Supplementary Material

Table S1a Studies Including Infants ≤28 Completed Weeks Gestation

Author/Year/ Country	Journal	Gestational Age Range (we	Primary Endpoint/ Outcome	Strengths/ Weaknesses	Findings pertaining to Head Siz	Head Size Reference	Neurodevelopmen Assessments
Bracewell MA et al, 2007, UK	Arch Dis Child Fetal Neonatal Ed.	≤25^{+6}	To study growth and blood pressure in extremely preterm children at 6 years	**Strengths:** Multicentre; large sample size of extremely premature infants; controlled for ethnicity **Weaknesses:** Head size not correlated withneurodevelopmental follow-up	• At 30 months OFC catch-up was significantly worse for those born at <23 weeks • Mean OFC at 6 years rose by 0.21 SD for each gestational week • Birth weight for gestational age had a significant independent additional effect on head size.	The Child Growth Foundation British 1990 reference	
Kuban, 2009, USA	Journal of Pediatrics	<28	To compare infants born with microcephaly and those with normal head size at birth at 2 years.	**Strengths** – Multicentre, large sample size **Weaknesses** – Loss to follow up - 20% of enrolled infants who survived to 24 months lost to follow up. No comment on infants who survived to discharge but not to 24 months	• Congenital microcephaly alone is not a risk factor, unless persistent • 71% with congenital microcephaly not microcephalic at 24 months • Microcephaly associated with growth restriction associated with poorer outcomes	Oxford UK data set (Birth) CDC data set (24 months)	Neurological examination @ 24 months BSITD3 MCHAT GMFCS
Kan E et al, 2008, Australia	Early Hum Dev.	23-27^{+6}	To determine associations between weight and head circumference, at birth and postnatally, with cognitive, academic and motor outcomes at age 8 years.	**Strengths:**Multicentre; Blinded assessors; Use of a control group; 93% follow up ;Detailed assessment @ 8years **Weaknesses:** Data from early 1990's; Missing data for head circumference at birth	• Preterm cohort had significantly smaller head size than the reference standard at all ages • OFC strongly related to cognitive, academic and motor outcomes at 2 and 8 years, not at birth • OFC catch-up between birth and 2 years associated with a favourable neurodevelopmental profile at age 8, however catch-up thereafter had minimal impact	British Growth Reference	Paediatric assessment @ 8years WISC-3 WRAT-3 MABC

Leviton A et al, 2010, USA	Early Hum Dev.	<28	To identify some of the antecedents of microcephaly at age 2years among children born before the 28th week of gestation.	**Strengths:**Multicentre, large numbers; high rates of follow up; considered social ethnic and perinatal factors **Weaknesses:** Observational study	• Antenatal phenomena (low virulence organisms in placenta, tobacco exposure) and correlates of social class influence postnatal head growth. • Pre-eclampsia/fetal indications to deliver preterm associated with a greater risk of microcephaly	CDC Data sets	BSITD-2 Motor Examination GMFCS
Kytnarova J, 2011, Czech republic	Journal of Paediatrics and Child Health	$22\text{-}27^{+6}$	To prospectively evaluate anthropometric parameters in children born as extremely premature neonates	**Strengths:** Examined extremely premature infants as a separate group **Weaknesses:** Single centre, Head size not correlated withneurodevelopmental follow-up; Social and ethnic factors not considered	• OFC significantly lower in extreme prematurity (<26 weeks) • Decline in head growth between 2 and 5 years	Sixth anthropological survey of children in the Czech Republic in 2001	
Farooqi A, 2006, Sweden	Pediatrics	<26	To examine growth development from birth to the age of 11 years	**Strengths:** Multicentre; use of a control population; considered social factors; excluded children with severe motor disability **Weaknesses:** Neurosensory impairment identified by review of medical records; No data on OFC between 4 and 11 years; Insufficient data for analysis of birth OFC	• OFC of premature infants significantly lower than controls at all ages analysed • No catch-up OFC growth after 6 months • Birth weight z scores predicted head size	United Kingdom Growth Chart	
Horemuzova E et al, 2012, Sweden	ActaPaediatrica	<26	To provide growth charts for clinical monitoring of extra-uterine growth from birth to full-term age	**Strengths:** Large cohort of very preterm infants **Weaknesses:** Single centre; no neurodevelopmental follow up	• OFC larger in boys at GA 23, 24 and 25 weeks • Head growth generally poor with a tendency to ‘catch-up’ before 40weeks CGA • Decreased gestational age and poor caloric intake indicators for poor overall growth	Constructed growth charts from data collected	

