

Neonatal parenteral nutrition

[D8] Ratio of carbohydrates to lipids

NICE guideline tbc

Evidence reviews

September 2019

Draft for consultation

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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1 What are the most effective relative 2 amounts of carbohydrate and lipids 3 (starting and target dose)?

4 Review question

5 What are the most effective relative amounts of carbohydrate and lipids (starting and target
6 dose)?

7 Introduction

8 Carbohydrate in the form of glucose is the main source of energy for most metabolic
9 processes in the body. Lipids provide essential fatty acids for brain development and are an
10 important source of energy. Together carbohydrates and lipids provide the non-nitrogen
11 energy in parenteral nutrition (PN).

12 A high relative amount of carbohydrate may result in hyperglycaemia, whilst too much lipid
13 can lead to hypertriglyceridemia. Optimising the relative amounts of carbohydrate and lipid
14 may reduce these problems.

15 Summary of the protocol

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

18 Table 1: Summary of the protocol (PICO table)

Population	<ul style="list-style-type: none">• 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	Ratio of carbohydrate to lipid
Comparison	Other ratios of carbohydrate to lipid
Outcomes	Critical <ul style="list-style-type: none">• Neurodevelopmental outcomes (general cognitive abilities at two years corrected age as measured by a validated scale)• Growth/Anthropometric measures:<ul style="list-style-type: none">○ Weight gain (g/kg/d)○ Linear growth○ Head circumference (mm)• Body composition (measured as lean mass, fat-free mass, fat mass, adipose tissue),• Adverse effects of PN<ul style="list-style-type: none">○ Infection (including sepsis)○ Hyperglycaemia○ Hypoglycaemia○ Hypertriglyceridemia○ Other PN associated liver disease• Nitrogen balance / nitrogen excretion• Metabolic acidosis

Important

- Mortality
- Length of hospital stay
- Nutritional intake (g/kg/day) (prescribed nitrogen/non-nitrogen, carbohydrates and lipids actually received)

1 PN: Parenteral nutrition.

2 For full details see the review protocol in appendix A. .

3 Clinical evidence

4 Included studies

5 As limited RCT evidence was available, we also included observational studies. Three
6 studies were identified for this review. One was an observational study (Chessex 1989) and
7 the other 2 are randomised controlled trials (RCTs) (Jones1995, Salas-Salvado 1993).

8 Two studies compared a high carbohydrate and low lipid PN to low carbohydrate and high
9 lipid PN (Chessex 1989, Jones 1995) and 1 study compared 3 different fat energy intakes
10 (Salas-Salvado 1993).

11 The included studies are summarised in Table 2.

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

14 Excluded studies

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

17 Summary of clinical studies included in the evidence review

18 Summaries of the studies included in this review is presented in Table 2.

19 **Table 2: Summary of included studies**

Study	Population	Intervention	Comparison	Outcomes	Comments
Chessex 1989	N = 11 (outcome measures were only available for 10)	<u>High carbohydrate and low lipid</u> (n=11)	<u>Low carbohydrate and high lipid</u> (n=11)	• Nitrogen excretion	2 day protocol Isocaloric regimens (70kcal/kg/day) Isoproteinic (2.5g/kg/day)
Canada Observational study		12 to 17 g/kg/day glucose 0 to 1 g/kg/day lipid Received on day 1	4 to 8 g/kg/day glucose 2.5 to 3 g/kg/day lipid Received on day 2		
	<u>Mean BW</u> 2.54kg (SD 0.54)				
	<u>Mean GA</u> 37 weeks (SD 3)				

Study	Population	Intervention	Comparison	Outcomes	Comments
Jones 1995 UK RCT	N = 18 <u>Mean GA</u> High carb: 38.2 weeks (SD 3.6) Low carb: 37.4 weeks (SD 2.4)	<u>High carbohydrate and low lipid (n=9)</u> 18.89 g/kg/day dextrose 0.5g/kg/day lipid	<u>Low carbohydrate and high lipid (n=9)</u> 10g/kg/day dextrose 4g/kg/day lipid	<ul style="list-style-type: none"> • Nitrogen excretion • Nitrogen balance 	3 days continuous TPN Similar calorie intake (86kcal/kg/day) and protein intake (2.5g/kg/day)
Salas-Salvado 1993 Spain RCT	N = 26 <u>Mean BW</u> Low lipid: 3272g (SD 780) Medium lipid: 2634g (SD 472) High lipid: 2883g (SD 646) <u>Mean GA</u> Low lipid: 39.7 weeks (SD 1.3) Medium lipid: 39 weeks (SD 2.7) High lipid: 38.9 weeks (SD 2.7)	<u>Medium lipid (n= 9)</u> Lipid energy = 29% <u>High Lipid (n=8)</u> Lipid energy = 40%	<u>Low lipid (n=9)</u> Lipid energy = 18 %	<ul style="list-style-type: none"> • Weight gain 	Isocaloric and isonitrogenous PN Energy, fat and glucose intake reported, but data does not have SD

1 *BW: Birth weight; GA: Gestational age; PN: Parenteral nutrition; RCT: Randomised controlled trial;*
2 *SD: standard deviation; TPN: Total parenteral nutrition.*

3 See appendix D for full evidence tables.

4 Quality assessment of clinical outcomes included in the evidence review

5 GRADE was conducted to assess the quality of outcomes. Evidence was identified for critical
6 outcomes, but no evidence was identified to provide data on important outcomes. The clinical
7 evidence profiles can be found in appendix F.

8 Economic evidence

9 Included studies

10 A systematic review of the economic literature was conducted but no economic studies were
11 identified which were applicable to this review question. A single economic search was

1 undertaken for all topics included in the scope of this guideline. Please see supplementary
2 material D for details.

3 **Excluded studies**

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

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

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

7 **Economic model**

8 No economic modelling was undertaken for this review because the committee agreed that
9 other topics were higher priorities for economic evaluation.

10 **Evidence statements**

11 **Clinical evidence statements**

12 ***High carbohydrate and low lipid versus Low carbohydrate and high lipid***

13 **Nitrogen excretion**

- 14 • Very low quality evidence from 1 RCT (n=18) showed a clinically important difference in
15 nitrogen excretion; those babies who received PN with low carbohydrate and high lipid
16 had lower nitrogen excretion as compared to those who had received high carbohydrate
17 and low lipid. However, there was high uncertainty around the effect: Mean difference
18 (MD) 0.04g/kg/day (95% CI -0.03to 0.11).
- 19 • Very low quality evidence from 1 observational study (n=10) showed a clinically important
20 difference in nitrogen excretion. Those babies who received low carbohydrate and high
21 lipid had a greater nitrogen excretion. However, there was uncertainty around the effect:
22 MD -24mg/kg/day (95% CI -50.31 to 2.31).

23 **Nitrogen balance**

- 24 • Low quality evidence from 1 RCT (n=18) showed a clinically important difference in
25 nitrogen balance. Those babies who had received PN with high carbohydrate and low lipid
26 had a lower nitrogen balance as compared to those who had received low carbohydrate
27 and high lipid PN. However, there was uncertainty around the effect: MD -0.05 (95% CI -
28 0.09 to -0.01).

29 ***Medium lipid (29%) versus low lipid (18%) PN***

30 **Weight gain**

- 31 • Very low quality evidence from 1 RCT (n=18) showed no clinically important difference
32 in weight gain over 3 days between babies who received a low lipid energy intake (18%)
33 as compared to those who received a medium lipid energy intake (29%). However,
34 there was high uncertainty around the effect: MD -0.1g/kg/day (95% CI -7.63 to 7.43)

1 **High lipid (40%) versus low lipid (18%) PN**

2 **Weight gain**

- 3 • Very low quality evidence from 1 RCT (n=17) showed a clinically important difference in
4 weight gain over 3 days between babies who received a high lipid energy intake (40%)
5 as compared to those who received a low lipid energy intake (18%); those babies
6 receiving high lipid energy had greater weight gain. However, there was high
7 uncertainty around the effect: MD 4.9g/kg/day (95% CI -4.42 to 14.22).
8

9 **High lipid (40%) versus medium lipid (29%) PN**

10 **Weight gain**

- 11 • Very low quality evidence from 1 RCT (n=17) showed a clinically important difference in
12 weight gain over 3 days between babies who received a high lipid energy intake (40%)
13 as compared to those who received a medium lipid energy intake (29%), those babies
14 receiving high lipid energy had greater weight gain. However, there was high
15 uncertainty around the effect: MD 5g/kg/day (95% CI -4.51 to 14.51).
16

17 **Economic evidence statements**

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

19 **Recommendations**

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

21 ***The outcomes that matter most***

22 The committee prioritised neurodevelopmental outcomes, anthropometric measures, body
23 composition, adverse events, nitrogen balance/nitrogen excretion and metabolic acidosis as
24 the critical outcomes. These were considered critical as carbohydrate in the form of glucose
25 is the main source of energy for most metabolic processes in the body (and therefore
26 influence body composition as well as anthropometric measures) whereas lipids provide
27 essential fatty acids for brain development and are an important source of energy (therefore
28 influence both neurodevelopment and growth). They also noted that higher levels of nitrogen
29 excretion leads to decreased nitrogen retention which would have a negative effect on
30 growth. The relative amounts may also influence the metabolic state of the baby which could
31 lead to adverse events, for example a high amount of glucose could result in hyperglycaemia
32 whilst too much lipid can lead to hypertriglyceridemia. The evidence identified only provided
33 data on anthropometric measures and nitrogen balance.

34 The committee considered mortality, length of hospital stay and nutritional intake as
35 important outcomes; however, these are likely influenced by a number of complex factors.
36 No evidence was identified with data on these outcomes.

37 ***The quality of the evidence***

38 The quality of evidence for this review was assessed using GRADE methodology. The
39 included evidence for outcomes was considered very low or low quality, indicating high
40 uncertainty in the effect. Evidence was downgraded due to risk of selection bias,
41 performance bias and detection bias. Studies were also very small which meant that data for
42 many outcomes were downgraded due to imprecision, the 95% confidence intervals crossed
43 either one or two default MID, suggesting the data was not precise. Although the evidence

1 was not downgraded based on the studies being old, it does suggest that the PN
2 formulations are not necessarily generalisable to current practice.

3 **Benefits and harms**

4 The committee discussed the evidence; however, they acknowledged that it was limited and
5 therefore the committee used the evidence presented, alongside their clinical knowledge and
6 expertise to make the recommendations by informal consensus.

7 The committee discussed that it is important that the ratios need to take into account the
8 dosages provided in the recommendations on individual constituents related to
9 carbohydrates and lipids (recommendations 1.4.7 and 1.4.8), and that it should be clear to
10 those prescribing PN, that when calculating the relative amounts of carbohydrate and lipid to
11 provide, the recommended dosages of each of these components should not be exceeded.

12 The committee discussed that only one of the included studies (Salas-Salvado 1993) was in
13 line with current practice, providing lipids in a range from 18 to 40% (meaning that the other
14 82 to 60% of non-nitrogen energy was made up of glucose) with better growth associated
15 with 40% lipid intake. The committee agreed that the evidence related to nitrogen balance
16 and excretion was inconclusive because the number of babies in the studies was low and
17 there was uncertainty around the findings. The committee noted that the evidence presented
18 was not sufficient to recommend anything which substantially differed from current practice.
19 The committee also acknowledged that the evidence from Salas-Salvado (1993) is
20 consistent with recommendations provided by the European Society of Paediatric
21 Gastroenterology, Hepatology and Nutrition (Koletzko 2005) as well as current practice.
22 Based on the evidence as well as knowledge and expertise, the committee agreed by
23 informal consensus that a range of 60 to 75% carbohydrate to 25 to 40% lipid should be
24 used. They decided not to recommend the lower end of the lipid range (18%) that was used
25 in the evidence because that would lead to a high glucose intake for which the risk of
26 hyperglycaemia was considered to be too high. Therefore the committee agreed a lower
27 level of 25% lipid was needed to limit the risk of hyperglycaemia, to provide sufficient
28 essential fatty acids, and fat soluble vitamins. In addition, lipid in PN reduces lipogenesis which
29 decreases energy expenditure, oxygen consumption and improves nitrogen retention. The
30 committee discussed how lowering the level of lipid below 25% risks suboptimal nutrition.
31 The committee also discussed more current research which has been conducted within the
32 UK (but that did not meet the criteria for this review question); the committee noted that these
33 studies provided 24% to 25% fat as their lower limits, which aligns with the
34 recommendations, and these studies did not report detrimental outcomes at these levels.

