



University of Warwick institutional repository: <http://go.warwick.ac.uk/wrap>

This paper is made available online in accordance with publisher policies. Please scroll down to view the document itself. Please refer to the repository record for this item and our policy information available from the repository home page for further information.

To see the final version of this paper please visit the publisher's website. Access to the published version may require a subscription.

Author(s): SAMARA, MUTHANNA; JOHNSON, SAMANTHA;
LAMBERTS, KOEN; MARLOW, NEIL; WOLKE, DIETER

Article Title: Eating problems at age 6 years in a whole population sample of extremely preterm children

Year of publication: 2010

Link to published version:

[http://dx.doi.org/ 10.1111/j.1469-8749.2009.03512.x](http://dx.doi.org/10.1111/j.1469-8749.2009.03512.x)

Publisher statement: The definitive version is available at www.blackwell-synergy.com

Eating problems at six years of age in a whole population sample of extremely preterm children

Muthanna Samara, Ph.D.*

Samantha Johnson, Ph.D.‡

Koen Lamberts, PhD.*

Neil Marlow M.D.‡

Dieter Wolke, Ph.D.* †

From the * University of Warwick, Department of Psychology, Coventry (UK); ‡ Institute for Women's Health, University College, London (UK); † University of Warwick, Health Science Research Institute, Warwick Medical School, Coventry (UK).

Corresponding Author:

Professor Dieter Wolke

Department of Psychology

The University of Warwick

Coventry CV4 7AL

Tel: +44 24 7652 3537

Fax: +44 24 7652 4225

Email: D.Wolke@warwick.ac.uk

Acknowledgement:

The research reported was supported by grants from BLISS, the premature infant charity, the Health Foundation, and Well-Being of Women (Drs Marlow and Wolke).

The EPICure Investigator Group included K. Costeloe (London), A. T. Gibson (Sheffield), E. M. Hennessy (London), N. Marlow (Nottingham), A. R. Wilkinson (Oxford), and D. Wolke (Warwick). Data were acquired by Drs Wolke and Marlow and the Developmental Panel researchers, as follows: psychologists: Emma Luck, Catherine Bamford, Helen Betteridge, Hanne Bruhn, Sandra Johnson, Iliana Magiati, Maria Morahan, Isabel Tsverik, and Muthanna Samara; pediatricians: Melanie Bracewell, Michele Cruwys, Ruth MacGregor, Lesley McDonald, Margaret Morton, Margaret Morris, and Sue Thomas. Administrative, technical, and material support was provided by Heather Palmer, Catherine Bamford, Emma Luck, and Melanie Bracewell.

Word Count: 3386

Abstract

Aim: To investigate the prevalence of eating problems and their association with neurological and behavioural disabilities and growth amongst extremely preterm children (EPC) at 6 years of age.

Method: A standard questionnaire about eating was completed by 223 parents of EPC (boys: N: 125, 56.1%; girls: N: 98, 43.9%) aged six years and born at 25 weeks of gestation or less (Mean: 24.5; SD: 0.7; Mean birth weight: 749.1g; SD: 116.8), and 148 parents of classmates born at term (boys: N: 66, 44.6%; girls: N: 82, 55.4%). All children had a neurological, cognitive and anthropometric assessment, and parents and teachers completed a behaviour scale.

Results: Extremely preterm children (EPC) were found to have more eating problems (OR: 3.6; CI 95%: 2.1-6.3) including oral-motor (OR: 5.2; CI 95%: 2.8-9.9), hypersensitivity (OR: 3.0; CI 95%: 1.6-5.6) and behavioural (OR: 3.8; CI 95%: 1.9-7.6) problems compared to control children. Group differences reduced after adjustment for cognitive impairment, neuromotor disability and other behaviour problems. EPC with eating problems were shorter, lighter, had lower mid arm circumference and lower Body Mass Index (BMI) even after adjusting for disabilities, gestational age, birth weight and feeding problems at 30 months.

Conclusions: Eating problems are still frequent in EPC at school age. They are only partly related to other disabilities but make an additional contribution to continued growth failure in extreme preterm children and may require early recognition and intervention.

Running Head: Eating problems of extremely preterm children.

Key words: Extreme Prematurity; growth; Eating Problems; Neurological Disabilities; learning difficulties.

Abbreviations: EP: Extremely Preterm; CC: Control Children; ES: Effect Size; IQ: Intelligence Quotient; HC: Head Circumference; BMI: Body Mass Index.

Surviving extremely preterm (EP) infants are at a significantly increased risk for long-term cognitive, motor, or behavioural impairments (1-3). **Preterm** infants often have feeding problems while in neonatal care including swallowing problems, oral sensory and motor dysfunction or fatigue during feeding. After discharge these include delayed feeding skill development, food refusal (4) and difficulty with the transition to solid foods often accompanied by growth faltering (5). Reasons proposed for these difficulties include immaturity and treatment related to preterm birth including parenteral or tube feeding, adverse oral motor experiences (6), and post-discharge health problems such as neurological or cognitive disabilities, all of which could complicate eating skill development for the child and increase parents' distress, depression, and feeling less confident in feeding (7).

There are few estimates concerning the prevalence of feeding problems of extremely preterm infants and none at school age (4) despite eating remaining a primary concern for parents post-discharge (8). Furthermore, it is unclear whether eating problems are specific or can be fully or mostly accounted for by general cognitive deficits, neuromotor or other behavioural problems often found in very preterm children (1, 3).

In this report we describe eating behaviour at 6 years of age for children born at a gestational age of 25 weeks or less in a whole population study. Firstly, do children born extremely preterm have clinically relevant eating problems more often compared to a full term children? Secondly, can eating problems be accounted for by co-morbidity including cognitive deficits or other neurological or behavioural disabilities? Finally, do eating problems in the clinical range have a significant impact on attained growth (height, weight, head circumference, mid-arm circumference and body mass index) at 6 years of age?

Methods

Participants

The population comprised all surviving children in the United Kingdom and Ireland, born at 25 weeks and 6 days of gestation or less from March through December 1995 (The EPICure Study; (3)). Of the 308 children known to be alive at 30 months, parents of 241 children (78%) consented to the study. Two hundred and four children were in mainstream education. Two hundred and twenty three parents (72%; out of a potential 308) completed the eating questionnaire. For each child assessed in mainstream school, we sought an age and sex-matched classmate as a comparison (3). One hundred and forty eight parents completed the eating questionnaire for the comparison children.