Costeloe K et al, 2012, UK	British Medical Journal	<26	To examine survival and developmental outcomes in cohort of infants born at <26 weeks in UK	**Strengths:** Large cohort; multicentre **Weaknesses**: Only comment on change in OFC z score from birth to EDD	• No improvement in OFC growth from birth to EDD seen in 2006 compared with 1995		
Dammann et al, 2010, USA	Neonatology	<28	To assess how illness severity measures predict death and illnesses in the newborn.	**Strengths**: Multicentre; large cohort; social factors considered. **Weaknesses:** Present developmental outcomes in relation to SNAP-II and SNAPPE-II scores but not in relation to head size.	• High SNAP-II and SNAPPE-II scores predicted infants with OFC >2 SD below expected mean at 24 months.	CDA datasets	Neurological examination@24 months BSITD-2 GMFCS
Leviton et al, 2011, USA	Early Human Development	23-28weeks	To evaluate if concentrations of inflammation-related proteins were eleviated in early postnatal blood specimens of preterm newborns who two years later had a small head	**Strengths**: Multicentre, large cohort **Weaknesses:** Neuroimaging and developmental follow up not included	• Microcephaly and small head associated with low gestational age and birth weight. • Elevated concentrations of inflammation related proteins associated with microcephaly and/or small head size at 2 years.	CDC datasets	
Ahmad I et al, 2010, USA	American Journal of Human Biology	23-42 weeks	To compare multimodal measurements of body composition	**Strengths:** Stratified according to gestational age **Weaknesses:** Small sample size; only data on birth OFC presented; Absolute OFC measurement presented rather than OFC percentile for gestational age	• Mean birth OFC (cms) 30.7 95%CI (29.8,31.5)		
Diekmann M et al, 2005, Germany	European Journal of Paediatrics	23-28 weeks	To investigate which postnatal growth pattern is ideal for extremely low birth weight infants	**Strengths:** Stratified by birthweight ; SGA babies analysed separately; intrauterine growth curves **Weaknesses:** Inclusion determined by birthweight rather than gestational age; data collected by retrospective chart review	• No significant difference found for weekly OFC growth velocity for SGA in comparison to AGA infants • Postnatal median growth was> 10^{th} percentile of intrauterine reference curves falling below the 10^{th} percentile after 33 weeks	Intrauterine growth curves - Voigt et al (1996)	