35 The committee agreed by informal consensus and based on experience and expertise that
36 the upper limit should be 40% fat as used in the included study. Even though there currently
37 is no evidence to firmly state the risks of a higher than 40% lipid provision the committee
38 agreed that this upper limit would be safe and not risk fatty liver or raised triglyceride levels.

39 Based on their clinical experience, the committee decided by informal consensus that
40 whenever the amount of PN is altered, (for instance when introducing enteral feeds) the
41 relative amounts should be kept within the same ranges of these recommendations, for the
42 reasons discussed above.

43 **Cost effectiveness and resource use**

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

45 The committee explained that recommendations pertaining to the optimal relative amounts of
46 carbohydrate and lipid would not incur extra resource implications to the health care system.

47 The committee noted that getting the relative amounts of carbohydrate and lipid for neonatal
48 parenteral nutrition may result in avoiding additional costs associated with adverse effects to

1 the NHS given that incorrect relative amounts of carbohydrate and lipid can result to adverse
2 events, for example hypoglycaemia, and also impact the growth and cognitive development
3 of the baby, and also metabolic ill health in later life which may require resource-intensive
4 management.

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

7 **References**

8 **Chessex 1989**

9 Chessex, P., Gagne, G., Pineault, M., Vaucher, J., Bisaillon, S., Brisson, G., Metabolic and
10 clinical consequences of changing from high-glucose to high-fat regimens in parenterally fed
11 newborn infants, *Journal of Pediatrics*, 115, 992-997, 1989

12 **Jones 1995**

13 Jones, M. O., Pierro, A., Garlick, P. J., McNurlan, M. A., Donnell, S. C., Lloyd, D. A., Protein
14 metabolism kinetics in neonates: effect of intravenous carbohydrate and fat, *Journal of*
15 *pediatric surgery*, 30, 458-62, 1995

16 **Koletzko 2005**

17 Koletzko, B., Goutle, O., Hunt, J., Krohn, K., Shamir, R., for the Parenteral Nutrition
18 Guidelines Working Group. Guidelines on Paediatric Parenteral Nutrition of the European
19 Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the
20 European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the
21 European Society of Pediatric Research (ESPR). *Journal of Pediatric, Gastroenterology and*
22 *Nutrition*, 41, S1-S4, 2005.

23 **Salas-Salvado 1993**

24 Salas-Salvado, J., Molina, J., Figueras, J., Masso, J., Marti-Henneberg, C., Jimenez, R.,
25 Effect of the quality of infused energy on substrate utilization in the newborn receiving total
26 parenteral nutrition, *Pediatric research*, 33, 112-7, 1993

27

28

1 Appendices

2 Appendix A – Review protocols

3 Review protocol for review question: What are the most effective relative amounts of carbohydrates and lipids (starting and target dose)?

5 Table 3: Review protocol for ratio of carbohydrates and lipids

Field (based on PRISMA-P)	Content
Review question	What are the most effective relative amounts of carbohydrates and lipids (starting and target dose)?
Type of review question	Intervention
Objective of the review	What is the optimal energy ratio and daily amounts of intravenous carbohydrates and lipids?
Eligibility criteria – population/disease/condition/issue/domain	<ul style="list-style-type: none"> • 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)	Ratio of carbohydrate to lipid
Eligibility criteria – comparator(s)/control or reference (gold) standard	Other ratios of carbohydrate to lipid
Outcomes and prioritisation	<p>Critical</p> <ul style="list-style-type: none"> • Neurodevelopmental outcomes (general cognitive abilities at two years corrected age as measured by a validated scale) • Growth/Anthropometric measures: <ul style="list-style-type: none"> ○ Weight gain (g/kg/d) ○ Linear growth ○ Head circumference (mm) • Body composition (measured as lean mass, fat-free mass, fat mass, adipose tissue), • Adverse effects of PN <ul style="list-style-type: none"> ○ Infection (including sepsis)

Field (based on PRISMA-P)	Content
	<ul style="list-style-type: none"> ○ Hyperglycaemia ○ Hypoglycaemia ○ Hypertriglyceridemia ○ Other PN associated liver disease ● Nitrogen balance / nitrogen excretion ● Metabolic acidosis <p>Important</p> <ul style="list-style-type: none"> ● Mortality ● Length of hospital stay ● Nutritional intake (g/kg/day) (prescribed nitrogen/non-nitrogen, carbohydrates and lipids actually received)
Eligibility criteria – study design	<p>Only published full text papers-</p> <ul style="list-style-type: none"> ● Systematic reviews of RCTs ● RCTs ● Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) ● Non-comparative studies (only if no evidence from RCTs or comparative cohort studies, limited data on critical outcomes to inform decision making) <p>No date restriction needed.</p> <p>Participant numbers (no restrictions for observational studies). For neurodevelopmental outcomes, studies with sample size of minimum 50 participants will be considered.</p> <p>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).</p>
Other inclusion exclusion criteria	<p>Inclusion:</p> <ul style="list-style-type: none"> ● Clinical settings that provide neonatal care or specialist paediatric care. ● UK and non-UK studies (non-UK studies from middle and high income countries according to WHO/World Bank criteria).
Proposed sensitivity/sub-group analysis, or meta-regression	<ul style="list-style-type: none"> ● Parents or carers whose first language is not English ● Parents or carers who have learning difficulties or disabilities <p>There are inequalities that have been identified relating to how information is provided to them and the type of support they need.</p>

Field (based on PRISMA-P)	Content
	<ul style="list-style-type: none"> • It is known that being a young woman (aged 17 years or under) or a woman with a low socioeconomic status increases the risk of giving birth to a baby preterm. These groups could require particular support and specific recommendations may be required to address their particular needs. <p>Stratified analysis:</p> <ul style="list-style-type: none"> • 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) <p>Subgroup analysis:</p> <p>The following groups will be considered for subgroup analysis:</p> <ul style="list-style-type: none"> • Population subgroups: <ul style="list-style-type: none"> ○ Age of baby ○ Preterm (extremely preterm <28 weeks' GA; very preterm: 28-31 weeks' GA; moderately preterm: 32-36 weeks' GA) ○ Birthweight: low birthweight (<2500g); very low birthweight (<1500g) and extremely low birthweight (<1000g) ○ First week of life and after first week of life ○ Critically ill babies or those requiring surgery (for example, inotropic support, therapeutic hypothermia or fluid restriction) <p>Confounders:</p> <p>Important confounders (when comparative observational studies are included for interventional reviews)</p> <ul style="list-style-type: none"> • Age of baby • Birthweight: low birthweight (<2500g); very low birthweight (<1500g) and extremely low birthweight (<1000g) • Sex of baby • Gestation (preterm vs. term) • For neurodevelopmental outcomes: <ul style="list-style-type: none"> ○ 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) • Underlying diseases (Chronic lung disease) • Other medications

Field (based on PRISMA-P)	Content
Selection process – duplicate screening/selection/analysis	<p>Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer.</p> <p>A random sample of the references identified in the search will be sifted by a second reviewer. This sample size will be 10% of the total, or 100 studies if the search identifies fewer than 1000 studies. All disagreements in study inclusion will be discussed and resolved between the two reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers.</p>
Data management (software)	<p>Pairwise meta-analyses, if possible, will be performed using Cochrane Review Manager (RevMan5).</p> <p>'GRADEpro' will be used to assess the quality of evidence for each outcome. Low income countries will be downgraded for indirectness.</p> <ul style="list-style-type: none"> • NGA STAR software will be used for generating bibliographies/citations, study sifting, data extraction and recording quality assessment using checklists (ROBIS (systematic reviews and meta-analyses); Cochrane risk of bias tool (RCTs or comparative cohort studies); Cochrane risk of bias tool (Non-randomised studies); Newcastle-Ottawa scale (Non-comparative studies)).
Information sources – databases and dates	<p>Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase.</p> <p>Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit.</p> <p>Supplementary search techniques: No supplementary search techniques were used.</p> <p>See appendix B for full strategies.</p>
Identify if an update	This is a new topic for the guideline and is not an update.
Author contacts	<p>Developer: The National Guideline Alliance</p> <p>https://www.nice.org.uk/guidance/indevelopment/gid-ng10037</p>
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).

Field (based on PRISMA-P)	Content
Data items – define all variables to be collected	For details please see appendix B.
Methods for assessing bias at outcome/study level	<p>Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual 2014</p> <p>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/</p>
Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual 2014
Methods for analysis – combining studies and exploring (in)consistency	For details of the methods please see supplementary material C.
Meta-bias assessment – publication bias, selective reporting bias	<p>For details please see section 6.2 of Developing NICE guidelines: the manual 2014</p> <p>If sufficient relevant RCTs evidence is available, publication bias will be explored using RevMan software to examine funnel plots.</p> <p>Trial registries will be examined to identify missing evidence: Clinical trials.gov, NIHR Clinical Trials Gateway.</p>
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014
Rationale/context – Current management	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	<p>A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Dr 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</p> <p>Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details of the methods please see supplementary material C.</p>
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.

Field (based on PRISMA-P)	Content
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.
PROSPERO registration number	Not registered with PROSPERO.

1 *BPD: Bronchopulmonary dysplasia; CDSR: Cochrane Database of Systematic Reviews; CCTR: Cochrane Controlled Trials Register; DARE: Database of Abstracts of Reviews*
2 *of Effects; GA: gestational age; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; ICF: International*
3 *Classification of Functioning, Disability and Health; IVH: Intraventricular haemorrhage of the newborn; MID: minimally important difference; NEC: Necrotising enterocolitis;*
4 *NGA: National Guideline Alliance; NIHR: National Institute for Health Research; NHS: National health service; NICE: National Institute for Health and Care Excellence; PN:*
5 *Parenteral nutrition; PRISMA-P: preferred reporting items for systematic review and meta-analysis protocols; PROSPERO: International prospective register of systematic*
6 *reviews; PVL: Periventricular leukomalacia; RCT: randomised controlled trial; RoB: risk of bias; ROBIS: risk of bias in systematic reviews; ROP: Retinopathy of prematurity;*
7 *SES: Social economic status; UK: United Kingdom; WHO: World Health Organisation.*

1 Appendix B – Literature search strategies

2 Literature search strategies for review question: What are the most effective 3 relative amounts of carbohydrate and lipids (starting and target dose)?

4

5 [Note: One combined search was conducted for questions D7 and D8]

6 Databases: Medline; Medline Epub Ahead of Print; and Medline In-Process & Other 7 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/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
19	INFUSIONS, INTRAVENOUS/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
20	CATHETERIZATION, CENTRAL VENOUS/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
21	exp CATHETERIZATION, PERIPHERAL/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
22	((parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
23	((peripheral\$ or central\$) adj3 line? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
24	(catheter\$ adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
25	(drip? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
26	or/15-25
27	NITROGEN/ and ratio?.ti,ab.
28	(ratio? adj10 nitrogen).mp.
29	exp PROTEINS/ and ratio?.ti,ab.
30	(ratio? adj10 (protein? or conalbumin or ovalbumin or avidin or ovomucin or phosvitin or whey or casein? or lactalbumin or lactoglobulin? or lactoferrin)).mp.
31	exp AMINO ACIDS/ and ratio?.mp.
32	(ratio? adj10 (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 Dextrothroxine 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-Amino adipic 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 Diazo oxonorleucine 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.
33	or/27-32
34	(nitrogen adj5 (nonnitrogen or non-nitrogen)).mp.
35	((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\$) adj10 nitrogen).mp.