This study was approved by the Trent Multicentre Research Ethics Committee and the local education authorities in Scotland.

Assessments

Feeding and Eating Behaviour Assessment: When the children were 30 months of age parents were asked whether their children had any feeding problems in a single item (9). At 6 years of age parents completed a specially developed eating questionnaire designed on the basis of a comprehensive review of the type of eating problems in general population studies (6). The scale included 19 items (see Appendix 1). A principal component factor analysis with varimax rotation yielded four factors with distinct high loadings of .48 or higher and acceptable eigenvalues > 1: Refusal-faddy eating problems (7 items: e.g., refuses to eat, is a faddy eater); Oral-motor problems (6 items: e.g., dribbles when drinking, has problems with biting crackers); Oral hypersensitivity problems (2 items: e.g., does not like things to be put

in his/her mouth); and Behavioural problems around meals (4 items: e.g., makes a mess, has tantrum during meals). A total eating difficulties score was also constructed and higher scores on each scale indicate more problems. See appendix 1 for the Cronbach's α (CA) of total eating problems and each subscale.

To derive clinical categories, each scale was dichotomized into normal versus clinical (score $>90^{\text{th}}$ percentile or near according to the control group) as suggested by other standard behaviour scales (1). If the child scored $<90^{\text{th}}$ percentile the eating behaviour was considered as normal (no eating difficulty). Parents were also asked if they felt that their child had an eating problem (mild or severe) or not and if the eating difficulties upset or distressed their child (a little, quite a lot, or a great deal).

Pervasive Behaviour Problems: Child behaviour was assessed with the Strengths and Difficulties Questionnaire (SDQ) (10), by parent and teacher report (1). Child behaviour was classified as follows: If the child scored $<90^{\text{th}}$ percentile in both parent and teacher report, the behaviour was considered as normal (no behaviour difficulty); mild difficulty refers to the classification of the child in the clinical range ($>90^{\text{th}}$ percentile) reported by either parent or teacher, while clinical pervasive behaviour problems refers to the classification of the child in the clinical range by both parent and teacher (1).

Cognitive Ability: Children were assessed with the Kaufman Assessment Battery for Children (K-ABC) at 6 years of age (11). The Mental Processing Component (MPC) provides an "overall cognitive score" (see (2)). Cognitive impairment was categorised according to conventional SD-banded cut-offs using the scores of the comparison group as reference data (mild – 1-2 SD below the mean; moderate – 2-3 SD below the mean; severe – more than 3 SD below the mean).

Disability Classification (neurological assessment): Mild disability included neurological signs with minimal functional consequences. Moderate disability included reasonable independence and ambulant cerebral palsy. Severe disability included non-ambulant cerebral palsy (see table 2) (3).

Growth Parameters: Weight was measured on identical weighing scales (Salter Housewares Ltd, UK), height using a standard stadiometer (Child Growth Foundation) and maximum occipito-frontal head circumference (OFC) and mid-arm circumference using a LASSO-O tape. Each measure was taken twice and the mean value computed. BMI was computed as weight/height².

Developmental Panel: The children were assessed by seven experienced developmental pediatricians and eight psychologists, who received formal training. Every second child's session was videotaped and randomly quality checked by the senior assessment pediatrician or psychologist (agreement of more than 90 percent).

Statistical Analysis

ANOVA was performed to compare between CC and EP groups and between sexes and effect sizes are reported as eta squared. Categorical outcomes were evaluated with chi-square tests for trends or Fisher's exact test as appropriate (SPSS 15.0). All statistical tests were two-sided. Odds ratios are reported with 95% confidence intervals comparing EP and CC, and boys and girls. **The 95% confidence intervals were obtained using bootstrapping (e.g., (12, 13) on 20,000 bootstrap samples, using the Bias Corrected and accelerated (BCa) method in MatLab R2009a (the Statistics Toolbox for MatLab).** Odds ratios approximate risk ratios when the incidence of the outcome in the study population (control group) is low (<.10%) (14). Selective dropout was determined by comparing neonatal, 12 and 30 months follow-up data of

those assessed at 6 years and those who were lost to follow-up. To test for the presence of specific eating problems, logistic regressions adjusted for cognitive disability (no/mild vs. moderate/severe), neuromotor disability (no vs. others), or pervasive behaviour disability (no vs. mild/severe) were computed. **Logistic regressions were also performed to test whether eating difficulties predict parent's acknowledgment of eating problems and distress of the child within the EP group.**

Correlations and partial correlations (adjusting for disabilities, gestational age, birth weight and feeding problems at 30 months) were performed to test the relationship between total eating problems and growth measures. Graph Pad Prism 5¹ software was used to design the graphs.

Results

Children lost to follow up (Drop-outs)

Compared to children who were assessed, dropouts (max. N: 85) were more likely to be from non-white ethnic origin (34.1% vs. 18.9%; $p = 0.004$), to have young mothers (> 21 years age: 24.7 % vs. 9.4%; $p = 0.001$), to live in overcrowded homes (49.4% vs. 21.5%; $p < 0.001$), to have experienced more than 1 serious life event by 30 months (48.2% vs. 23.3%, $p < 0.001$), to suffer from cerebral palsy at 30 months (30.8% vs. 15.6%; $p = 0.007$), to have a lower psychomotor development index score (PDI mean 78.7 vs. 84.8; $p = 0.015$), to have more feeding problems (42.4% vs. 30.4%; $p = 0.049$) and more likely to be diagnosed with overall severe disability (40% vs. 25%; $p = 0.014$) at 30 months of age. No differences were found in any of the assessed 9 neonatal complications (e.g., prenatal steroid treatment), 5 other

¹ GraphPad Software, Inc., San Diego, CA, USA

socioeconomic factors (e.g., mother is single or separated), and 6 developmental and growth parameters (e.g., weight, height) up to 30 months (see: (1, 3)).

