideline Alliance https://www.nice.org.uk/guidance/indevelopment/gid-ng10037
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014
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 Developing NICE guidelines: the manual 2014. 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 http://www.gradeworkinggroup.org/.
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual 2014
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please of the methods please see supplementary material C.

Field (based on PRISMA-P)	Content
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Alliance (NGA) and chaired by Joe Fawke (Consultant Neonatologist and Honorary Senior Lecturer, University Hospitals Leicester NHS Trust) in line with section 3 of Developing NICE guidelines: the manual 2014. Staff from the NGA 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 please see the methods see supplementary material 3.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for those working in the NHS, public health and social care in England
PROSPERO registration number	Not applicable

BPD: bronchopulmonary dysplasia; GA: gestational age; GRADE: Grading of Recommendations Assessment, Development and Evaluation; IV: intravenous; IVH: intraventricular haemorrhage; NEC: necrotising enterocolitis; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; PN: parenteral nutrition; PVL: periventricular leukomalacia; RCT: randomised controlled trial; ROP: retinopathy of prematurity; RR: risk ratio; SD: standard deviation; SES: socioeconomic status

Appendix B – Literature search strategies

Literature search strategies for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

One combined search was conducted for the research questions.

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	PREMATURE BIRTH/
4	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 (birth? or born)).ab,ti.
5	exp INFANT, PREMATURE/
6	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 infan$).ti,ab.
7	(pre#mie? or premie or premies).ti,ab.
8	exp INFANT, LOW BIRTH WEIGHT/
9	(low adj3 birth adj3 weigh$ adj5 infan$).ti,ab.
10	((LBW or VLBW) adj5 infan$).ti,ab.
11	INTENSIVE CARE, NEONATAL/
12	INTENSIVE CARE UNITS, NEONATAL/
13	NICU?.ti,ab.
14	or/1-13
15	PARENTERAL NUTRITION/
16	PARENTERAL NUTRITION, TOTAL/
17	PARENTERAL NUTRITION SOLUTIONS/
18	ADMINISTRATION, INTRAVENOUS/
19	INFUSIONS, INTRAVENOUS/
20	CATHETERIZATION, CENTRAL VENOUS/
21	exp CATHETERIZATION, PERIPHERAL/
22	(parenteral$ or intravenous$ or intra-venous$ or IV or venous$ or infusion?).ti,ab.
23	((peripheral$ or central$) adj3 (line? or catheter$)).ti,ab.
24	drip?.ti,ab.
25	or/15-24
26	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 (amino acid? or Alanine or Pantothenic Acid or Lysinoalanine or Mimosine or Chloromethyl Ketone? or Aspartic Acid or Isoaspartic Acid or N-Methylaspartate or Potassium Magnesium Aspartate or Glutamate? or 1-Carboxyglutamic Acid or Glutamic Acid or Sodium Glutamate or Pemetrexed or Polyglutamic Acid or Pyrrolidonecarboxylic Acid or Arginine or Argininosuccinic Acid or Benzoylarginine-2-Naphthylamide or Benzoylarginine Nitroanilide or Homoarginine or Nitroarginine or omega-N-Methylarginine or Tosylarginine Methyl Ester or Asparagine or Glutamine or Proglumide or Lysine or Hydroxylysine or Polylysine or Ornithine or Eflornithine or Aminoisobutyric Acids or Isoleucine or Leucine or Valine or 2-Amino-5-phosphonovalerate or Valsartan or Dextrothyroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyldopa or Levodopa or Methyldopa or Fenclonine or N-Formylmethionine or p-Fluorophenylalanine or Thyroxine or Thyronine? or Diiodothyronine? or Triiodothyronine or Tryptophan or 5-Hydroxytryptophan or Tyrosine or Betalain? or Betacyanin? or Diiodotyrosine or Melanin? or Methyltyrosine? or Monoiodotyrosine or Phosphotyrosine or Cycloleucine or Desmosine or Histidine or Ergothioneine or Methylhistidine? or Imino Acid? or Azetidinecarboxylic Acid or Proline or Captopril or Fosinopril or Hydroxyproline or Technetium Tc 99m or Isodesmosine or NG-Nitroarginine Methyl Ester or Citrulline or Cystathionine or Cystine or Diaminopimelic Acid or Homocystine or 2-Aminoadipic Acid or Carbocysteine or Methionine or Racemethionine or Threonine or Phosphothreonine or Cysteine or Serine or Azaserine or Droxidopa or Enterobactin or Phosphoserine or Cysteic Acid or Acetylcysteine or Selenocysteine or Ethionine or Homocysteine or S-Adenosylhomocysteine or S-Adenosylmethionine or Buthionine Sulfoximine or Selenomethionine or Vitamin U or Penicillamine or S-Nitroso-N-Acetylpenicillamine or Thiorphan or Tiopronin or Aminobutyrate? or gamma-Aminobutyric Acid or Pregabalin or Vigabatrin or Aminocaproate? or Aminocaproic Acid or Norleucine or Diazooxonorleucine or Aminolevulinic Acid or Canavanine or Creatine or Phosphocreatine or Glycine? or Allylglycine or Glycocholic Acid or Glycodeoxycholic Acid or Glycochenodeoxycholic Acid or Sarcosine or Homoserine or Kynurenine or Oxamic Acid or Phosphoamino Acid? or Quisqualic Acid)).mp.
27	(g adj3 kg adj3 (d or day) adj5 (amino acid? or Alanine or Pantothenic Acid or Lysinoalanine or Mimosine or Chloromethyl Ketone? or Aspartic Acid or Isoaspartic Acid or N-Methylaspartate or Potassium Magnesium Aspartate or Glutamate? or 1-Carboxyglutamic Acid or Glutamic Acid or Sodium Glutamate or Pemetrexed or Polyglutamic Acid or

#	Searches
	Pyrrolidonecarboxylic Acid or Arginine or Argininosuccinic Acid or Benzoylarginine-2-Naphthylamide or Benzoylarginine Nitroanilide or Homoarginine or Nitroarginine or omega-N-Methylarginine or Tosylarginine Methyl Ester or Asparagine or Glutamine or Proglumide or Lysine or Hydroxylysine or Polylysine or Ornithine or Eflornithine or Aminoisobutyric Acids or Isoleucine or Leucine or Valine or 2-Amino-5-phosphonovalerate or Valsartan or Dextrothyroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyldopa or Levodopa or Methyldopa or Fenclonine or N-Formylmethionine or p-Fluorophenylalanine or Thyroxine or Thyronine? or Diiodothyronine? or Triiodothyronine or Tryptophan or 5-Hydroxytryptophan or Tyrosine or Betalain? or Betacyanin? or Diiodotyrosine or Melanin? or Methyltyrosine? or Monoiodotyrosine or Phosphotyrosine or Cycloleucine or Desmosine or Histidine or Ergothioneine or Methylhistidine? or Imino Acid? or Azetidinecarboxylic Acid or Proline or Captopril or Fosinopril or Hydroxyproline or Technetium Tc 99m or Isodesmosine or NG-Nitroarginine Methyl Ester or Citrulline or Cystathionine or Cystine or Diaminopimelic Acid or Homocystine or 2-Aminoadipic Acid or Carbocysteine or Methionine or Racemethionine or Threonine or Phosphothreonine or Cysteine or Serine or Azaserine or Droxidopa or Enterobactin or Phosphoserine or Cysteic Acid or Acetylcysteine or Selenocysteine or Ethionine or Homocysteine or S-Adenosylhomocysteine or S-Adenosylmethionine or Buthionine Sulfoximine or Selenomethionine or Vitamin U or Penicillamine or S-Nitroso-N-Acetylpenicillamine or Thiorphan or Tiopronin or Aminobutyrate? or gamma-Aminobutyric Acid or Pregabalin or Vigabatrin or Aminocaproate? or Aminocaproic Acid or Norleucine or Diazooxonorleucine or Aminolevulinic Acid or Canavanine or Creatine or Phosphocreatine or Glycine? or Allylglycine or Glycocholic Acid or Glycodeoxycholic Acid or Glycochenodeoxycholic Acid or Sarcosine or Homoserine or Kynurenine or Oxamic Acid or Phosphoamino Acid? or Quisqualic Acid)).mp.
28	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 (Lipid? or intralipid? or Ceroid or Fat? or Cholesterol? or Oil? or Fatty Acid? or Omega-3 or Omega-6 or Linolenic Acid? or Docosahexaenoic Acid? or Eicosapentaenoic Acid? or Ricinoleic Acid? or Triolein or Caprylate? or Decanoic Acid? or Decanoate? or Eicosanoic Acid? or Endocannabinoid? or Eicosanoid? or Arachidonic Acid? or Hydroxyeicosatetraenoic Acid? or eicosatetraenoic Acid? or Isoprostane? or Neuroprostane? or Leukotriene? or SRS-A or Thromboxane? or Eicosatetraynoic Acid? or Eicosatrienoic Acid? or Lipoxin? or Linoleic Acid? or Lubiprostone or Capsaicin or Erucic Acid? or Oleic Acid? or Undecylenic Acid? or Gefarnate or Ionomycin or Oxylipin? or Sorbic Acid? or Heptanoic Acid? or Atorvastatin Calcium or Heptanoate? or Lauric Acid? or Laurate? or Mupirocin or Mycolic Acid? or Mycophenolic Acid? or Myristic Acid? or Myristate? or Palmitic Acid? or Palmitate? or Palmitoyl Coenzyme A or Prostanoic Acid? or Sodium Morrhuate or Stearic Acid? or Stearate? or Thioctic Acid? or Glyceride? or Diglyceride? or Monoglyceride? or Triglyceride? or Triacetin or Glycolipid? or Cord Factor? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Polyisoprenyl Phosphate Sugar? or Polyisoprenyl Phosphate Monosaccharide? or Polyisoprenyl Phosphate Oligosaccharide? or Lipofuscin or Lipopolysaccharide? or O Antigen? or Lipoprotein? or Apolipoprotein? or ATP Binding Cassette Transporter Sub-Family G Member 5 or ATP Binding Cassette Transporter Sub-Family G Member 8 or Chylomicron? or Apoprotein or Phospholipid? or Glycerophosphate? or Phosphatidic Acid? or Glycerophospholipid? or Glycerylphosphorylcholine or Phosphatidylcholine? or Dimyristoylphosphatidylcholine or Dipalmitoylphosphatidylcholine or Lecithin? or Phosphatidylethanolamine? or Phosphatidylglycerol? or Cardiolipin? or Phosphatidylinositol? or Phosphatidylserine? or Phospholipid Ether? or Plasmalogen? or Platelet Activating Factor or Lysophospholipid? or Lysophosphatidylcholine? or Sphingomyelin? or Proteolipid? or Sphingolipid? or Sterol? or Adosterol or Cholecalciferol or Hydroxycholecalciferol? or Calcifediol or Dihydroxycholecalciferol? or Calcitriol or Dihydroxyvitamin D3 or Azacosterol or Cholestanol or Dehydrocholesterol? or Desmosterol or 19-Iodocholesterol or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or 25-Hydroxyvitamin D2 or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)).mp.
29	(g adj3 kg adj3 (d or day) adj5 (Lipid? or intralipid? or Ceroid or Fat? or Cholesterol? or Oil? or Fatty Acid? or Omega-3 or Omega-6 or Linolenic Acid? or Docosahexaenoic Acid? or Eicosapentaenoic Acid? or Ricinoleic Acid? or Triolein or Caprylate? or Decanoic Acid? or Decanoate? or Eicosanoic Acid? or Endocannabinoid? or Eicosanoid? or Arachidonic Acid? or Hydroxyeicosatetraenoic Acid? or eicosatetraenoic Acid? or Isoprostane? or Neuroprostane? or Leukotriene? or SRS-A or Thromboxane? or Eicosatetraynoic Acid? or Eicosatrienoic Acid? or Lipoxin? or Linoleic Acid? or Lubiprostone or Capsaicin or Erucic Acid? or Oleic Acid? or Undecylenic Acid? or Gefarnate or Ionomycin or Oxylipin? or Sorbic Acid? or Heptanoic Acid? or Atorvastatin Calcium or Heptanoate? or Lauric Acid? or Laurate? or Mupirocin or Mycolic Acid? or Mycophenolic Acid? or Myristic Acid? or Myristate? or Palmitic Acid? or Palmitate? or Palmitoyl Coenzyme A or Prostanoic Acid? or Sodium Morrhuate or Stearic Acid? or Stearate? or Thioctic Acid? or Glyceride? or Diglyceride? or Monoglyceride? or Triglyceride? or Triacetin or Glycolipid? or Cord Factor? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Polyisoprenyl Phosphate Sugar? or Polyisoprenyl Phosphate Monosaccharide? or Polyisoprenyl Phosphate Oligosaccharide? or Lipofuscin or Lipopolysaccharide? or O Antigen? or Lipoprotein? or Apolipoprotein? or ATP Binding Cassette Transporter Sub-Family G Member 5 or ATP Binding Cassette Transporter Sub-Family G Member 8 or Chylomicron? or Apoprotein or Phospholipid? or Glycerophosphate? or Phosphatidic Acid? or Glycerophospholipid? or Glycerylphosphorylcholine or Phosphatidylcholine? or Dimyristoylphosphatidylcholine or Dipalmitoylphosphatidylcholine or Lecithin? or Phosphatidylethanolamine? or Phosphatidylglycerol? or Cardiolipin? or Phosphatidylinositol? or Phosphatidylserine? or Phospholipid Ether? or Plasmalogen? or Platelet Activating Factor or Lysophospholipid? or Lysophosphatidylcholine? or Sphingomyelin? or Proteolipid? or Sphingolipid? or Sterol? or Adosterol or Cholecalciferol or Hydroxycholecalciferol? or Calcifediol or Dihydroxycholecalciferol? or Calcitriol or Dihydroxyvitamin D3 or Azacosterol or Cholestanol or Dehydrocholesterol? or Desmosterol or 19-Iodocholesterol or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or 25-Hydroxyvitamin D2 or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)).mp.
30	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 (Carbohydrate? or Amino Sugar? or Hexosamine? or Fructosamine or Galactosamine or Acetylgalactosamine or Glucosamine or Acetylglucosamine or Muramic Acid? or Acetylmuramyl-Alanyl-Isoglutamine or Neuraminic Acid? or Sialic Acid? or N-Acetylneuraminic Acid or Deoxy Sugar? or Deoxyglucose or Fluorodeoxyglucose F18 or Deoxyribose or Fucose or Rhamnose or Sucrose or High Fructose Corn Syrup or Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or