Table S1b Studies Including Infants 28-32 Completed Weeks Gestation

Author/Year/ Country	Journal	Gestational Age Range (weeks)	Primary Endpoint	Strengths/ Weaknesses	Findings pertaining to Head Size	Head Size Reference	Neurodevelopmental Assessments
Neubauer et al, 2013, Austria	ActaPaediatrica	24 -32	To examine the association between neurodevelopmental outcome and head circumference in a cohort of very preterm infants and in this context to investigate the relevance of suboptimal head size.	**Strengths:** Prospective, adjusted for social and perinatal factors **Weaknesses:** Extremely premature infants not analysed as a separate group; Ethnicity not considered	• OFC catch-up growth seen between discharge and 3 months • Suboptimal head size at birth did not predict outcome at any age • At 3 months suboptimal head size was a strong predictor for both cognitive and psychomotor development at 12 and 24 months	Growth charts developed by Pan et al.	BSITD 2 @ 12 and 24 months CGA
Cooke R. W. 2005, UK	Arch Dis Child Fetal Neonatal Ed.	<32	To examine associations between cognitive and minor motor problems in preterm children and perinatal and postnatal clinical factors.	**Strengths:**Multicentre; neurodevelopmental follow-up at 7 years **Weaknesses:** 102(27%) Children lost to follow up	• OFC at 7 years independently significantly related to IQ. • OFC at 7 years associated with parenchymal brain lesions on neonatal ultrasound.	"4 in 1" growth charts (Growth Foundation)	WISC 3 MABC
Tan M et al, 2008, UK	Arch Dis Child Fetal Neonatal Ed.	<29	To examine the feasibility of providing macronutrients at amounts above current recommendations (hyperalimentation) to improve nutrition and head growth in preterm infants.	**Strengths:** Randomized controlled trial **Weaknesses:** Single centre; unblinded; small sample size	• Factors significantly associated with OFC> 2 SD below mean at 36 weeks CGA were days to full feeds; CRIB 2 score; SD score of first recorded OFC; cumulative protein and energy deficits	Gairdner Pearson growth reference	
Franz AR, 2009, Germany	Pediatrics	<30	To determine whether intrauterine, early neonatal, or postdischarge growth is associated	**Strengths:** Neurodevelopmental follow-up to 5.4 years; perinatal and social factors considered in analyses **Weaknesses:** Single centre;	• The median SD score for OFC decreases from birth to discharge and further decreases at follow up • OFC growth from birth to discharge is an important	Microsoft Excel add-in LMSgrowth (version 2.14;)	Neurological Examination KABC

			with neurocognitive and motor-developmental outcome in extremely preterm infants.	lack of data on nutritional intake	predictor of neurologic and gross motor development at 5.4 years		
Maguire, 2008, Netherlands	Pediatrics	<32	To investigate the effect of basic elements of developmental care on days of respiratory support and intensive care, growth, and neuromotor development at term age in infants who were born at <32 weeks' gestation	**Strengths**: Multicentre; social and ethnic factors considered **Weaknesses**: High attrition rates from recruitment to follow up; unblinded	• Developmental care interventions had no significant effect on OFC		Neurological Examination
Biasini A et al, 2012, Italy	The Journal of Maternal-Fetal and Neonatal Medicine	23-32	To investigate growth and neurological outcome in preterm infants fed with human milk and extra-protein supplementation as routine practice.	**Weaknesses:** Single centre; Small sample size; significant differences in basic characteristics between groups; neurodevelopmental follow-up only to 9 months.	• Up to 9 months CGA extra protein group showed better OFC catch up growth. • GDMS did not show any significant difference between groups at 9 months CGA.		GDMS MilaniComparetti and AmielTison neurological assessment
Zachariassen et al, 2011, Denmark	Pediatrics	23 – 32	To determine if the addition of a multinutrient human milk fortifier to mother's milk while breastfeeding very preterm infants after hospital discharge is possible and whether it influences first-year growth	**Strengths:** Multicentre; prospective randomized controlled trial; social factors considered **Weaknesses**: 25% of neonates excluded (those with severe diseases or circumstances influencing feeding ability at discharge); 25% non consent rate; Characteristics of study group significantly different to non consent group; unblinded ; per protocol analysis performed because of many changes in nutrition in all groups	• Boys showed higher OFC score within all 3 groups from term until 12 months • Mean OFC z score nadir at 3 months CGA • OFC from term to 4 months significantly higher in girls breastfeeding combined with EBM fortification	Niklasson et al Swedish growth reference	