Eating behaviour differences

EP children were found to have more problems in the total eating problems scale ($p < 0.001$; Effect Size “ES” = .080); oral-motor ($p < 0.001$; ES = .099); refusal-faddy ($p = 0.026$; ES = .016); behavioural ($p < 0.001$; ES = .076) and hypersensitivity subscales ($p < 0.001$; ES = .052) compared to control children (see table 1). Boys were found to have more oral-motor difficulties ($p = 0.001$; ES = .124) and higher behavioural problems ($p = 0.013$; ES = .087) compared to girls (see table 1). The interaction between group and sex was not significant.

Table 1

Compared to CC, EP children had more frequent total eating difficulties in the clinical range (Odds Ratio (OR): 3.6; 95% CI: 2.1-6.3; $p < 0.001$), oral-motor problems (OR: 5.2; 95% CI: 2.8-9.9; $p < 0.001$), behavioural problems (OR: 3.0; 95% CI: 1.6-5.6; $p < 0.001$) and hypersensitivity problems (OR: 3.8; 95% CI: 1.9-7.6; $p < 0.001$) (table 1).

Both boys and girls in the EP group had more total eating difficulties (boys: $p < 0.001$; girls: $p = 0.001$), oral-motor problems ($p < 0.001$), behavioural (boys: $p = 0.005$; girls: $p = 0.023$) and hypersensitivity (boys: $p = 0.001$; girls: $p = 0.031$) problems than their same-sexed counterparts in the CC group (table 1). Within the EP group boys were more likely to have oral-motor problems than girls (OR: 2.2; 95% CI: 1.2-3.9; $p = 0.007$). EP boys compared to EP girls also had more often hypersensitivity problems (OR: 2.1; 95% CI: 1.1-4.2; $p = 0.019$).

Gestation, disability and eating difficulties

Significant associations between gestation at birth and total eating difficulties ($p = 0.003$) and hypersensitivity problems ($p = 0.038$) in EP children were found (table 2). Cognitive impairment and neuromotor disability were associated with an increased prevalence of clinical oral-motor problems ($p = 0.022$; $p < 0.001$), and hypersensitivity problems ($p < 0.001$; $p < 0.001$). Pervasive behaviour difficulties showed significant associations with all eating problem scales: total eating difficulties ($p < 0.001$), oral-motor problems ($p = 0.001$), refusal faddy problems ($p = 0.010$), behavioural eating problems ($p < 0.001$), and hypersensitivity problems ($p = 0.001$) in the clinical range (table 2).

Table 2

Group differences between EP and CC in Hypersensitivity and Behavioural problems became non-significant after adjustment for cognitive abilities, neuromotor disability and pervasive behavioural difficulties together (table 3). In contrast, even after adjustment for all variables, Total eating difficulties and Oralmotor problems still differed between EP and controls and are thus only partly explained by these disabilities.

Table 3

Table 4 shows that total eating difficulties and the subscales significantly predicted parents' judgment of significant eating difficulties and distress of the child within the EP group.

Table 4

Eating problems and growth parameters

Extremely preterm children without eating problems (normal range) had significantly poorer attained growth than control children without eating problems in weight (mean difference: 2.6 kg (95% CI: 1.6-3.7; $p < 0.001$)) (Figure 1), height (mean difference: 3.1 cm (95% CI: 1.6-4.6; $p < 0.001$)), head circumference (mean difference: 1.4 cm (95% CI: 1.03-1.8; $p < 0.001$)), mid arm circumference (mean difference: 1.2 cm (95% CI: 0.7-1.7; $p < 0.001$)) and the BMI was lower (mean difference: 1.2 (95% CI: 0.8-1.7; $p < 0.001$)) (Appendix 2). The mean differences were even larger between EP and CC who had eating problems (clinical range): height (4.2 cm (95% CI: 1.2-7.1; $p = 0.006$)) and head circumference (1.7 cm (95% CI: 0.8-2.6; $p < 0.001$)) (Appendix 2). In contrast, the differences in weight (2.1 kg (95% CI: 0.5-3.7; $p = 0.013$)) (Figure 1), mid arm circumference (0.8 cm (95% CI: 0.04-1.6; $p = 0.049$)) and BMI (0.7 (95% CI: 0.07-1.3; $p = 0.029$)) were similar to those found between EP and CC without eating problems.

Comparison within the EP group of children with and without eating problems showed that those with eating problems weight less (mean difference: 1.1 kg (95% CI: 0.09-2.1; $p = 0.033$)) (Figure 1), had smaller heads (mean difference: 0.6 cm (95% CI: 0.2-1.1; $p = 0.009$)) and lower BMI (mean difference: 0.5 (95% CI: 0.04-0.96; $p = 0.032$)) (Appendix 2) but no significant differences were found for height and mid arm circumference. In contrast, those with eating problems within the control group had only lower BMI (mean difference: 1.1 (95% CI: 0.1-2.0; $p = 0.028$)).

Figure 1

Correlations of total eating problems and growth parameters amongst EP children indicated that with increasing eating problems EP children were lighter (Spearman rho = -0.242 , $N=223$, $p < 0.001$), shorter (Spearman rho = -0.232 , $N=220$, p

< 0.001), had smaller head circumference (Spearman rho = -.211, N=221, p = 0.002), smaller mid arm circumference (Spearman rho = -.165, N=221, p = 0.014) and lower BMIs (Spearman rho = -.164, N=220, p = 0.015). The partial correlations remained significant between total eating problems and weight (r = -.204, N=203, p = 0.003), height (r = -.149, N=203, p = 0.033), mid arm (r = -.156, N=203, p = 0.025) and BMI (r = -.162, N=203, p = 0.021) even when adjusting for gestational age, birth weight, feeding problems at 30 months, and cognitive, neuromotor and pervasive behaviour disabilities but not anymore for head circumference (r = -.087, N=213, p = 0.213).

Discussion

In this whole population cohort of extremely preterm children, we found a considerable excess of eating problems. These difficulties continue to cause significant distress and are perceived as significant problems by the parents. Total eating problems at 6 years of age in extremely preterm children are only partly explained by other disabilities; in particular differences to control children in total and oral motor problems remain after adjustment for disabilities. The eating problems in EP children significantly correlate with poorer attained growth at 6 years of age beyond the prediction afforded by disabilities, gestation, birthweight and early feeding problems.