#	Searches
	Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Glycopeptide? or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Glycoprotein? or AC133 Antigen or ADAM$ Protein? or Fertilin? or Cholesterol Ester Transfer Protein? or Fibrillin? or Lipopolysaccharide? or Glycoside? or Anthocyanin? or Atractyloside or Digitonin or Acetyldigitoxin? or Acetyldigoxin? or Medigoxin or Lanatoside? or Deslanoside or Proscillaridin or Strophanthin? or Cymarine or Ouabain or Chromomycin? or Galactoside? or Methylgalactoside? or Nitrophenylgalactoside? or Thiogalactoside? or Glucoside? or Amygdalin or Arbutin or Canagliflozin or Chloralose or Esculin or Methylglucoside? or 3-O-Methylglucose or Thioglucoside? or Glucosinolate? or Glycosylated Hemoglobin A or Lincosamide? or Mannoside? or Methylmannoside? or Methylglycoside? or Novobiocin or Nucleoside? Nucleotide? or Adenosine Diphosphate or O-Acetyl-ADP-Ribose or Cyclic ADP-Ribose or Cytidine Diphosphate Diglyceride? or Guanosine Diphosphate or Uridine Diphosphate or Olivomycin? or Phlorhizin or Saponin? or Escin or Ginsenoside? or Holothurin or Quillaja Saponin? or Solanine or Teichoic Acid? or Thioglycoside? or Tomatine or Monosaccharide? or Carbasugar? or Heptose? or Mannoheptulose or Hexose? or Fructose or Galactose or Glucose or Mannose or Sorbose or Imino Sugar? or Imino Furanose? or Imino Pyranose? or 1-Deoxynojirimycin or Ketose? or Dihydroxyacetone or Xylulose or Pentose? or Arabinose or Ribose or Xylose or Tetrose? or Thiosugar? or Triose? or Glyceraldehyde or Polysaccharide? or Alginate? or Carrageenan or Chitin or Chitosan or Ficoll or Fructan? or Inulin or Galactan? or Agar or Glucan? or Lentinan or Sizofiran or Zymosan or Cellulose or Cellobiose or Hypromellose Derivative? or Methylcellulose or Carboxymethylcellulose Sodium or Dextran? or Glycogen or Isomaltose or Maltose or Starch or Amylopectin or Amylose or Dextrin? or Cyclodextrin? or Hydroxyethyl Starch Derivative? or Trehalose or Glycosaminoglycan? or Chondroitin or Dermatan Sulfate or Heparitin Sulfate or Hyaluronic Acid or Keratan Sulfate or Mannan? or Oligosaccharide? or Disaccharide? or Lactose or Lactulose or Melibiose or Sucralfate or Oligosaccharide? or Trisaccharide? or Acarbose or Raffinose or Pectin? or Pentosan Sulfuric Polyester or Bambermycin? or Lipid A or O Antigen? or Prebiotic? or Prodigiozan or Proteoglycan? or Aggrecan? or CD44 Antigen? or Versican? or Heparan Sulfate Proteoglycan? or Small Leucine-Rich Proteoglycan? or Biglycan or Decorin or Fibromodulin or Lumican or Sepharose or Xylan? or Sugar Acid? or Ascorbic Acid or Dehydroascorbic Acid or Diketogulonic Acid or Glucaric Acid or Gluconate? or Glyceric Acid? or Diphosphoglyceric Acid? or Diphosphoglycerate or Tartrate? or Tartronate? or Uronic Acid? or Glucuronate? or Glucuronic Acid or Hexuronic Acid? or Iduronic Acid or Sugar Alcohol? or Dithioerythritol or Dithiothreitol or Erythritol or Erythrityl Tetranitrate or Galactitol or Dianhydrogalactitol or Mitolactol or Glycerol or Inositol or Phytic Acid or Mitobronitol or Ribitol or Sorbitol or Isosorbide or Xylitol or Sugar Phosphate? or Dihydroxyacetone Phosphate or Glycerophosphate? or Glycerylphosphorylcholine or Hexosephosphate? or Fructosephosphate? or Fructosediphosphate? or Galactosephosphate? or Glucosephosphate? or Glucose-6-Phosphate or Hexosediphosphate? or Mannosephosphate? or Pentosephosphate? or Phosphoribosyl Pyrophosphate or Ribosemonophosphate? or Ribulosephosphate? or Polyisoprenyl Phosphate or Dolichol Monophosphate Mannose)).mp.
31	(g adj3 kg adj3 (d or day) adj5 (Carbohydrate? or Amino Sugar? or Hexosamine? or Fructosamine or Galactosamine or Acetylgalactosamine or Glucosamine or Acetylglucosamine or Muramic Acid? or Acetylmuramyl-Alanyl-Isoglutamine or Neuraminic Acid? or Sialic Acid? or N-Acetylneuraminic Acid or Deoxy Sugar? or Deoxyglucose or Fluorodeoxyglucose F18 or Deoxyribose or Fucose or Rhamnose or Sucrose or High Fructose Corn Syrup or Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Glycopeptide? or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Glycoprotein? or AC133 Antigen or ADAM$ Protein? or Fertilin? or Cholesterol Ester Transfer Protein? or Fibrillin? or Lipopolysaccharide? or Glycoside? or Anthocyanin? or Atractyloside or Digitonin or Acetyldigitoxin? or Acetyldigoxin? or Medigoxin or Lanatoside? or Deslanoside or Proscillaridin or Strophanthin? or Cymarine or Ouabain or Chromomycin? or Galactoside? or Methylgalactoside? or Nitrophenylgalactoside? or Thiogalactoside? or Glucoside? or Amygdalin or Arbutin or Canagliflozin or Chloralose or Esculin or Methylglucoside? or 3-O-Methylglucose or Thioglucoside? or Glucosinolate? or Glycosylated Hemoglobin A or Lincosamide? or Mannoside? or Methylmannoside? or Methylglycoside? or Novobiocin or Nucleoside? Nucleotide? or Adenosine Diphosphate or O-Acetyl-ADP-Ribose or Cyclic ADP-Ribose or Cytidine Diphosphate Diglyceride? or Guanosine Diphosphate or Uridine Diphosphate or Olivomycin? or Phlorhizin or Saponin? or Escin or Ginsenoside? or Holothurin or Quillaja Saponin? or Solanine or Teichoic Acid? or Thioglycoside? or Tomatine or Monosaccharide? or Carbasugar? or Heptose? or Mannoheptulose or Hexose? or Fructose or Galactose or Glucose or Mannose or Sorbose or Imino Sugar? or Imino Furanose? or Imino Pyranose? or 1-Deoxynojirimycin or Ketose? or Dihydroxyacetone or Xylulose or Pentose? or Arabinose or Ribose or Xylose or Tetrose? or Thiosugar? or Triose? or Glyceraldehyde or Polysaccharide? or Alginate? or Carrageenan or Chitin or Chitosan or Ficoll or Fructan? or Inulin or Galactan? or Agar or Glucan? or Lentinan or Sizofiran or Zymosan or Cellulose or Cellobiose or Hypromellose Derivative? or Methylcellulose or Carboxymethylcellulose Sodium or Dextran? or Glycogen or Isomaltose or Maltose or Starch or Amylopectin or Amylose or Dextrin? or Cyclodextrin? or Hydroxyethyl Starch Derivative? or Trehalose or Glycosaminoglycan? or Chondroitin or Dermatan Sulfate or Heparitin Sulfate or Hyaluronic Acid or Keratan Sulfate or Mannan? or Oligosaccharide? or Disaccharide? or Lactose or Lactulose or Melibiose or Sucralfate or Oligosaccharide? or Trisaccharide? or Acarbose or Raffinose or Pectin? or Pentosan Sulfuric Polyester or Bambermycin? or Lipid A or O Antigen? or Prebiotic? or Prodigiozan or Proteoglycan? or Aggrecan? or CD44 Antigen? or Versican? or Heparan Sulfate Proteoglycan? or Small Leucine-Rich Proteoglycan? or Biglycan or Decorin or Fibromodulin or Lumican or Sepharose or Xylan? or Sugar Acid? or Ascorbic Acid or Dehydroascorbic Acid or Diketogulonic Acid or Glucaric Acid or Gluconate? or Glyceric Acid? or Diphosphoglyceric Acid? or Diphosphoglycerate or Tartrate? or Tartronate? or Uronic Acid? or Glucuronate? or Glucuronic Acid or Hexuronic Acid? or Iduronic Acid or Sugar Alcohol? or Dithioerythritol or Dithiothreitol or Erythritol or Erythrityl Tetranitrate or Galactitol or Dianhydrogalactitol or Mitolactol or Glycerol or Inositol or Phytic Acid or Mitobronitol or Ribitol or Sorbitol or Isosorbide or Xylitol or Sugar Phosphate? or Dihydroxyacetone Phosphate or Glycerophosphate? or Glycerylphosphorylcholine or Hexosephosphate? or Fructosephosphate? or Fructosediphosphate? or Galactosephosphate? or Glucosephosphate? or Glucose-6-Phosphate or Hexosediphosphate? or Mannosephosphate? or Pentosephosphate? or Phosphoribosyl Pyrophosphate or Ribosemonophosphate? or Ribulosephosphate? or Polyisoprenyl Phosphate or Dolichol Monophosphate Mannose)).mp.
32	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 macronutrient?).mp.
33	exp AMINO ACIDS/ad [Administration & Dosage]
34	exp LIPIDS/ad [Administration & Dosage]

#	Searches
35	exp PROSTAGLANDINS/ad [Administration & Dosage]
36	34 not 35
37	exp CARBOHYDRATES/ad [Administration & Dosage]
38	exp HEPARIN/ad [Administration & Dosage]
39	exp GLYCOPEPTIDES/ad [Administration & Dosage]
40	exp AMINOGLYCOSIDES/ad [Administration & Dosage]
41	or/38-40
42	37 not 41
43	FAT EMULSIONS, INTRAVENOUS/
44	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 36 or 42
45	14 and 25 and 44
46	14 and 43
47	45 or 46
48	limit 47 to english language
49	LETTER/
50	EDITORIAL/
51	NEWS/
52	exp HISTORICAL ARTICLE/
53	ANECDOTES AS TOPIC/
54	COMMENT/
55	CASE REPORT/
56	(letter or comment*).ti.
57	or/49-56
58	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
59	57 not 58
60	ANIMALS/ not HUMANS/
61	exp ANIMALS, LABORATORY/
62	exp ANIMAL EXPERIMENTATION/
63	exp MODELS, ANIMAL/
64	exp RODENTIA/
65	(rat or rats or mouse or mice).ti.
66	or/59-65
67	48 not 66

Databases: Embase; and Embase Classic

#	Searches
1	NEWBORN/
2	(neonat$ or newborn$ or new-born$ or baby or babies).ti,ab.
3	PREMATURITY/
4	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 (birth? or born)).ab,ti.
5	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 infan$).ti,ab.
6	(pre#mie? or premie or premies).ti,ab.
7	exp LOW BIRTH WEIGHT/
8	(low adj3 birth adj3 weigh$ adj5 infan$).ti,ab.
9	((LBW or VLBW) adj5 infan$).ti,ab.
10	NEWBORN INTENSIVE CARE/
11	NEONATAL INTENSIVE CARE UNIT/
12	NICU?.ti,ab.
13	or/1-12
14	PARENTERAL NUTRITION/
15	TOTAL PARENTERAL NUTRITION/
16	PERIPHERAL PARENTERAL NUTRITION/
17	PARENTERAL SOLUTIONS/
18	INTRAVENOUS FEEDING/
19	INTRAVENOUS DRUG ADMINISTRATION/
20	exp INTRAVENOUS CATHETER/
21	(parenteral$ or intravenous$ or intra-venous$ or IV or venous$ or infusion?).ti,ab.
22	((peripheral$ or central$) adj3 (line? or catheter$)).ti,ab.
23	drip?.ti,ab.
24	or/14-23
25	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 (amino acid? or Alanine or Pantothenic Acid or Lysinoalanine or Mimosine or Chloromethyl Ketone? or Aspartic Acid or Isoaspartic Acid or N-Methylaspartate or Potassium Magnesium Aspartate or Glutamate? or 1-Carboxyglutamic Acid or Glutamic Acid or Sodium Glutamate or Pemetrexed or Polyglutamic Acid or Pyrrolidonecarboxylic Acid or Arginine or Argininosuccinic Acid or Benzoylarginine-2-Naphthylamide or Benzoylarginine Nitroanilide or Homoarginine or Nitroarginine or omega-N-Methylarginine or Tosylarginine Methyl Ester or Asparagine or Glutamine or Proglumide or Lysine or Hydroxylysine or Polylysine or Ornithine or Eflornithine or Aminoisobutyric Acids or Isoleucine or Leucine or Valine or 2-Amino-5-phosphonovalerate or Valsartan or Dextrothyroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyldopa or Levodopa or Methyldopa or Fenclonine or N-Formylmethionine or p-Fluorophenylalanine or Thyroxine or Thyronine? or

#	Searches
	Diiodothyronine? or Triiodothyronine or Tryptophan or 5-Hydroxytryptophan or Tyrosine or Betalain? or Betacyanin? or Diiodotyrosine or Melanin? or Methyltyrosine? or Monoiodotyrosine or Phosphotyrosine or Cycloleucine or Desmosine or Histidine or Ergothioneine or Methylhistidine? or Imino Acid? or Azetidinecarboxylic Acid or Proline or Captopril or Fosinopril or Hydroxyproline or Technetium Tc 99m or Isodesmosine or NG-Nitroarginine Methyl Ester or Citrulline or Cystathionine or Cystine or Diaminopimelic Acid or Homocystine or 2-Aminoadipic Acid or Carbocysteine or Methionine or Racemethionine or Threonine or Phosphothreonine or Cysteine or Serine or Azaserine or Droxidopa or Enterobactin or Phosphoserine or Cysteic Acid or Acetylcysteine or Selenocysteine or Ethionine or Homocysteine or S-Adenosylhomocysteine or S-Adenosylmethionine or Buthionine Sulfoximine or Selenomethionine or Vitamin U or Penicillamine or S-Nitroso-N-Acetylpenicillamine or Thiorphan or Tiopronin or Aminobutyrate? or gamma-Aminobutyric Acid or Pregabalin or Vigabatrin or Aminocaproate? or Aminocaproic Acid or Norleucine or Diazooxonorleucine or Aminolevulinic Acid or Canavanine or Creatine or Phosphocreatine or Glycine? or Allylglycine or Glycocholic Acid or Glycodeoxycholic Acid or Glycochenodeoxycholic Acid or Sarcosine or Homoserine or Kynurenine or Oxamic Acid or Phosphoamino Acid? or Quisqualic Acid)).mp.
26	(g adj3 kg adj3 (d or day) adj5 (amino acid? or Alanine or Pantothenic Acid or Lysinoalanine or Mimosine or Chloromethyl Ketone? or Aspartic Acid or Isoaspartic Acid or N-Methylaspartate or Potassium Magnesium Aspartate or Glutamate? or 1-Carboxyglutamic Acid or Glutamic Acid or Sodium Glutamate or Pemetrexed or Polyglutamic Acid or Pyrrolidonecarboxylic Acid or Arginine or Argininosuccinic Acid or Benzoylarginine-2-Naphthylamide or Benzoylarginine Nitroanilide or Homoarginine or Nitroarginine or omega-N-Methylarginine or Tosylarginine Methyl Ester or Asparagine or Glutamine or Proglumide or Lysine or Hydroxylysine or Polylysine or Ornithine or Eflornithine or Aminoisobutyric Acids or Isoleucine or Leucine or Valine or 2-Amino-5-phosphonovalerate or Valsartan or Dextrothyroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyldopa or Levodopa or Methyldopa or Fenclonine or N-Formylmethionine or p-Fluorophenylalanine or Thyroxine or Thyronine? or Diiodothyronine? or Triiodothyronine or Tryptophan or 5-Hydroxytryptophan or Tyrosine or Betalain? or Betacyanin? or Diiodotyrosine or Melanin? or Methyltyrosine? or Monoiodotyrosine or Phosphotyrosine or Cycloleucine or Desmosine or Histidine or Ergothioneine or Methylhistidine? or Imino Acid? or Azetidinecarboxylic Acid or Proline or Captopril or Fosinopril or Hydroxyproline or Technetium Tc 99m or Isodesmosine or NG-Nitroarginine Methyl Ester or Citrulline or Cystathionine or Cystine or Diaminopimelic Acid or Homocystine or 2-Aminoadipic Acid or Carbocysteine or Methionine or Racemethionine or Threonine or Phosphothreonine or Cysteine or Serine or Azaserine or Droxidopa or Enterobactin or Phosphoserine or Cysteic Acid or Acetylcysteine or Selenocysteine or Ethionine or Homocysteine or S-Adenosylhomocysteine or S-Adenosylmethionine or Buthionine Sulfoximine or Selenomethionine or Vitamin U or Penicillamine or S-Nitroso-N-Acetylpenicillamine or Thiorphan or Tiopronin or Aminobutyrate? or gamma-Aminobutyric Acid or Pregabalin or Vigabatrin or Aminocaproate? or Aminocaproic Acid or Norleucine or Diazooxonorleucine or Aminolevulinic Acid or Canavanine or Creatine or Phosphocreatine or Glycine? or Allylglycine or Glycocholic Acid or Glycodeoxycholic Acid or Glycochenodeoxycholic Acid or Sarcosine or Homoserine or Kynurenine or Oxamic Acid or Phosphoamino Acid? or Quisqualic Acid)).mp.
27	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 (Lipid? or intralipid? or Ceroid or Fat? or Cholesterol? or Oil? or Fatty Acid? or Omega-3 or Omega-6 or Linolenic Acid? or Docosahexaenoic Acid? or Eicosapentaenoic Acid? or Ricinoleic Acid? or Triolein or Caprylate? or Decanoic Acid? or Decanoate? or Eicosanoic Acid? or Endocannabinoid? or Eicosanoid? or Arachidonic Acid? or Hydroxyeicosatetraenoic Acid? or eicosatetraenoic Acid? or Isoprostane? or Neuroprostane? or Leukotriene? or SRS-A or Thromboxane? or Eicosatetraynoic Acid? or Eicosatrienoic Acid? or Lipoxin? or Linoleic Acid? or Lubiprostone or Capsaicin or Erucic Acid? or Oleic Acid? or Undecylenic Acid? or Gefarnate or Ionomycin or Oxylipin? or Sorbic Acid? or Heptanoic Acid? or Atorvastatin Calcium or Heptanoate? or Lauric Acid? or Laurate? or Mupirocin or Mycolic Acid? or Mycophenolic Acid? or Myristic Acid? or Myristate? or Palmitic Acid? or Palmitate? or Palmitoyl Coenzyme A or Prostanoic Acid? or Sodium Morrhuate or Stearic Acid? or Stearate? or Thioctic Acid? or Glyceride? or Diglyceride? or Monoglyceride? or Triglyceride? or Triacetin or Glycolipid? or Cord Factor? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Polyisoprenyl Phosphate Sugar? or Polyisoprenyl Phosphate Monosaccharide? or Polyisoprenyl Phosphate Oligosaccharide? or Lipofuscin or Lipopolysaccharide? or O Antigen? or Lipoprotein? or Apolipoprotein? or ATP Binding Cassette Transporter Sub-Family G Member 5 or ATP Binding Cassette Transporter Sub-Family G Member 8 or Chylomicron? or Apoprotein or Phospholipid? or Glycerophosphate? or Phosphatidic Acid? or Glycerophospholipid? or Glycerylphosphorylcholine or Phosphatidylcholine? or Dimyristoylphosphatidylcholine or Dipalmitoylphosphatidylcholine or Lecithin? or Phosphatidylethanolamine? or Phosphatidylglycerol? or Cardiolipin? or Phosphatidylinositol? or Phosphatidylserine? or Phospholipid Ether? or Plasmalogen? or Platelet Activating Factor or Lysophospholipid? or Lysophosphatidylcholine? or Sphingomyelin? or Proteolipid? or Sphingolipid? or Sterol? or Adosterol or Cholecalciferol or Hydroxycholecalciferol? or Calcifediol or Dihydroxycholecalciferol? or Calcitriol or Dihydroxyvitamin D3 or Azacosterol or Cholestanol or Dehydrocholesterol? or Desmosterol or 19-Iodocholesterol or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or 25-Hydroxyvitamin D2 or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)).mp.
28	(g adj3 kg adj3 (d or day) adj5 (Lipid? or intralipid? or Ceroid or Fat? or Cholesterol? or Oil? or Fatty Acid? or Omega-3 or Omega-6 or Linolenic Acid? or Docosahexaenoic Acid? or Eicosapentaenoic Acid? or Ricinoleic Acid? or Triolein or Caprylate? or Decanoic Acid? or Decanoate? or Eicosanoic Acid? or Endocannabinoid? or Eicosanoid? or Arachidonic Acid? or Hydroxyeicosatetraenoic Acid? or eicosatetraenoic Acid? or Isoprostane? or Neuroprostane? or Leukotriene? or SRS-A or Thromboxane? or Eicosatetraynoic Acid? or Eicosatrienoic Acid? or Lipoxin? or Linoleic Acid? or Lubiprostone or Capsaicin or Erucic Acid? or Oleic Acid? or Undecylenic Acid? or Gefarnate or Ionomycin or Oxylipin? or Sorbic Acid? or Heptanoic Acid? or Atorvastatin Calcium or Heptanoate? or Lauric Acid? or Laurate? or Mupirocin or Mycolic Acid? or Mycophenolic Acid? or Myristic Acid? or Myristate? or Palmitic Acid? or Palmitate? or Palmitoyl Coenzyme A or Prostanoic Acid? or Sodium Morrhuate or Stearic Acid? or Stearate? or Thioctic Acid? or Glyceride? or Diglyceride? or Monoglyceride? or Triglyceride? or Triacetin or Glycolipid? or Cord Factor? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Polyisoprenyl Phosphate Sugar? or Polyisoprenyl Phosphate Monosaccharide? or Polyisoprenyl Phosphate Oligosaccharide? or Lipofuscin or Lipopolysaccharide? or O Antigen? or Lipoprotein? or

