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The EPICure study: Growth and blood pressure at 6 years of age following extremely preterm birth

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ABSTRACT

Background: Preterm children are at risk for reduced growth in early childhood, which may predispose them to later changes in blood pressure. We studied growth and blood pressure (BP) in extremely preterm (EP) children at age 6 years.

Methods: We evaluated children who were born at 25 completed weeks of gestation or less in the United Kingdom and Ireland in 1995 when they reached early school age. Children underwent standardized assessments, including auxology and sitting blood pressure.

Results: Of 308 surviving children, 241 (78 percent) were assessed at a median age of 6 years 4 months; 160 full term classmates acted as a comparison group. Compared to classmates, EP children were 1.2 standard deviations (SD) lighter, 0.97SD shorter, BMI was 0.95SD lower and head circumference 1.3SD lower. Compared to 2.5 years of age, EP children showed catch up in terms of weight by 0.37SD, height by 0.42SD and head circumference by 0.13SD. Systolic and diastolic BP were lower by 2.3mmHg and 2.4mmHg respectively in EP children but these differences were accounted for by differences in height and BMI. Maternal smoking in pregnancy was associated with lower BP, children born before 24 weeks had higher systolic and children given postnatal steroids higher diastolic pressures.

Conclusions: Poor postnatal growth seen after birth and at in the third year persists into school age. Catch up growth reduces some of the early deficit but is least for head growth. Despite serious postnatal growth restriction blood pressure appears similar in both EP and term classmates.

INTRODUCTION

Poor longitudinal growth in childhood is common in children born at lower gestational ages. We recently reported growth to 30 months age for a national cohort of extremely preterm (EP) children, identifying poor longitudinal growth, poor weight gain and smaller head size compared to population norms. (1) Poor postnatal growth was associated with a range of clinical factors including weight for gestation at birth, long courses of postnatal corticosteroids and later feeding difficulties. Head growth in particular was associated with later serious disability but overall it was not related to developmental test scores at 30 months age corrected for prematurity in those able to do them.

Growth after birth (2) and over the first year (3, 4) may affect later cardiovascular risk but this risk needs to be balanced for all babies against the need for reasonable postnatal growth, particularly of head size to achieve adequate neurological (5) or cognitive outcomes. (6, 7) Although developmental outcome has been shown to be related to postnatal growth, most evidence is for children with low birthweight for gestation.(8) Many children who survive birth at borderline viability have significant periods of postnatal growth failure, probably due to inadequate early nutritional intake or utilisation. (9) Thus the long term consequences of early growth failure in EP children remain to be identified.

Our earlier study (1) is part of an ongoing longitudinal evaluation of children born in the United Kingdom and Republic of Ireland at 25 completed weeks of gestation or less (The EPICure study). Over 10 months in 1995 we identified 1289 livebirths between 20 and 25 weeks of gestation; 308 survived beyond the first year after birth. We have reported a range of outcomes for this group at discharge from hospital (10) and at 30 months age corrected for prematurity. (1, 11-13) Recently we re-evaluated this cohort at 6 years of age and demonstrated persisting high levels of disability and emerging cognitive impairments. (14) We also measured growth and blood pressure (BP) with the objectives of comparing their outcomes with a comparison group of contemporary term-born children, of investigating their relationships with earlier predictors, and reporting catch-up growth.

METHODS

The derivation and characteristics of this EP cohort have been described, (1, 10, 12) as have the details of the 6 year evaluation. (14) The population represents all surviving children born at 25 weeks 6 days gestational age or less from March through December 1995. Of the 308 children known to be alive at 30 months, the parents of 241 children consented to the study.

There were 204 children in mainstream education. For each of these, we sought an age and sex-matched classmate as a comparison. (14) We were able to assess 160 term born children. All children were assessed by a paediatrician and a psychologist after training in the techniques used for the study.

We carried out physical and neuropsychological evaluations, supplemented by a clinical history obtained by parental questionnaire, as previously described. (14) Weight was measured on identical weighing scales (Salter Housewares Ltd, UK) or on clinic equipment. Height was measured using a standard stadiometer (Child Growth Foundation™). Measurements of maximum occipito-frontal head circumference (OFC) and mid arm circumference were made using a LASSO-O™ tape respectively. BP was measured at the end of each assessment in the sitting child's right arm, using a mercury sphygmomanometer taking the first and fifth Korotkoff sounds as systolic and diastolic pressures, respectively.

Standard deviation scores (SD or “z” scores) for weight, height, body mass index (BMI) and head circumference at 6 years were calculated from UK population norms using age since birth. (15) Comparisons were made with data already collected at birth and EDD (weight and OFC), and at 30 months (weight, height, OFC and BMI).