Both extremely **preterm** boys and girls were more likely to have eating problems than their classmates. However, EP boys, as previously shown (2, 3) had twice as often cognitive and neurological problems, factors that partly explain the sex difference in oral hypersensitivity. Boys in the EP group were also more likely than girls to suffer oral-motor problems, an indicator of generally more delayed development in boys compared to girls. Our findings add that oral-motor dysfunction

persists beyond infancy (7) in a third of extremely preterm children. Furthermore, oral hypersensitivity and behavioural eating problems are still found in a quarter of extremely preterm children at early school-age while food refusal or faddy eating is only slightly more common. Infants and toddlers with neurological impairments (4, 15) are more likely to experience eating problems and have more difficulties in dealing with higher textured food. Our findings indicate that those EP children with neurological or cognitive disabilities, often occurring together in the same child (3), contribute but do not fully account for eating problems observed (15). In particular , oral motor and oral hypersensitivity are increased in children with cerebral palsy (15) found in 12% of EP children (3). Furthermore, learning disabilities as indicated by low cognitive scores are also associated with overall and specifically oral-motor and hypersensitivity problems but did not explain them (16). While impaired oral motor eating skills may be transient and likely to resolve in some EP infants, others may be early indicators of neurodevelopmental impairment (17) due to brain damage (18) and both the neurodevelopmental and eating problems are persistent. The more **preterm** the infant the longer the dependency on tube feeding. As shown here, those infants born at extremely low gestation with neurodevelopmental problems are at greatest risk of developing tactile defensiveness and oral hypersensitivity (6, 19).

In contrast, refusal to eat, the most frequent problem encountered in general population samples of infants (20) was only slightly increased compared to control children. Refusal to eat is often related to difficult and irregular temperament and negative emotionality (21) and frequently leads to higher levels of conflict, non-contingency, and maternal intrusiveness during feeding interactions (22) resulting more often in secondary problems including hyperactive behaviour (23) or distress (24). The behavioural eating problems were explained by general behavioural

problems of the children both at home and at school rather than confined to the eating situation. This is another indicator that the pervasive and multiple problems common among extremely preterm children (1, 2), rather than parenting difficulties, are a major contributor to eating problems in these children. Nevertheless, the eating, and in particular, the behavioural and oral hypersensitivity problems were perceived by the parents as difficulties and as distressing. Thus eating problems put an additional burden on families of impaired extremely **preterm** children (25).

EP children (with and without eating problems) were smaller than control children (26). However, EP children with eating problems were significantly smaller and had less muscle mass than those without eating problems. In particular, poor weight gain and the development of muscle was lowest within EP children with eating problems as reported previously (4, 9). The relationship of eating problems with poor growth in our study was not explained by other disabilities, gestation, birth weight or more physical activity (i.e., hyperactivity). Thus, although disabilities partly contribute to eating problems, it appears that the poor nutritional intake associated with eating problems in EP children explain some of the growth deficits in these children. Eating problems in infants are highly persistent throughout childhood (27) and have been found to increase the risk of other cognitive, behavioural and psychosocial problems (28) in general population samples due to malnutrition. Thus, even in children with significant disability rectifying eating problems may potentially improve their growth and possibly their cognitive development (29).

Overall, considering the stress caused to the child and caretaker, eating problems are not trivial for the families (30). Interventions suggested include oral motor therapy to reduce oral-motor deficits and oral hypersensitivity (31).

Furthermore, Fucile et al. (32) have shown that intervention before the transition from

tube to oral feeding may prevent some of the 'early' feeding difficulties in preterm children. On the other hand, behavioural therapy can be effective in treating behavioural eating problems (15). Early advice and support to parents whose preterm infants experience eating problems may reduce perceived eating difficulties (33) and increase the parental confidence in parenting and nurturing children .

This study has a number of strengths including large sample size, and the inclusion of a control group in the same neighborhood. **The logistic regressions before and after adjusting for disability factors included bootstrapping to determine 95% confidence intervals and provided very similar values to those produced by SPSS but safer estimates of effect size ranges.** Limitations are that we were unable to recruit a comparison child for each preterm child in mainstream classes (see: (3)). Previous research (34), has shown that eating disorder questionnaires and interviews are highly correlated but may slightly overestimate the rate of eating problems (35). A structured feeding assessment including direct observation or structured testing of oral motor skills (36) would have been desirable but not feasible within a half day comprehensive psychological and medical examination. Furthermore, those participants who did not attend the assessments were more likely to be from socially disadvantaged families. While there were no differences regarding medical variables, early feeding behaviour or growth, cerebral palsy and overall disability were more frequent in those lost to follow-up than those assessed (see: (1, 3)). Thus, the reported rate of eating problems, often associated with other disability or social deprivation (15) reported here is likely to be an underestimation of the true rate in the total EP population (37).

In conclusion, at school age, extremely preterm children still have a 2 to 5 times increased risk of eating problems and these are only partly accounted for by co-

existing neurological, developmental or pervasive behavioural impairments. Eating problems in EP children increase the risk of growth problems. Clinicians should be aware of the distress caused to the children and families and early intervention and identification and early referral may alleviate some of the problems for the children and caretakers (38).