#	Searches
	Apolipoprotein? or ATP Binding Cassette Transporter Sub-Family G Member 5 or ATP Binding Cassette Transporter Sub-Family G Member 8 or Chylomicron? or Apoprotein or Phospholipid? or Glycerophosphate? or Phosphatidic Acid? or Glycerophospholipid? or Glycerylphosphorylcholine or Phosphatidylcholine? or Dimyristoylphosphatidylcholine or Dipalmitoylphosphatidylcholine or Lecithin? or Phosphatidylethanolamine? or Phosphatidylglycerol? or Cardiolipin? or Phosphatidylinositol? or Phosphatidylserine? or Phospholipid Ether? or Plasmalogen? or Platelet Activating Factor or Lysophospholipid? or Lysophosphatidylcholine? or Sphingomyelin? or Proteolipid? or Sphingolipid? or Sterol? or Adosterol or Cholecalciferol or Hydroxycholecalciferol? or Calcifediol or Dihydroxycholecalciferol? or Calcitriol or Dihydroxyvitamin D3 or Azacosterol or Cholestanol or Dehydrocholesterol? or Desmosterol or 19-Iodocholesterol or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or 25-Hydroxyvitamin D2 or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)).mp.
29	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 (Carbohydrate? or Amino Sugar? or Hexosamine? or Fructosamine or Galactosamine or Acetylgalactosamine or Glucosamine or Acetylglucosamine or Muramic Acid? or Acetylmuramyl-Alanyl-Isoglutamine or Neuraminic Acid? or Sialic Acid? or N-Acetylneuraminic Acid or Deoxy Sugar? or Deoxyglucose or Fluorodeoxyglucose F18 or Deoxyribose or Fucose or Rhamnose or Sucrose or High Fructose Corn Syrup or Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Glycopeptide? or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Glycoprotein? or AC133 Antigen or ADAM$ Protein? or Fertilin? or Cholesterol Ester Transfer Protein? or Fibrillin? or Lipopolysaccharide? or Glycoside? or Anthocyanin? or Atractyloside or Digitonin or Acetyldigitoxin? or Acetyldigoxin? or Medigoxin or Lanatoside? or Deslanoside or Proscillaridin or Strophanthin? or Cymarine or Ouabain or Chromomycin? or Galactoside? or Methylgalactoside? or Nitrophenylgalactoside? or Thiogalactoside? or Glucoside? or Amygdalin or Arbutin or Canagliflozin or Chloralose or Esculin or Methylglucoside? or 3-O-Methylglucose or Thioglucoside? or Glucosinolate? or Glycosylated Hemoglobin A or Lincosamide? or Mannoside? or Methylmannoside? or Methylglycoside? or Novobiocin or Nucleoside? Nucleotide? or Adenosine Diphosphate or O-Acetyl-ADP-Ribose or Cyclic ADP-Ribose or Cytidine Diphosphate Diglyceride? or Guanosine Diphosphate or Uridine Diphosphate or Olivomycin? or Phlorhizin or Saponin? or Escin or Ginsenoside? or Holothurin or Quillaja Saponin? or Solanine or Teichoic Acid? or Thioglycoside? or Tomatine or Monosaccharide? or Carbasugar? or Heptose? or Mannoheptulose or Hexose? or Fructose or Galactose or Glucose or Mannose or Sorbose or Imino Sugar? or Imino Furanose? or Imino Pyranose? or 1-Deoxynojirimycin or Ketose? or Dihydroxyacetone or Xylulose or Pentose? or Arabinose or Ribose or Xylose or Tetrose? or Thiosugar? or Triose? or Glyceraldehyde or Polysaccharide? or Alginate? or Carrageenan or Chitin or Chitosan or Ficoll or Fructan? or Inulin or Galactan? or Agar or Glucan? or Lentinan or Sizofiran or Zymosan or Cellulose or Cellobiose or Hypromellose Derivative? or Methylcellulose or Carboxymethylcellulose Sodium or Dextran? or Glycogen or Isomaltose or Maltose or Starch or Amylopectin or Amylose or Dextrin? or Cyclodextrin? or Hydroxyethyl Starch Derivative? or Trehalose or Glycosaminoglycan? or Chondroitin or Dermatan Sulfate or Heparitin Sulfate or Hyaluronic Acid or Keratan Sulfate or Mannan? or Oligosaccharide? or Disaccharide? or Lactose or Lactulose or Melibiose or Sucralfate or Oligosaccharide? or Trisaccharide? or Acarbose or Raffinose or Pectin? or Pentosan Sulfuric Polyester or Bambermycin? or Lipid A or O Antigen? or Prebiotic? or Prodigiozan or Proteoglycan? or Aggrecan? or CD44 Antigen? or Versican? or Heparan Sulfate Proteoglycan? or Small Leucine-Rich Proteoglycan? or Biglycan or Decorin or Fibromodulin or Lumican or Sepharose or Xylan? or Sugar Acid? or Ascorbic Acid or Dehydroascorbic Acid or Diketogulonic Acid or Glucaric Acid or Gluconate? or Glyceric Acid? or Diphosphoglyceric Acid? or Diphosphoglycerate or Tartrate? or Tartronate? or Uronic Acid? or Glucuronate? or Glucuronic Acid or Hexuronic Acid? or Iduronic Acid or Sugar Alcohol? or Dithioerythritol or Dithiothreitol or Erythritol or Erythrityl Tetranitrate or Galactitol or Dianhydrogalactitol or Mitolactol or Glycerol or Inositol or Phytic Acid or Mitobronitol or Ribitol or Sorbitol or Isosorbide or Xylitol or Sugar Phosphate? or Dihydroxyacetone Phosphate or Glycerophosphate? or Glycerylphosphorylcholine or Hexosephosphate? or Fructosephosphate? or Fructosediphosphate? or Galactosephosphate? or Glucosephosphate? or Glucose-6-Phosphate or Hexosediphosphate? or Mannosephosphate? or Pentosephosphate? or Phosphoribosyl Pyrophosphate or Ribosemonophosphate? or Ribulosephosphate? or Polyisoprenyl Phosphate or Dolichol Monophosphate Mannose)).mp.
30	(g adj3 kg adj3 (d or day) adj5 (Carbohydrate? or Amino Sugar? or Hexosamine? or Fructosamine or Galactosamine or Acetylgalactosamine or Glucosamine or Acetylglucosamine or Muramic Acid? or Acetylmuramyl-Alanyl-Isoglutamine or Neuraminic Acid? or Sialic Acid? or N-Acetylneuraminic Acid or Deoxy Sugar? or Deoxyglucose or Fluorodeoxyglucose F18 or Deoxyribose or Fucose or Rhamnose or Sucrose or High Fructose Corn Syrup or Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Glycopeptide? or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Glycoprotein? or AC133 Antigen or ADAM$ Protein? or Fertilin? or Cholesterol Ester Transfer Protein? or Fibrillin? or Lipopolysaccharide? or Glycoside? or Anthocyanin? or Atractyloside or Digitonin or Acetyldigitoxin? or Acetyldigoxin? or Medigoxin or Lanatoside? or Deslanoside or Proscillaridin or Strophanthin? or Cymarine or Ouabain or Chromomycin? or Galactoside? or Methylgalactoside? or Nitrophenylgalactoside? or Thiogalactoside? or Glucoside? or Amygdalin or Arbutin or Canagliflozin or Chloralose or Esculin or Methylglucoside? or 3-O-Methylglucose or Thioglucoside? or Glucosinolate? or Glycosylated Hemoglobin A or Lincosamide? or Mannoside? or Methylmannoside? or Methylglycoside? or Novobiocin or Nucleoside? Nucleotide? or Adenosine Diphosphate or O-Acetyl-ADP-Ribose or Cyclic ADP-Ribose or Cytidine Diphosphate Diglyceride? or Guanosine Diphosphate or Uridine Diphosphate or Olivomycin? or Phlorhizin or Saponin? or Escin or Ginsenoside? or Holothurin or Quillaja Saponin? or Solanine or Teichoic Acid? or Thioglycoside? or Tomatine or Monosaccharide? or Carbasugar? or Heptose? or Mannoheptulose or Hexose? or Fructose or Galactose or Glucose or Mannose or Sorbose or Imino Sugar? or Imino Furanose? or Imino Pyranose? or 1-Deoxynojirimycin or Ketose? or Dihydroxyacetone or Xylulose or Pentose? or Arabinose or Ribose or Xylose or Tetrose? or Thiosugar? or Triose? or Glyceraldehyde or Polysaccharide? or Alginate? or Carrageenan or Chitin or Chitosan or Ficoll or Fructan? or Inulin or Galactan? or Agar or Glucan? or Lentinan or Sizofiran or Zymosan or Cellulose or Cellobiose or Hypromellose Derivative? or Methylcellulose or Carboxymethylcellulose Sodium or Dextran? or Glycogen or Isomaltose or Maltose or Starch or Amylopectin or Amylose or Dextrin? or Cyclodextrin? or Hydroxyethyl Starch Derivative? or Trehalose or Glycosaminoglycan? or Chondroitin or Dermatan Sulfate or Heparitin Sulfate or Hyaluronic Acid or Keratan Sulfate or

#	Searches
	Mannan? or Oligosaccharide? or Disaccharide? or Lactose or Lactulose or Melibiose or Sucralfate or Oligosaccharide? or Trisaccharide? or Acarbose or Raffinose or Pectin? or Pentosan Sulfuric Polyester or Bambermycin? or Lipid A or O Antigen? or Prebiotic? or Prodigiozan or Proteoglycan? or Aggrecan? or CD44 Antigen? or Versican? or Heparan Sulfate Proteoglycan? or Small Leucine-Rich Proteoglycan? or Biglycan or Decorin or Fibromodulin or Lumican or Sepharose or Xylan? or Sugar Acid? or Ascorbic Acid or Dehydroascorbic Acid or Diketogulonic Acid or Glucaric Acid or Gluconate? or Glyceric Acid? or Diphosphoglyceric Acid? or Diphosphoglycerate or Tartrate? or Tartronate? or Uronic Acid? or Glucuronate? or Glucuronic Acid or Hexuronic Acid? or Iduronic Acid or Sugar Alcohol? or Dithioerythritol or Dithiothreitol or Erythritol or Erythrityl Tetranitrate or Galactitol or Dianhydrogalactitol or Mitolactol or Glycerol or Inositol or Phytic Acid or Mitobronitol or Ribitol or Sorbitol or Isosorbide or Xylitol or Sugar Phosphate? or Dihydroxyacetone Phosphate or Glycerophosphate? or Glycerylphosphorylcholine or Hexosephosphate? or Fructosephosphate? or Fructosediphosphate? or Galactosephosphate? or Glucosephosphate? or Glucose-6-Phosphate or Hexosediphosphate? or Mannosephosphate? or Pentosephosphate? or Phosphoribosyl Pyrophosphate or Ribosemonophosphate? or Ribulosephosphate? or Polyisoprenyl Phosphate or Dolichol Monophosphate Mannose)).mp.
31	((Dose? or Dosage? or Regimen? or Amount? or Optimal$ or Optimis$ or Requir$ or Target? or Rate? or Increment$ or Safe$ or Efficacy or Initiat$ or Start$ or Introduc$ or Receiv$ or Administer$) adj5 macronutrient?).mp.
32	exp AMINO ACIDS/do [Drug Dose]
33	exp LIPID/do [Drug Dose]
34	exp PROSTAGLANDIN/do [Drug Dose]
35	33 not 34
36	exp CARBOHYDRATE/do [Drug Dose]
37	exp HEPARIN/do [Drug Dose]
38	exp GLYCOPEPTIDE/do [Drug Dose]
39	exp AMINOGLYCOSIDE/do [Drug Dose]
40	or/37-39
41	36 not 40
42	exp AMINO ACIDS/
43	exp LIPID/
44	exp PROSTAGLANDIN/
45	43 not 44
46	exp CARBOHYDRATE/
47	exp HEPARIN/
48	exp GLYCOPEPTIDE/
49	exp AMINOGLYCOSIDE/
50	or/47-49
51	46 not 50
52	OPTIMAL DRUG DOSE/
53	RECOMMENDED DRUG DOSE/
54	DRUG DOSE REGIMEN/
55	DOSE CALCULATION/
56	DRUG DOSE COMPARISON/
57	DRUG DOSE ESCALATION/
58	DRUG DOSE INCREASE/
59	DRUG DOSE INTENSIFICATION/
60	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 35 or 41
61	42 or 45 or 51
62	52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
63	13 and 24 and 60
64	13 and 24 and 61 and 62
65	or/63-64
66	limit 65 to english language
67	letter.pt. or LETTER/
68	note.pt.
69	editorial.pt.
70	CASE REPORT/ or CASE STUDY/
71	(letter or comment*).ti.
72	or/67-71
73	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
74	72 not 73
75	ANIMAL/ not HUMAN/
76	NONHUMAN/
77	exp ANIMAL EXPERIMENT/
78	exp EXPERIMENTAL ANIMAL/
79	ANIMAL MODEL/
80	exp RODENT/
81	(rat or rats or mouse or mice).ti.
82	or/74-81
83	66 not 82