Itabashi K et al, 2007, Japan	Early Hum Dev	24.0 – 31.9	This aims to conduct a comparative study of the height catch-up rate in preterm small for gestational age (SGA) infants during early childhood by gestational age and identify the factors affecting short stature in comparison to full-term SGA infants	**Strengths:** Multicentre; 32-37 week and term groups included; maternal OFC considered in >32 week infants; **Weaknesses:** Results applicable only to Japanese population; small sample size of very preterm infants; missing data limited study to longitudinal assessment at 5 years	• In infants born>32 weeks head circumference at birth is a significant factor affecting height catch-up at 5 years		
Tan M et al, 2008, UK	Arch Dis Child Fetal Neonatal Ed.	< 29 weeks	To explore the relationships between early nutrition, post-natal head growth, quantitative magnetic resonance imaging and developmental outcome in the first year	**Strengths:** MR data included **Weaknesses:** 32% of recruited infants were excluded or did not have parental consent ; 1.5 Tesla MR scanner; Quality of scans inadequate for brain volume measurements in up to 25%; BSITD assessor not blinded; developmental outcome not primary outcome	• Good correlation between OFC measurement and total brain volume • No significant differences in OFC and BSITD scores in infants randomised to receive hyperalimentation or standard feeding • Pooled data showed that energy deficit in the first 28 days correlates significantly with total brain volume and BSITD scores at 3 months CGA	Gairdner Pearson growth reference	BSITD2
Cockerill J et al, 2006, UK	Arch Dis Child Fetal Neonatal Ed.	≤32 weeks	To evaluate weight gain and head growth between birth and term in a contemporary cohort of preterm infants, taking into account breast milk intake and illness severity.	**Strengths:** Controlled for social factors **Weaknesses**: Single centre; small sample size; infants remaining in unit at ≥37 weeks not representative of entire population	• Highly significant correlation between weight standard deviation score gain (SDSG) and OFC SDSG • Accelerated postnatal head growth which was enhanced by breast milk	1990 British Growth Reference	
Löfqvist C et al, 2006, Sweden	Pediatrics	<32 weeks	To investigate whether retinal vascular growth retardation is paralleled by brain growth retardation	**Strengths**: Multicentre; adjusted for other neonatal morbidities **Weaknesses**: Small sample size	• Degree of head growth restriction postnatally corresponded to degree of ROP • Serum IGF-1 levels from birth to 31 weeks CGA correlate with OFC • Decline in head growth shown to precede occurrence of	Swedish reference standard	

			in premature infants		proliferative ROP		
Sakurai M et al, 2008, Japan	Pediatrics international	23 – 32 weeks	To determine the frequency and contributing factors of EUGR in infants ≥32 weeks of gestational age.	**Strengths**: Multicentre ; stepwise logistic regression analysis of many neonatal factors **Weaknesses**: Cross sectional design	• Lower gestational age strongly influences extrauterine head growth. • Even at low gestational ages significant brain sparing effects seen.		
Miller J et al, 2012, Australia	American Journal of Clinical Nutrition	<31 weeks	To assess the effect of human milk fortified with a higher-protein HMF on growth in preterm infants	**Strengths:**Randomised controlled study **Weaknesses:** Single centre; small sample size; OFC not a primary outcome measure	• No significant differences in head growth between babies randomised to higher protein or control fortifier.	New South Wales birthweight percentile charts	
Herrmann KR et al, 2010, USA	Nutrition in Clinical practice	<32 weeks	To test the hypothesis that premature infants would grow adequately when they received more than 50 kcal/kg per day of parenteral nutrition	**Strengths**: Infants stratified by birthweight; use of intrauterine percentiles **Weaknesses**: Single centre; small sample size	• OFC remained > 10TH percentile for intrauterine growth for all except 24 week GA cohort. • Study participants' (early parenteral nutrition) OFC was 1 SD > mean OFC in the comparison group.	Babson and Benda intrauterine growth data	
Karna P, 2005, USA	Paediatric and Perinatal Epidemiology	23 – 29 weeks	To provide new national reference values for extremely preterm neonates.	**Strengths**: Multicentre; large sample size; ethnicity considered **Weaknesses**: Large number (28%) excluded due to missing maternal information	• Average increase in OFC was 0.99cms per week of gestation • OFC larger for boys and twins and did not differ by race	Multiple growth charts used : Lubchenco growth charts Usher and McLean growth charts Thomas et al growth charts	
Maas C et al, 2013, Germany	Neonatology	<32 weeks	To evaluate the effects of accelerated enteral feeding advancement on the time to full enteral feeds, on early postnatal growth as well as on the frequency of necrotizing enterocolitis and	**Strengths**: >50% cohorts <28weeks gestational age **Weakness**: Single centre; small sample size; observational design	• No benefit observed in OFC growth with more rapid feeding and higher protein and energy in the first 3 weeks of life	LMS growth	