#	Searches
36	((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\$) adj10 (protein? or conalbumin or ovalbumin or avidin or ovomucin or phosvitin or whey or casein? or lactalbumin or lactoglobulin? or lactoferrin)).mp.
37	((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\$) adj10 (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 Dextrothroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyl-dopa or Levodopa or Methyl-dopa 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-Amino adipic 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 Homocystine 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 Diazo oxonorleucine or Aminoevalulinic 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.
38	or/35-37
39	((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\$) adj10 (nonnitrogen or non-nitrogen)).mp.
40	NITROGEN/ad [Administration & Dosage]
41	exp PROTEINS/ad [Administration & Dosage]
42	exp AMINO ACIDS/ad [Administration & Dosage]
43	or/40-42
44	exp LIPIDS/ and ratio?.ti,ab.
45	exp PROSTAGLANDINS/ and ratio?.ti,ab.
46	44 not 45
47	((ratio? or amount?) adj10 (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 Eicosatetraenoic 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 Prostanoid 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.
48	or/46-47
49	exp CARBOHYDRATES/ and ratio?.ti,ab.
50	exp HEPARIN/ and ratio?.ti,ab.
51	exp GLYCOPEPTIDES/ and ratio?.ti,ab.
52	exp AMINOGLYCOSIDES/ and ratio?.ti,ab.
53	or/50-52
54	49 not 53
55	((ratio? or amount?) adj10 (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

#	Searches
	Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? 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 Galactose? 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 Methylglucoside? 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 Tarttronate? 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 Glycerolphosphorylcholine 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.
56	or/54-55
57	FAT EMULSIONS, INTRAVENOUS/ and ratio?.ti,ab.
58	(ratio? adj10 macronutrient?).mp.
59	((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\$) adj10 macronutrient?).mp.
60	or/58-59
61	((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\$) adj10 (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 Eicosatetraenoic 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 Oxylin? 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 Prostanoid 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 Glycerolphosphorylcholine 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 Cholesterol 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.
62	((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\$) adj10 (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

#	Searches
	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 Acetyldigoxin? 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.
63	exp LIPIDS/ad [Administration & Dosage]
64	exp PROSTAGLANDINS/ad [Administration & Dosage]
65	63 not 64
66	exp CARBOHYDRATES/ad [Administration & Dosage]
67	exp HEPARIN/ad [Administration & Dosage]
68	exp GLYCOPEPTIDES/ad [Administration & Dosage]
69	exp AMINOGLYCOSIDES/ad [Administration & Dosage]
70	or/67-69
71	66 not 70
72	ENERGY INTAKE/ and ratio?.ti,ab.
73	ENERGY METABOLISM/ and ratio?.ti,ab.
74	(energy adj10 ratio?).ti,ab.
75	or/72-74
76	14 and 26 and 33
77	14 and 26 and 34
78	14 and 26 and 38 and (39 or 61 or 62)
79	14 and 26 and 43 and (65 or 71)
80	or/76-79
81	14 and 26 and 48
82	14 and 26 and 56
83	14 and 57
84	14 and 26 and 60
85	14 and 26 and 61 and 62
86	14 and 26 and 65 and 71
87	or/81-86
88	14 and 26 and 75
89	80 or 87 or 88
90	limit 89 to english language
91	LETTER/
92	EDITORIAL/
93	NEWS/
94	exp HISTORICAL ARTICLE/
95	ANECDOTES AS TOPIC/
96	COMMENT/
97	CASE REPORT/
98	(letter or comment*).ti.
99	or/91-98
100	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
101	99 not 100

#	Searches
102	ANIMALS/ not HUMANS/
103	exp ANIMALS, LABORATORY/
104	exp ANIMAL EXPERIMENTATION/
105	exp MODELS, ANIMAL/
106	exp RODENTIA/
107	(rat or rats or mouse or mice).ti.
108	or/101-107
109	90 not 108

1

2 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/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
20	exp INTRAVENOUS CATHETER/ and (nutrition\$ or feed\$ or fed\$).ti,ab.
21	((parenteral\$ or intravenous\$ or intra-venous\$ or IV or venous\$ or infusion?) adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
22	((peripheral\$ or central\$) adj3 line? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
23	(catheter\$ adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
24	(drip? adj3 (nutrition\$ or feed\$ or fed\$)).ti,ab.
25	or/14-24
26	NITROGEN/ and ratio?.ti,ab.
27	(ratio? adj10 nitrogen).mp.
28	PROTEIN/ and ratio?.ti,ab.
29	(ratio? adj10 (protein? or conalbumin or ovalbumin or avidin or ovomucin or phosvitin or whey or casein? or lactalbumin or lactoglobulin? or lactoferrin)).mp.
30	exp AMINO ACIDS/ and ratio?.ti,ab.
31	(ratio? adj10 (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 Methylidopa 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 Diazo oxonorleucine 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.
32	or/26-31
33	(nitrogen adj5 (nonnitrogen or non-nitrogen)).mp.
34	((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\$) adj10 nitrogen).mp.

#	Searches
35	((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\$) adj10 (protein? or conalbumin or ovalbumin or avidin or ovomucin or phosvitin or whey or casein? or lactalbumin or lactoglobulin? or lactoferrin)).mp.
36	((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\$) adj10 (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 Dextrothroxine or Phenylalanine or Dihydroxyphenylalanine or Cysteinyl-dopa or Levodopa or Methyl-dopa 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-Amino adipic 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 Diazo oxonorleucine or Aminovulvinic Acid or Aminovanine 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.
37	or/34-36
38	((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\$) adj10 (nonnitrogen or non-nitrogen)).mp.
39	NITROGEN/do [Drug Dose]
40	PROTEIN/do [Drug Dose]
41	exp AMINO ACIDS/do [Drug Dose]
42	or/39-41
43	exp LIPID/ and ratio?.ti,ab.
44	exp PROSTAGLANDIN/ and ratio?.ti,ab.
45	43 not 44
46	((ratio? or amount?) adj10 (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 Eicosatetraenoic 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 Prostanoid 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.
47	or/45-46
48	exp CARBOHYDRATE/ and ratio?.ti,ab.
49	exp HEPARIN/ and ratio?.ti,ab.
50	exp GLYCOPEPTIDE/ and ratio?.ti,ab.
51	exp AMINOGLYCOSIDE/ and ratio?.ti,ab.
52	or/49-51
53	48 not 52
54	((ratio? or amount?) adj10 (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

#	Searches
	Glycoconjugate? or Glycolipid? or Galactolipid? or Glycosphingolipid? or Ganglioside? or Sulfoglycosphingolipid? or Ceramide? or Cerebroside? or Galactosylceramide? or Glucosylceramide? 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 Methylglucoside? 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-Deoxyojirimycin 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 Tarttronate? 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 Glycerolphosphorylcholine 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.
55	or/53-54
56	MACRONUTRIENT/ and ratio?.ti,ab.
57	(ratio? adj10 macronutrient?).mp.
58	((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\$) adj10 macronutrient?).mp.
59	or/56-58
60	((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\$) adj10 (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 Eicosatetraenoic 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 Oxylin? 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 Prostanoid 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 Glycerolphosphorylcholine 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 Cholesterol 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.
61	((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\$) adj10 (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

#	Searches
	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 Acetyldigoxin? 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 Sifofiran 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 Heparin 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 Tarttronate? 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.
62	exp LIPID/do [Drug Dose]
63	exp PROSTAGLANDIN/do [Drug Dose]
64	62 not 63
65	exp CARBOHYDRATE/do [Drug Dose]
66	exp HEPARIN/do [Drug Dose]
67	exp GLYCOPEPTIDE/do [Drug Dose]
68	exp AMINOGLYCOSIDE/do [Drug Dose]
69	or/66-68
70	65 not 69
71	CALORIC INTAKE/ and ratio?.ti,ab.
72	ENERGY METABOLISM/ and ratio?.ti,ab.
73	(energy adj10 ratio?).ti,ab.
74	or/71-73
75	13 and 25 and 32
76	13 and 25 and 33
77	13 and 25 and 37 and (38 or 60 or 61)
78	13 and 25 and 42 and (64 or 70)
79	or/75-78
80	13 and 25 and 47
81	13 and 25 and 55
82	13 and 25 and 59
83	13 and 25 and 60 and 61
84	13 and 25 and 64 and 70
85	or/80-84
86	13 and 25 and 74
87	79 or 85 or 86
88	limit 87 to english language
89	letter.pt. or LETTER/
90	note.pt.
91	editorial.pt.
92	CASE REPORT/ or CASE STUDY/
93	(letter or comment*).ti.
94	or/89-93
95	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
96	94 not 95
97	ANIMAL/ not HUMAN/
98	NONHUMAN/
99	exp ANIMAL EXPERIMENT/
100	exp EXPERIMENTAL ANIMAL/

#	Searches
101	ANIMAL MODEL/
102	exp RODENT/
103	(rat or rats or mouse or mice).ti.
104	or/96-103
105	88 not 104

1

2 **Databases: Cochrane Central Register of Controlled Trials; Cochrane Database of**
3 **Systematic Reviews; Database of Abstracts of Reviews of Effects; and Health**
4 **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	#18 or #19 or #20 or #21
#23	(nutrition* or feed* or fed*):ti,ab
#24	#22 and #23
#25	((parenteral* or intravenous* or intra-venous* or IV or venous* or infusion?) near/3 (nutrition* or feed* or fed*)):ti,ab
#26	((peripheral* or central*) near/3 line? near/3 (nutrition* or feed* or fed*)):ti,ab
#27	(catheter* near/3 (nutrition* or feed* or fed*)):ti,ab
#28	(drip? near/3 (nutrition* or feed* or fed*)):ti,ab
#29	#15 or #16 or #17 or #24 or #25 or #26 or #27 or #28
#30	MeSH descriptor: [Nitrogen] this term only
#31	MeSH descriptor: [Proteins] explode all trees
#32	MeSH descriptor: [Amino Acids] explode all trees
#33	#30 or #31 or #32
#34	ratio*:ti,ab
#35	#33 and #34
#36	(ratio* near/10 nitrogen):ti,ab
#37	(ratio* near/10 (protein* or conalbumin or ovalbumin or avidin or ovomucin or phosvitin or whey or casein* or lactalbumin or lactoglobulin* or lactoferrin)):ti,ab
#38	(ratio* near/10 ("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 Methyl-dopa 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-Aminoacidipic 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 Diazoaxonorleucine or "Aminolevulinic Acid" or Canavanine or Creatine or Phosphocreatine or Glycine* or Allylglycine or "Glycocholic Acid" or "Glycodeoxycholic

#	Searches
	Acid" or "Glycochenodeoxycholic Acid" or Sarcosine or Homoserine or Kynurenine or "Oxamic Acid" or "Phosphoamino Acid*" or "Quisqualic Acid")):ti,ab
#39	#35 or #36 or #37 #38
#40	(nitrogen near/5 (nonnitrogen or non-nitrogen)):ti,ab
#41	((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/10 nitrogen):ti,ab
#42	((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/10 (protein* or conalbumin or ovalbumin or avidin or ovomucin or phosvitin or whey or casein* or lactalbumin or lactoglobulin* or lactoferrin)):ti,ab
#43	((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/10 ("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 Aminornithine 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 Methylidopa 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
#44	#41 or #42 or #43
#45	((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/10 (nonnitrogen or non-nitrogen)):ti,ab
#46	MeSH descriptor: [Nitrogen] this term only and with qualifier(s): [administration & dosage - AD]
#47	MeSH descriptor: [Proteins] explode all trees and with qualifier(s): [administration & dosage - AD]
#48	MeSH descriptor: [Amino Acids] explode all trees and with qualifier(s): [administration & dosage - AD]
#49	#46 or #47 or #48
#50	MeSH descriptor: [Lipids] explode all trees
#51	ratio?:ti,ab
#52	#50 and #51
#53	MeSH descriptor: [Prostaglandins] explode all trees
#54	ratio?:ti,ab
#55	#53 and #54
#56	#52 not #55
#57	((ratio? or amount?) near/10 (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 "Eicosatetraenoic 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 Oxylin? 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 Cholesterol or Dehydrocholesterol? or Desmosterol or "19-Iodocholesterol" or Oxysterol? or Hydroxycholesterol? or Ketocholesterol? or Ergocalciferol? or "25-Hydroxyvitamin