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	MeSH descriptor: [PREMATURE BIRTH] this term only
4	((preterm* or pre-term* or prematur* or pre-matur*) near/5 (birth* or born)):ti,ab
5	MeSH descriptor: [INFANT, PREMATURE] explode all trees
6	((preterm* or pre-term* or prematur* or pre-matur*) near/5 infan*):ti,ab
7	(pre#mie? or premie or premies):ti,ab
8	MeSH descriptor: [INFANT, LOW BIRTH WEIGHT] explode all trees
9	(low near/3 birth near/3 weigh* near/5 infan*):ti,ab
10	((LBW or VLBW) near/5 infan*):ti,ab
11	MeSH descriptor: [INTENSIVE CARE, NEONATAL] this term only
12	MeSH descriptor: [INTENSIVE CARE UNITS, NEONATAL] this term only
13	NICU?:ti,ab
14	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13
15	MeSH descriptor: [PARENTERAL NUTRITION] this term only
16	MeSH descriptor: [PARENTERAL NUTRITION, TOTAL] this term only
17	MeSH descriptor: [PARENTERAL NUTRITION SOLUTIONS] this term only
18	MeSH descriptor: [ADMINISTRATION, INTRAVENOUS] this term only
19	MeSH descriptor: [INFUSIONS, INTRAVENOUS] this term only
20	MeSH descriptor: [CATHETERIZATION, CENTRAL VENOUS] this term only
21	MeSH descriptor: [CATHETERIZATION, PERIPHERAL] explode all trees
22	(parenteral* or intravenous* or intra-venous* or IV or venous* or infusion*):ti,ab
23	((peripheral* or central*) near/3 (line? or catheter*)):ti,ab
24	drip?:ti,ab
25	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
26	((Dose? or Dosage? or Regimen? or Amount? or Optimal* or Optimis* or Requir* or Target? or Rate? or Increment* or Safe* or Efficacy or Initiat* or Start* or Introduc* or Receiv* or Administer*) near/5 (amino acid? or Alanine or Pantothenic Acid or Lysinoalanine or Mimosine or Chloromethyl Ketone? or Aspartic Acid or Isoaspartic Acid or N-Methylaspartate or Potassium Magnesium Aspartate or Glutamate? or 1-Carboxyglutamic Acid or Glutamic Acid or Sodium Glutamate or Pemetrexed or Polyglutamic Acid or Pyrrolidonecarboxylic Acid or Arginine or Argininosuccinic Acid or Benzoylarginine-2-Naphthylamide or Benzoylarginine Nitroanilide or Homoarginine or Nitroarginine or omega-N-Methylarginine or Tosylarginine Methyl Ester or Asparagine or Glutamine or Proglumide or Lysine or Hydroxylysine or Polylysine or Ornithine or Eflornithine or Aminoisobutyric Acids or Isoleucine or Leucine or Valine or 2-Amino-5-phosphonovalerate or Valsartan or Dextrothyroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyldopa or Levodopa or Methyldopa or Fenclonine or N-Formylmethionine or p-Fluorophenylalanine or Thyroxine or Thyronine? or Diiodothyronine? or Triiodothyronine or Tryptophan or 5-Hydroxytryptophan or Tyrosine or Betalain? or Betacyanin? or Diiodotyrosine or Melanin? or Methyltyrosine? or Monoiodotyrosine or Phosphotyrosine or Cycloleucine or Desmosine or Histidine or Ergothioneine or Methylhistidine? or Imino Acid? or Azetidinecarboxylic Acid or Proline or Captopril or Fosinopril or Hydroxyproline or Technetium Tc 99m or Isodesmosine or NG-Nitroarginine Methyl Ester or Citrulline or Cystathionine or Cystine or Diaminopimelic Acid or Homocystine or 2-Aminoadipic Acid or Carbocysteine or Methionine or Racemethionine or Threonine or Phosphothreonine or Cysteine or Serine or Azaserine or Droxidopa or Enterobactin or Phosphoserine or Cysteic Acid or Acetylcysteine or Selenocysteine or Ethionine or Homocysteine or S-Adenosylhomocysteine or S-Adenosylmethionine or Buthionine Sulfoximine or Selenomethionine or Vitamin U or Penicillamine or S-Nitroso-N-Acetylpenicillamine or Thiorphan or Tiopronin or Aminobutyrate? or gamma-Aminobutyric Acid or Pregabalin or Vigabatrin or Aminocaproate? or Aminocaproic Acid or Norleucine or Diazooxonorleucine or Aminolevulinic Acid or Canavanine or Creatine or Phosphocreatine or Glycine? or Allylglycine or Glycocholic Acid or Glycodeoxycholic Acid or Glycochenodeoxycholic Acid or Sarcosine or Homoserine or Kynurenine or Oxamic Acid or Phosphoamino Acid? or Quisqualic Acid)) :ti,ab
27	(g adj3 kg adj3 (d or day) near/5 (amino acid? or Alanine or Pantothenic Acid or Lysinoalanine or Mimosine or Chloromethyl Ketone? or Aspartic Acid or Isoaspartic Acid or N-Methylaspartate or Potassium Magnesium Aspartate or Glutamate? or 1-Carboxyglutamic Acid or Glutamic Acid or Sodium Glutamate or Pemetrexed or Polyglutamic Acid or Pyrrolidonecarboxylic Acid or Arginine or Argininosuccinic Acid or Benzoylarginine-2-Naphthylamide or Benzoylarginine Nitroanilide or Homoarginine or Nitroarginine or omega-N-Methylarginine or Tosylarginine Methyl Ester or Asparagine or Glutamine or Proglumide or Lysine or Hydroxylysine or Polylysine or Ornithine or Eflornithine or Aminoisobutyric Acids or Isoleucine or Leucine or Valine or 2-Amino-5-phosphonovalerate or Valsartan or Dextrothyroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyldopa or Levodopa or Methyldopa or Fenclonine or N-Formylmethionine or p-Fluorophenylalanine or Thyroxine or Thyronine? or Diiodothyronine? or Triiodothyronine or Tryptophan or 5-Hydroxytryptophan or Tyrosine or Betalain? or Betacyanin? or Diiodotyrosine or Melanin? or Methyltyrosine? or Monoiodotyrosine or Phosphotyrosine or Cycloleucine or Desmosine or Histidine or Ergothioneine or Methylhistidine? or Imino Acid? or Azetidinecarboxylic Acid or Proline or Captopril or Fosinopril or Hydroxyproline or Technetium Tc 99m or Isodesmosine or NG-Nitroarginine Methyl Ester or Citrulline or Cystathionine or Cystine or Diaminopimelic Acid or Homocystine or 2-Aminoadipic Acid or Carbocysteine or Methionine or Racemethionine or Threonine or Phosphothreonine or Cysteine or Serine or Azaserine or Droxidopa or Enterobactin or Phosphoserine or Cysteic Acid or Acetylcysteine or Selenocysteine or Ethionine or Homocysteine or S-Adenosylhomocysteine or S-Adenosylmethionine or Buthionine Sulfoximine or Selenomethionine or Vitamin U or Penicillamine or S-Nitroso-N-Acetylpenicillamine or Thiorphan or Tiopronin or Aminobutyrate? or gamma-Aminobutyric Acid or Pregabalin or Vigabatrin or Aminocaproate? or Aminocaproic Acid or Norleucine or Diazooxonorleucine or Aminolevulinic Acid or Canavanine or Creatine or Phosphocreatine or Glycine? or Allylglycine or Glycocholic Acid or Glycodeoxycholic Acid or Glycochenodeoxycholic Acid or Sarcosine or Homoserine or Kynurenine or Oxamic Acid or Phosphoamino Acid? or Quisqualic Acid)) :ti,ab

#	Searches
28	((Dose? or Dosage? or Regimen? or Amount? or Optimal* or Optimis* or Requir* or Target? or Rate? or Increment* or Safe* or Efficacy or Initiat* or Start* or Introduc* or Receiv* or Administer*) near/5 (Lipid? or intralipid? or Ceroid or Fat? or Cholesterol? or Oil? or Fatty Acid? or Omega-3 or Omega-6 or Linolenic Acid? or Docosahexaenoic Acid? or Eicosapentaenoic Acid? or Ricinoleic Acid? or Triolein or Caprylate? or Decanoic Acid? or Decanoate? or Eicosanoic Acid? or Endocannabinoid? or Eicosanoid? or Arachidonic Acid? or Hydroxyeicosatetraenoic Acid? or eicosatetraenoic Acid? or Isoprostane? or Neuroprostane? or Leukotriene? or SRS-A or Thromboxane? or Eicosatetraynoic Acid? or Eicosatrienoic Acid? or Lipoxin? or Linoleic Acid? or Lubiprostone or Capsaicin or Erucic Acid? or Oleic Acid? or Undecylenic Acid? or Gefarnate or Ionomycin or Oxylipin? or Sorbic Acid? or Heptanoic Acid? or Atorvastatin Calcium or Heptanoate? or Lauric Acid? or Laurate? or Mupirocin or Mycolic Acid? or Mycophenolic Acid? or Myristic Acid? or Myristate? or Palmitic Acid? or Palmitate? or Palmitoyl Coenzyme A or Prostanoic Acid? or Sodium Morrhuate or Stearic Acid? or Stearate? or Thioctic Acid? or Glyceride? or Diglyceride? or Monoglyceride? or Triglyceride? or Triacetin or Glycolipid? or Cord Factor? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Polyisoprenyl Phosphate Sugar? or Polyisoprenyl Phosphate Monosaccharide? or Polyisoprenyl Phosphate Oligosaccharide? or Lipofuscin or Lipopolysaccharide? or O Antigen? or Lipoprotein? or Apolipoprotein? or ATP Binding Cassette Transporter Sub-Family G Member 5 or ATP Binding Cassette Transporter Sub-Family G Member 8 or Chylomicron? or Apoprotein or Phospholipid? or Glycerophosphate? or Phosphatidic Acid? or Glycerophospholipid? or Glycerylphosphorylcholine or Phosphatidylcholine? or Dimyristoylphosphatidylcholine or Dipalmitoylphosphatidylcholine or Lecithin? or Phosphatidylethanolamine? or Phosphatidylglycerol? or Cardiolipin? or Phosphatidylinositol? or Phosphatidylserine? or Phospholipid Ether? or Plasmalogen? or Platelet Activating Factor or Lysophospholipid? or Lysophosphatidylcholine? or Sphingomyelin? or Proteolipid? or Sphingolipid? or Sterol? or Adosterol or Cholecalciferol or Hydroxycholecalciferol? or Calcifediol or Dihydroxycholecalciferol? or Calcitriol or Dihydroxyvitamin D3 or Azacosterol or Cholestanol or Dehydrocholesterol? or Desmosterol or 19-Iodocholesterol or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or 25-Hydroxyvitamin D2 or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)) :ti,ab
29	(g adj3 kg adj3 (d or day) near/5 (Lipid? or intralipid? or Ceroid or Fat? or Cholesterol? or Oil? or Fatty Acid? or Omega-3 or Omega-6 or Linolenic Acid? or Docosahexaenoic Acid? or Eicosapentaenoic Acid? or Ricinoleic Acid? or Triolein or Caprylate? or Decanoic Acid? or Decanoate? or Eicosanoic Acid? or Endocannabinoid? or Eicosanoid? or Arachidonic Acid? or Hydroxyeicosatetraenoic Acid? or eicosatetraenoic Acid? or Isoprostane? or Neuroprostane? or Leukotriene? or SRS-A or Thromboxane? or Eicosatetraynoic Acid? or Eicosatrienoic Acid? or Lipoxin? or Linoleic Acid? or Lubiprostone or Capsaicin or Erucic Acid? or Oleic Acid? or Undecylenic Acid? or Gefarnate or Ionomycin or Oxylipin? or Sorbic Acid? or Heptanoic Acid? or Atorvastatin Calcium or Heptanoate? or Lauric Acid? or Laurate? or Mupirocin or Mycolic Acid? or Mycophenolic Acid? or Myristic Acid? or Myristate? or Palmitic Acid? or Palmitate? or Palmitoyl Coenzyme A or Prostanoic Acid? or Sodium Morrhuate or Stearic Acid? or Stearate? or Thioctic Acid? or Glyceride? or Diglyceride? or Monoglyceride? or Triglyceride? or Triacetin or Glycolipid? or Cord Factor? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Polyisoprenyl Phosphate Sugar? or Polyisoprenyl Phosphate Monosaccharide? or Polyisoprenyl Phosphate Oligosaccharide? or Lipofuscin or Lipopolysaccharide? or O Antigen? or Lipoprotein? or Apolipoprotein? or ATP Binding Cassette Transporter Sub-Family G Member 5 or ATP Binding Cassette Transporter Sub-Family G Member 8 or Chylomicron? or Apoprotein or Phospholipid? or Glycerophosphate? or Phosphatidic Acid? or Glycerophospholipid? or Glycerylphosphorylcholine or Phosphatidylcholine? or Dimyristoylphosphatidylcholine or Dipalmitoylphosphatidylcholine or Lecithin? or Phosphatidylethanolamine? or Phosphatidylglycerol? or Cardiolipin? or Phosphatidylinositol? or Phosphatidylserine? or Phospholipid Ether? or Plasmalogen? or Platelet Activating Factor or Lysophospholipid? or Lysophosphatidylcholine? or Sphingomyelin? or Proteolipid? or Sphingolipid? or Sterol? or Adosterol or Cholecalciferol or Hydroxycholecalciferol? or Calcifediol or Dihydroxycholecalciferol? or Calcitriol or Dihydroxyvitamin D3 or Azacosterol or Cholestanol or Dehydrocholesterol? or Desmosterol or 19-Iodocholesterol or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or 25-Hydroxyvitamin D2 or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)) :ti,ab
30	((Dose? or Dosage? or Regimen? or Amount? or Optimal* or Optimis* or Requir* or Target? or Rate? or Increment* or Safe* or Efficacy or Initiat* or Start* or Introduc* or Receiv* or Administer*) near/5 (Carbohydrate? or Amino Sugar? or Hexosamine? or Fructosamine or Galactosamine or Acetylgalactosamine or Glucosamine or Acetylglucosamine or Muramic Acid? or Acetylmuramyl-Alanyl-Isoglutamine or Neuraminic Acid? or Sialic Acid? or N-Acetylneuraminic Acid or Deoxy Sugar? or Deoxyglucose or Fluorodeoxyglucose F18 or Deoxyribose or Fucose or Rhamnose or Sucrose or High Fructose Corn Syrup or Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Glycopeptide? or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Glycoprotein? or AC133 Antigen or ADAM* Protein? or Fertilin? or Cholesterol Ester Transfer Protein? or Fibrillin? or Lipopolysaccharide? or Glycoside? or Anthocyanin? or Atractyloside or Digitonin or Acetyldigitoxin? or Acetyldigoxin? or Medigoxin or Lanatoside? or Deslanoside or Proscillaridin or Strophanthin? or Cymarine or Ouabain or Chromomycin? or Galactoside? or Methylgalactoside? or Nitrophenylgalactoside? or Thiogalactoside? or Glucoside? or Amygdalin or Arbutin or Canagliflozin or Chloralose or Esculin or Methylglucoside? or 3-O-Methylglucose or Thioglucoside? or Glucosinolate? or Glycosylated Hemoglobin A or Lincosamide? or Mannoside? or Methylmannoside? or Methylglycoside? or Novobiocin or Nucleoside? Nucleotide? or Adenosine Diphosphate or O-Acetyl-ADP-Ribose or Cyclic ADP-Ribose or Cytidine Diphosphate Diglyceride? or Guanosine Diphosphate or Uridine Diphosphate or Olivomycin? or Phlorhizin or Saponin? or Escin or Ginsenoside? or Holothurin or Quillaja Saponin? or Solanine or Teichoic Acid? or Thioglycoside? or Tomatine or Monosaccharide? or Carbasugar? or Heptose? or Mannoheptulose or Hexose? or Fructose or Galactose or Glucose or Mannose or Sorbose or Imino Sugar? or Imino Furanose? or Imino Pyranose? or 1-Deoxynojirimycin or Ketose? or Dihydroxyacetone or Xylulose or Pentose? or Arabinose or Ribose or Xylose or Tetrose? or Thiosugar? or Triose? or Glyceraldehyde or Polysaccharide? or Alginate? or Carrageenan or Chitin or Chitosan or Ficoll or Fructan? or Inulin or Galactan? or Agar or Glucan? or Lentinan or Sizofiran or Zymosan or Cellulose or Cellobiose or Hypromellose Derivative? or Methylcellulose or Carboxymethylcellulose Sodium or Dextran? or Glycogen or Isomaltose or Maltose or Starch or Amylopectin or Amylose or Dextrin? or Cyclodextrin? or Hydroxyethyl Starch Derivative? or Trehalose or