This study was approved by the Trent Multicentre Research Ethics Committee. Informed signed consent for this assessment was obtained from all the families.

Statistical Analysis

Data were double-entered and outliers were verified before combination with the main study data set for analysis with SPSS for Windows software (release 14.0, SPSS, Chicago). Univariate and multivariate regression analyses were performed using STATA, version 9.0 (Stata Corp, College Station, Texas, USA). A forward stepwise procedure was used to establish independent factors associated with growth as previously.(11) For regression analyses, to avoid extreme outliers, SD scores at 6 years were truncated at the following values: weight +2.5 (n=1), head circumference -4.5 (n=5), BMI, -4 (n=4), and for change in SD scores from 30m, head circumference -2.5 (n=3), +2.5 (n=2) and height -2.5 (n=2) +2 (n=1) .

In analysing associations with BP, BMI for height (the residual of linear regression) rather than BMI was used. For investigation of earlier predictors of later BP in the EP cohort, the residuals of BP on height and BMI rather than actual BP values have been used to avoid confounding by the effects of perinatal variables on growth. No adjustments have been made for multiple testing.

RESULTS

Two hundred and forty one children (78% of 308 survivors) participated at a median age of 76 months (range 62-87 months; 51% boys). They were representative of the whole population of survivors over a range of perinatal variables and of 47 children not assessed at 6 years but evaluated at 2½ years. (14) The comparison group had a median age of 74 months (range 61-86 months; 44% boys).

Of the EP children assessed at 6 years there was information from birth for weight (n=241), OFC (n=166); from estimated date of delivery for weight (n=225), height (n=66), OFC (n=214) and from the 30 month assessment for weight (n=226), height (n=216), OFC (n=231) and BMI (n=212). Of the 160 comparison children, measurements were obtained for weight (n=159), height (n=159) and OFC (n=160).

The mean birthweight (relative to UK standard data) of the EP children who were assessed at 6 years, was for the gestations ≤23 , 24 and 25 weeks, +0.70 SD, +0.37 SD and +0.07 SD respectively.

Figure 1 shows raw data for weight and OFC of the EP and comparison children, relative to the 0.4th, 50th and 99.6th percentiles for girls and boys. At 6 years extremely preterm children were still smaller than their peers in each of the four main growth measures: mean difference in SD scores for weight was 1.25 SD (95%CI: 1.0, 1.50), for height 0.97 SD (0.75, 1.19), for head circumference 1.30 SD (1.07, 1.53) and for BMI 0.95 SD (0.70, 1.20) (all p<.001; table 1).

Table 1: Standard deviation scores for growth parameters for EPICure children and for comparison children at 6 year assessment

	n	Extremely preterm Mean (sd)	Comparison Mean (sd)	Difference in Means (CI)
OFC SDS	239/160	-1.63 (1.29)	-0.33 (1.02)	-1.3 (-1.5;-1.1)
Weight SDS	241/159	-1.18 (1.34)	0.07 (1.18)	-1.2 (-1.5;-1.0)
Height SDS	237/159	-0.95 (1.12)	-0.00 (1.08)	-.95 (-1.2;-0.7)
BMI SDS	237/158	-0.87 (1.30)	0.11 (1.14)	-.98 (-1.2;-0.7)

These differences remained after elimination of children with cerebral palsy (weight: 1.29SD, height: 0.87SD, head circumference 1.16SD; all p<0.001). Further excluding children with other severe disabilities at 6 years and adjusting for height, the comparison children's head circumference remained 0.69SD (95% CI: 0.46, 0.92) greater than that of the remaining EP children, whose head circumference was itself 0.33SD (95%CI: -0.03, 7.0; p=0.07) greater than those with cerebral palsy or severe disability.

SD scores from the 30 month assessment were recalculated using chronological age so that intervening growth could be evaluated. The change in weight standard deviation score from 30 months to 6 years was +0.37 SD (95% CI 0.23, 0.50) (p<.001), for height +0.42 SD (0.31, 0.52) (p<.001) and for OFC +0.13 SD (0.00, 0.25) (p=05; table 2). There was no change in BMI over this period (95% CI -0.18, 0.18). Thus, some catch up was observed in weight and height but less in head growth. Figure 2 shows the mean changes in SD scores from birth for weight (A) and OFC (B) for those children for whom we had measures at each age relative to chronological age; correcting for prematurity would raise these values slightly closer to the mean.

Table 2: Change in standard deviation scores between 30 months and 6 years of age for extremely preterm children who were examined at both time points.