#	Searches
	D2" or Dihydrotachysterol or Lanosterol or Phytosterol? or Brassinosteroid? or Ecdysteroid? or Sitosterol? or Stigmasterol or Withanolide? or Solanine or Polyhydroxyalkanoate?)):ti,ab
#58	#56 or #57
#59	MeSH descriptor: [Carbohydrates] explode all trees
#60	ratio?:ti,ab
#61	#59 and #60
#62	MeSH descriptor: [Heparin] explode all trees
#63	MeSH descriptor: [Glycopeptides] explode all trees
#64	MeSH descriptor: [Aminoglycosides] explode all trees
#65	#62 or #63 or #64
#66	ratio?:ti,ab
#67	#65 and #66
#68	#61 not #67
#69	((ratio? or amount?) near/10 (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 Cyamarine 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-Deoxyxojirimycin" 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 "Heparin 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
#70	#68 or #69
#71	MeSH descriptor: [Fat Emulsions, Intravenous] this term only
#72	ratio?:ti,ab
#73	#71 and #72
#74	(ratio? near/10 macronutrient?):ti,ab
#75	((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/10 macronutrient?):ti,ab
#76	#74 or #75
#77	((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/10 (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 "Eicosatetraenoic 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

#	Searches
	Glycerolipid? 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 Cholesterol 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
#78	((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/10 (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 Attractiloid 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
#79	MeSH descriptor: [Lipids] explode all trees and with qualifier(s): [administration & dosage - AD]
#80	MeSH descriptor: [Prostaglandins] explode all trees and with qualifier(s): [administration & dosage - AD]
#81	#79 not #80
#82	MeSH descriptor: [Carbohydrates] explode all trees and with qualifier(s): [administration & dosage - AD]
#83	MeSH descriptor: [Heparin] explode all trees and with qualifier(s): [administration & dosage - AD]
#84	MeSH descriptor: [Glycopeptides] explode all trees and with qualifier(s): [administration & dosage - AD]
#85	MeSH descriptor: [Aminoglycosides] explode all trees and with qualifier(s): [administration & dosage - AD]
#86	#83 or #84 or #85
#87	#82 not #86
#88	MeSH descriptor: [Energy Intake] this term only
#89	MeSH descriptor: [Energy Metabolism] this term only
#90	#88 or #89
#91	ratio?:ti,ab
#92	#90 and #91
#93	(energy near/10 ratio?):ti,ab
#94	#92 or #93

#	Searches
#95	#14 and #29 and #39
#96	#14 and #29 and #40
#97	#14 and #29 and #44 and (#45 or #77 or #78)
#98	#14 and #29 and #49 and (#81 or #87)
#99	#95 or #96 or #97 or #98
#100	#14 and #29 and #58
#101	#14 and #29 and #70
#102	#14 and #73
#103	#14 and #29 and #76
#104	#14 and #29 and #77 and #78
#105	#14 and #29 and #81 and #87
#106	#100 or #101 or #102 or #103 or #104 or #105
#107	#14 and #29 and #94
#108	#99 or #106 or #107

1

2

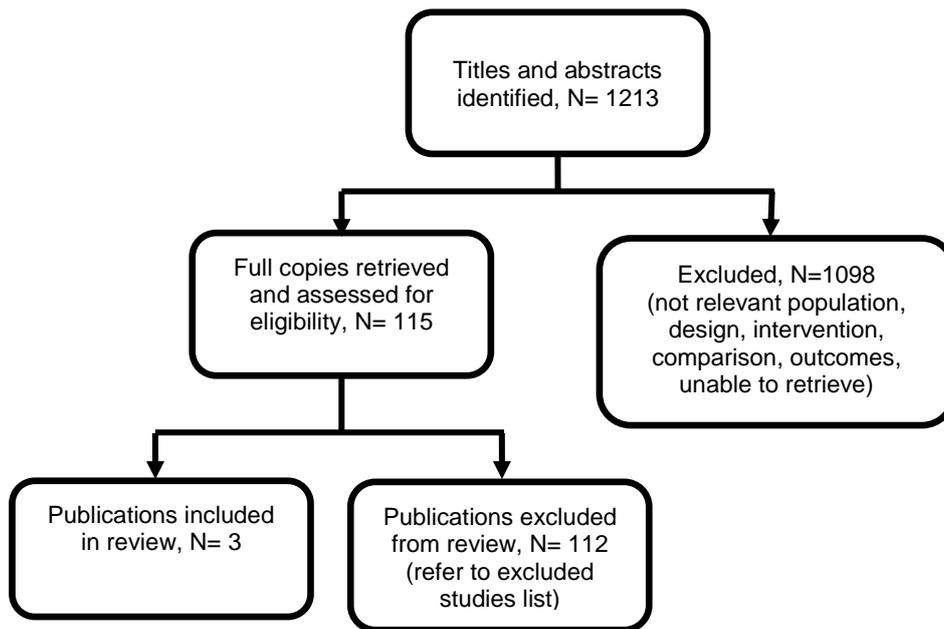
1 Appendix C – Clinical evidence study selection

2 Clinical study selection for review question: What are the most effective relative 3 amounts of carbohydrates and lipids (starting and target dose)?

4

5 Figure 1: PRISMA flow chart of clinical article selection for review question on 6 effective relative amounts of carbohydrates and lipids.

7



8

9

1 Appendix D – Clinical evidence tables

2 Clinical evidence tables for review question: What are the most effective relative amounts of carbohydrates and lipids (starting and target dose)?

4 Table 4: Clinical evidence tables for included studies

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
<p>Full citation Chessex, P., Gagne, G., Pineault, M., Vaucher, J., Bisailon, S., Brisson, G., Metabolic and clinical consequences of changing from high-glucose to high-fat regimens in parenterally fed newborn infants, Journal of Pediatrics, 115, 992-997, 1989 Ref Id 688679</p> <p>Country/ies where the study was carried out Canada</p> <p>Study type Observational study (Non-randomised cross-over study)</p> <p>Aim of the study To assess the clinical and metabolic effects</p>	<p>Sample size n=11 newborn infants</p> <p>Characteristics Gestational age (weeks) - mean \pmSD 37 (3)</p> <p>Age at study (days) - mean \pmSD 8 (3)</p> <p>Birth weight (kg) - mean \pmSD 2.54 (0.54)</p> <p>Weight at study (kg) - mean \pmSD 2.41 (0.57)</p> <p>Parenteral energy and macronutrient intakes Energy (kcal/kg/day) - mean \pmSD High-glucose: 64 (6)</p>	<p>Interventions Day 1 high-glucose intake (12 to 17 gm/kg/day) and low-lipid intake (0 to 1 gm/kg/day)</p> <p>Day 2 Low-glucose (4 to 8 gm/kg/day) and high-lipid (2.5 to 3 gm/kg/day)</p>	<p>Details Parenteral nutrition was initiated because of a gastrointestinal condition precluding oral feeding, such as oesophageal plus duodenal or jejunal atresia (n=7), perforated necrotising enterocolitis (n=2), gastroschisis (n=1) and malrotation with volvulus (n=1).</p> <p>Prior to commencing the study, a 5 to 8-day postsurgical period of stabilisation was allowed to minimise the impact of post-operative catabolism on the study results.</p> <p>Energy intake was progressively increased to reach maintenance energy requirements (60 kcal/kg/day) by the time of the study.</p>	<p>Results Nitrogen excretion (mg/kg/day) - mean \pmSD High-glucose (n=10): 148 (29) High-lipid (n=10): 172 (31) Difference: -24 (10); p<0.05</p>	<p>Limitations Cochrane risk of bias tool for non-randomised trials (ROBINS-I)</p> <p>Confounding bias: Low risk of bias</p> <p>Selection of participant's bias: Low risk of bias (infants received both interventions)</p> <p>Classification of interventions bias: Low risk of bias</p> <p>Deviations from intended interventions bias: Low risk of bias</p> <p>Missing data bias: Low risk of bias (all infants evaluable)</p> <p>Measurement of outcomes bias: High risk of bias (outcome assessors not blinded)</p>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
<p>of changing from a high-carbohydrate to high-lipid regimen during initiation of parenteral nutrition</p> <p>Study dates Not stated</p> <p>Source of funding Grants from the Medical Research Council of Canada and Travenol Canada Inc</p>	<p>High-lipid: 64 (6)</p> <p>Glucose (gm/kg/day) - mean \pmSD High-glucose: 14.5 (1.4) High-lipid: 6.1 (1.2)</p> <p>Non-protein energy intake as glucose (%) - mean \pmSD High-glucose: 96.5 (7.8) High-lipid: 40.2 (4.6)</p> <p>Lipids (gm/kg/day) - mean \pmSD High-glucose: 0.2 (0.4) High-lipid: 2.8 (0.2)</p> <p>Non-protein energy intake as lipid (%) - mean \pmSD High-glucose: 3.5 (7.8) High-lipid: 59.7 (4.6)</p> <p>Amino acids (gm/kg/day) - mean \pmSD High-glucose: 2.4 (0.2) High-lipid: 2.4 (0.2)</p>		<p>Total parenteral nutrition was administered through a peripheral line. Infusion rate of amino acid plus dextrose solution was controlled with an IVAC pump and the rate of fat emulsion was controlled with a syringe pump.</p> <p>Statistical analyses Data presented as mean and standard deviation (SD). Analysis of variance used to compare data for repeated measures.</p>		<p>Selection of the reported results bias: Low risk of bias (all outcomes reported)</p> <p>Other information Potential for carryover effect from treatment on day 1 to day 2.</p>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	<p>Inclusion criteria</p> <p>Babies required to be clinically stable.</p> <p>Birth weight >1500 gm.</p> <p>No jaundice, proven infection, or respiratory problem requiring oxygen supplementation.</p> <p>Able to receive 3 gm/kg/day of lipid emulsion at the time of the study.</p> <p>Exclusion criteria</p> <p>Not stated</p>				
<p>Full citation</p> <p>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</p> <p>Ref Id</p> <p>606424</p> <p>Country/ies where the study was carried out</p> <p>UK</p>	<p>Sample size</p> <p>Total: n=14 infants</p> <p>Intervention: n=9 metabolic studies</p> <p>Comparison: n=9 metabolic studies</p> <p>Characteristics</p> <p>Gestational age (weeks) - mean \pmSEM</p> <p>Intervention: 37.4 (0.8)</p> <p>Comparison: 38.2 (1.2)</p>	<p>Interventions</p> <p>Intervention -Low carbohydrate and high lipid</p> <p>mean \pmSEM: 10.0 (0.01) g/kg/day carbohydrate (dextrose); 4.09 (0.03) g/kg/day fat (intralipid 20%); protein 2.51 (0.01) g/kg/day; 86.16 (0.60) kcal/kg/day total calories)</p> <p>Comparison High Carbohydrate and low lipid</p>	<p>Details</p> <p>All infants received 3 days of continuous TPN with similar caloric intake (86 kcal/kg/day) and protein intake (2.5 g/kg/day). The volume of TPN varied from 120 to 180 mL/kg/day according to the infant's requirements. No enteral feeds were administered.</p> <p>On the third day of the study, infants received a priming dose of 15 μmol/kg of [¹³C]leucine, followed by a 6-hour infusion at 6 μmol/kg/hour.</p>	<p>Results</p> <p>Nitrogen balance (g/kg/day) - mean \pmSEM</p> <p>Intervention: 0.29 (0.02)</p> <p>Comparison: 0.24 (0.02)</p>	<p>Limitations</p> <p>Cochrane risk of bias tool</p> <p>Selection bias</p> <p>Random sequence generation: Unclear risk. Infants were randomly allocated post-operation, however no details provided on the randomisation.</p> <p>Allocation concealment: Unclear risk. No information provided on allocation.</p> <p>Performance bias</p> <p>Blinding of participants and personnel: Unclear risk. Infants would be unaware of their assignment and it would be likely</p>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
<p>Study type Randomised controlled trial</p> <p>Aim of the study To assess the effects of carbohydrate/lipid ratios on nitrogen balance and protein metabolism kinetics in stable newborn infants receiving isonitrogenous and isocaloric total parenteral nutrition (TPN)</p> <p>Study dates Not reported</p> <p>Source of funding Supported by the Scottish Office Agriculture and Fisheries Department</p>	<p>Postnatal age (days) - mean \pmSEM Intervention: 14.6 (4.1) Comparison: 13.3 (2.8)</p> <p>Days post-operation - mean \pmSEM Intervention: 9.1 (2.0) Comparison: 8.5 (2.3)</p> <p>Weight (kg) - mean \pmSEM Intervention: 3.26 (0.2) Comparison: 3.03 (0.2)</p> <p>Inclusion criteria Stable newborn infants</p> <p>Exclusion criteria Infants with sepsis. Infants requiring ventilatory support</p>	<p>- mean \pmSEM: 18.89 (0.03) g/kg/day carbohydrate (dextrose); 0.5 (0.01) g/kg/day fat (intralipid 20%); 2.5 (0.01) g/kg/day protein; 85.61 (0.45) kcal/kg/day total calories.</p>	<p>Infants were studied in an incubator in a thermoneutral environment</p> <p>Statistical analyses Data presented as means \pmSEM. Unpaired t test used to determine the between group differences. (Data converted to SD for inclusion in Meta-analysis)</p>		<p>those responsible for nursing and clinical procedures would not be blinded for safety reasons.</p> <p>Detection bias Blinding of outcome assessment: Low risk. Outcomes are objective.</p> <p>Attrition bias Incomplete outcome data: Low risk. There were no study withdrawals.</p> <p>Reporting bias Selective reporting: Low risk. All outcomes reported.</p> <p>Other bias Other sources of bias: Low risk.</p> <p>Other information All infants had undergone an operation for a gastrointestinal tract anomaly, and received postoperative TPN because it was anticipated that the gastrointestinal tract could not be used for a minimum of 7 days after the operation. The study started at least 4 days post operation, when the infant's general condition had stabilised.</p>
Full citation	Sample size	Interventions	Details	Results	Limitations