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	Glycosaminoglycan? or Chondroitin or Dermatan Sulfate or Heparitin Sulfate or Hyaluronic Acid or Keratan Sulfate or Mannan? or Oligosaccharide? or Disaccharide? or Lactose or Lactulose or Melibiose or Sucralfate or Oligosaccharide? or Trisaccharide? or Acarbose or Raffinose or Pectin? or Pentosan Sulfuric Polyester or Bambermycin? or Lipid A or O Antigen? or Prebiotic? or Prodigiozan or Proteoglycan? or Aggrecan? or CD44 Antigen? or Versican? or Heparan Sulfate Proteoglycan? or Small Leucine-Rich Proteoglycan? or Biglycan or Decorin or Fibromodulin or Lumican or Sepharose or Xylan? or Sugar Acid? or Ascorbic Acid or Dehydroascorbic Acid or Diketogulonic Acid or Glucaric Acid or Gluconate? or Glyceric Acid? or Diphosphoglyceric Acid? or Diphosphoglycerate or Tartrate? or Tartronate? or Uronic Acid? or Glucuronate? or Glucuronic Acid or Hexuronic Acid? or Iduronic Acid or Sugar Alcohol? or Dithioerythritol or Dithiothreitol or Erythritol or Erythrityl Tetranitrate or Galactitol or Dianhydrogalactitol or Mitolactol or Glycerol or Inositol or Phytic Acid or Mitobronitol or Ribitol or Sorbitol or Isosorbide or Xylitol or Sugar Phosphate? or Dihydroxyacetone Phosphate or Glycerophosphate? or Glycerylphosphorylcholine or Hexosephosphate? or Fructosephosphate? or Fructosediphosphate? or Galactosephosphate? or Glucosephosphate? or Glucose-6-Phosphate or Hexosediphosphate? or Mannosephosphate? or Pentosephosphate? or Phosphoribosyl Pyrophosphate or Ribosemonophosphate? or Ribulosephosphate? or Polyisoprenyl Phosphate or Dolichol Monophosphate Mannose)) :ti,ab
31	(g adj3 kg adj3 (d or day) near/5 (Carbohydrate? or Amino Sugar? or Hexosamine? or Fructosamine or Galactosamine or Acetylgalactosamine or Glucosamine or Acetylglucosamine or Muramic Acid? or Acetylmuramyl-Alanyl-Isoglutamine or Neuraminic Acid? or Sialic Acid? or N-Acetylneuraminic Acid or Deoxy Sugar? or Deoxyglucose or Fluorodeoxyglucose F18 or Deoxyribose or Fucose or Rhamnose or Sucrose or High Fructose Corn Syrup or Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? or Globoside? or Lactosylceramide? or Trihexosylceramide? or Sphingomyelin? or Psychosine or Glycosylphosphatidylinositol? or Glycopeptide? or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Glycoprotein? or AC133 Antigen or ADAM* Protein? or Fertilin? or Cholesterol Ester Transfer Protein? or Fibrillin? or Lipopolysaccharide? or Glycoside? or Anthocyanin? or Atractyloside or Digitonin or Acetyldigitoxin? or Acetyldigoxin? or Medigoxin or Lanatoside? or Deslanoside or Proscillaridin or Strophanthin? or Cymarine or Ouabain or Chromomycin? or Galactoside? or Methylgalactoside? or Nitrophenylgalactoside? or Thiogalactoside? or Glucoside? or Amygdalin or Arbutin or Canagliflozin or Chloralose or Esculin or Methylglucoside? or 3-O-Methylglucose or Thioglucoside? or Glucosinolate? or Glycosylated Hemoglobin A or Lincosamide? or Mannoside? or Methylmannoside? or Methylglycoside? or Novobiocin or Nucleoside? Nucleotide? or Adenosine Diphosphate or O-Acetyl-ADP-Ribose or Cyclic ADP-Ribose or Cytidine Diphosphate Diglyceride? or Guanosine Diphosphate or Uridine Diphosphate or Olivomycin? or Phlorhizin or Saponin? or Escin or Ginsenoside? or Holothurin or Quillaja Saponin? or Solanine or Teichoic Acid? or Thioglycoside? or Tomatine or Monosaccharide? or Carbasugar? or Heptose? or Mannoheptulose or Hexose? or Fructose or Galactose or Glucose or Mannose or Sorbose or Imino Sugar? or Imino Furanose? or Imino Pyranose? or 1-Deoxynojirimycin or Ketose? or Dihydroxyacetone or Xylulose or Pentose? or Arabinose or Ribose or Xylose or Tetrose? or Thiosugar? or Triose? or Glyceraldehyde or Polysaccharide? or Alginate? or Carrageenan or Chitin or Chitosan or Ficoll or Fructan? or Inulin or Galactan? or Agar or Glucan? or Lentinan or Sizofiran or Zymosan or Cellulose or Cellobiose or Hypromellose Derivative? or Methylcellulose or Carboxymethylcellulose Sodium or Dextran? or Glycogen or Isomaltose or Maltose or Starch or Amylopectin or Amylose or Dextrin? or Cyclodextrin? or Hydroxyethyl Starch Derivative? or Trehalose or Glycosaminoglycan? or Chondroitin or Dermatan Sulfate or Heparitin Sulfate or Hyaluronic Acid or Keratan Sulfate or Mannan? or Oligosaccharide? or Disaccharide? or Lactose or Lactulose or Melibiose or Sucralfate or Oligosaccharide? or Trisaccharide? or Acarbose or Raffinose or Pectin? or Pentosan Sulfuric Polyester or Bambermycin? or Lipid A or O Antigen? or Prebiotic? or Prodigiozan or Proteoglycan? or Aggrecan? or CD44 Antigen? or Versican? or Heparan Sulfate Proteoglycan? or Small Leucine-Rich Proteoglycan? or Biglycan or Decorin or Fibromodulin or Lumican or Sepharose or Xylan? or Sugar Acid? or Ascorbic Acid or Dehydroascorbic Acid or Diketogulonic Acid or Glucaric Acid or Gluconate? or Glyceric Acid? or Diphosphoglyceric Acid? or Diphosphoglycerate or Tartrate? or Tartronate? or Uronic Acid? or Glucuronate? or Glucuronic Acid or Hexuronic Acid? or Iduronic Acid or Sugar Alcohol? or Dithioerythritol or Dithiothreitol or Erythritol or Erythrityl Tetranitrate or Galactitol or Dianhydrogalactitol or Mitolactol or Glycerol or Inositol or Phytic Acid or Mitobronitol or Ribitol or Sorbitol or Isosorbide or Xylitol or Sugar Phosphate? or Dihydroxyacetone Phosphate or Glycerophosphate? or Glycerylphosphorylcholine or Hexosephosphate? or Fructosephosphate? or Fructosediphosphate? or Galactosephosphate? or Glucosephosphate? or Glucose-6-Phosphate or Hexosediphosphate? or Mannosephosphate? or Pentosephosphate? or Phosphoribosyl Pyrophosphate or Ribosemonophosphate? or Ribulosephosphate? or Polyisoprenyl Phosphate or Dolichol Monophosphate Mannose)) :ti,ab
32	((Dose? or Dosage? or Regimen? or Amount? or Optimal* or Optimis* or Requir* or Target? or Rate? or Increment* or Safe* or Efficacy or Initiat* or Start* or Introduc* or Receiv* or Administer*) near/5 macronutrient?) :ti,ab
33	MeSH descriptor: [AMINO ACIDS] explode all trees and with qualifier(s): [Administration & dosage - AD]
34	MeSH descriptor: [LIPIDS] explode all trees and with qualifier(s): [Administration & dosage - AD]
35	MeSH descriptor: [PROSTAGLANDINS] explode all trees and with qualifier(s): [Administration & dosage - AD]
36	#34 not #35
37	MeSH descriptor: [CARBOHYDRATES] explode all trees and with qualifier(s): [Administration & dosage - AD]
38	MeSH descriptor: [HEPARIN] explode all trees and with qualifier(s): [Administration & dosage - AD]
39	MeSH descriptor: [GLYCOPEPTIDES] explode all trees and with qualifier(s): [Administration & dosage - AD]
40	MeSH descriptor: [AMINOGLYCOSIDES] explode all trees and with qualifier(s): [Administration & dosage - AD]
41	#38 or #39 or #40
42	#37 not #41
43	MeSH descriptor: [FAT EMULSIONS, INTRAVENOUS] this term only
44	#26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #36 or #42
45	#14 and #25 and #44
46	#14 and #43
47	#45 or #46

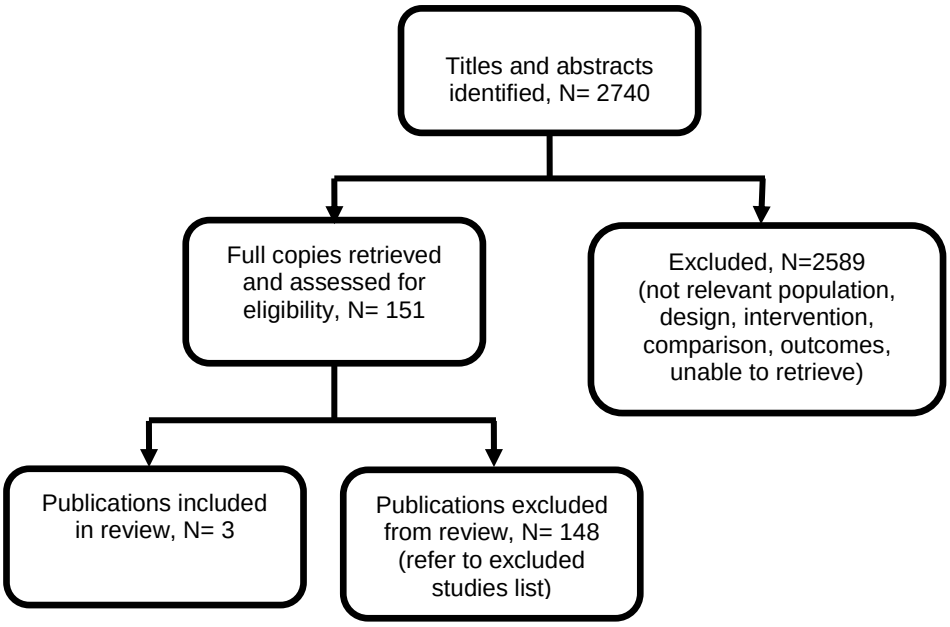
Appendix C – Clinical evidence study selection

Clinical study selection for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

Figure 1: PRISMA Flow chart of clinical article selection for review questions on optimal target dose and approach for carbohydrates



Appendix D – Clinical evidence tables

Clinical evidence tables for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

Table 4: Clinical evidence table for included studies

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
Full citation Forsyth, J. S., Murdock, N., Crighton, A., Low birthweight infants and total parenteral nutrition immediately after birth. III. Randomised study of energy substrate utilisation, nitrogen balance, and carbon dioxide production, Archives of Disease in Childhood, Fetal and neonatal edition. 73, F13-6, 1995 Ref Id 439240 Country/ies where the study was carried out	Sample size n = 20 randomised Characteristics Mean (SE) birthweight 1314 (65)g; mean (SE) gestation 30.9 (0.4) weeks Inclusion criteria None stated. Exclusion criteria None stated.	Interventions Infants were randomly allocated immediately after birth to either a low or high carbohydrate (glucose) intake; after 24 hours they were changed to the alternative regimen which was continued for 24 hours. High glucose regimen: 12g/kg/day (8.3mg/kg/minute) Low glucose regimen: 8g/kg/day (5.5mg/kg/minute)	Details PN was infused using neonatal infusion pumps and fat and protein intakes were kept constant throughout the study (for both glucose regimens). Indirect calorimetry was conducted for at least 2 hours for each regimen and urine was collected to measure nitrogen. Power analysis: Not stated Statistical analyses: Outcomes were	Results Outcome: Nutritional glucose intake (g/kg/day) High glucose regimen (n = 20), mean (SE): 12.2 (0.4) Low glucose regimen (n = 20), mean (SE): 8.3 (0.2)	Limitations Cochrane risk of bias tool Selection bias Random sequence generation: Unclear risk. Infants were randomly allocated immediately after birth, however no details provided on the randomisation. Allocation concealment: Unclear risk. Infants were randomly allocated immediately after birth, however no details provided on the randomisation. Performance bias

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
United Kingdom (Scotland) Study type Cross-over RCT Aim of the study To investigate energy substrate utilisation and nitrogen balance in low birthweight infants receiving total parental nutrition and compare two different glucose intakes on carbon dioxide production during the first days of life. Study dates Not stated. Source of funding Chest, Heart and Stroke Association (Scotland); Scottish Home and Health Department; Cow & Gate Nutricia.			compared using ANOVA and paired t tests.		Blinding of participants and personnel: Unclear risk. Infants would be unaware of their assignment and it would be likely those responsible for nursing and clinical procedures would not be blinded for safety reasons, however this would unlikely effect clinical care. Detection bias Blinding of outcome assessment: Low risk. Outcomes are objective. Attrition bias Incomplete outcome data: Low risk for energy intake (no missing data). High risk for protein retention as no information provided on dropouts (n=8). Reporting bias Selective reporting: Low risk. All outcomes reported (Nitrogen balance reported as protein retention). Other bias

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
					Other sources of bias: High risk. A Latin square crossover experimental design was used where each infant serves as his or her own control. Regimens were alternated each 24 hour period following allocation immediately after birth. Other information Authors recommend a parenteral regimen consisting of glucose 10-12 g/kg/day, amino acids 1.5-2.0 g/kg/day, and lipid 1.8-2.0 g/kg/day to meet energy and protein requirements for the maintenance and continued growth of infants considered to be sufficiently unwell
Full citation Morgan, C., McGowan, P., Herwitker, S., Hart, A. E., Turner, M. A., Postnatal head growth in preterm infants: a randomized controlled parenteral nutrition study, Pediatrics, 133, e120-8, 2014 Ref Id	Sample size n = 227 met birth weight/gestation criteria n = 196 eligible to take part (n=10 early deaths, n=8 unexpected to survive, n=3 congenital anomaly, n=10 early cranial ultrasound scan anomaly)	Interventions All infants received the control PN as soon as possible after birth. Infants were randomised to SCAMP or control, where feasible before 72 hours of age or at least within 120 hours of age. Once randomised, infants maintained their assigned regimen throughout, with	Details Details of PN/enteral nutrition, fluid, and drug infusion were recorded using routine nursing charts. PN was discontinued if enteral feed exceeded 75% total. Amino acid, glucose, lipid and energy intake were calculated from	Results Infection (late onset of sepsis >72 hours, n) at 28 days post treatment: SCAMP: 21/74 Control: 29/76 Infection (late onset of sepsis	Limitations Cochrane risk of bias tool Selection bias Random sequence generation: Low risk. Block randomisation codes generated in Stata 10. Allocation concealment: Low risk. Codes were sealed

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
378475 Country/ies where the study was carried out UK Study type RCT Aim of the study Comparison of standardised concentrated with added macronutrients (SCAMP) parenteral nutrition with control PN to improve early head circumference growth in preterm infants Study dates October 2009 to July 2012 Source of funding Bliss via the Innovation in Care Programme; Newborn appeal; National Institute for Health Research (through the Cheshire, Merseyside and North Wales Medicines for	n = 150 randomised (SCAMP n = 74; Control n = 76; n=40 refused consent, n=6 unavailable for consent) n = 135 available for analysis (SCAMP n = 66 [n = 8 deaths before 28 days]; Control n = 69 [n= 7 deaths before 28 days]) Characteristics Gestational age (mean GA weeks, SD): 26.7 (1.3) Birth weight (mean g, SD): 892 (170.5) Gender (male): 83/150 Age PN started (median, IQR): 3(2-7) Clinical Risk Index for Babies score (mean, SD): 10.8 (2.3) Inclusion criteria Babies born at <29 weeks gestation, birth weight <1200g, admitted to NICU within 48 hours of birth Exclusion criteria Babies who were not likely to survive, major congenital or chromosomal	the study intervention continuing for 28 completed days of life. SCAMP: Standardised, concentrated neonatal parenteral nutrition formulation used in clinical practice with additional macronutrients (Total calorie intake, kcal/kg per day = 108; maximum protein g/kg per day = 3.8; maximum lipid, g/kg per day = 3.8, maximum glucose g/kg per day = 15.6). Control: Standardised, concentrated neonatal parenteral nutrition formulation used in clinical practice without any additional macronutrients (Total calorie intake, kcal/kg per day = 85; maximum protein g/kg per day = 2.8; maximum lipid, g/kg per day = 2.8, maximum glucose g/kg per day = 13.5).	published PN composition data. Electronic patient records were used to collect patient demographic, mortality, and morbidity data (obtained for 36 weeks correct gestational age (CGA) survivors with additional 28-day survivor outcomes for morbidities related to PN complications). Statistical analysis: Analysis was conducted using Stata 11, SPSS 20 and R 2.15.1. Primary outcome was analysed using a general linear model, controlling for stratum based on gestational age, and checked with sensitivity analyses. Longitudinal joint modelling of head circumference and survival was conducted. Between group t tests, chi squared tests and linear models were	>72 hours, n) at 36 weeks GA: SCAMP: 26/63 Control: 28/64 Mortality at 28 days post treatment (n): SCAMP: 8/74 Control: 7/76 Mortality at 36 weeks GA (corrected age) (n): SCAMP: 11/63 Control: 12/64 Weight change at day 7 (mean g, SD): SCAMP: 25 (102.137) Control: 5 (116.271) Weight change at day 14 (mean g, SD): SCAMP: 135 (108.204) Control: 91 (121.272) Weight change at day 21 (mean g, SD):	in opaque serially numbered envelopes and given to the pharmacy. Once parental consent was confirmed, the pharmacy opened envelopes sequentially and provided the allocation. Performance bias Blinding of participants and personnel: Unclear risk. Caregivers and parents were blinded but pharmacists were not blinded due to safety reasons. Authors report this is unlikely to have affected clinical care. Detection bias Blinding of outcome assessment: Low risk. Outcomes were objective. Complete blinding to intervention at cot side. Attrition bias Incomplete outcome data: Low risk. There were no study withdrawals (apart from deaths).

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
Children Research Network).	complications, parenchymal brain lesions at <48 hours age measured by cranial ultrasound, no parental consent		generated as appropriate.	SCAMP: 238 (116.97) Control: 174 (139.079) Weight change at day 28 post treatment (mean g, SD): SCAMP: 360 (147.37) Control: 314 (160.35) Weight change at 36 weeks GA (Corrected age) (mean, g, SD): SCAMP: 1173 (204.651) Control: 1078 (245.014) Head circumference change at 7 days (mean mm, SD): SCAMP: 4 (8.485) Control: 3 (9.592) Head circumference change at 14 days (mean mm, SD): SCAMP: 12 (8.485) Control: 10 (9.592)	Reporting bias Selective reporting: Low risk. All outcomes reported. Other bias Other sources of bias: Low risk. None Other information Study was not powered to assess differences in major complications.