	No of data pairs	30 months Mean (sd)	6 years Mean (sd)	Mean of Differences (CI)
OFC SDS	231	-1.76 (1.42)	-1.63 (1.30)	0.13 (0.00,0.25)
Weight SDS	226	-1.58 (1.32)	-1.21 (1.32)	0.37 (0.23,0.50)
Height SDS	216	-1.39 (1.14)	-0.97 (1.10)	0.42 (0.31,0.52)
BMI SDS	212	-0.88 (1.34)	-0.88 (1.30)	0.0 (-0.18,0.18)

The relationship between perinatal variables and growth parameters were examined in sequential regression analysis, as described previously (11) The relationships between outcomes and sequentially occuring variables was similar to the results for the 30 month analysis (table 3).[10] There were some differences in growth measures between ethnic groups: at 6 years Afro-Caribbean children were taller, the white children lighter and the children with mother's from the Indian subcontinent no longer had a significantly smaller head circumferences.

Birthweight for gestational age remained strongly associated with all growth outcomes at 6 years except BMI, where the independent effect was 0.11 (-0.06, 0.28; p=0.2). The effects per SD of birthweight after adjustment for factors arising prior to leaving hospital are similar for head circumference 0.32SD at 30 months and 0.31D at 6 years, while for weight (0.33SD, 0.27SD) and height (0.32SD, 0.20SD) the respective associations are smaller at 6 years. Gestational age was related only to head circumference (0.24SD per gestational week at 6 years; 0.29 SD at 30 months). Problems while in hospital, particularly necrotising enterocolitis, severe changes on first chest radiograph and longer courses of steroids were related to the same growth outcomes as at 30 months, except that steroids were no longer related to weight at 6 years. Head growth is related to height (r=0.32 EP, r= 0.42 comparison) so the independent effects for head circumference adjusted for height are also shown in Table 3, to indicate which factors specifically affect relative head growth rather than those mediated through association with linear growth. Fewer factors are associated with relatively poor growth velocity between 30 months and 6 years (table 3).

Table 3: Factors associated with growth at 6 years (in truncated standard deviation scores) corrected for chronological age in extremely preterm infants.

Independent risk factors arising before discharge from hospital

		Weight	Head circumference	Height	Head circumference for height [a]	BMI
1	White ethnic groups (v all others)	-0.76 (-1.14, -0.38)***			0.62 (0.25,0.99)***	
2	Black ethnic groups (v all others)			1.00 (0.63, 1.36)***		
3	Birthweight SD score (per SD)	0.27 (0.1,0.43)***	0.31 (0.25, 0.47)***	0.20 (0.07, 0.33)**	0.20 (0.04, 0.35)*	
4	Gestation age (per week)		0.24 (0.03, 0.44)*		0.24 (0.03, 0.44)*	
5	First chest radiograph (severe changes v mild or no x-ray)	-0.47 (-0.82, -0.14)**		-0.34 (-0.60,0.07)**		
6	First temperature ≥35°C (yes v no)			0.30 (0.01, 0.59)*		
7	Enteral feeding begun by day 7 (yes v no)	0.47 (0.16, 0.78)**		0.31 (0.06, 0.57)*		0.39 (0.07, 0.71)*
8	Definite or probably NEC (yes v no)	-0.95 (-1.8, -.13)**	-1.22 (-2.0, -0.45)**	-0.82 (-1.45, -0.19)**		
9	Any postnatal steroids for CLD (yes v no)		0.16 (- 0.24, 0.56)			
10	Systemic steroid for CLD (per week)		-0.073 (-0.13, -0.02)**		-0.046 (-0.09, -0.01)*	
11	More than 8w of steroids for CLD (yes v no)			-0.59 (-1.13, -0.04)*		

Independent risk factors measured at 30 month follow up, after adjustment for significant factors above.					
Adjusted for:	1,3,5,7 (not 8)	3,4,9,10 (not 8)	2,3,5,6,7 (not 8/11)	1,3,4,10.	
Feeding problems at 30 months (yes v no)	-0.44 (-0.77, -0.10)	-0.31 (-0.62, 0)*	-0.34 (-0.61, -0.07)*		
Given feeding supplements at 30 months (yes v no)	-1.1 (-1.9, -0.35)**		-1.3 (-2.0, -0.54)***		
Mothers age at the birth (per 10 years)		0.30 (0.06, 0.54)*		0.29 (0.04, 0.55) *	
Severe neuromotor delay at 30 months (yes v no)		-1.1 (-1.6, -0.55)***		-0.71 (-1.3, -0.14)*	
Parent in non manual employment (v others)					-0.37 (-0.70, -0.03)*
Independent risk factors associated with poor growth velocity between 30 months and 6 years.					
Neonatal chest X-ray (yes v no)		-0.28 (-0.52, -0.03)*			
Given feeding supplements at 30 months (yes v no)		-0.76 (-1.32, -0.20)**	-0.43 (-0.74, 0.08)*		
Neonatal Surgery (per procedure)	-0.15 (-0.28, -0.02)*		-0.22 (-0.43, -0.01)*		
Severe neuromotor delay at 30 months (yes v no)			-0.42 (-0.84, -0.01)*		

a residuals of regression of head circumference on height in whole study group; * p≤0.05; ** p≤0.01; *** p≤0.001

NEC – necrotising enterocolitis; CLD – chronic lung disease

As head growth is often compromised in those with severe brain injury, the analysis was repeated for children without cerebral palsy or severe disability at 6 years. While the effects of birthweight for gestation, feeding difficulties at 2 years, necrotising enterocolitis (NEC) and ethnicity remained very similar, the effects of gestational age and postnatal steroids were weaker and no longer statistically significant.