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
<p>Salas-Salvado, J., Molina, J., Figueras, J., Masso, J., Marti-Henneberg, C., Jimenez, R., Effect of the quality of infused energy on substrate utilization in the newborn receiving total parenteral nutrition, <i>Pediatric research</i>, 33, 112-7, 1993</p> <p>Ref Id 606778</p> <p>Country/ies where the study was carried out Spain</p> <p>Study type Randomised controlled trial</p> <p>Aim of the study To assess the energy substrate use, gas exchange, and protein metabolism for three different isocaloric, isonitrogenous total parenteral nutrition (TPN) solutions (with varied proportions of calories from fat and glucose) in newborn infants</p> <p>Study dates Not stated</p>	<p>N=26</p> <p>Group A: N=9 Group B: N=9 Group C: N=8</p> <p>Characteristics Birth weight (g) - mean \pmSD Group A: 3272 (780) Group B: 2634 (472) Group C: 2883 (646)</p> <p>Weight at study (g) - mean \pmSD Group A: 3221 (735) Group B: 2629 (575) Group C: 2906 (589)</p> <p>Gestational age (week) mean \pmSD Group A: 39.7 (1.3) Group B: 39.0 (2.7) Group C: 38.9 (2.7)</p> <p>Gender (male/female) - n Group A: 5/4 Group B: 4/5 Group C: 4/4</p> <p>Hypoxic ischaemic encephalopathy - n</p>	<p>Group A: Fat energy (18%) Group B: Fat energy (29%) Group C: Fat energy (40%)</p>	<p>Total PN commenced on day 1 and stabilised by day 5, differing only in the source of non-protein calories (glucose and fat). Non-protein energy intake was provided as a mixture of glucose and long-chain fatty acids.</p> <p>TPN delivered in 20 infants via peripheral catheter, and via central catheter in 6 infants. Non-protein energy intake provided by separate infusion of long-chain fatty acids and glucose over 24 hours. Parenteral solutions were prepared in the hospital pharmacy under aseptic conditions and administered at a constant infusion rate over 24 hours.</p> <p>Statistical analyses Data presented as mean \pmSD. Non-parametric Mann-Whitney tests used for comparisons between groups.</p>	<p>Weight gain over 3 days (g/kg/day) mean \pmSD Group A: 8.4 (7.9) Group B: 8.3 (8.4)</p> <p>Glucose intake (g/kg/day) - mean Group A: 19.2 Group B: 16.8 Group C: 14.4</p> <p>Fat intake (g/kg/day) - mean Group A: 1.5 Group B: 2.5 Group C: 3.5</p>	<p>Cochrane risk of bias tool Selection bias Random sequence generation: Unclear risk (No details provided on the method of randomisation).</p> <p>Allocation concealment: Unclear risk (No information provided on the method of allocation).</p> <p>Performance bias Blinding of participants and personnel: Unclear risk (Infants would be unaware of their assignment however it is unclear whether personnel were blinded).</p> <p>Detection bias Blinding of outcome assessment: Unclear risk (Outcomes are objective, but no details provided).</p> <p>Attrition bias Incomplete outcome data: Unclear risk (The study does not comment on withdrawals or exclusions).</p> <p>Reporting bias Selective reporting: Low risk (selective outcome reporting not detected).</p> <p>Other bias</p>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Supported in part by the European Society of Parenteral and Enteral Nutrition and the ORDESA, NUTREXPA Society	Group A: 8 Group B: 7 Group C: 5 Necrotising enterocolitis - n Group A: 1 Group B: 1 Group C: 1 Gastroschisis - n Group A: 0 Group B: 0 Group C: 1 Inclusion criteria <ul style="list-style-type: none"> • Newborn infants with unchanging clinical condition, in whom total PN was clinically indicated. • 24 hours haemodynamic stabilisation period preceding the study. Exclusion criteria Not stated				Other sources of bias: Low risk (no other bias detected). Other information Two infants in Group A and Group B, and 4 infants in Group C were administered phenobarbital.

1 PN: Parenteral nutrition; ROBINS-I: risk of bias in non-randomised studies of interventions; SD: standard deviation; SEM: standard error of the mean; TNP: Total
 2 parenteral nutrition; UK: United Kingdom.

3

1 **Appendix E – Forest plots**

2 **Forest plots for review question: What are the most effective relative amounts of** 3 **carbohydrates and lipids (starting and target dose)?**

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

1 Appendix F – GRADE tables

2 GRADE tables for review question: What are the most effective relative amounts of carbohydrates and lipids (starting and target dose)?

4 Table 5: Clinical evidence profile for comparison high carbohydrate and low lipid versus low carbohydrate and high lipid

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High carb and low lipid	Low carb and high lipid	Relative (95% CI)	Absolute		
Nitrogen excretion (g/kg/day) (follow-up mean 3 days; Better indicated by lower values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	9	9	-	MD 0.04 higher (0.03 lower to 0.11 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Nitrogen excretion (mg/kg/day) (follow-up mean 2 days; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ³	none	10*	10*	-	MD 24 lower (50.31 lower to 2.31 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Nitrogen balance (follow-up mean 3 days; Better indicated by lower values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ⁴	none	9	9	-	MD 0.05 lower (0.09 to 0.01 lower)	⊕⊕⊕⊕ LOW	CRITICAL

5 CI: confidence interval; MD; mean difference.

6 ¹ Serious risk of bias due to unclear selection bias, no details are provided about randomisation or allocation procedures. Unclear if study personnel were blind to treatment allocation.

7 ² Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses two default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (-0.03 and 0.03).

8 ³ 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 (-15.5).

9 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 (-0.01).

1 *cross over study – 10 babies, acting as their own control

2 **Table 6: Clinical evidence profile for medium lipid (29%) versus low lipid (18%)**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Medium lipid (29%)	Low lipid (18%)	Relative (95% CI)	Absolute		
Weight gain (follow-up mean 3 days; Better indicated by higher values)												
1	randomised trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	9	9	-	MD 0.1 lower (7.63 lower to 7.43 higher)	⊕000 VERY LOW	CRITICAL

3 *CI: confidence interval; MD; mean difference.*

4 ¹ Very serious risk of bias due to unclear allocation methods, unclear randomisation methods, including sequence generation. Risk of performance and detection bias as unclear if care staff, or assessors were blind to treatment

5 ² Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses two default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (-3.95 and 3.95).

7 **Table 7: Clinical evidence profile for high lipid (40%) versus low lipid (18%)**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High lipid (40%)	Low lipid (18%)	Relative (95% CI)	Absolute		
Weight gain (follow-up mean 3 days; Better indicated by higher values)												
1	randomised trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	9	8	-	MD 4.9 higher (4.42 lower to 14.22 higher)	⊕000 VERY LOW	CRITICAL

8 *CI: confidence interval; MD; mean difference.*

9 ¹ Very serious risk of bias due to unclear allocation methods, unclear randomisation methods, including sequence generation. Risk of performance and detection bias as unclear if care staff, or assessors were blind to treatment

10 ² Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses two default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (-3.95 and 3.95).

1

2 **Table 8: Clinical evidence profile for high lipid (40%) versus medium lipid (29%)**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High lipid (40%)	Medium lipid (29%)	Relative (95% CI)	Absolute		
Weight gain (follow-up mean 3 days; Better indicated by higher values)												
1	randomised trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	9	8	-	MD 5 higher (4.51 lower to 14.51 higher)	⊕000 VERY LOW	CRITICAL

3

CI: confidence interval; MD; mean difference.

4

¹ Very serious risk of bias due to unclear allocation methods, unclear randomisation methods, including sequence generation. Risk of performance and detection bias as unclear if care staff, or assessors were blind to treatment

5

² Evidence was downgraded by 2 due to very serious imprecision, 95% confidence interval crosses two default MID for continuous outcomes, calculated as 0.5 x SD control at baseline (-4.2 and 4.2).

6

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

2 **Economic evidence study selection for review question: What are the most effective** 3 **relative amounts of carbohydrates and lipids (starting and target dose)?**

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

6

1 **Appendix H – Economic evidence tables**

2 **Economic evidence tables for review question: What are the most effective relative** 3 **amounts of carbohydrates and lipids (starting and target dose)?**

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

1 **Appendix I – Economic evidence profiles**

2 **Economic evidence profiles for review question: What are the most effective relative** 3 **amounts of carbohydrates and lipids (starting and target dose)?**

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

5

1 Appendix J – Economic analysis

2 Economic analysis for review question: What are the most effective relative amounts 3 of carbohydrates and lipids (starting and target dose)?

4 No economic analysis was conducted for this review question.

5 Appendix K – Excluded studies

6 Excluded studies for review question: What are the most effective relative amounts of 7 carbohydrates and lipids (starting and target dose)?

8 Clinical studies

9 **Table 9: Excluded studies and reasons for their exclusion (one search was conducted for**
10 **two review questions; D7 and D8)**

Study	Reason for Exclusion
Adamkin, D. H., McClead, R. E., Jr., Desai, N. S., McCulloch, K. M., Marchildon, M. B., Comparison of two neonatal intravenous amino acid formulations in preterm infants: a multicenter study, <i>Journal of perinatology : official journal of the California Perinatal Association</i> , 11, 375-82, 1991	Intervention does not fit the inclusion criteria: Different AA intakes.
Aiken, C. G. A., Pathogenesis of metabolic acidosis in preterm infants, <i>Journal of Paediatrics and Child Health</i> , 48, 135, 2012	Conference abstract - insufficient information.
Altman, R. P., Randolph, J. G., Application and hazards of total parenteral nutrition in infants, <i>Annals of Surgery</i> , 174, 85-90, 1971	Study design and population does not meet protocol eligibility criteria - babies aged 3 days 10 15 weeks; presented as case reports.
Anderson, T. L., Muttart, C. R., Bieber, M. A., Nicholson, J. F., Heird, W. C., A controlled trial of glucose versus glucose and amino acids in premature infants, <i>Journal of Pediatrics</i> , 94, 947-51, 1979	Intervention does not fit the inclusion criteria: Glucose vs. Glucose AA.
Asch, M. J., Huxtable, R. F., Hays, D. M., High calorie parenteral therapy in infants and children, <i>Arch.Surg.</i> , 104, 434-437, 1972	Study intervention does not meet protocol eligibility criteria - starting and target doses not reported.
Bassiouny, Mohamed R., Almarsafawy, Hala, Abdel-Hady, Hesham, Nasef, Nehad, Hammad, Tarek A., Aly, Hany, A randomized controlled trial on parenteral nutrition, oxidative stress, and chronic lung diseases in preterm infants, <i>Journal of pediatric gastroenterology and nutrition</i> , 48, 363-9, 2009	Intervention does not fit the inclusion criteria: Different AA intakes.
Biagetti, C., Bellagamba, M. P., D'Ascenzo, R., Burattini, I., Cogo, P. E., Carnielli, V. P., Increasing amino acid and non-protein energy in preterms on parenteral nutrition: Higher rate of sepsis and no benefit in short-term growth, <i>Archives of Disease in Childhood</i> , 99, A132, 2014	Study design does not meet eligibility criteria - conference abstract.
Bonsante, F., Iacobelli, S., Chantegret, C., Martin, D., Gouyon, J.B., The effect of parenteral nitrogen and energy intake on electrolyte balance in the preterm	Intervention does not fit the inclusion criteria: Different AA intakes.