References

1. Samara M, Marlow N, Wolke D. Pervasive Behavior Problems at 6 Years of Age in a Total-Population Sample of Children Born at ≤ 25 Weeks of Gestation. *Pediatrics* 2008;122(3):562-573.
2. Wolke D, Samara M, Bracewell M, Marlow N. Specific Language Difficulties and School Achievement in Children Born at 25 Weeks of Gestation or Less. *The Journal of Pediatrics* 2008;152(2):256-262.e1.
3. 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.
4. Cerro N, Zeunert S, Simmer KN, Daniels LA. Eating behaviour of children 1.5-3.5 years born preterm: Parents' perceptions. *Journal of Paediatrics and Child Health* 2002;38(1):72-78.
5. Gewolb IH, Vice FL. Maturation changes in the rhythms, patterning, and coordination of respiration and swallow during feeding in preterm and term infants. *Developmental Medicine & Child Neurology* 2006b;48(7):589-594.
6. Reilly S, Skuse D, Wolke D. The nature and consequences of feeding problems in infancy. In: Cooper PJ, Stein A, editors. *Childhood Feeding Problems and Adolescent Eating Disorders*. London: Routledge; 2006. p. 7-40.
7. Mathisen B, Worrall L, O'Callaghan MO, Wall C, Shepherd RW. Feeding problems and dysphagia in six-month-old extremely low birth weight infants. *Advances in Speech-Language Pathology* 2000;2:9-17.
8. Pridham K, Saxe R, Limbo R. Feeding issues for mothers of very low-birth-weight, premature infants through the first year *Journal of Perinatal and Neonatal Nursing Research* 2004;18:161-169.
9. 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 *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2003 88:F492-500.
10. Goodman R. Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child Adolesc Psychiatry* 2001;40(11):1337-45.
11. Kaufman A, Kaufman N. *Kaufman Assessment Battery for Children*. Minnesota: Circle Pines; 1983.
12. Efron B. Nonparametric estimates of standard error: The jackknife, the bootstrap and other methods. *Biometrika* 1981;3:589-599.

13. Efron B, Tibshirani R. An Introduction to the Bootstrap: Chapman & Hall/CRC; 1993.
14. Zhang J, Yu KF. What's the Relative Risk? A Method of Correcting the Odds Ratio in Cohort Studies of Common Outcomes. *JAMA* 1998;280:1690-1691.
15. Schädler G, Süß-Burghart H, Toschke A, von Voss H, von Kries R. Feeding disorders in ex-prematures: causes - response to therapy - long term outcome. *European Journal of Pediatrics* 2007;166(8):803-808.
16. Bosma JF. Postnatal ontogeny of performances of the pharynx, larynx, and mouth. *American Review of Respiratory Disease* 1985;131:510-515.
17. Palmer MM, Heyman MB. Developmental outcome for neonates with dysfunctional and disorganized sucking patterns: Preliminary findings Infant-Toddler Intervention: The Transdisciplinary Journal 1999 9:299-308.
18. Braun M, Palmer MM. A pilot study of oral-motor dysfunction in 'at risk' infants. *Pediatrics* 1985;5:13-25.
19. Dodrill P, McMahan S, Ward E, Weir K, Donovan T, Riddle B. Long-term oral sensitivity and feeding skills of low-risk pre-term infants. *Early Human Development* 2004;76(1):23-37.
20. Wolke D, Skuse D, Reilly S. The management of infant feeding problems. In: Cooper PJ, Stein A, editors. *Childhood Feeding Problems and Adolescent Eating Disorders*. London: Routledge; 2006. p. 41-91.
21. McDermott BM, Mamun AA, Najman JM, Williams GM, O'Callaghan MJ, Bor W. Preschool Children Perceived by mothers as Irregular Eaters: Physical and Psychosocial Predictors from a Birth Cohort Study. *Journal of Developmental and Behavioral Pediatrics* 2008;29(3):197-205.
22. Lindberg L, Bohlin G, Hagekull B, Palmerus K. Interactions between mothers and infants showing food refusal. *Infant Mental Health Journal* 1996;17(4):334-347.
23. Dahl M, Rydell AM, Sundelin C. Children with early refusal to eat: follow-up during primary school. *Acta Paediatrica* 1994;83:54-58.
24. Jacobi C, Agras WS, Bryson S, Hammer LD. Behavioral validation, Precursors and Concomitants of picky Eating in Childhood. *J Am Acad Child Adolesc Psychiatry* 2003;42:76-84.
25. Mathisen B, Worrall L, Masel J, Wall C, Shepherd RW. Feeding problems in infants with gastroesophageal reflux disease: a controlled study. *Journal of Paediatrics and Child Health* 1999;35:163 - 169

26. Elliman A, Bryan E, Walker J, Harvey D. The growth of low-birthweight children. *Acta Paediatr Scand* 1992;81:311-314.
27. Dahl M, Rydell AM, Sundelin C. Children with early refusal to eat: Follow-up during primary school. *Acta Paediatrica Scandinavia* 1994;83:54-58.
28. Esparó G, Canals J, Jane C, Ballespi S, Vinas F, Domenech E. Feeding problems in nursery children: prevalence and psychosocial factors *Acta Paediatrica* 2004;93:663 - 668.
29. Heird WC. Determination of nutritional requirements in preterm infants, with special reference to 'catch-up' growth. *Seminars in Neonatology* 2001;6(5):365-375.
30. Blissett J, Meyer C, Haycraft E. Maternal mental health and child feeding problems in a non-clinical group. *Eating Behaviours* 2007;8:311-318.
31. Carroll L, Reilly S. The therapeutic approach to the child with feeding difficulty: II. management and treatment. In: Sullivan PB, Rosenbloom L, editors. *Feeding the Disabled Child*. London: Mac Keith Press; 1996.
32. Fucile S, Gisel EG, Lau C. Effect of an oral stimulation program on sucking skill maturation of preterm infants. *Developmental Medicine & Child Neurology* 2005;47(3):158-162.
33. Satter E. The feeding relationship: Problems and interventions. *J. Pediatr.* 1990;117:S191-S189.
34. Mond JM, Hay PJ, Rodgers B, Owen C, Beumont PJV. Validity of the Eating Disorder Examination Questionnaire (EDE-Q) in screening for eating disorders in community samples. *Behaviour Research and Therapy* 2004;42(5):551-567.
35. Wilfley DE, Schwartz MB, Spurrell EB, Fairburn CG. Assessing the specific psychopathology of binge eating disorder patients: interview or self-report? *Behaviour Research and Therapy* 1997;35:1151-1159.
36. Reilly S, Skuse D, Mathisen B, Wolke D. The objective rating of oral-motor functions during feeding. *Dysphagia* 1995;10:177-191.
37. Wolke D, Söhne B, Ohrt B, Riegel K. Follow-up of preterm children: important to document dropouts. *The Lancet* 1995;345 (8947):447.
38. Wolke D. Frequent problems in infancy and toddler years: excessive crying, sleeping and feeding difficulties. In: Bergmann KE, Bergmann RL, editors. *Health promotion and disease prevention in the family*. Berlin: De Gruyter; 2003. p. 44-88.