From EP children we recorded blood pressure for 208 and systolic pressures only in a further 6 children. The blood pressures from 158 comparison children became our reference data. Mean systolic and diastolic pressures for EP children were 89.3mmHg (SD11.8) and 57.6mmHg (SD 9.5), respectively compared to 91.7mmHg (SD 9.9) and 60.1mmHg (SD 9.4) for the comparison group. These differences were significant (systolic: -2.3mmHg (-4.62, -0.07) p=0.043; diastolic: -2.4mmHg (-4.4, -0.47) p=0.015). Mean differences diminished and became non-significant when adjusted for height and BMI for height (table 4). Among the EP children diastolic BP adjusted for height and weight was slightly higher in children with cerebral palsy but not significantly so (systolic difference: 0mmHg (-4.0, 4.0) p=1.0, diastolic difference: 2.7mmHg (-0.7, 6.0) p=0.11). EP children had greater variability in systolic BP than the comparison children, both unadjusted (p=0.02) and after adjustment for height and BMI (p=0.004, Bartlett's test for equal variances). For diastolic BP the relationship with common variables (BMI, height, mid upper arm circumference (MUAC), age, sex and ethnicity) was similar in the two groups but there was a suggestion that the relationship of height (shorter in EP children) (adjusted for BMI) and systolic BP differed between EP and comparison children (coefficients 0.78 v 0.45 mmHg per cm).

Table 4: Associates of systolic and diastolic blood pressure in extremely preterm and comparison children. Results expressed as effect size in mmHg with 95% confidence intervals.

	Extremely preterm	Comparison
Systolic		
Height (/cm)	0.78 (.53, 1.0)	0.45 (.23, .66)
BMI for height*	1.35 (.40, 2.3)	2.1 (1.3, 2.8)
Diastolic		
Height (/cm)	0.47 (.26, .69)	0.31 (.09,.53)
BMI for height*	1.1 (.37, 1.9)	0.97 (.20,1.7)
Afro-Caribbean ethnic group	3.7 (-.1, 7.5)	6.0 (.9, 11.2)

* calculated as the residuals of the regression of BMI on height in all the children.

Within EP children, multiple regression was undertaken to assess whether there were significant independent relationships of adjusted blood pressure (for height and BMI) with perinatal variables. The 4 children who had had a stoma or intestinal resection for NEC had markedly higher BP than the others (+10mmHg for diastolic and +16mmHg for systolic pressure); they are excluded from further analyses of perinatal associates with BP. Adjusted systolic BP was independently associated with maternal smoking in pregnancy (-4.1mmHg (-7.1; -1.1)), birth <24 weeks (10.8mmHg (5.6; 16)) and marginally with an antenatal cervical suture (4.6mmHg (-0.4; 9.6). Adjusted diastolic BP was independently associated with maternal smoking in pregnancy (-3.0mmHg (-5.5; -0.5)) and use of postnatal steroids (3.2mmHg (0.5; 5.8)) and cervical suture (6.0 (1.8; 10.0). Growth velocity during the three time epochs (birth to full term; to 30 months; to 6 years) was not associated with adjusted blood pressure values at 6 years.

DISCUSSION

These data demonstrate that being born extremely preterm is associated with poor longitudinal somatic growth, with little catch up over the pre-school years. By 6 years the EP children remain significantly shorter, lighter and with smaller head circumferences than reference data or, a group of classmates. Between 2½ and 6 years there has been some catch up in height (0.42SD) and weight (0.37SD) but less in head circumference (0.13SD). These findings are mirrored in the subset of children for whom we have data at each age (figure 2).

By 30 months head size catch up was significantly worse for babies born at 23 weeks of gestation or less than at 24 or 25 weeks (1) which persisted at six years – mean head circumference at 6 years rising by 0.21 SD for each gestational week. It might be expected that head growth would be proportionate to height and indeed many factors are associated with both, however gestational age and birthweight for gestational age had significant independent additional effects on head circumference. The effect of gestation and postnatal steroid use were weaker in children without cerebral palsy or severe disability reflecting the increased risk of these outcomes with lower gestational age and/or the need for longer periods of post natal steroids. We identified few associates of poor growth from 30 months to 6 years; the group of children who had need for food supplementation at 30 months, presumably because of earlier growth concerns, are falling further behind at 6 years.