Study	Reason for Exclusion
infant, European Journal of Clinical Nutrition, 65, 1088-1093, 2011	
Bresson, J. L., Bader, B., Rocchiccioli, F., Mariotti, A., Ricour, C., Sachs, C., Rey, J., Protein-metabolism kinetics and energy-substrate utilization in infants fed parenteral solutions with different glucose-fat ratios, The American journal of clinical nutrition, 54, 370-6, 1991	Outcome of interest does not fit the inclusion criteria: metabolism.
Bulbul, Ali, Okan, Fusun, Bulbul, Lida, Nuhoglu, Asiye, Effect of low versus high early parenteral nutrition on plasma amino acid profiles in very low birth-weight infants, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 25, 770-6, 2012	Study intervention does not meet protocol eligibility criteria - focus on high vs low amino acids; only target non-protein calories reported; lipids and carbohydrates same for all babies.
Callaghan, F., Morgan, C., Target parenteral protein attainment in parenterally fed preterm infants following the implementation of the concentrated macronutrients in parenteral standardised solutions (CoMPaSS) programme, Journal of Pediatric Gastroenterology and Nutrition, 64, 805, 2017	Abstract.
Can, E., Bulbul, A., Uslu, S., Comert, S., Bolat, F., Nuhoglu, A., Evaluation of two different types of parenteral nutrition on early growth of preterm infants, Early Human Development, 86, S85, 2010	Study design does not meet eligibility criteria - conference abstract.
Can, E., Bülbül, A., Uslu, S., Cömert, S., Bolat, F., Nuhoğlu, A., Effects of aggressive parenteral nutrition on growth and clinical outcome in preterm infants, Pediatrics International, 54, 869-874, 2012	Study intervention does not meet protocol eligibility criteria - starting and target nitrogen: non-nitrogen energy not reported; target lipid: carbohydrate ratios not reported.
Can, Emrah, Bulbul, Ali, Uslu, Sinan, Comert, Serdar, Bolat, Fatih, Nuhoglu, Asiye, Effects of aggressive parenteral nutrition on growth and clinical outcome in preterm infants, Pediatrics international : official journal of the Japan Pediatric Society, 54, 869-74, 2012	Intervention does not fit the inclusion criteria: Different AA and lipid intakes.
Chen, W. J., Oashi, E., Kasai, M., Amino acid metabolism in parenteral nutrition: with special reference to the calorie: nitrogen ratio and the blood urea nitrogen level, Metabolism: clinical and experimental, 23, 1117-23, 1974	Intervention does not fit the inclusion criteria: Different AA intakes.
Collins, C. T., Gibson, R. A., Miller, J., McPhee, A. J., Willson, K., Smithers, L. G., Makrides, M., Carbohydrate intake is the main determinant of growth in infants born <33 weeks' gestation when protein intake is adequate, Nutrition, 24, 451-7, 2008	Study intervention does not meet protocol eligibility criteria - energy intake reported as medians for all macronutrients for parenteral and enteral nutrients; lipid: carbohydrate ratios not reported.
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 when protein intake is adequate, Nutrition (Burbank, Los Angeles County, Calif.), 24, 451-7, 2008	Intervention does not fit the inclusion criteria: No comparator of interest.

Study	Reason for Exclusion
Cooke, R. J., Yeh, Y. Y., Gibson, D., Debo, D., Bell, G. L., Soybean oil emulsion administration during parenteral nutrition in the preterm infant: effect on essential fatty acid, lipid, and glucose metabolism, <i>The Journal of pediatrics</i> , 111, 767-73, 1987	Outcome of interest does not meet the inclusion criteria: Metabolism.
Cooke, R. J., Zee, P., Yeh, Y. Y., Safflower oil emulsion administration during parenteral nutrition in the preterm infant. 1. Effect on essential fatty acid status, <i>Journal of pediatric gastroenterology and nutrition</i> , 4, 799-803, 1985	Outcome of interest does not meet the inclusion criteria: Essential fatty acid.
D'Ascenzo, R, D'Egidio, S, Angelini, L, Bellagamba, Mp, Manna, M, Pompilio, A, Cogo, Pe, Cogo, Pe, Carnielli, Vp, Parenteral nutrition of preterm infants with a lipid emulsion containing 10% fish oil: effect on plasma lipids and long-chain polyunsaturated fatty acids, <i>Journal of Pediatrics</i> , 159, 33-38.e1, 2011	Intervention does not fit the inclusion criteria: Difference in type of lipid (fish vs. soybean).
De Curtis, M., Dito, L., Lucchini, R., Terrin, G., Nutrition of very low birth-weight infants, <i>Italian Journal of Pediatrics</i> , 40, 2014	Conference abstract.
Deshpande, Girish C., Simmer, Karen, Mori, Trevor, Croft, Kevin, Parenteral lipid emulsions based on olive oil compared with soybean oil in preterm (<28 weeks' gestation) neonates: a randomised controlled trial, <i>Journal of pediatric gastroenterology and nutrition</i> , 49, 619-25, 2009	Intervention does not fit the inclusion criteria: Difference in lipid type (olive vs. soybean).
Deshpande, Girish, Simmer, Karen, Deshmukh, Mangesh, Mori, Trevor A., Croft, Kevin D., Kristensen, Judy, Fish Oil (SMOFlipid) and olive oil lipid (Clinoleic) in very preterm neonates, <i>Journal of pediatric gastroenterology and nutrition</i> , 58, 177-82, 2014	Intervention does not fit the inclusion criteria: Difference in lipid type (olive vs. fish).
DeSilva, Shayana, Hana, Mervat, Sutija, Vesna G., Raziuddin, Khaja, Effect of amino acids on glucose tolerance and hyperkalemia in very low birth weight infants, <i>Journal of Perinatal Medicine</i> , 30, 128-31, 2002	Study does not meet protocol eligibility criteria - babies received same PN regimen.
Dinerstein, A., Nieto, R. M., Solana, C. L., Perez, G. P., Otheguy, L. E., Largaia, A. M., Early and aggressive nutritional strategy (parenteral and enteral) decreases postnatal growth failure in very low birth weight infants, <i>Journal of Perinatology</i> , 26, 436-42, 2006	Intervention does not fit the inclusion criteria: Different AA and lipid intakes.
Dolanski, E. A., Stahlman, M. T., Meng, H. C., Parenteral alimentation of premature infants under 1,200 grams, <i>Southern medical journal</i> , 66, 41-6, 1973	Study does not meet protocol eligibility criteria - PN methods/process; energy ratio and amounts of carbohydrates and lipids not reported.
Dudrick, S. J., Ruberg, R. L., Principles and practice of parenteral nutrition, <i>Gastroenterology</i> , 61, 901-10, 1971	Study design does not meet protocol eligibility criteria - narrative review.
Duffy, B., Gunn, T., Collinge, J., Pencharz, P., The effect of varying protein quality and energy intake on the nitrogen metabolism of parenterally fed very low birthweight (less than 1600 g) infants, <i>Pediatric Research</i> , 15, 1040-4, 1981	Intervention does not fit the inclusion criteria: Different sources of AA.

Study	Reason for Exclusion
Filler, R. M., Eraklis, A. J., Care of the critically ill child: intravenous alimentation, <i>Pediatrics</i> , 46, 456-61, 1970	Study design does not meet protocol eligibility criteria - narrative on PN.
Filler, R. M., Eraklis, A. J., Rubin, V. G., Das, J. B., Long-term total parenteral nutrition in infants, <i>The New England journal of medicine</i> , 281, 589-94, 1969	Study does not meet protocol eligibility criteria - babies aged 15 to 60 days (outcomes not reported separately); relative amounts of energy or carbohydrates and lipids not reported.
Fivez, Tom, Kerklaan, Dorian, Verbruggen, Sascha, Vanhorebeek, Ilse, Verstraete, Soren, Tibboel, Dick, Guerra, Gonzalo Garcia, Wouters, Pieter J., Joffe, Ari, Joosten, Koen, Mesotten, Dieter, Van den Berghe, Greet, Impact of withholding early parenteral nutrition completing enteral nutrition in pediatric critically ill patients (PEPaNIC trial): study protocol for a randomized controlled trial, <i>Trials</i> , 16, 202, 2015	Study protocol.
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, <i>Archives of Disease in Childhood, Fetal and neonatal edition</i> . 73, F13-6, 1995	Comparator of interest does not meet the inclusion criteria: Population served as their own controls. Minimal change in lipid intake (difference of 0.01 g/kg/d).
Fosel, T. H., Uth, M., Wilhelm, W., Gruness, V., Comparison of two solutions with different glucose concentrations for infusion therapy during laparotomies in infants, <i>Infusionstherapie und Transfusionsmedizin</i> , 23, 80-4, 1996	Participants do not fit the inclusion criteria: Infants aged 5-14 months.
Gobel, Y., Koletzko, B., Bohles, H. J., Engelsberger, I., Forget, D., Le Brun, A., Peters, J., Zimmermann, A., Parenteral fat emulsions based on olive and soybean oils: A randomized clinical trial in preterm infants, <i>Journal of Pediatric Gastroenterology and Nutrition</i> , 37, 161-167, 2003	Intervention does not fit the inclusion criteria: Difference in lipid type (olive vs. soybean).
Hay Jr, W. W., Intravenous nutrition of the very preterm neonate, <i>Acta Paediatrica, International Journal of Paediatrics</i> , 94, 47-56, 2005	Study design not relevant to protocol - not a systematic review.
Hays, D. M., Kaplan, M. S., Mahour, G. H., Strauss, J., Huxtable, R. F., High-calorie infusion therapy following surgery in low-birth-weight infants: metabolic problems encountered, <i>Surgery</i> , 71, 834-41, 1972	Study intervention does not meet protocol eligibility criteria - all babies received same PN; only target calories for glucose reported.
Heird, W. C., Driscoll, J. M., Jr., Schullinger, J. N., Grebin, B., Winters, R. W., Intravenous alimentation in pediatric patients, <i>The Journal of pediatrics</i> , 80, 351-72, 1972	Study design not relevant to protocol - not a systematic review.
Heird, W. C., Winters, R. W., Total intravenous alimentation, <i>American journal of diseases of children</i> (1960), 126, 287-9, 1973	Study design does not meet protocol eligibility criteria - narrative.
Hendry, P. G., James, B. E., MacMahon, R. A., Nitrogen balance studies during oral and complete intravenous feeding of small premature infants, <i>Australian Paediatric Journal</i> , 14, 6-10, 1978	Intervention does not fit the inclusion criteria: Different types of AA.
Hirai, Y., Sanada, Y., Hasegawa, S., Fujiwara, T., Iwakiri, K., Total parenteral nutrition in low-birth-weight neonates with complicated surgical	Study does not meet protocol eligibility criteria - infants received same PN regimen.