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
				Head circumference change at 21 days (mean mm, SD): SCAMP: 21 (9.381) Control: 17 (10.63) Head circumference change at 28 days post treatment (mean mm, SD): SCAMP: 31 (10.583) Control: 25 (11.247) Head circumference change at 36 weeks GA corrected age (mean mm, SD) SCAMP: 76 (8.888) Control: 71 (10.075)	
Full citation Pineault, M., Chessex, P., Bisaillon, S., Brisson, G., Total parenteral nutrition in the newborn: impact of the quality of infused energy on nitrogen metabolism, American Journal of Clinical	Sample size N=16 (all babies were included in both the high glucose [low fat] and low glucose [high fat] groups 60 kcal/kg-1/d-1; high glucose: n=8	Interventions Babies were divided into two groups based on calorie intake needed to either maintain energy requirements (60 kcal/kg-1/d-1) or achieve normal growth (80 kcal/kg-1/d-1). Each baby completed two nutrition phases where	Details Each infant received two 6-day periods of isocaloric and isonitrogenous (450 mg/kg-1/day-1) infusions, provided through a peripheral line. The only difference between	Results Nitrogen balance (mg/kg-1/day-1) - mean (SE) 60 kcal/kg-1/d-1; high glucose (n=8) 216 (27.0)	Limitations Quality of study assessed using ROBINS-I Confounding bias: Low risk. Selection of participants' bias: Low risk.

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
Nutrition, 47, 298-304, 1988 Ref Id 394278 Country/ies where the study was carried out Canada Study type Observational study (cohort study with crossover component (component of interest for this review question is crossover component)) Aim of the study To determine the influences of the quality (level and source) of infused energy on nitrogen metabolism. Study dates Not stated. Source of funding Medical Research Council of Canada.	60 kcal/kg-1/d-1; low glucose: n=8 80 kcal/kg-1/d-1; high glucose: n=8 80 kcal/kg-1/d-1; low glucose: n=8 Characteristics Reported based on calorie intake, not glucose intake (as comparing glucose intake was not aim of study) Gestational age (weeks) - mean (SE) 60 kcal/kg-1/d-1: 36 (1) 80 kcal/kg-1/d-1: 34 (1) Age at study (days) - mean (SE) 60 kcal/kg-1/d-1: 9 (1) 80 kcal/kg-1/d-1: 11 (2) Birthweight (g) - mean (SE) 60 kcal/kg-1/d-1: 2293 (147) 80 kcal/kg-1/d-1: 2006 (169) Weight at study (g) - mean (SE) 60 kcal/kg-1/d-1: 2102 (153) 80 kcal/kg-1/d-1: 1850 (174)	they received either high glucose [low fat] or low glucose [high fat]. Parental nutrition for the four groups comprised of: 60 kcal/kg-1/d-1; high glucose: 11 g/kg/-1/day-1 glucose; 1g/kg-1/d-1 lipids. 60 kcal/kg-1/d-1; low glucose: 5 g/kg/-1/day-1 glucose; 3g/kg-1/d-1 lipids. 80 kcal/kg-1/d-1; high glucose: 17g/kg-1/day-1 glucose; 1g/kg-1/day-1 lipids 80 kcal/kg-1/d-1; low glucose: 11g/kg-1/day-1 glucose; 3g/kg-1/day-1 lipids	the two periods was the source of calories (quantities of glucose and lipids). The caloric value of amino acids and glucose were 5.2kcal/g and 3.4kcal/g, respectively. All infusions provided 150 mL/kg/day of total fluids, 3mmol/kg/day sodium, 2mmol/kg/day potassium, 2mmol/kg/day chloride, 1mmol/kg/day calcium, 0.125mmol/kg/day magnesium, 0.8mmol/kg/day phosphorus, 300µg/kg/day zinc, 40µg/kg/day copper and 2.5ml/day multivitamins. Assisted ventilation and supplementary oxygen were not required. Statistical analyses: ANOVA was used to compare results of	60 kcal/kg-1/d-1; low glucose (n=8): 224 (18.0) 80 kcal/kg-1/d-1; high glucose (n=8): 250 (8.0) 80 kcal/kg-1/d-1; low glucose (n=8): 245 (10.0) Nitrogen retention (%) - mean (SE) 60 kcal/kg-1/d-1; high glucose (n=8): 49.7 (5.8) 60 kcal/kg-1/d-1; low glucose (n=8): 52.0 (4.2) 80 kcal/kg-1/d-1; high glucose (n=8): 57.1 (1.9) 80 kcal/kg-1/d-1; low glucose (n=8): 55.9 (2.2) Nutritional glucose intake (g/kg-1/d-1) - mean (SE) 60 kcal/kg-1/d-1; high glucose (n=8): 10.9 (0.3) 60 kcal/kg-1/d-1; low glucose (n=8): 5.4 (0.2)	Classification of interventions bias: Low risk. Intervention groups clearly defined. Deviations from intended interventions bias: Unclear risk. Protocol violations, if any occurred, are not reported. Missing data bias: Low risk. Data for head circumference was missing for one baby in the 80 kcal/kg-1/d-1 group; no other missing data. Measurement of outcomes bias: Low risk. Unlikely that outcome assessors were blind to intervention for safety reasons but all outcomes are objective. Selection of the reported results bias: High risk. It was not possible to include the growth outcomes for this review question as these are reported based on

Study Details	Participants	Interventions	Methods	Outcomes and results	Comments
	Duodenal atresia - number (%) 60 kcal/kg-1/d-1: 2 (25) 80 kcal/kg-1/d-1: 0 (0) Gastroschisis - number (%) 60 kcal/kg-1/d-1: 2 (25) 80 kcal/kg-1/d-1: 2 (25) Necrotizing enterocolitis - number (%) 60 kcal/kg-1/d-1: 3 (37.5) 80 kcal/kg-1/d-1: 4 (50) Oesophageal atresia - number (%) 60 kcal/kg-1/d-1: 1 (12.5) 80 kcal/kg-1/d-1: 1 (12.5) Feeding intolerance - number (%) 60 kcal/kg-1/d-1: 0 (0) 80 kcal/kg-1/d-1: 1 (12.5) Inclusion criteria Appropriate-for-gestational-age newborn infants demonstrating unchanging clinical conditions. Exclusion criteria Not stated.		nutrient and calorie intakes, nitrogen retention, 3-methylhistidine, glycaemia, and blood urea nitrogen. In the case of missing data from one of the periods, Student's t-test was used.	80 kcal/kg-1/d-1; high glucose (n=8): 15.6 (0.2) 80 kcal/kg-1/d-1; low glucose (n=8): 11.2 (0.3)	calorie intake only, not glucose intake. Other information Unclear wash-out period between interventions, suggesting potential for carry-over effect from one intervention to the other.

ANOVA: analysis of variance; CGA: correct for gestational age; GA: gestational age; IQR: interquartile range; NICU: neonatal intensive care unit; RCT: randomised controlled trial; ROBINS-I: risk of bias for non-randomised studies of interventions; SCAMP: standardised, concentrated, additional macronutrients parenteral nutrition; SE: standard error.

Appendix E – Forest plots

Forest plots for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

No meta-analysis was conducted for this review; therefore there are no forest plots.

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

No meta-analysis was conducted for this review; therefore there are no forest plots.

Appendix F – GRADE tables

GRADE tables for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

Table 4: Evidence profile for comparison higher versus lower glucose intake

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Higher glucose	Lower glucose	Relative (95% CI)	Absolute	Quality	Importance
Infection including sepsis at 28 days - 15.6g/kg/day vs 13.5g/kg/day glucose (follow-up 28 days)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	21/74 (28.4%)	29/76 (38.2%)	RR 0.74 (0.47 to 1.18)	99 fewer per 1000 (from 202 fewer to 69 more)	⊕⊕⊕O MODERATE	CRITICAL
Infection including sepsis at 36 weeks CGA - 15.6g/kg/day vs 13.5g/kg/day glucose												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	26/63 (41.3%)	28/64 (43.8%)	RR 0.94 (0.63 to 1.41)	26 fewer per 1000 (from 162 fewer to 179 more)	⊕⊕OO LOW	CRITICAL
Mortality at 28 days - 15.6g/kg/day vs 13.5g/kg/day glucose												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	8/74 (10.8%)	7/76 (9.2%)	RR 1.17 (0.45 to 3.07)	16 more per 1000 (from 51 fewer to 191 more)	⊕⊕OO LOW	IMPORTANT
Mortality at 36 weeks CGA - 15.6g/kg/day vs 13.5g/kg/day glucose												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Higher glucose	Lower glucose	Relative (95% CI)	Absolute	Quality	Importance
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11/63 (17.5%)	12/64 (18.8%)	RR 0.93 (0.44 to 1.95)	13 fewer per 1000 (from 105 fewer to 178 more)	⊕⊕OO LOW	IMPORTANT
Nitrogen balance (mg/kg/day) - 60kcal; 11g/kg/day vs 5g/kg/day glucose (Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	8[ł]	8[ł]	-	MD 8 lower (30.49 lower to 14.49 higher)	⊕OOO VERY LOW	IMPORTANT
Nitrogen balance (mg/kg/day) - 80kcal; 17g/kg/day vs 11g/kg/day glucose (Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	8[ł]	8[ł]	-	MD 5 higher (3.87 lower to 13.87 higher)	⊕OOO VERY LOW	IMPORTANT
Nitrogen retention (%) - 60kcal; 11g/kg/day vs 5g/kg/day glucose (Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	8[ł]	8[ł]	-	MD 2.3 lower (7.26 lower to 2.66 higher)	⊕OOO VERY LOW	IMPORTANT
Nitrogen retention (%) - 80kcal; 17g/kg/day vs 11g/kg/day glucose (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	8[ł]	8[ł]	-	MD 1.2 higher (0.81 lower to 3.21 higher)	⊕OOO VERY LOW	IMPORTANT
Weight (g) change at day 7 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	66	69	-	MD 20 higher (16.88 lower to 56.88 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Weight (g) change at day 14 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	66	69	-	MD 44 higher (5.27 to 82.73 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Weight (g) change at day 21 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Higher glucose	Lower glucose	Relative (95% CI)	Absolute		
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	66	69	-	MD 64 higher (20.72 to 107.28 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Weight (g) change at day 28 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[9]	none	66	69	-	MD 46 higher (5.91 lower to 97.91 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Weight (g) change at 36 weeks CGA - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[10]	none	62	62	-	MD 95 higher (15.54 to 174.46 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Head circumference (cm) change at day 7 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	66	69	-	MD 1 higher (2.05 lower to 4.05 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Head circumference (cm) change at day 14 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[11]	none	66	69	-	MD 2 higher (1.05 lower to 5.05 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Head circumference (cm) change at day 21 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[12]	none	66	69	-	MD 4 higher (0.62 to 7.38 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Head circumference (cm) change at day 28 - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[13]	none	66	69	-	MD 6 higher (2.32 to 9.68 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Head circumference (cm) change at 36 weeks CGA - 15.6g/kg/day vs 13.5g/kg/day glucose (Better indicated by higher values)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Higher glucose	Lower glucose	Relative (95% CI)	Absolute	Quality	Importance
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[14]	none	63	63	-	MD 5 higher (1.68 to 8.32 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Actual glucose intake (g/kg/day) - 60kcal; 11g/kg/day vs 5g/kg/day glucose (Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	8[f]	8[f]	-	MD 5.5 higher (5.25 to 5.75 higher)	⊕⊕OO LOW	IMPORTANT
Actual glucose intake (g/kg/day) - 80kcal; 17g/kg/day vs 11g/kg/day glucose (Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	8[f]	8[f]	-	MD 4.4 higher (4.15 to 4.65 higher)	⊕⊕OO LOW	IMPORTANT
Actual glucose intake (g/kg/day) - 12g/kg/day vs 8g/kg/day glucose (Better indicated by higher values)												
1	randomised trials	serious[15]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20[f]	20[f]	-	MD 3.9 higher (3.7 to 4.1 higher)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; CGA: correct for gestational age; MD: mean difference; RR: risk ratio.
[1] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for dichotomous outcomes (0.80).
[2] Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses two default MID for dichotomous outcomes (0.80 and 1.25).
[3] Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses both MID for continuous outcomes, calculated as 0.5 x SD control at baseline (-9.00 and 9.00).
[4] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (5.00).
[5] Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses both default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (-2.1 and 2.1).
[6] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (1.10).
[7] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (60.64).
[8] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (69.54).
[9] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (80.15).
[10] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (122.51).

[11] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (4.80).
[12] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (5.32).
[13] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (5.62).
[14] Evidence was downgraded by 1 due to serious imprecision, 95% confidence interval crosses one default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (5.04).
[15]Evidence was downgraded by 1 due serious risk of bias; unclear process of randomisation, unclear allocation concealment, and high risk of bias for other sources of bias.
[t] Cross over study – babies acted as their own controls.

Appendix G – Economic evidence study selection

Economic evidence study selection for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

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 questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

No evidence was identified which was applicable to these review questions.

Appendix I – Health economic evidence profiles

Economic evidence profiles for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

No evidence was identified which was applicable to these review questions.

Appendix J – Health economic analysis

Economic evidence analysis for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

No economic analysis was conducted for these review questions.

Appendix K – Excluded studies

Excluded clinical and economic studies for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

Clinical studies

Table 5: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
A. S. P. E. N. Intravenous Amino Acids National Shortage Task Force, Vanek, Vincent W., Mirtallo, Jay, Robinson, Larry, Kochevar, Marty, Guenter, Peggi, Parenteral nutrition amino acids product shortage considerations, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 28, 524-7, 2013	Non-systematic review.
Agus, M. S. D., Javid, P. J., Piper, H. G., Wypij, D., Duggan, C. P., Ryan, D. P., Jaksic, T., The effect of insulin infusion upon protein metabolism in neonates on extracorporeal life support, Annals of Surgery, 244, 536-543, 2006	Population in the study were not given PN.
Agus, M. S., Hirshberg, E., Srinivasan, V., Faustino, E. V., Luckett, P. M., Curley, M. A., Alexander, J., Asaro, L. A., Coughlin-Wells, K., Duva, D., French, J., Hasbani, N., Sisko, M. T., Soto-Rivera, C. L., Steil, G., Wypij, D., Nadkarni, V. M., Design and rationale of Heart and Lung Failure - Pediatric INsulin Titration Trial (HALF-PINT): A randomized clinical trial of tight glycemic control in hyperglycemic critically ill children, Contemporary clinical trials, 53, 178-187, 2017	Population in the study were not given PN.
Al-Shahwani, Noora H., Sigalet, David L., Pathophysiology, prevention, treatment, and outcomes of intestinal failure-associated liver disease, Pediatric surgery international, 33, 405-411, 2017	Narrative review.
Altman, R. P., Randolph, J. G., Application and hazards of total parenteral nutrition in infants, Annals of Surgery, 174, 85-90, 1971	Study design not relevant.
Barennes, Hubert, Pussard, Eric, Improving the management of dysglycemia in children in the developing world, The American journal of tropical medicine and hygiene, 92, 6-8, 2015	Not PN.
Beardsall, K., Vanhaesebrouck, S., Ogilvy-Stuart, A. L., Vanhole, C., Palmer, C. R., Ong, K., Vanweissenbruch, M., Midgley, P., Thompson, M., Thio, M., Cornette, L., Ossuetta, I., Iglesias, I., Theyskens, C., De Jong, M., Gill, B., Ahluwalia, J. S., De Zegher, F., Dunger, D. B., Prevalence and determinants of hyperglycemia in very low birth weight infants: Cohort analyses of the NIRTURE study, Journal of Pediatrics, 157, 715, 2010	Follow up study of Beardsall 2008.
Beardsall, K., Vanhaesebrouck, S., Ogilvy-Stuart, A. L., Vanhole, C., Palmer, C. R., Van Weissenbruch, M.,	The study comparison was early vs late insulin.

Study	Reason for Exclusion
Midgley, P., Thompson, M., Thio, M., Cornette, L., Ossuetta, I., Iglesias, I., Theyskens, C., De Jong, M., Ahluwalia, J. S., De Zegher, F., Dunger, D. B., Early insulin therapy in very-low-birth-weight infants, New England Journal of Medicine, 359, 1873-1884, 2008	
Becroft, D. M., Dix, M. R., Farmer, K., Intramuscular iron-dextran and susceptibility of neonates to bacterial infections. In vitro studies, Archives of Disease in Childhood, 52, 778-81, 1977	Intramuscular intervention.
Bell, E. F., Filer, L. J., Jr., Stegink, L. D., Plasma glutamate and aspartate concentrations in young infants on Neopham, Acta chirurgica Scandinavica. Supplementum, 517, 29-37, 1983	Comparison not relevant.
Bennett, Catherine, Fagan, Elyse, Chaharbakhshi, Edwin, Zamfirova, Ina, Flicker, Jai, Implementing a Protocol Using Glucose Gel to Treat Neonatal Hypoglycemia, Nursing for women's health, 20, 64-74, 2016	Not PN.
Beyreiss, K., Rautenbach, M., Utilization and turnover rate of fructose during continuous intravenous infusion in pre-term and term newborns in dependence on age, Biology of the Neonate, 24, 330-43, 1974	Outcomes not relevant.
Beyreiss, K., Rautenbach, M., Absorption and turnover of fructose in small for date infants compared to true pre term infants, Acta Medica Auxologica, 7, 113-120, 1975	Outcomes not relevant.
Bier, D. M., Leake, R. D., Haymond, M. W., Arnold, K. J., Gruenke, L. D., Sperling, M. A., Kipnis, D. M., Measurement of 'true' glucose production rates in infancy and childhood with 6,6-dideuteroglucose, Diabetes, 26, 1016-1023, 1977	Mixed population of newborns and children, outcomes in the study reported in graphical format.
Binder, N. D., Raschko, P. K., Benda, G. I., Reynolds, J. W., Insulin infusion with parenteral nutrition in extremely low birth weight infants with hyperglycemia, Journal of Pediatrics, 114, 273-280, 1989	Retrospective analysis.
Biswas, S., Buffery, J., Enoch, H., Bland, M., Markiewicz, M., Walters, D., Pulmonary effects of triiodothyronine (T3) and hydrocortisone (HC) supplementation in preterm infants less than 30 weeks gestation: Results of the THORN trial - Thyroid hormone replacement in neonates, Pediatric Research, 53, 48-56, 2003	Intervention and comparator were hydrocortisone glucose vs glucose.
Bombardirova, E., Belyaeva, I., Petrichyuk, S., Semenova, G., Ivanov, V., The use of metabolic therapy in treatment premature infants with severe cerebral ischemia, Journal of Perinatal Medicine, 41, 2013	Study topic not of interest, not PN.
Bottino,Marcela, Cowett,Richard M., Sinclair,John C., Interventions for treatment of neonatal hyperglycemia in very low birth weight infants, Cochrane Database of Systematic Reviews, -, 2011	Individual studies checked for inclusion.
Bowie, M. D., Mulligan, P. B., Schwartz, R., Intravenous glucose tolerance in the normal newborn infant: The effects of a double dose of glucose and insulin, Pediatrics, 31, 590-598, 1963	Outcomes not of interest.
Brand, P. L. P., Molenaar, N. L. D., Kaaijk, C., Wierenga, W. S., Neurodevelopmental outcome of hypoglycaemia in healthy, large for gestational age, term newborns, Archives of Disease in Childhood, 90, 78-81, 2005	Retrospective analysis.