			focal intestinal perforation in very premature infants				
Cheong et al, 2008, Australia	Pediatrics	<30 weeks	To establish the relationship between head circumference with brain MRI at term-equivalent age and to relate head circumference with neurodevelopmental outcome at 2 years	**Strengths**: Social factors considered; MR scans scored blindly by 2 independent raters; high follow up rate for neurodevelopmental assessments (94%) **Weaknesses:** Quantitative volumetric MR analysis not possible in 13%**;** Birth OFC only available in 130 (57%)	• Microcephaly increased from 7.5% at term to 29.7% at 2 years • No significant relationship between OFC and white/grey matter abnormalities on MRI. • Strong correlation found between OFC and brain volume at birth • At 2 years CGA microcephaly associated with poor development and increased rate of CP	British Growth Reference Data	BSITD 2 Standardized Neurological Examination Assessment of Vision and Hearing
Van der Lugt et al, 2010, Netherlands	BMC Pediatrics	24 – 32 weeks	To investigated the effects of neonatal hyperglycemia on growth and neurobehavioral outcome at 2 years of age	**Strengths:** Large sample size; adjusted for potential confounders; subgroup analyses by gestational age and birth weight **Weaknesses:** Single centre; retrospective design can only outline association ; multiple potential confounding factors	• OFC at 2 years not different in infants exposed to hyperglycaemia compared to unexposed neonates		Neurological Examination (Hempel 1993) CBCL/2-3
Vinall et al, 2013, Canada	Sci. Transl. Med.	24 – 32 weeks	To examine the association between neonatal growth and diffusion tensor imaging measures of microstructural cortical development in infants born very preterm	**Strengths:** Analyses considered many medical confounders; **Weaknesses:**Singlecentre; small sample size within each category of injury; <27 weeks not analyzed as a separate group;1.5 Telsa MR	• Impaired head growth between 32 and 40 weeks associated with delayed microstructural development of the cortical grey matter, independent of birth weight, brain injury and systemic illness.		
Vinall et al, 2012, Canada	Pain	< 32 weeks	To examine whether neonatal pain is related to postnatal body and head growth in infants born very preterm	**Strengths**: Identified and controlled for key indicators of potential medical confounders **Weaknesses**: Single centre; small sample size	• Lower birth OFC, more neonatal pain and longer duration of mechanical ventilation independently associated with decreased OFC percentile at 32 weeks CGA • Lower birth OFC, longer duration of mechanical ventilation and hydrocortisone exposure rather than pain independently	Sex specific British Columbia population based data	

					associated with decreased OFC percentile at 40 weeks CGA • Accelerated head growth relative to body growth seen after 32 weeks CGA.		
Euser et al, 2011, Netherlands	Horm Res Paediatr	< 32 weeks	To test the effect of the IGF1 192-bp allele on cranial and linear growth and body mass index from birth until age 5 years, and on IQ and serum IGF-1 at age 19 years	**Strengths:** Multicentre; adjusted for birth weight and socioeconomic status **Weaknesses**: Study cohort born in 1983; Sample studied not representative of general preterm population	• Homozygosity for the IGF1 promoter 192-bp allele associated with a slower cranial growth from birth until 5 years but not IQ at 19 years of age. • OFC at 5 years positively associated with IQ at age 19	Birth: Swedish References for Preterm Infants(Niklasson et al 1991) Follow up: Dutch reference values(Fredriks et al 2000)	
Rijken M et al, 2007, Netherlands	Early Hum Dev.	23.7-31.9	To assess the relationship between growth, perinatal factors and neurodevelopmental outcome.	**Strengths:**Multicentre;Controlled for ethnicity and perinatal variables **Weaknesses:** Limited number of infants with microcephaly	• Smaller OFC associated with mental and psychomotor delay and abnormal neurological exam • Catch up head growth poorer in SGA infants • Postnatal use of dexamethasone negatively associated with head circumference	Dutch growth charts	Neurological examination @ term; 12 and 24 months BSITD1