Table 1. Total eating difficulties and its subscales assessed at 6 years for 223 children born at 25 weeks of gestation or less and 148 age matched classmates for comparison (Mean and standard deviation are shown together with the proportion of the clinical range of the comparison group by sex).

Eating Difficulties	Comparison group			Extremely preterm group			Odds Ratio ¹ for clinical range
	Number/number with information	Mean (SD)	Clinical Range (%)	Number/number with information	Mean (SD)	Clinical Range (%)	
Total Eating Difficulties	19/148	6.1 (4.9)*	12.8%*	76/218	10.0 (7.4)*	34.9%*	3.6 (2.1-6.5)
Boys	8/66	6.1 (5.1)	12.1%*	43/122	10.5 (7.3)	35.2%*	3.9 (1.7-9.0)
Girls	11/82	6.1 (4.7)	13.4%†	33/96	9.4 (7.5)	34.4%†	3.4 (1.6-7.2)
Oralmotor Difficulties	13/148	0.4 (1.0)*	8.8%*	72/215	1.8 (2.5)*	33.5%*	5.2 (2.8-10.3)
Boys	9/66	0.6 (1.3)†	13.6%*	49/120	2.2 (2.7)†	40.8%*	4.4 (1.9-9.6)
Girls	4/82	0.3 (0.6)†	4.9%*	23/95	1.4 (2.3)†	24.2%*	6.2 (2.1-18.9)
Refusal Faddy Problems	16/148	3.9 (3.5)‡	10.8%	38/223	4.9 (4.0)‡	17.0%	1.7 (0.9-3.3)
Boys	7/66	3.6 (3.4)	10.6%	19/125	4.8 (3.7)	15.2%	1.5 (0.6-3.8)
Girls	9/82	4.3 (3.5)	11.0%	19/98	5.3 (4.3)	19.4%	1.9 (0.8-4.6)
Behavioural Problems	14/148	1.4 (1.4)*	9.5%*	52/219	2.3 (1.7)*	23.7%*	3.0 (1.6-5.8)
Boys	6/66	1.6 (1.4)‡	9.1%†	31/123	2.5 (1.8)‡	25.2%†	3.4 (1.3-8.5)
Girls	8/82	1.3 (1.4)‡	9.8%‡	21/96	2.1 (1.7)‡	21.9%‡	2.6 (1.1-6.2)
Hypersensitivity Problems	11/148	0.1 (0.5)*	7.4%*	50/213	0.5 (1.0)*	23.5%*	3.8 (1.9-8.0)
Boys	6/66	0.1 (0.4)	9.1%†	35/120	0.6 (1.1)	29.2%†	4.1 (1.6-10.4)
Girls	5/82	0.1 (0.5)	6.1%‡	15/93	0.4 (0.9)	16.1%‡	2.9 (1.0-8.5)

¹ 95% Confidence Intervals based on 20,000 bootstrap samples, using the Bias Corrected and accelerated (BCa) method

* $p < 0.001$; † $p < 0.01$; ‡ $p < 0.05$ for differences between extremely preterm and comparison groups

Table 2. Gestational age at birth, severity and type of disability and total eating difficulties and its subscales at six years of age among extremely preterm children

	Total Eating Difficulties (N: 218)		Oral-motor Problems (N: 215)		Refusal Faddy Problems (N: 223)		Behavioural Problems (N: 219)		Hypersensitivity Problems (N: 213)	
	Normal	Clinical	Normal/Borderline	Clinical	Normal	Clinical	Normal	Clinical	Normal	Clinical
Gestational age		†								‡
<=23 weeks	13 (59.1%)	9 (40.9%)	12 (60%)	8 (40%)	19 (86.4%)	3 (13.6%)	14 (63.6%)	8 (36.4%)	18 (81.8%)	4 (18.2%)
24	34 (50%)	34 (50.0%)	39 (59.1%)	27 (40.9%)	57 (83.8%)	11 (16.2%)	50 (74.6%)	17 (25.4%)	41 (65.1%)	22 (34.9%)
25	95 (74.2%)	33 (25.8%)	92 (71.3%)	37 (28.7%)	109 (82%)	24 (18%)	103 (79.2%)	27 (20.8%)	104 (81.3%)	24 (18.8%)
Overall Cognition				‡						*
No disability (score, >94)	44 (68.8%)	20 (31.3%)	46 (71.9%)	18 (28.1%)	54 (84.4%)	10 (15.6%)	53 (85.5%)	9 (14.5%)	57 (90.5%)	6 (9.5%)
Mild disability (score, 82–94)	49 (71%)	20 (29%)	51 (75%)	17 (25%)	57 (80.3%)	14 (19.7%)	52 (75.4%)	17 (24.6%)	54 (80.6%)	13 (19.4%)
Moderate disability (score, 70–81)	27 (60%)	18 (40%)	28 (62.2%)	17 (37.8%)	34 (73.9%)	12 (26.1%)	31 (67.4%)	15 (32.6%)	35 (81.4%)	8 (18.6%)
Severe disability (score, >69)	22 (55%)	18 (45%)	18 (47.4%)	20 (52.6%)	40 (95.2%)	2 (4.8%)	31 (73.8%)	11 (26.2%)	17 (42.5%)	23 (57.5%)
Neuromotor				*						*
No disability	113 (66.1%)	58 (33.9%)	125 (74%)	44 (26%)	141 (82%)	31 (18%)	134 (79.8%)	34 (20.2%)	135 (81.6%)	30 (18.2%)
Abnormal signs	14 (66.7%)	7 (33.3%)	10 (47.6%)	11 (52.4%)	18 (81.8%)	4 (18.2%)	13 (59.1%)	9 (40.9%)	14 (70%)	6 (30%)
CP ambulatory	10 (66.7%)	5 (33.3%)	7 (50%)	7 (50%)	15 (100%)	0 (0%)	10 (66.7%)	5 (33.3%)	10 (66.7%)	5 (33.3%)
CP, nonambulatory	5 (45.5%)	6 (54.5%)	1 (9.1%)	10 (90.9%)	11 (78.6%)	3 (21.4%)	10 (71.4%)	4 (28.6%)	4 (30.8%)	9 (69.2%)
Pervasive Total Difficulties-SDQ		*		*		‡		*		†
No Disability	89 (80.9%)	21 (19.1%)	85 (78.7%)	23 (21.3%)	100 (90.9%)	10 (9.1%)	103 (93.6%)	7 (6.4%)	94 (85.5%)	16 (14.5%)
Mild Disability	36 (50.7%)	35 (49.3%)	40 (57.1%)	30 (42.9%)	56 (75.7%)	18 (24.3%)	43 (60.6%)	28 (39.4%)	49 (74.2%)	17 (25.8%)
Severe Disability	17 (47.2%)	19 (52.8%)	18 (50%)	18 (50%)	28 (75.7%)	9 (24.3%)	20 (55.6%)	16 (44.4%)	20 (55.6%)	16 (44.4%)