Study	Reason for Exclusion
Calkins, K. L., Venick, R. S., Devaskar, S. U., Complications Associated with Parenteral Nutrition in the Neonate, Clinics in Perinatology, 41, 331-345, 2014	Narrative review.
Campbell, M. A., Ferguson, I. C., Hutchison, J. H., Kerr, M. M., Diagnosis and treatment of hypoglycaemia in the newborn, Archives of Disease in Childhood, 42, 353-60, 1967	Study topic not of interest, diagnostic testing.
Candy, D. C., Parenteral nutrition in paediatric practice: a review, Journal of human nutrition, 34, 287-96, 1980	Review.
Carlson,S.J., Current nutrition management of infants with chronic lung disease, Nutrition in Clinical Practice, 19, 581-586, 2004	Narrative review.
Carter, P. E., Lloyd, D. J., Duffty, P., Glucagon for hypoglycaemia in infants small for gestational age, Archives of Disease in Childhood, 63, 1264-1266, 1988	Study not relevant.
Chacko, S. K., Ordonez, J., Sauer, P. J. J., Sunehag, A. L., Gluconeogenesis is not regulated by either glucose or insulin in extremely low birth weight infants receiving total parenteral nutrition, Journal of Pediatrics, 158, 891-896, 2011	Outcomes not relevant.
Chacko, S. K., Sunehag, A. L., Gluconeogenesis continues in premature infants receiving total parenteral nutrition, Archives of Disease in Childhood: Fetal and Neonatal Edition, 95, F413-F418, 2010	Outcomes no relevant.
Chaudhari, S., Kadam, S., Total parenteral nutrition in neonates, Indian Pediatrics, 43, 953-964, 2006	Narrative review.
Chawla, D., Thukral, A., Agarwal, R., Deorari, A. K., Paul, V. K., Parenteral nutrition, Indian Journal of Pediatrics, 75, 377-383, 2008	Narrative review; individual studies checked for carbs.
Chen,F.S., Chung,M.Y., Huang,C.B., Hyperglycemia in very low birth weight premature infants, Clinical Neonatology, 8, 5-8, 2001	Retrospective study.
Chilimindris, C. P., The current status of parenteral nutritional therapy, Maryland state medical journal, 27, 61-5, 1978	Old, non-systematic review.
Chirinian, N., Shah, V., Does decreasing the frequency of changing intravenous administration sets (>24 h) increase the incidence of sepsis in neonates receiving total parenteral nutrition?, Paediatrics and Child Health (Canada), 17, 501-504, 2012	Not a relevant intervention.
Chowning, R., Adamkin, D. H., Table to quickly calculate glucose infusion rates in neonates, Journal of Perinatology, 35, 463, 2015	Study design not relevant.
Christensen, M. L., Helms, R. A., Mauer, E. C., Storm, M. C., Plasma carnitine concentration and lipid metabolism in infants receiving parenteral nutrition, The Journal of pediatrics, 115, 794-8, 1989	No relevant outcomes.
Cochran, E. B., Phelps, S. J., Helms, R. A., Parenteral nutrition in pediatric patients, Clinical pharmacy, 7, 351-366, 1988	Narrative review.
Collins, Carmel T., Gibson, Robert A., Miller, Jacqueline, McPhee, Andrew J., Willson, Kristyn, Smithers, Lisa G., Makrides, Maria, Carbohydrate intake is the main determinant of growth in infants born <33 weeks' gestation	Retrospective audit.

Study	Reason for Exclusion
when protein intake is adequate, Nutrition (Burbank, Los Angeles County, Calif.), 24, 451-7, 2008	
Collins, J. W., Jr., Hoppe, M., Brown, K., Edidin, D. V., Padbury, J., Ogata, E. S., A controlled trial of insulin infusion and parenteral nutrition in extremely low birth weight infants with glucose intolerance, The Journal of pediatrics, 118, 921-7, 1991	Intervention not relevant.
Conway, A., Williams, T., Care of the critically ill newborn: parenteral alimentation, The American journal of nursing, 76, 574-7, 1976	Narrative review.
Cornblath, M., Wybregt, S. H., Baens, G. S., Studies of carbohydrate metabolism in the newborn infant. vii. tests of carbohydrate tolerance in premature infants, Pediatrics, 32, 204-220, 1963	Outcomes not relevant.
Costello, I., Powell, C., Williams, A. F., Sodium glycerophosphate in the treatment of neonatal hypophosphataemia, Archives of Disease in Childhood, 73, F44-F45, 1995	Comparison not relevant.
Cowett, R. M., Oh, W., Pollak, A., Schwartz, R., Stonestreet, B. S., Glucose disposal of low birth weight infants: Steady state hyperglycemia produced by constant intravenous glucose infusion, Pediatrics, 63, 389-396, 1979	Not a PN study.
Cowett, R. M., Oh, W., Schwartz, R., Persistent glucose production during glucose infusion in the neonate, Journal of Clinical Investigation, 71, 467-475, 1983	Not the right comparison; glucose vs saline.
Cowett, R. M., Susa, J. B., Oh, W., Schwartz, R., Glucose kinetics in glucose-infused small for gestational age infants, Pediatric Research, 18, 74-79, 1984	Intervention/outcomes not relevant.
Dani, C., Poggi, C., Nutrition and bronchopulmonary dysplasia, Journal of Maternal-Fetal and Neonatal Medicine, 25, 37-40, 2012	Study design not relevant.
Disma, N., Mameli, L., Montobbio, G., De Benedetto, S., Locatelli, B. G., Sonzogni, V., Benigni, A., Prussiani, V., Comparison between Sterofundin (and glucose 1%) and Normal Saline (with glucose 1%) for intraoperative fluid management in children aged <36 months undergoing major surgery. Multisite, Randomized, Open Trial, Paediatric Anaesthesia, 23, 286, 2013	Conference abstract, population age not relevant.
Dobryanskyy, D., Dobush, O., Salabay, Z., Detsyk, O., Dubrovna, Y., Borysiuk, O., Risk factors of hyperglycemia in very low birth weight newborn infants, European Journal of Pediatrics, 175, 1615, 2016	Risk factors study.
Driscoll, J. M., Jr., Heird, W. C., Schullinger, J. N., Gongaware, R. D., Winters, R. W., Total intravenous alimentation in low-birth-weight infants: a preliminary report, The Journal of pediatrics, 81, 145-53, 1972	Study design not relevant.
Dudrick, S. J., Ruberg, R. L., Principles and practice of parenteral nutrition, Gastroenterology, 61, 901-10, 1971	Old guidelines.
Dweck, H. S., Cassady, G., Glucose intolerance in infants of very low birth weight. I. Incidence of hyperglycemia in infants of birth weights 1,100 grams or less, Pediatrics, 53, 189-95, 1974	Narrative review.

Study	Reason for Exclusion
Dweck, H., Brans, Y., Milstead, R., Cassady, G., Glucose intolerance in infants less than 1000 grams: The effects of a double dose of glucose, Pediatric Research, 7, 386, 1973	Outcomes not relevant.
Dweck,H.S., Neonatal hypoglycemia and hyperglycemia: two unique perinatal metabolic problems, Postgraduate Medicine, 60, 118-124, 1976	Narrative review.
Edstrom, K., Thalme, B., Infants of mothers with a high and of mothers with a low insulin response to glucose infusion. Glucose tolerance, insulin response and clinical appearance during the early neonatal period, Journal of Perinatal Medicine, 3, 21-33, 1975	Narrative review.
Ekblad, H., Kero, P., Takala, J., Stable glucose balance in premature infants with fluid restriction and early enteral feeding, Acta Paediatrica Scandinavica, 76, 438-443, 1987	Intervention is not PN.
Embleton, N. D., Simmer, K., Practice of parenteral nutrition in VLBW and ELBW infants, World Review of Nutrition & Dietetics, 110, 177-89, 2014	Review. No relevant sections.
Ergin, H., Ozdemir, O. M., Cirali, C., Korkut, M., Growth failure of very low birth weigth neonates at discharge, European Journal of Pediatrics, 175 (11), 1719, 2016	Combination treatment. Cohort.
Falcao, M. C., Ramos, J. L., Prediction of hyperglycemia in preterm newborn infants, Revista do Hospital das Clinicas, 54, 3-8, 1999	Study design not relevant.
Falcao,M.C., Leone,C.R., Ramos,J.L., Is glycosuria a reliable indicator of adequacy of glucose infusion rate in preterm infants?, Sao Paulo Medical Journal = Revista Paulista de Medicina, 117, 19-24, 1999	Outcome not of interest.
Falorni, A., Fracassini, F., Massi-Benedetti, F., Maffei, S., Glucose metabolism and insulin secretion in the newborn infant. Comparisons between the responses observed the first and seventh day of life to intravenous and oral glucose tolerance tests, Diabetes, 23, 172-8, 1974	Outcomes not relevant.
Filler, R. M., Eraklis, A. J., Care of the critically ill child: intravenous alimentation, Pediatrics, 46, 456-61, 1970	Exclude. Old review.
Fitzgerald,M.J., Goto,M., Myers,T.F., Zeller,W.P., Early metabolic effects of sepsis in the preterm infant: lactic acidosis and increased glucose requirement, Journal of Pediatrics, 121, 951-955, 1992	Unclear how much dextrose was administered through IV at start and at end of study.
Forsyth,J.S., Crighton,A., Low birthweight infants and total parenteral nutrition immediately after birth. I. Energy expenditure and respiratory quotient of ventilated and non-ventilated infants, Archives of Disease in Childhood Fetal and Neonatal Edition, 73, F4-F7, 1995	Outcomes not relevant.
Fosel, T. H., Uth, M., Wilhelm, W., Gruness, V., Comparison of two solutions with different glucose concentrations for infusion therapy during laparotomies in infants, Infusionstherapie und Transfusionsmedizin, 23, 80-4, 1996	Age of population not relevant.
Fox, H. A., Krasna, I. H., Total intravenous nutrition by peripheral vein in neonatal surgical patients, Pediatrics, 52, 14-20, 1973	Old review.
Frey, G., Hyperalimentation: a review, Arizona Medicine, 30, 613-619, 1973	Old review.
Friel, J. K., Bessie, J. C., Belkhode, S. L., Edgecombe, C., Steele-Rodway, M., Downton, G., Kwa, P. G., Aziz, K.,	Comparison/outcomes not relevant.

Study	Reason for Exclusion
Thiamine, riboflavin, pyridoxine, and vitamin C status in premature infants receiving parenteral and enteral nutrition, Journal of Pediatric Gastroenterology and Nutrition, 33, 64-69, 2001	
Galderisi, A., Facchinetti, A., Steil, G. M., Ortiz-Rubio, P., Cobelli, C., Trevisanuto, D., Neonatal hypoglycemia continuous glucose monitoring: A randomized controlled trial in preterm infants, Diabetes technology & therapeutics, 18, 2016	Study is investigating effectiveness of glucose monitor vs no glucose monitor in neonates.
Galderisi, Alfonso, Facchinetti, Andrea, Steil, Garry M., Ortiz-Rubio, Paulina, Cavallin, Francesco, Tamborlane, William V., Baraldi, Eugenio, Cobelli, Claudio, Trevisanuto, Daniele, Continuous Glucose Monitoring in Very Preterm Infants: A Randomized Controlled Trial, Pediatrics, 2017	Study is investigating effectiveness of glucose monitor vs no glucose monitor in neonates.
Ganzevoort, W., Rep, A., Bonsel, G. J., Fetter, W. P. F., Van Sonderen, L., De Vries, J. I. P., Wolf, H., A randomised controlled trial comparing two temporising management strategies, one with and one without plasma volume expansion, for severe and early onset pre-eclampsia, BJOG: An International Journal of Obstetrics and Gynaecology, 112, 1358-1368, 2005	Not a relevant intervention.
Gentz, J. C. H., Warrner, R., Persson, B. E. H., Cornblath, M., Intravenous glucose tolerance, plasma insulin, free fatty acids and beta-hydroxybutyrate in underweight newborn infants, Acta Paediat.Scand., 58, 218-223, 1960	Not PN study.
Georges, J. M., Glucose management and nutritional support of low-birth-weight neonates, The Journal of perinatal & neonatal nursing, 6, 71-7, 1992	Narrative review.
Gladtke, E., Rind, H., Von Hattingberg, H. M., Attempts to influence the pharmacokinetics off glucose in newborns, Mschr.Kinderheilk., 117, 245-247, 1969	Outcomes not relevant.
Glynn, A., Barr, S., Lewis, A., Tuthill, D. P., A national audit of parenteral nutrition practise in UK neonatal intensive care units: Is practise consistent with guidelines?, Archives of Disease in Childhood: Education and Practice Edition, 98, A30-A31, 2013	Not a relevant review.
Gradin, M., Finnstrom, O., Schollin, J., Feeding and oral glucose - Additive effects on pain reduction in newborns, Early Human Development, 77, 57-65, 2004	Outcomes not relevant.
Grasso, S., Distefano, G., Messina, A., Vigo, R., Reitano, G., Effect of glucose priming on insulin response in the premature infant, Diabetes, 24, 291-4, 1975	Outcomes not relevant.
Grasso, S., Fallucca, F., Romeo, M. G., Distefano, G., Sciullo, E., Reitano, G., Glucagon and insulin secretion in low birthweight preterm infants. The effect of glucose infusion, Acta Paediatrica Scandinavica, 79, 280-285, 1990	Outcomes not relevant.
Hay, William W., Jr., Strategies for feeding the preterm infant, Neonatology, 94, 245-54, 2008	Narrative review.
Hay, William W., Jr., Intravenous nutrition of the very preterm neonate, Acta paediatrica (Oslo, Norway : 1992). Supplement, 94, 47-56, 2005	Narrative review.
Hays, D. M., Kaplan, M. S., Mahour, G. H., Strauss, J., Huxtable, R. F., High-calorie infusion therapy following	Outcomes not relevant.