Study	Reason for Exclusion
disorders; effects and difficulties, The Japanese journal of surgery, 11, 175-83, 1981	
Iacobelli, S., Bonsante, F., Vintejoux, A., Gouyon, J. B., Standardized parenteral nutrition in preterm infants: early impact on fluid and electrolyte balance, Neonatology, 98, 84-90, 2010	Study design does not meet the inclusion criteria - cohort study. Intervention not relevant - comparison of standard versus individualised bags.
Ibrahim, Hassan M., Jeroudi, Majied A., Baier, R. J., Dhanireddy, Ramasubbareddy, Krouskop, Richard W., Aggressive early total parental nutrition in low-birth-weight infants, Journal of perinatology : official journal of the California Perinatal Association, 24, 482-6, 2004	Intervention does not fit the inclusion criteria: Early vs. late PN.
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	Study does not meet protocol eligibility criteria - relationship between sodium, potassium, calcium, magnesium, chlorine and phosphorous.
Janeiro, P., Cunha, M., Marques, A., Moura, M., Barroso, R., Carreiro, H., Caloric intake and weight gain in a neonatal intensive care unit, European Journal of Pediatrics, 169, 99-105, 2010	Study intervention does not meet protocol eligibility criteria - not nitrogen vs non-nitrogen energy; starting and target dose for lipids: carbohydrates not clear.
Joffe, Ari, Anton, Natalie, Lequier, Laurance, Vandermeer, Ben, Tjosvold, Lisa, Larsen, Bodil, Hartling, Lisa, Nutritional support for critically ill children, Cochrane Database of Systematic Reviews, 2016	Intervention does not fit the inclusion criteria: EN vs. PN.
Johnson, Patricia J., Review of macronutrients in parenteral nutrition for neonatal intensive care population, Neonatal network : NN, 33, 29-34, 2014	Study type does not fit the inclusion criteria: Commentary review.
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	Ratio of carbohydrate to lipid not clear and no comparison group. Outcomes not relevant to protocol - correlation to glucose intake.
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	Study does not meet protocol eligibility criteria - case reports; energy and carbohydrate: lipid ratios not reported.
Kanarek, K. S., Williams, P. R., Curran, J. S., Total parenteral nutrition in infants and children, Advances in pediatrics, 29, 151-81, 1982	Not relevant to protocol - not a systematic review.
Kandil, H., Darwish, O., Hammad, S., Zagloul, N., Halliday, D., Millward, J., Nitrogen balance and protein turnover during the growth failure in newly born low-birth-weight infants, The American journal of clinical nutrition, 53, 1411-7, 1991	Conference abstract.
Kesiak, M., Nowiczewski, M., Talar, T., Gulczynska, E., Early use of intravenous lipids in two different doses in the group of very low birth weight newborns - RCT, Early Human Development, 86, S86, 2010	Conference abstract.
Khan, Z., Morris, N., Unterrainer, H., Haiden, N., Holasek, S. J., Urlesberger, B., Effect of standardized feeding protocol on nutrient supply and postnatal growth of preterm infants: A prospective study, Journal of Neonatal-Perinatal	Study intervention does not meet protocol eligibility criteria - relative amounts of nitrogen:non-nitrogen or carbohydrates: lipids not reported.

Study	Reason for Exclusion
MedicineJ Neonatal Perinatal Med, 11, 11-19, 2018	
Kotiya, P., Zhao, X., Cheng, P., Zhu, X., Xiao, Z., Wang, J., Fish oil- and soy oil-based lipid emulsions in neonatal parenteral nutrition: a systematic review and meta-analysis, European journal of clinical nutrition, 70, 1106-1115, 2016	Intervention type does not meet the inclusion criteria: Fish vs. Soy oil.
Lenclen, R., Crauste-Manciet, S., Narcy, P., Boukhouna, S., Geffray, A., Guerrault, M. N., Bordet, F., Brossard, D., Assessment of implementation of a standardized parenteral formulation for early nutritional support of very preterm infants, European Journal of Pediatrics, 165, 512-518, 2006	Study design does not meet inclusion criteria - retrospective study. Interventions not relevant, comparison of standardised versus individualised PN (additionally the lipid intake is the same across interventions).
Lindblad, B. S., Settergren, G., Feychting, H., Persson, B., Total parenteral nutrition in infants. Blood levels of glucose, lactate, pyruvate, free fatty acids, glycerol, d-beta-hydroxybutyrate, triglycerides, free amino acids and insulin, Acta paediatrica Scandinavica, 66, 409-19, 1977	Includes ineligible infants (aged 2 to 10 months) and outcomes are not reported separately in eligible infants.
Lindblad, B. S., Settergren, G., Feychting, H., Persson, B., Total parenteral nutrition in infants. Blood levels of glucose, lactate, pyruvate, free fatty acids, glycerol, D beta hydroxybutyrate, triglycerides, free amino acids and insulin, Acta Paediatrica Scandinavica, 66, 409-419, 1977	Study population does not meet protocol eligibility criteria - babies aged 2 days to 10 months; caloric intake not reported for 1 treatment group.
Malloy, M. H., Rassin, D. K., Richardson, C. J., Total parenteral nutrition in sick preterm infants: effects of cysteine supplementation with nitrogen intakes of 240 and 400 mg/kg/day, Journal of Pediatric Gastroenterology and Nutrition, 3, 239-44, 1984	Comparison not relevant to protocol - high versus low nitrogen.
Martin, Camilia R., Brown, Yolanda F., Ehrenkranz, Richard A., O'Shea, T. Michael, Allred, Elizabeth N., Belfort, Mandy B., McCormick, Marie C., Leviton, Alan, Extremely Low Gestational Age Newborns Study, Investigators, Nutritional practices and growth velocity in the first month of life in extremely premature infants, Pediatrics, 124, 649-57, 2009	Data provided does not present outcomes for different lipid to carbohydrate ratios.
Mayes, K., Tan, M. J., Morgan, C., Hyperalimentation results in paradoxical fall in tyrosine levels in very preterm infants receiving parenteral nutrition, Archives of disease in childhood., 97, A51, 2012	Study design does not meet eligibility criteria - conference abstract.
McIntosh, N., Mitchell, V., A clinical trial of two parenteral nutrition solutions in neonates, Archives of Disease in Childhood, 65, 692-9, 1990	Intervention type does not meet the inclusion criteria: Different types of AA.
Morgan, C, Herwitker, S, Badhawi, I, Hart, A, Tan, M, Mayes, K, Newland, P, Turner, Ma, SCAMP: standardised, concentrated, additional macronutrients, parenteral nutrition in very preterm infants: a phase IV randomised, controlled exploratory study of macronutrient intake, growth and other aspects of neonatal care, BMC Pediatrics, 11, 53, 2011	Study protocol.

Study	Reason for Exclusion
Morgan, C., Burgess, L., Grosdenier, M., Green, J., McGowan, P., Turner, M. A., Hyperalimentionation and blood glucose control in very preterm infants: A randomised controlled parenteral nutrition study, Archives of Disease in Childhood: Fetal and Neonatal Edition, 99, A2-A3, 2014	Conference abstract - insufficient information.
Morgan, C., Burgess, L., Grosdenier, M., McGowan, P., Turner, M. A., Hyperalimentionation and blood glucose control in very preterm infants: The randomised controlled scamp nutrition study, Archives of Disease in Childhood, 99, A208, 2014	Conference abstract - insufficient information.
Morgan, C., McGowan, P., Herwitker, S., Hart, A. E., Turner, M. A., Early postnatal head growth in very preterm infants: The randomised controlled scamp nutrition study, Journal of Neonatal-Perinatal Medicine, 6, 197, 2013	Abstract.
Morgan, C., McGowan, P., Herwitker, S., Hart, A. E., Turner, M. A., Preventing early postnatal head growth failure in very preterm infants: The randomised controlled scamp nutrition study, Archives of Disease in Childhood: Education and Practice Edition, 98, 2013	Conference abstract.
Morgan, C., Parry, S., Tan, M., Neurodevelopmental outcome at 2.5 years in very preterm infants randomised to receive two different parenteral nutrition regimens at birth: The SCAMP nutrition study, Journal of Pediatric Gastroenterology and Nutrition, 64, 764, 2017	Conference abstract - insufficient information.
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	Study design does not meet eligibility criteria - conference abstract.
Morgan, Colin, Herwitker, Shakeel, Badhawi, Isam, Hart, Anna, Tan, Maw, Mayes, Kelly, Newland, Paul, Turner, Mark A., SCAMP: standardised, concentrated, additional macronutrients, parenteral nutrition in very preterm infants: a phase IV randomised, controlled exploratory study of macronutrient intake, growth and other aspects of neonatal care, BMC pediatrics, 11, 53, 2011	Study design does not meet protocol eligibility criteria - study protocol.
Morgan, Colin, McGowan, Patrick, Herwitker, Shakeel, Hart, Anna E., Turner, Mark A., Postnatal head growth in preterm infants: a randomized controlled parenteral nutrition study, Pediatrics, 133, e120-8, 2014	Intervention does not meet inclusion criteria – high AA and lipids vs. low AA and lipids.
Murdock, N., Crighton, A., Nelson, L. M., Forsyth, J. S., Low birthweight infants and total parenteral nutrition immediately after birth. II. Randomised study of biochemical tolerance of intravenous glucose, amino acids, and lipid, Archives of disease in childhood. Fetal and neonatal edition, 73, F8-12, 1995	Intervention type does not meet the inclusion criteria: Glucose vs. glucose AA/lipid.
Najm, S., Lofqvist, C., Hellgren, G., Engstrom, E., Lundgren, P., Hard, A. L., Lapillonne, A., Savman, K., Nilsson, A. K., Andersson, M. X., Smith, L. E.	Intervention type does not meet the inclusion criteria: Compares different types of lipid solutions.

Study	Reason for Exclusion
H., Hellstrom, A., Effects of a lipid emulsion containing fish oil on polyunsaturated fatty acid profiles, growth and morbidities in extremely premature infants: A randomized controlled trial, <i>Clinical Nutrition ESPEN</i> , 20, 17-23, 2017	
O'Neill Jr, J. A., Meng, H. C., Caldwell, M. D., Stahlman, M. T., Metabolic evaluation of a synthetic amino acid mixture for parenteral nutrition in infants and children, <i>Journal of Pediatric Surgery</i> , 11, 979-985, 1976	Study population does not meet protocol eligibility criteria - includes neonates and children aged 1 month to 15 years; unclear whether neonates pre-term or term babies aged up to 28 days.
O'Neill, J. A., Caldwell, M. D., Meng, H. C., Otten, A., Stahlman, M. T., Use of a 10% l-amino acid solution with glucose in pediatric parenteral nutrition, <i>Acta chirurgica Scandinavica. Supplementum</i> , 466, 106-7, 1976	Study does not meet protocol eligibility criteria - unclear whether neonates eligible for inclusion; starting and target amounts for nitrogen: non-nitrogen energy and lipids: carbohydrates not reported.
Ong, E. G., Eaton, S., Wade, A. M., Horn, V., Losty, P. D., Curry, J. I., Sugarman, I. D., Klein, N. J., Pierro, A., Randomized clinical trial of glutamine-supplemented versus standard parenteral nutrition in infants with surgical gastrointestinal disease, <i>British journal of surgery</i> , 99, 929-938, 2012	Study does not meet protocol eligibility criteria - relative amounts of nutrition provided at start of study not reported; energy intake reported as an outcome.
Osborn, D. A., Schindler, T., Jones, L. J., Sinn, J. K. H., Bolisetty, S., Higher versus lower amino acid intake in parenteral nutrition for newborn infants, <i>Cochrane Database of Systematic Reviews</i> , 2018, CD005949, 2018	Systematic review - references checked.
Pawlik, Dorota, Lauterbach, Ryszard, Walczak, Maria, Hurkala, Joanna, Sherman, Michael P., Fish-oil fat emulsion supplementation reduces the risk of retinopathy in very low birth weight infants: a prospective, randomized study, <i>JPEN. Journal of parenteral and enteral nutrition</i> , 38, 711-6, 2014	Intervention type does not meet the inclusion criteria: Fish vs. Soy/olive oil.
Peden, V. H., Karpel, J. T., Total parenteral nutrition in premature infants, <i>The Journal of pediatrics</i> , 81, 137-44, 1972	Study intervention does not meet protocol eligibility criteria - relative amounts of starting does for nitrogen: non-nitrogen energy and carbohydrates: lipids not reported.
Pencharz, P., Beesley, J., Sauer, P., Van Aerde, J., Canagarayar, U., Renner, J., McVey, M., Wesson, D., Swyer, P., Total-body protein turnover in parenterally fed neonates: Effects of energy source studied by using [15N]glycine and [1-13C]leucine, <i>American Journal of Clinical Nutrition</i> , 50, 1395-1400, 1989	Study intervention does not meet protocol eligibility criteria - starting and target doses not reported.
Pineault, M., Chessex, P., Bisailon, S., Brisson, G., Total parenteral nutrition in the newborn: impact of the quality of infused energy on nitrogen metabolism, <i>American Journal of Clinical Nutrition</i> , 47, 298-304, 1988	Included study for D7: Nitrogen/non-nitrogen.
Quan, M., Wang, D., The early-life nutritional status and progress in nutritional support strategy of extremely low birth weight infants in China, <i>Journal of Pediatric Gastroenterology and Nutrition</i> , 62, 819, 2016	Abstract.
Ribed Sanchez, A., Romero Jimenez, R. M., Sanchez De Orgaz, M. C., De Juan, A., Tovar Pozo, M., Diaz Garzon, J., Sanjurjo Saez, M.,	Abstract.