* $p < 0.001$; † $p < 0.01$; ‡ $p < 0.05$ for differences between gestation ages and disability groups

Table 3. Odds ratios¹ for clinical scores for total eating difficulties and the subscales before and after adjustment for general cognitive scores, neuromotor or/and pervasive total behavioural difficulties (SDQ).

	Unadjusted	Adjusted for categorized MPC+	Adjusted for neuromotor	Adjusted for pervasive total behaviour difficulties SDQ	Adjusted for all variables\$
Total Eating Difficulties	3.6 (2.1-6.5)*	3.0 (1.6-5.5)*	3.5 (1.9-6.4)*	2.7 (1.5-5.0)†	2.5 (1.3-4.8)†
Oralmotor Problems	5.2 (2.8-10.3)*	3.7 (1.8-7.8)*	3.6 (1.8-7.4)*	4.1 (2.2-8.2)*	2.7 (1.3-5.7)†
Refusal Faddy Problems	1.7 (0.9-3.3)	1.8 (0.9-3.6)	1.8 (0.9-3.6)	1.3 (0.7-2.6)	1.6 (0.8-3.3)
Behavioural Problems	3.0 (1.6-5.8)†	2.4 (1.2-5.0)‡	2.4 (1.2-5.0)†	1.7 (0.8-3.5)	1.6 (0.7-3.6)
Hypersensitivity Problems	3.8 (1.9-8.0)*	2.5 (1.1-6.0)‡	2.8 (1.3-6.3)†	3.0 (1.5-6.4)†	1.9 (0.8-4.7)

¹ 95% Confidence Intervals based on 20,000 bootstrap samples, using the Bias Corrected and accelerated (BCa) method

* $p < 0.001$; † $p < 0.01$; ‡ $p < 0.05$ for differences between extremely preterm and comparison groups

+ < -2 SD vs. > -2SD (No and mild vs. moderate and severe); \$ Cognitive, neuromotor and pervasive behaviour difficulties

Table 4. Odds ratios¹ for total eating difficulties and the subscales predicting parents' acknowledgment of eating problems and the distress caused to their children among extremely preterm children.

	Parents'	Distress
	acknowledgment of	
	eating problems	
Total Eating Difficulties	1.4 (1.3-1.6)*	1.3 (1.1-1.4)*
Oralmotor Problems	1.6 (1.3-1.9)*	1.5 (1.2-2.0)*
Refusal Faddy Problems	1.6 (1.4-1.8)*	1.2 (1.01-1.4)‡
Behavioural Problems	1.8 (1.5-2.2)*	1.5 (1.1-2.2)‡
Hypersensitivity Problems	2.2 (1.7-3.1)*	1.8 (1.1-3.1)†

¹ 95% Confidence Intervals based on 20,000 bootstrap samples, using the Bias Corrected and accelerated (BCa) method

* $p < 0.001$; † $p < 0.01$; ‡ $p < 0.05$

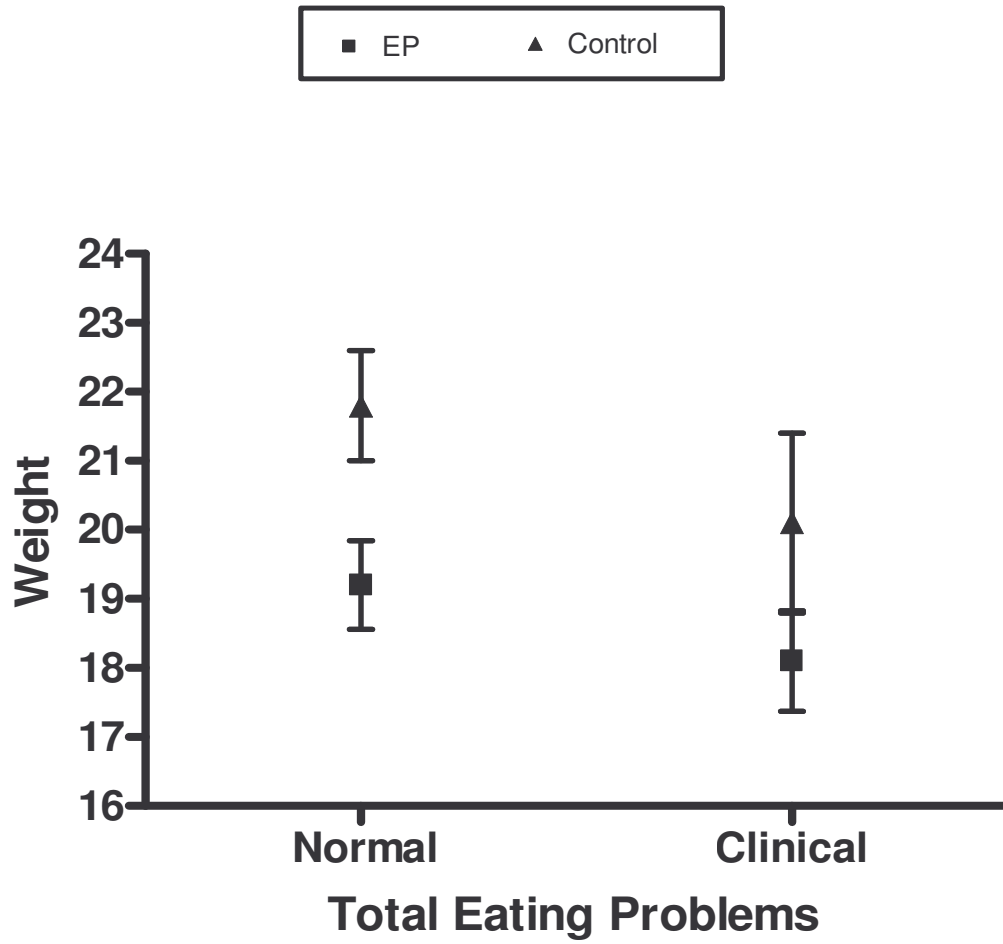


Figure 1: Measured weight (kg) parameters at 6 years for EP and control children with (clinical) and without (normal) eating problems