Our data appear at variance with a smaller study of 52 children born in 1988-1991 at <29 weeks of gestation where catch up to the mean was demonstrated in sequential measurements of weight and height over the first 7 years. (16) Most of these children were more mature at birth than our EP children but those children <27 weeks of gestation were not significantly different from those born at 27-28 weeks. In contrast other population studies of <32 weeks of gestation children have demonstrated similar poor growth over the first 5 years of life (17) .

Most studies of growth in middle childhood have described children born at very or extremely low birthweight (<1500g (VLBW) and <1000g (ELBW) respectively). It is difficult to make direct comparison with such studies as they include an excess of more mature but growth restricted infants for whom later growth performance may be different. (17, 18) Indeed in our study birthweight for gestational age was highly associated with growth parameters. Almost all studies have identified that VLBW or preterm children are relatively slim and this was true of our population. Furthermore, mean BMI SD score has remained constant between 2½ and 6 years. A low fat mass may place preterm children at decreased risk for adult obesity and for the associated increase risk of cardiovascular morbidity. (19)

Studies of ELBW children to adolescence (19, 20) have not demonstrated complete catch-up in height, although one has shown catch up for head growth for 12-16 year olds (10) so it is plausible that further follow up may show improvements in head growth.

No studies have evaluated blood pressure in middle childhood in EP populations, in contrast to VLBW children in adolescence or adult life. (20-25) Generally, studies at older ages show a significant increment in systolic and diastolic pressures but, in contrast, Saigal and colleagues reported no differences in BP in their adolescent ELBW cohort (26), with mean gestational age of 27 weeks. It should be noted that differences in BP in middle childhood are often small and even whole population studies such as ours, where blood pressure is assessed as part of a global assessment may be too small to detect such differences.

Some studies suggest that it is only preterm small for gestational age infants who are at risk of increased BP. (27, 28). Although our EP children were heavier than average at birth they demonstrate serious extra uterine growth failure. Many preterm growth restricted infants in previous studies would have suffered poor growth at the same maturational age

The extent to which blood pressure tracks from middle childhood to adult life is poorly understood. Studies have reported conflicting results, although none have studied such an immature population as ours. The effects of low weight at birth and high weight velocity after birth may be additive and weight gain from birth may be the stronger predictor. (32, 33) Indeed lower birthweight and greater weight gain between 1 and 5 years of age have been associated with higher systolic blood pressure in young adult life (34) and endothelial function in preterm adolescents may be enhanced following slower growth in the first 2 weeks post delivery. (35) This suggests that even short periods of early catch-up growth are bad for later cardiovascular health. Rapid weight gain in childhood has been associated with further increase in risk, but only in boys who were light at birth. (36) Further analysis suggested that this “adiposity rebound” occurs at around 2 years of age. (37) Given the poor immediate postnatal growth of EP children, (10) the lack of significant catch up over the first 2½ years, (1) the lower blood pressures observed in this study, and the finding of similar blood pressures in adult life for extremely low birthweight children, (26) these EP children may not be at higher risk of later cardiovascular disease. Current EP children may have better growth outcomes because of enhanced attention to nutritional care.

We also demonstrated a negative association between smoking during pregnancy and high BP, consistent with a study that showed smoking reduced BP at age 7.5-8 years if gestation was <33wks, but increased it if gestation was >33 wks. (29) Women who stop smoking in pregnancy have heavier babies than those who don't (30) and term babies who suffer growth retardation in the first trimester are heavier than those who don't. (31) It could be speculated that the babies whose mother's smoked were at a potential growth advantage once born, an effect negated by EP birth.

This cohort of extremely preterm children remain much shorter, lighter and slimmer than their classroom peers and head growth has not shown significant catch up over the past 3-4 years. Despite these growth changes, we did not observe any significant differences in blood pressure after correction for height and BMI. Blood pressure must be monitored in further follow-up but currently our findings seem to indicate little risk for increased blood pressure in adult life provided they stay relatively slim.

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Legends

Figure 1: Measured growth parameters at 6 years for EPICure index children and for comparison group: Weight (upper graphs) and head circumference (lower graphs) for boys (left graphs) and girls (right graphs). Reference lines are taken from growth standards (15)

Figure 2: Change in weight and head circumference standard deviation scores between birth, expected date of delivery (EDD), 30 months and 6 years of age (uncorrected for prematurity). Data are shown only for children who had measures at each age.