Study	Reason for Exclusion
surgery in low-birth-weight infants: metabolic problems encountered, Surgery, 71, 834-41, 1972	
Hecker, J. F., Duffy, B. J., Fong, T., Wyer, M., Failure of intravenous infusions in neonates, Journal of Paediatrics and Child Health, 27, 175-9, 1991	Topic not relevant.
Heird, W. C., Anderson, T. L., Nutritional requirements and methods of feeding low birth weight infants, Current problems in pediatrics, 7, 1-40, 1977	Narrative review.
Heird, W. C., Driscoll, J. M., Jr., Schullinger, J. N., Grebin, B., Winters, R. W., Intravenous alimentation in pediatric patients, The Journal of pediatrics, 80, 351-72, 1972	Old review.
Heird, W. C., Jensen, C. L., Gomez, M. R., Practical aspects of achieving positive energy balance in low birth weight infants, The Journal of pediatrics, 120, S120-8, 1992	Energy intake, not specific to carbohydrates.
Heird, W. C., Winters, R. W., Total intravenous alimentation, American journal of diseases of children (1960), 126, 287-9, 1973	Old review.
Hertz, D. E., Karn, C. A., Liu, Y. M., Liechty, E. A., Denne, S. C., Intravenous glucose suppresses glucose production but not proteolysis in extremely premature newborns, The Journal of clinical investigation, 92, 1752-8, 1993	Outcomes not of interest, not relevant study design.
Horvath, M., Mestyan, I., Mestyan, J., Iatrogenic hyperosmolality in critically ill low birth weight infants, Acta Paediatrica Academiae Scientiarum Hungaricae, 16, 231-242, 1975	Outcomes not relevant.
Hosono, S., Ohono, T., Kimoto, H., Nagoshi, R., Shimizu, M., Nozawa, M., Preventive management of hypoglycemia in very low-birthweight infants following indomethacin therapy for patent ductus arteriosus, Pediatrics International, 43, 465-468, 2001	Retrospective study.
Hsiao, Chien-Chou, Tsai, Ming-Luen, Chen, Chih-Chen, Lin, Hung-Chih, Early optimal nutrition improves neurodevelopmental outcomes for very preterm infants, Nutrition reviews, 72, 532-40, 2014	Old review.
Hung, K. C., Su, B. H., Lin, T. W., Peng, C. T., Tsai, C. H., Glucose-insulin infusion for the early treatment of non-oliguric hyperkalemia in extremely-low-birth-weight infants, Acta paediatrica Taiwanica = Taiwan er ke yi xue hui za zhi, 42, 282-6, 2001	Outcomes not relevant.
Jacob, J., Davis, R. F., Differences in serum glucose determinations in infants with umbilical artery catheters, Journal of perinatology : official journal of the California Perinatal Association, 8, 40-42, 1988	Topic not relevant.
Jain, Ashish, Aggarwal, Rajiv, Jeeva Sankar, M., Agarwal, Ramesh, Deorari, Ashok K., Paul, Vinod K., Hypoglycemia in the newborn, Indian Journal of Pediatrics, 77, 1137-42, 2010	Narrative review.
Jain,A., Aggarwal,R., Jeevasanker,M., Agarwal,R., Deorari,A.K., Paul,V.K., Hypoglycemia in the newborn, Indian Journal of Pediatrics, 75, 63-67, 2008	Conference abstract.
James, B. E., Hendry, P. G., MacMahon, R. A., Total parenteral nutrition of premature infants. I. Requirement for macronutrient elements, Australian Paediatric Journal, 15, 62-66, 1979	Old review.

Study	Reason for Exclusion
Janjua, Halima S., Mahan, John D., Patel, Hiren P., Mentser, Mark, Schwaderer, Andrew L., Continuous infusion of a standard combination solution in the management of hyperkalemia, Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 26, 2503-8, 2011	Retrospective study.
Johnson, J. D., Albritton, W. L., Sunshine, P., Hyperammonemia accompanying parenteral nutrition in newborn infants, The Journal of pediatrics, 81, 154-61, 1972	Old review.
Johnson, P. J., Review of macronutrients in parenteral nutrition for neonatal intensive care population, Neonatal network : NN, 33, 29-34, 2014	Review.
Jones, M. O., Pierro, A., Garlick, P. J., McNurlan, M. A., Donnell, S. C., Lloyd, D. A., Protein metabolism kinetics in neonates: effect of intravenous carbohydrate and fat, Journal of pediatric surgery, 30, 458-62, 1995	Combination treatment.
Jones, M. O., Pierro, A., Hammond, P., Nunn, A., Lloyd, D. A., Glucose utilization in the surgical newborn infant receiving total parenteral nutrition, Journal of pediatric surgery, 28, 1121-5, 1993	Outcomes not relevant.
Joosten, K. F., Verhoeven, J. J., Hazelzet, J. A., Energy expenditure and substrate utilization in mechanically ventilated children, Nutrition (Burbank, Los Angeles County, Calif.), 15, 444-8, 1999	Topic not relevant.
Kaemmer, A., Miller, J. D., Hyperalimentation in infancy. Experiences at the Maine Medical Center, The Journal of the Maine Medical Association, 63, 200-passim, 1972	Old review.
Kalhan, S. C., Parimi, P., Van Beek, R., Gilfillan, C., Saker, F., Gruca, L., Sauer, P. J., Estimation of gluconeogenesis in newborn infants, American journal of physiology. Endocrinology and metabolism, 281, E991-7, 2001	Measured glucose clearance.
Kalikstad, Betty, Skjerdal, Ase, Hansen, Thor Willy Ruud, Compatibility of drug infusions in the NICU, Archives of Disease in Childhood, 95, 745-8, 2010	Topic not relevant.
Kanarek, K. S., Williams, P. R., Curran, J. S., Total parenteral nutrition in infants and children, Advances in pediatrics, 29, 151-81, 1982	Not carbohydrate PN.
Kandula, T., Fox, L., Davis, P. G., Glucagon in neonatal hypoglycaemia, Journal of Paediatrics and Child Health, 46, 67, 2010	Retrospective study.
Keir, A., Hansen, A., Jankov, R., Callum, J., Acker, J., Co-infusion of dextrose-containing solutions and packed red blood cells does not adversely affect in vitro red blood cell quality, Transfusion, 53, 33A, 2013	Study design not relevant.
Keshen, T., Miller, R., Jahoor, F., Jaksic, T., Reeds, P. J., Glucose production and gluconeogenesis are negatively related to body weight in mechanically ventilated, very low birth weight neonates, Pediatric Research, 41, 132-138, 1997	Topic not relevant.
Keuth, U., Sodium bicarbonate-glucose infusion in the treatment of the respiratory distress syndrome of the	Comparisons/outcomes not relevant.

Study	Reason for Exclusion
premature and newborn infant. A six-year survey, German medical monthly, 12, 522-6, 1967	
King, K. C., Neonatal hypoglycemia, Children's Hospital Quarterly, 5, 97-105, 1993	Narrative review.
King, K. C., Schwartz, R., Yamaguchi, K., Adam, P. A., Lack of gastrointestinal enhancement of the insulin response to glucose in newborn infants, The Journal of pediatrics, 91, 783-6, 1977	Outcomes presented in graphical format.
King, R. A., Smith, R. M., Dahlenburg, G. W., Long term postnatal development of insulin secretion in early premature infants, Early Human Development, 13, 285-94, 1986	Outcomes not relevant.
Kirk, E. L., Audit to determine whether current parenteral nutrition regimens for pre-term infants on the neonatal unit are in accordance with international guidelines, Archives of Disease in Childhood, 94, e2, 2009	Study design not relevant.
Kirsten, G. F., Feeding the Larger Low-Birthweight Infant in a Resource-Poor Environment, Nestle Nutrition Institute workshop series, 81, 123-134, 2015	Study design not relevant.
Koletzko, B, Poindexter, B, Uauy, R, Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines. , 110, 2014	Studies for carbohydrates checked.
Kubota, A., Okada, A., Nezu, R., Kamata, S., Imura, K., Takagi, Y., Hyperbilirubinemia in neonates associated with total parenteral nutrition, Journal of Parenteral and Enteral Nutrition, 12, 602-606, 1988	Retrospective study.
Kulkarni, Sakil, Mercado, Velma, Rios, Mirta, Arboleda, Richard, Gomara, Roberto, Muinos, William, Reeves-Garcia, Jesse, Hernandez, Erick, Breast milk is better than formula milk in preventing parenteral nutrition-associated liver disease in infants receiving prolonged parenteral nutrition, Journal of Pediatric Gastroenterology and Nutrition, 57, 383-8, 2013	Retrospective study.
Kumpf, V. J., Parenteral nutrition-associated liver disease in adult and pediatric patients, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 21, 279-290, 2006	Narrative review.
Kutamba, E., Lubega, S., Mugalu, J., Ouma, J., Mupere, E., Dextrose boluses versus burette dextrose infusions in prevention of hypoglycemia among preterms admitted at Mulago Hospital: an open label randomized clinical trial, African health sciences, 14, 502-9, 2014	Comparator treatment not PN but glucose given through a burette.
Lafeber, H. N., Sulkers, E. J., Chapman, T. E., Sauer, P. J., Glucose production and oxidation in preterm infants during total parenteral nutrition, Pediatric Research, 28, 153-7, 1990	Outcomes not relevant.
Lai, Nai Ming, Ahmad, Kamar Azanna, Choo, Yao Mun, Kong, Juin Yee, Ngim, Chin Fang, Fluid supplementation for neonatal unconjugated hyperbilirubinaemia, Cochrane Database of Systematic Reviews, 2017	Checked individual studies.
Lai, Nai Ming, Rajadurai, Samuel V, Tan, Kenneth, Increased energy intake for preterm infants with (or developing) bronchopulmonary dysplasia/chronic lung disease, Cochrane Database of Systematic Reviews, 2006	Outcomes not relevant.

Study	Reason for Exclusion
Larsson, L. E., Nilsson, K., Niklasson, A., Andreasson, S., Ekstrom-Jodal, B., Influence of fluid regimens on perioperative blood-glucose concentrations in neonates, British Journal of Anaesthesia, 64, 419-424, 1990	Comparison not relevant.
Le Compte,A.J., Lynn,A.M., Lin,J., Pretty,C.G., Shaw,G.M., Chase,J.G., Pilot study of a model-based approach to blood glucose control in very-low-birthweight neonates, BMC Pediatrics, 12, 117-, 2012	Population were hyperglycaemic at start of study.
Le Dune, M. A., Intravenous glucose tolerance and plasma insulin studies in small for dates infants, Archives of Disease in Childhood, 47, 111-114, 1972	Intervention not relevant.
Lilien, L. D., Grajwer, L. A., Pildes, R. S., Treatment of neonatal hypoglycemia with continuous intravenous glucose infusion, Journal of Pediatrics, 91, 779-782, 1977	Outcomes reported in graphical format.
Lilien, L. D., Pildes, R. S., Srinivasan, G., Voora, S., Yeh, T. F., Treatment of neonatal hypoglycemia with minibolus and intravenous glucose infusion, The Journal of pediatrics, 97, 295-8, 1980	Outcomes not relevant.
Lilien, L. D., Rosenfield, R. L., Baccaro, M. M., Pildes, R. S., Hyperglycemia in stressed small premature neonates, The Journal of pediatrics, 94, 454-9, 1979	Outcomes not relevant.
Mayes, K., Tan, M., Morgan, C., Effect of hyperalimentation and insulin-treated hyperglycemia on tyrosine levels in very preterm infants receiving parenteral nutrition, Jpen: Journal of Parenteral & Enteral Nutrition, 38, 92-8, 2014	Carbohydrate intake was dependent on fluid allowance and the same fluid protocol was used for both groups.
Miralles,R.E., Lodha,A., Perlman,M., Moore,A.M., Experience with intravenous glucagon infusions as a treatment for resistant neonatal hypoglycemia, Archives of Pediatrics and Adolescent Medicine, 156, 999-1004, 2002	Retrospective study.
Mohnike, K., Blankenstein, O., Pfuetzner, A., Potzsch, S., Schober, E., Steiner, S., Hardy, O. T., Grimberg, A., Van Waarde, W. M., Long-term non-surgical therapy of severe persistent congenital hyperinsulinism with glucagon, Hormone Research, 70, 59-64, 2008	Retrospective study.
Morgan, C., Parry, S., Tan, M., Neurodevelopmental outcome in very preterm infants randomized to receive two different parenteral nutrition regimens: The scamp nutrition study, Journal of Neonatal-Perinatal Medicine, 10, 220-221, 2017	Abstract only.
Morgan, Colin, Burgess, Laura, High Protein Intake Does Not Prevent Low Plasma Levels of Conditionally Essential Amino Acids in Very Preterm Infants Receiving Parenteral Nutrition, JPEN. Journal of parenteral and enteral nutrition, 41, 455-462, 2017	Outcomes not relevant - plasma amino acid levels.
Murakami, R., Katsura, N., Nakamura, H., Matsuo, T., Response to glucagon of low-birth-weight infants with early intravenous glucose infusion, Kobe Journal of Medical Sciences, 22, 229-237, 1976	Intervention not relevant.
Nili, F., Ghafuri, M., Hypoglycemia in sick preterm infants and the therapeutic effect of 12.5% dextrose in water compared with 10% dextrose in water, Acta Medica Iranica, 43, 182-186, 2005	Intervention not PN.
Oliven, A., King, K. C., Kalhan, S. C., Gastrointestinal enhanced insulin release in response to glucose in newborn	Topic not relevant.

Study	Reason for Exclusion
infants, Journal of Pediatric Gastroenterology and Nutrition, 5, 220-5, 1986	
Pohlandt, F., Heinze, E., Fussganger, F., Mayer, V., Teller, W., Insulin secretion in human neonates during long term infusion of glucose, Acta endocrinologica. Supplementum, 173, 122, 1973	Not PN; old study.
Pribylova, H., Melichar, V., Sabata, V., The effect of prenatal fructose infusions upon metabolic condition of the newborn, Biology of the Neonate, 32, 108-112, 1977	Population not relevant.
Pribylova,J., Kozlova,J., Glucose and galactose infusions in newborns of diabetic and healthy mothers, Biology of the Neonate, 36, 193-197, 1979	Outcomes reported in graphical format.
Roelants, Jorine A., Vlaardingerbroek, Hester, van den Akker, Chris H. P., de Jonge, Rogier C. J., van Goudoever, Johannes B., Vermeulen, Marijn J., Two-Year Follow-up of a Randomized Controlled Nutrition Intervention Trial in Very Low-Birth-Weight Infants, JPEN. Journal of parenteral and enteral nutrition, 42, 122-131, 2018	Intervention not relevant - levels of glucose do not differ between groups.
Sinclair,J.C., Bottino,M., Cowett,R.M., Interventions for prevention of neonatal hyperglycemia in very low birth weight infants, Cochrane database of systematic reviews (Online), 2011. Date of Publication, -, 2011	Individual studies checked for inclusion.
Spath, Cornelia, Zamir, Itay, Sjostrom, Elisabeth Stoltz, Domellof, Magnus, Use of Concentrated Parenteral Nutrition Solutions is Associated with Improved Nutrient Intakes and Postnatal Growth in Very Low-Birth-Weight Infants, JPEN. Journal of parenteral and enteral nutrition, 2019	Insufficient information reported - not possible to compare total prescribed glucose intake in the original and concentrated PN arms as additional glucose (to that contained in the main bag) was given in the original arm (amount not reported) and glucose is expressed as g/100ml and it is unclear if prescribed fluid amount was the same for both arms.
Sunehag, A. L., Parenteral glycerol enhances gluconeogenesis in very premature infants, Pediatric Research, 53, 635-641, 2003	Not an RCT.
Sunehag, A. L., Haymond, M. W., Schanler, R. J., Reeds, P. J., Bier, D. M., Gluconeogenesis in very low birth weight infants receiving total parenteral nutrition, Diabetes, 48, 791-800, 1999	Intervention not relevant.
Tan, M., Parry, S., Morgan, C., Neurodevelopmental outcome in very preterm infants randomised to receive two different parenteral nutrition regimens: The SCAMP nutrition study, Archives of Disease in Childhood, 101, A5, 2016	Combination treatment.
Tottman, A. C., Bloomfield, F. H., Cormack, B. E., Harding, J. E., Mohd Slim, M. A., Weston, A. F., Alsweiler, J. M., Relationships between Early Nutrition and Blood Glucose Concentrations in Very Preterm Infants, Journal of Pediatric Gastroenterology and Nutrition, 66, 960-966, 2018	Intervention not relevant - concentration of carbohydrates was the same (although fluid differed) for both arms with the exception of ELBW babies. Results were not presented separately for ELBW babies.
Tuncer, M., Occurrence of hyperglycemia and hypoglycemia in premature and malnourished premature infants during glucose infusion in the first 48 hours of life, The Turkish journal of pediatrics, 20, 108-15, 1978	Outcomes not relevant.

Study	Reason for Exclusion
Usher, R., Reduction of mortality from respiratory distress syndrome of prematurity with early administration of intravenous glucose and sodium bicarbonate, Pediatrics, 32, 966-975, 1963	Comparison not relevant.
Uthaya, S., Liu, X., Babalis, D., Dore, C., Warwick, J., Bell, J., Thomas, L., Ashby, D., Durighel, G., Ederies, A., Yanez-Lopez, M., Modi, N., Nutritional Evaluation and Optimisation in Neonates (NEON) trial of amino acid regimen and intravenous lipid composition in preterm parenteral nutrition: a randomised double-blind controlled trial, Efficacy and Mechanism Evaluation, 3, 2016	Comparisons not relevant (amount of carbohydrates is not different between groups)
Vanhatalo, T., Tammela, O., Glucose infusions into peripheral veins in the management of neonatal hypoglycemia - 20% instead of 15%?, Acta Paediatrica, International Journal of Paediatrics, 99, 350-353, 2010	Population was not admitted to NICU, they did not require hospitalisation.
Zamir, Itay, Tornevi, Andreas, Abrahamsson, Thomas, Ahlsson, Fredrik, Engstrom, Eva, Hallberg, Boubou, Hansen-Pupp, Ingrid, Sjostrom, Elisabeth Stoltz, Domellof, Magnus, Hyperglycemia in Extremely Preterm Infants-Insulin Treatment, Mortality and Nutrient Intakes, The Journal of pediatrics, 200, 104-110.e1, 2018	Comparison not relevant - infants with and without hyperglycaemia.

Economic studies

No economic evidence was identified for these reviews. See supplementary material D for further information.

Appendix L – Research recommendations

Research recommendations for review questions:

What is the optimal target dosage for carbohydrates in preterm and term babies who are receiving parenteral nutrition and neonatal care?

What is the optimal way (starting dose and approach to increment, if employed) to achieve this target dosage for carbohydrates?

No research recommendation was made for this review.