Study	Reason for Exclusion
Early aggressive parenteral nutrition in preterm infants, <i>International Journal of Clinical Pharmacy</i> , 35, 983, 2013	
Ribed Sanchez, Almudena, Romero Jimenez, Rosa Ma, Sanchez Gomez de Orgaz, Ma Carmen, Sanchez Luna, Manuel, Sanjurjo Saez, Maria, Aggressive parenteral nutrition and growth velocity in preterm infants, <i>Nutricion hospitalaria</i> , 28, 2128-34, 2013	No comparison of interest.
Riskin, ArieH, Hartman, Corina, Shamir, Raanan, Parenteral Nutrition in Very Low Birth Weight Preterm Infants, <i>The Israel Medical Association journal</i> : IMAJ, 17, 310-5, 2015	Study design does not meet protocol eligibility criteria - narrative review.
Roelants, Jorine A., Vlaardingbroek, 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, <i>JPEN. Journal of parenteral and enteral nutrition</i> , 42, 122-131, 2018	Study intervention does not meet protocol eligibility criteria - focus on lipids amino acids; ratios not clearly reported.
Rubecz, I., Mestyan, J., Soltesz, G., Horvath, M., Metabolic and hormonal effects of alternate infusion of hypertonic glucose and aminosol-glucose in premature infants, <i>Acta paediatrica Academiae Scientiarum Hungaricae</i> , 15, 301-21, 1974	Study does not meet protocol eligibility criteria - no comparator group; all babies received the same PN regimen.
Rubin, M., Moser, A., Naor, N., Merlob, P., Pakula, R., Sirota, L., Effect of three intravenously administered fat emulsions containing different concentrations of fatty acids on the plasma fatty acid composition of premature infants, <i>The Journal of pediatrics</i> , 125, 596-602, 1994	Intervention type does not meet the inclusion criteria: Compares different types of lipids.
Schanler, R. J., Shulman, R. J., Prestridge, L. L., Parenteral nutrient needs of very low birth weight infants, <i>Journal of Pediatrics</i> , 125, 961-8, 1994	Intervention type does not meet the inclusion criteria: Differ in calcium gluconate and potassium monobasic-dibasic phosphate.
Simmer, K., Rao, S. C., Early introduction of lipids to parenterally-fed preterm infants, <i>Cochrane Database of Systematic Reviews</i> , 2005	Systematic review - relevant references checked.
Stensvold, H. J., Lang, A. M., Strommen, K., Abrahamsen, T. G., Ogland, B., Pripp, A. H., Ronnestad, A. E., Strictly controlled glucose infusion rates are associated with a reduced risk of hyperglycaemia in extremely low birth weight preterm infants, <i>Acta Paediatrica, International Journal of Paediatrics</i> , 107, 442-449, 2018	Study intervention does not meet protocol eligibility criteria - babies received same intake of carbohydrates and lipids during 2 study periods.
Tan, M. J., Cooke, R. W., Improving head growth in very preterm infants - A randomised controlled trial I: Neonatal outcomes, <i>Archives of Disease in Childhood: Fetal and Neonatal Edition</i> , 93, f337-f341, 2008	Intervention does not meet protocol - Hyperalimented PN vs. standard PN.
Tan, M., Parry, S., Morgan, C., Neurodevelopmental outcome in very preterm infants randomised to receive two different parenteral nutrition regimens: The SCAMP nutrition study, <i>Archives of Disease in Childhood</i> , 101, A5, 2016	Conference abstract.

Study	Reason for Exclusion
te Braake, F. W., van den Akker, C. H., Wattimena, D. J., Huijmans, J. G., van Goudoever, J. B., Amino acid administration to premature infants directly after birth, <i>Journal of Pediatrics</i> , 147, 457-461, 2005	Study intervention does not meet protocol eligibility criteria - babies received same amounts of glucose and lipids; focus on amino acids delivered early or late.
Thakur, A., Kansal, B. K., Saini, A., Kler, N., Garg, P., Modi, M., Soni, A., Saluja, S., Effect of aggressive versus standard nutritional regime on growth of extremely low birth weight infants-A randomized controlled trial, <i>Journal of Pediatric Gastroenterology and Nutrition</i> , 66, 1089, 2018	Study design does not meet eligibility criteria - conference abstract.
Torer, Birgin, Hanta, Deniz, Ozdemir, Zeliha, Cetinkaya, Bilin, Gulcan, Hande, An aggressive parenteral nutrition protocol improves growth in preterm infants, <i>The Turkish journal of pediatrics</i> , 57, 236-41, 2015	Study intervention does not meet protocol eligibility criteria - focus on high dose lipids and amino acids vs low dose lipids and amino acids; ratios not clearly reported.
Tottman, A. C., Bloomfield, F. H., Cormack, B. E., Harding, J. E., Mohd Slim, M. A., Weston, A. F., Alswailer, J. M., Relationships between Early Nutrition and Blood Glucose Concentrations in Very Preterm Infants, <i>Journal of Pediatric Gastroenterology and Nutrition</i> , 66, 960-966, 2018	Study intervention does not meet protocol eligibility criteria - starting and target lipids: carbohydrates not clear.
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, <i>Efficacy and Mechanism Evaluation</i> , 3, 2016	Intervention type does not meet the inclusion criteria: High AA vs low AA.
Uthaya, Sabita, Liu, Xinxue, Babalis, Daphne, Dore, Caroline J., Warwick, Jane, Bell, Jimmy, Thomas, Louise, Ashby, Deborah, Durighel, Giuliana, Ederies, Ash, Yanez-Lopez, Monica, Modi, Neena, Nutritional Evaluation and Optimisation in Neonates: a randomized, double-blind controlled trial of amino acid regimen and intravenous lipid composition in preterm parenteral nutrition, <i>The American journal of clinical nutrition</i> , 103, 1443-52, 2016	Intervention type does not meet the inclusion criteria: High AA vs low AA.
Uthaya, Sabita, Liu, Xinxue, Babalis, Daphne, Dore, Caroline, Warwick, Jane, Bell, Jimmy, Thomas, Louise, Ashby, Deborah, Durighel, Giuliana, Ederies, Ash, Yanez-Lopez, Monica, Modi, Neena, 2016	Study interventions do not meet protocol eligibility criteria - starting energy for non-nitrogen: nitrogen not reported; same amount of carbohydrates: lipids administered.
Van Aerde, J. E., Sauer, P. J., Pencharz, P. B., Smith, J. M., Heim, T., Swyer, P. R., Metabolic consequences of increasing energy intake by adding lipid to parenteral nutrition in full-term infants, <i>The American journal of clinical nutrition</i> , 59, 659-62, 1994	Ineligible intervention - comparison of lipid and non-lipid containing parenteral nutrition.
van den Akker, C. H., te Braake, F. W., Schierbeek, H., Rietveld, T., Wattimena, D. J., Bunt, J. E., van Goudoever, J. B., Albumin synthesis in premature neonates is stimulated by parenterally administered amino acids during the	Study intervention does not meet protocol eligibility criteria - glucose vs glucose amino acids (lipids withheld; only nonprotein energy reported as an outcome).

Study	Reason for Exclusion
first days of life, American Journal of Clinical NutritionAm J Clin Nutr, 86, 1003-8, 2007	
van den Akker, C. H., te Braake, F. W., Weisglas-Kuperus, N., van Goudoever, J. B., Observational outcome results following a randomized controlled trial of early amino acid administration in preterm infants, Journal of Pediatric Gastroenterology and Nutrition, 59, 714-719, 2014	Study intervention does not meet protocol eligibility criteria - glucose vs amino acid; starting and target energy not reported; amount of lipid not reported.
van Puffelen, E., Vanhorebeek, I., Joosten, K. F. M., Wouters, P. J., Van den Berghe, G., Verbruggen, S. C. A. T., Early versus late parenteral nutrition in critically ill, term neonates: a preplanned secondary subgroup analysis of the PEPaNIC multicentre, randomised controlled trial, The Lancet Child and Adolescent Health, 2, 505-515, 2018	Study intervention does not meet protocol eligibility criteria - babies receive same PN regimen but early vs late administration.
Vlaardingerbroek, H., Roelants, J. A., Rook, D., Dorst, K., Schierbeek, H., Vermes, A., Vermeulen, M. J., van Goudoever, J. B., van den Akker, C. H., Adaptive regulation of amino acid metabolism on early parenteral lipid and high-dose amino acid administration in VLBW infants - a randomized, controlled trial, Clinical nutrition (Edinburgh, Scotland), 33, 982-990, 2014	Study intervention does not meet protocol eligibility criteria - amino acids lipids vs high amino acids lipids; ratios not clearly reported.
Vlaardingerbroek, H., Rook, D., Van Den Akker, C. H. P., Vermeulen, M. J., Van Goudoever, J. B., Can early parenteral lipid and high dose amino acid administration improve growth in VLBW infants?, Archives of Disease in Childhood, 97, A397, 2012	Study design does not meet eligibility criteria - conference abstract.
Vlaardingerbroek, H., Vermeulen, M. J., Rook, D., van den Akker, C. H., Dorst, K., Wattimena, J. L., Vermes, A., Schierbeek, H., van Goudoever, J. B., Safety and efficacy of early parenteral lipid and high-dose amino acid administration to very low birth weight infants, Journal of Pediatrics, 163, 638-44.e1-5, 2013	Study intervention does not meet protocol eligibility criteria - amino acids lipids vs high amino acids lipids; ratios not clearly reported.
Wagner, J. V., Moe-Byrne, T., Grover, Z., McGuire, W., Glutamine supplementation for young infants with severe gastrointestinal disease, Cochrane database of systematic reviews (Online), 7, CD005947, 2012	Systematic review - references checked.
Wolf, H., Melichar, V., von Berg, W., Kerstan, J., Intravenous alimentation with a mixture of fat, carbohydrates and amino acids in small immature newborn infants--a preliminary report, Die Infusionstherapie, 1, 479-81, 1974	Not relevant to protocol - does not assess different carbohydrate to lipid ratios.
Xie, E., Sun, J., Shen, Y., Ju, H., Li, J., Zhang, G., Huang, P., Influence of early rapidly increased amino acid dosaging on nitrogen balance and growth in preterm infants, Chinese journal of clinical nutrition, 22, 136-140, 2014	Study does not meet protocol eligibility criteria - non-English language (Chinese).
Yu, V. Y. H., James, B., Hendry, P., MacMahon, R. A., Total parenteral nutrition in very low birthweight infants: A controlled trial, Archives of Disease in Childhood, 54, 653-661, 1979	Intervention type does not meet the inclusion criteria: PN vs. EN.

Study	Reason for Exclusion
Zhao, Yiyang, Wu, Yang, Pei, Jiao, Chen, Zude, Wang, Qi, Xiang, Bo, Safety and efficacy of parenteral fish oil-containing lipid emulsions in premature neonates, Journal of pediatric gastroenterology and nutrition, 60, 708-16, 2015	Study does not meet protocol eligibility criteria - comparison of different lipid emulsions.
Zlotkin, S. H., Bryan, M. H., Anderson, G. H., Intravenous nitrogen and energy intakes required to duplicate in utero nitrogen accretion in prematurely born human infants, The Journal of pediatrics, 99, 115-20, 1981	Included study for D7: Nitrogen/non-nitrogen.
Zlotkin, S. H., Intravenous nitrogen intake requirements in full-term newborns undergoing surgery, Pediatrics, 73, 493-6, 1984	Outcome of interest does not fit the inclusion criteria.

1

2 Economic studies

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

5

1 **Appendix L – Research recommendations**

- 2 **Research recommendations for review question: What are the most effective relative**
- 3 **amounts of carbohydrates and lipids (starting and target dose)?**
- 4 No research recommendation was made for this review.