What is known on this topic:

- Growth following preterm birth may be poor in middle childhood with variable catch up
- There is conflicting evidence whether blood pressure is elevated following very preterm birth

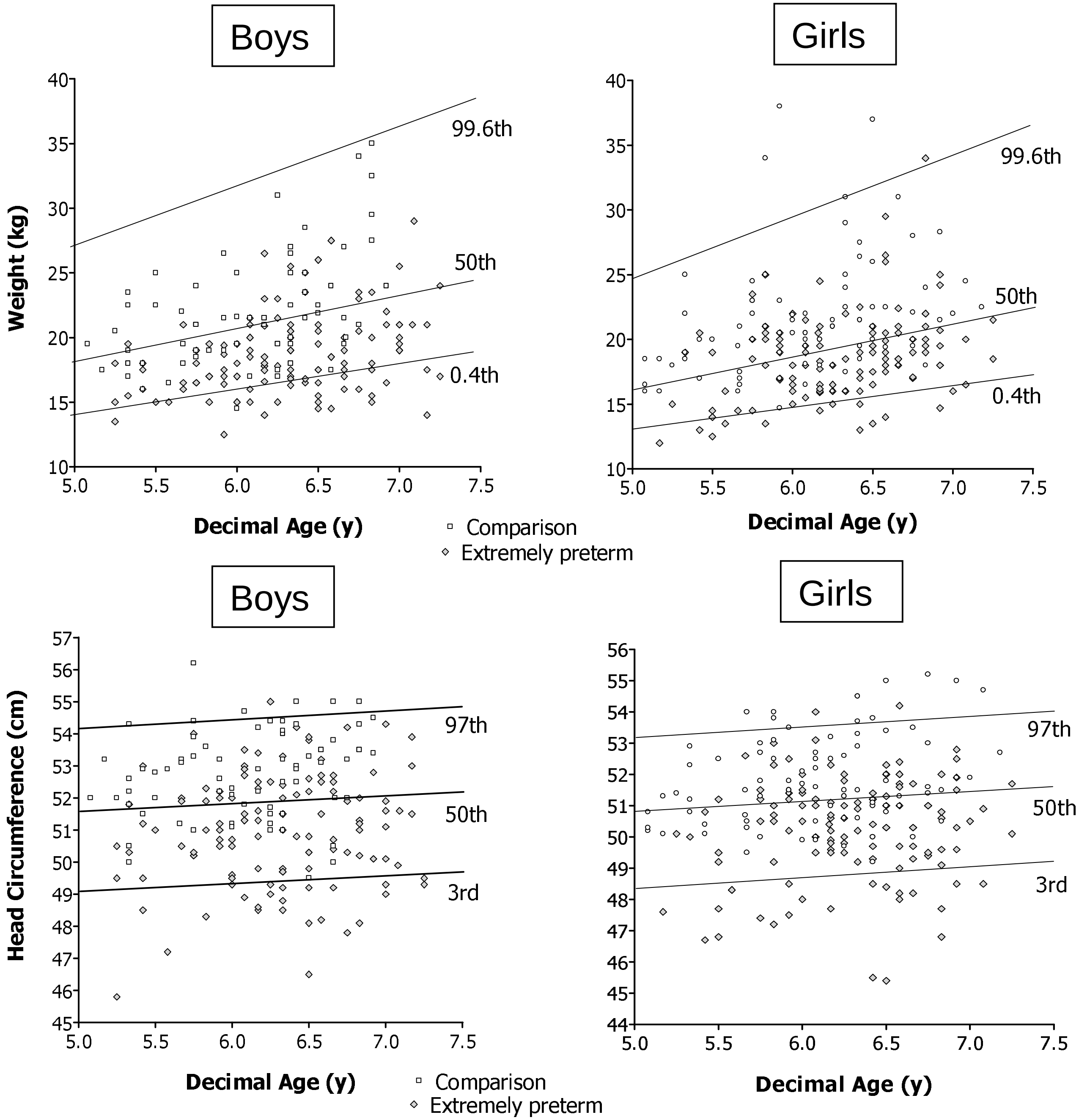
What this study adds:

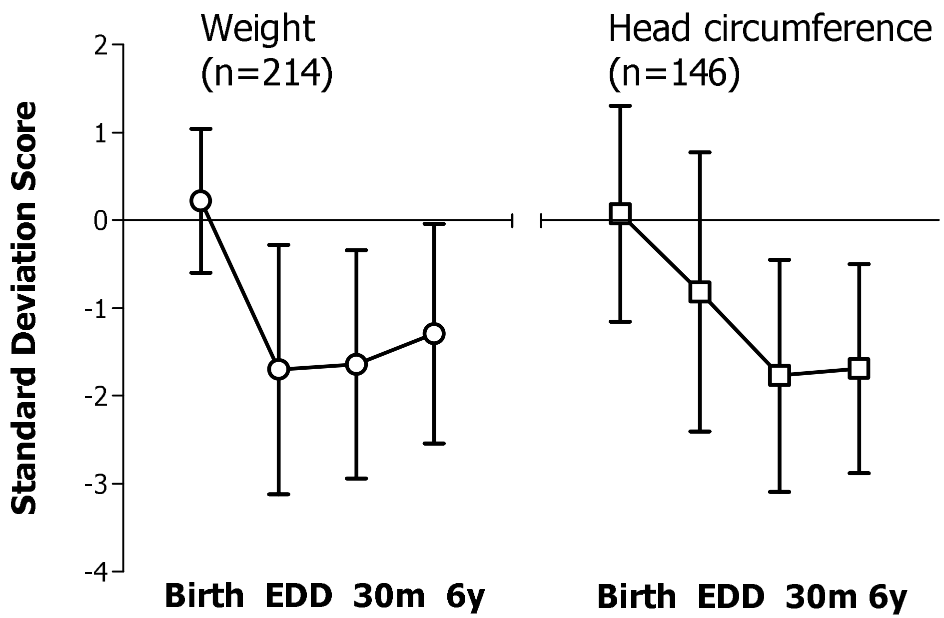
- Extremely preterm children are smaller, lighter and have smaller head circumferences at early school age than their peers.
- Small degrees of catch up in weight and height, but not in head circumference are observed between 2½ and 6 years
- Blood pressure appears lower in extremely preterm infants at 6 years but after correction for confounders no differences are apparent from their peers.

REFERENCES

1. Wood NS, Costeloe K, Gibson AT, Hennessy EM, Marlow N, Wilkinson AR. The EPICure study: growth and associated problems in children born at 25 weeks of gestational age or less. Arch Dis Child Fetal Neonatal Ed 2003;88(6):F492-500.
2. Singhal A, Kattenhorn M, Cole TJ, Deanfield J, Lucas A. Preterm birth, vascular function, and risk factors for atherosclerosis. Lancet 2001;358(9288):1159-60.
3. Singhal A, Cole TJ, Lucas A. Early nutrition in preterm infants and later blood pressure: two cohorts after randomised trials. Lancet 2001;357(9254):413-9.
4. Hemachandra AH, Howards PP, Furth SL, Klebanoff MA. Birth weight, postnatal growth, and risk for high blood pressure at 7 years of age: results from the Collaborative Perinatal Project. Pediatrics 2007;119(6):e1264-70.
5. Lucas A, Fewtrell MS, Davies PS, Bishop NJ, Clough H, Cole TJ. Breastfeeding and catch-up growth in infants born small for gestational age. Acta Paediatr 1997;86(6):564-9.
6. Skuse D, Pickles A, Wolke D, Reilly S. Postnatal growth and mental development: evidence for a "sensitive period". J Child Psychol Psychiatry 1994;35(3):521-45.
7. Corbett SS, Drewett RF, Wright CM. Does a fall down a centile chart matter? The growth and developmental sequelae of mild failure to thrive. Acta Paediatr 1996;85(11):1278-83.
8. Lucas A, Morley R, Cole TJ, Gore SM, Lucas PJ, Crowle P, et al. Early diet in preterm babies and developmental status at 18 months. Lancet 1990;335(8704):1477-81.
9. Cooke RJ, Ainsworth SB, Fenton AC. Postnatal growth retardation: a universal problem in preterm infants. Arch Dis Child Fetal Neonatal Ed 2004;89(5):F428-30.
10. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. Pediatrics 2000;106(4):659-71.
11. Wood NS, Costeloe K, Gibson AT, Hennessy EM, Marlow N, Wilkinson AR. The EPICure study: associations and antecedents of neurological and developmental disability at 30 months of age following extremely preterm birth. Arch Dis Child Fetal Neonatal Ed 2005;90(2):F134-40.
12. Wood NS, Marlow N, Costeloe K, Gibson AT, Wilkinson AR. Neurologic and developmental disability after extremely preterm birth. EPICure Study Group. N Engl J Med 2000;343(6):378-84.
13. Marlow N. Pulmonary outcomes for the extremely preterm infant. Biol Neonate 2000;78:239-240.
14. Marlow N, Wolke D, Bracewell MA, Samara M. Neurologic and developmental disability at six years of age after extremely preterm birth. N Engl J Med 2005;352(1):9-19.
15. The Child Growth Foundation. British 1990 growth reference for height, weight, BMI and h/c. London: The Child Growth Foundation; 1996.
16. Niklasson A, Engstrom E, Hard A-L, Wikland KA, Hellstrom A. Growth in very preterm children: a longitudinal study. Pediatric Research 2003;54(6):899-905.
17. Gutbrod T, Wolke D, Soehne B, Ohrt B, Riegel K. Effects of gestation and birth weight on the growth and development of very low birthweight small for gestational age infants: a matched group comparison. Arch Dis Child Fetal Neonatal Ed 2000;82(3):F208-14.
18. Bardin C, Piuze G, Papageorgiou A. Outcome at 5 years of age of SGA and AGA infants born less than 28 weeks of gestation. Seminars in Perinatology 2004;28(4):288-94.
19. Fewtrell MS, Lucas A, Cole TJ, Wells JCK. Prematurity and reduced body fatness at 8-12 y of age. American Journal of Clinical Nutrition 2004;80(2):436-40.