-Appendix 1- Eating Questionnaire

Refusal-faddy eating problems (Cronbach's α (CA) for total sample: 0.90; extremely preterm (EP) 0.91; control children (CC): 0.89; eigenvalue 6.5):

1. Refuses to eat.
2. Has no appetite.
3. Is a faddy eater.
4. Leaves most of the food offered.
5. Is a slow eater.
6. Eats too little.
7. Is a picky eater.

Oral-motor problems (CA: 0.84; EP: 0.83; CC: 0.70; eigenvalue 2.7):

1. Dribbles when drinking.
2. Has problems with biting crackers.
3. Has problems with chewing meat/dried fruits.
4. Gags or chokes on food.
5. Has problems with swallowing.
6. Needs help with eating.

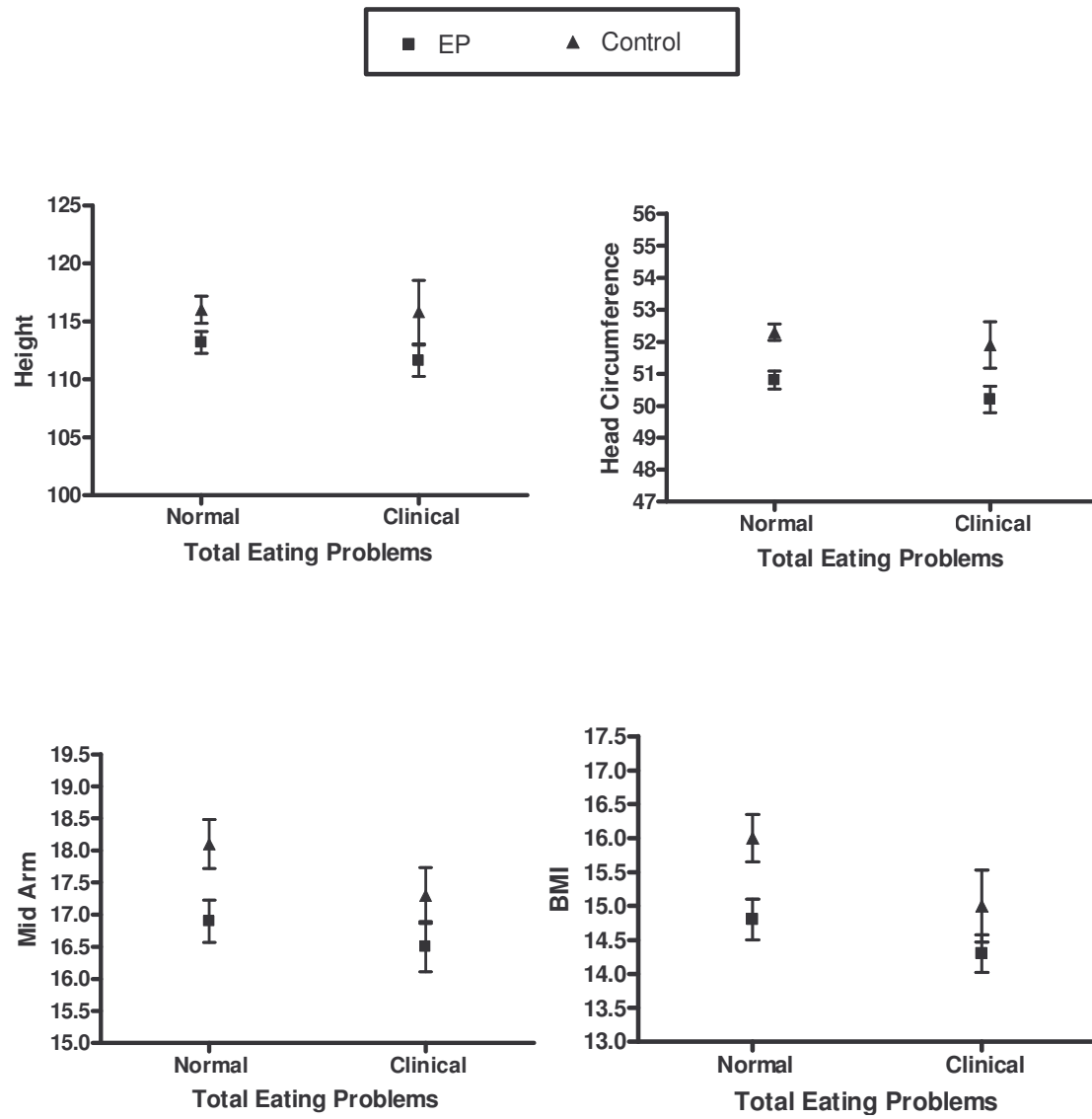
Oral hypersensitivity problems (CA: 0.79; EP 0.81; CC: 0.64; eigenvalue 1.3):

1. Does not like things to be put in his/her mouth (e.g. toothbrush).
2. Does not like to be touched around the mouth.

Behavioural problems around meals (CA: 0.55; EP 0.52; CC: 0.53; eigenvalue 1.2):

1. Makes a mess.
2. Has tantrums during meals.
3. Can't sit still during mealtimes.
4. Eats too much.

Total eating difficulties score: CA: 0.88; EP 0.88; CC: 0.84



Appendix 2: Measured growth parameters at 6 years for EP and control children (Height (cm), Head Circumference (cm), Mid Arm (cm) and Body Mass Index (BMI)) with (clinical) and without (normal) eating problems.