Table 4: Clinical evidence table for included studies

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

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

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

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

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

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

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

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

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