20. Doyle LW, Faber B, Callanan C, Morley R. Blood pressure in late adolescence and very low birth weight. Pediatrics 2003;111(2):252-7.
21. Doyle LW, Ford GW, Davis NM, Callanan C. Antenatal corticosteroid therapy and blood pressure at 14 years of age in preterm children.[see comment]. Clinical Science 2000;98(2):137-42.
22. Hack M, Schluchter M, Cartar L, Rahman M. Blood pressure among very low birth weight (<1.5 kg) young adults. Pediatric Research 2005;58(4):677-84.
23. Pharoah PO, Stevenson CJ, West CR. Association of blood pressure in adolescence with birthweight. Archives of Disease in Childhood Fetal & Neonatal Edition 1998;79(2):F114-8.
24. Irving RJ, Belton NR, Elton RA, Walker BR. Adult cardiovascular risk factors in premature babies. Lancet 2000;355(9221):2135-6.
25. Kistner A, Jacobson L, Jacobson SH, Svensson E, Hellstrom A. Low gestational age associated with abnormal retinal vascularization and increased blood pressure in adult women. Pediatric Research 2002;51(6):675-80.
26. Saigal S, Stoskopf BL, Streiner DL, Burrows E. Physical growth and current health status of infants who were of extremely low birth weight and controls at adolescence. Pediatrics 2001;108(2):407-15.
27. Cheung YF, Wong KY, Lam BC, Tsoi NS. Relation of arterial stiffness with gestational age and birth weight. Arch Dis Child 2004;89(3):217-21.
28. Rahiala E, Tenhola S, Vanninen E, Herrgard E, Tikanoja T, Martikainen A. Ambulatory blood pressure in 12-year-old children born small for gestational age. Hypertension 2002;39(4):909-13.
29. Morley R, Leeson Payne C, Lister G, Lucas A. Maternal smoking and blood pressure in 7.5 to 8 year old offspring. Arch Dis Child 1995;72(2):120-4.
30. Li CQ, Windsor RA, Perkins L, Goldenberg RL, Lowe JB. The impact on infant birth weight and gestational age of cotinine-validated smoking reduction during pregnancy. Jama 1993;269(12):1519-24.
31. Hemachandra AH, Klebanoff MA. Use of serial ultrasound to identify periods of fetal growth restriction in relation to neonatal anthropometry. Am J Hum Biol 2006;18(6):791-7.
32. Primatesta P, Falaschetti E, Poulter NR. Birth weight and blood pressure in childhood: results from the Health Survey for England. Hypertension 2005;45(1):75-9.
33. Huxley RR, Shiell AW, Law CM. The role of size at birth and postnatal catch-up growth in determining systolic blood pressure: a systematic review of the literature. J Hypertens 2000;18(7):815-31.
34. Law CM, Shiell AW, Newsome CA, Syddall HE, Shinebourne EA, Fayers PM, et al. Fetal, infant, and childhood growth and adult blood pressure: a longitudinal study from birth to 22 years of age. Circulation 2002;105(9):1088-92.
35. Singhal A, Cole TJ, Fewtrell M, Deanfield J, Lucas A. Is slower early growth beneficial for long-term cardiovascular health? Circulation 2004;109(9):1108-13.
36. Eriksson JG, Forsen T, Tuomilehto J, Osmond C, Barker DJ. Early growth and coronary heart disease in later life: longitudinal study. Bmj 2001;322(7292):949-53.
37. Barker DJ, Osmond C, Forsen TJ, Kajantie E, Eriksson JG. Trajectories of growth among children who have coronary events as adults. N Engl J Med 2005;353(17):1802-9.


Boys
Girls
Weight (kg)
99.6th
50th
0.4th
Decimal Age (y)
Comparison
Extremely preterm
Boys
Girls
Head Circumference (cm)
97th
50th
3rd
Decimal Age (y)
Comparison
Extremely preterm


Weight
(n=214)
Head circumference
(n=146)
Standard Deviation Score
2
1
0
-1
-2
-3
-4
Birth EDD 30m 6y
Birth EDD 30m 6y