Published in final edited form as:
Paediatr Perinat Epidemiol. 2011 July ; 25(4): 377–387. doi:10.1111/j.1365-3016.2011.01193.x.

Duration of Gestation, Size at Birth and Later Childhood Behaviour

Seungmi Yang[1,2], **Eric Fombonne**[3,4], and **Michael S. Kramer**[1,2,3]

[1]Department of Epidemiology, Biostatistics and Occupational Health, McGill University

[2]The Research Institute of Montreal Children's Hospital, McGill University Health Centre

[3]Department of Pediatrics, McGill University

[4]Department of Psychiatry, McGill University

SUMMARY

Although many previous studies have reported an association between preterm birth or small size at birth and later behaviour, multiple methodological limitations threaten the validity of causal inferences from reported associations. The authors have examined the association between gestational age and gestational age-specific size at birth (weight, length, and head circumference) and behaviour in a large sample of children born healthy at term. The data were from the 6.5-year follow-up of 13,889 Belarusian children who participated in PROBIT, a cluster-randomized trial of a breastfeeding promotion intervention. Child behaviour was measured using the parent and teacher versions of Strengths and Difficulties Questionnaire (SDQ). Differences in SDQ scores by gestational age and by birthweight, birth length, and birth head circumference standardized for gestational age and sex (z-scores) were analyzed after controlling for potentially confounding maternal and family factors. There was no association between gestational age and child behaviour after adjusting for potential confounding factors. Lower birthweight for gestational age was significantly associated with higher scores in problem behaviours including total difficulties, conduct problems, hyperactivity, emotional symptoms, and peer problems. Similar but smaller differences were observed with birth length and birth head circumference, but those differences were attenuated with adjustment for birthweight. The patterns of association were consistent in both parent and teacher assessments. Among school-age children born at term within normal range of birthweight, foetal growth, but not gestational age, was associated with behavioural problem scores.

INTRODUCTION

Many previous studies have reported an association between preterm birth[1] or small size at birth[2–8] and later behaviour, such as hyperactivity/attention deficit,[2–6] conduct problems or aggressive behaviors[6] and emotional problems.[5, 7] These findings have been interpreted as evidence for the foetal origins of later behaviour.

However, several studies are based on cut-offs for birthweight, including extremely low (<1000 g),[3, 4] very low (<1500 g),[2, 5, 9] and low birthweight (<2000 g or 2500 g), [6, 8] usually compared with "normal" birthweight (≥2500 g). However, birthweight is determined not only by fetal growth but also by the duration of gestation, and low birthweight can therefore result from either preterm birth or restricted fetal growth.[10] Thus, it is important to take

Correspondence: Seungmi Yang. The Research Institute of McGill University Health Centre, 4060 Ste-Catherine West (Place Toulon), Montreal, Quebec H3Z 2Z3. Telephone: (514) 934-1934 ext. 22434, Fax: (514) 412-4331. seungmi.yang@mcgill.ca.

gestational age into account when studying the association between birthweight and behavioural outcomes. Studies that statistically adjusted for gestational age or used gestational age-specific birthweight have reported inconsistent findings.[11–15] Moreover, some studies have not controlled for other important potentially confounding factors, including family socioeconomic circumstance[11] and maternal smoking and drinking during pregnancy.[14, 15] Finally, despite numerous studies, only a handful have examined the association among healthy children born at term and reported inconsistent results.[16–19] All except one[19] of the previous studies have based on relatively small sample sizes.[16–18]

Gestational duration has rarely been examined as a primary determinant of behavioural outcomes among term births. Recent studies, however, have shown that length of gestation is associated with cerebrovascular disease,[20] insulin resistance,[21] and depressive symptoms[22] independent of birthweight. This suggests that both gestational duration and size at birth may have unique roles for later health outcomes. The objectives of our study were therefore to examine whether gestational age and fetal "growth," as reflected by birthweight, length, and head circumference standardized for gestational age and sex, are independently associated with behaviors at age 6.5 years among a large sample of healthy children who were born at or after term.

METHODS

Study Participants

Participants of the present study were children enrolled in the Promotion of Breastfeeding Intervention Trial (PROBIT) who were followed up at age 6.5 years. A full description of PROBIT has been published elsewhere.[23] In brief, PROBIT is a cluster-randomized controlled trial of a breastfeeding promotion intervention modelled on the WHO/UNICEF Baby-Friendly Hospital Initiative. A total of 17,046 mothers and their healthy singleton infants born at ≥37 completed weeks of gestation with birthweight ≥2500 g were recruited from 31 maternity hospitals and affiliated polyclinics during their postpartum stay between June 1996 and December 1997 in the Republic of Belarus. After regular follow-up visits during the first year of life, 13,889 of the children were interviewed and examined at age 6.5 years. The study received approval from the Institutional Review Board of the Montreal Children's Hospital, and signed consent in Russian was obtained from the parents.

Measures

Child behaviour was measured using the Strengths and Difficulties Questionnaire (SDQ).[24] The SDQ is a brief behavioural screening questionnaire for children and adolescents from ages 4 to 16 years and consists of 5 subscales (hyperactivity, conduct problems, emotional symptoms, peer problems and prosocial behaviour), each with 5 items. Each item is rated as not true (0), somewhat true (1) or certainly true (2). The score for each of the 5 scales is generated by summing the scores for the 5 items, each ranging from 0 to 10. The 4 subscales scores (hyperactivity, conduct problems, emotional symptoms, and peer problems) are then summed to generate a total difficulties score. The SDQ has been validated against other measures of child behaviour problems, including the Child Behaviour Checklist (CBCL).[25] The SDQ has also been shown to compare favourably with other measures for identifying hyperactivity and attention problems.[26, 27] Several studies have demonstrated the cross-cultural validity of the SDQ in European and developing countries.[26, 28]

At the 6.5-year follow-up visit, a parent accompanying the child (usually [92%] the mother) was asked to complete the SDQ while awaiting the child's examination and interview. Of the total of 13,889 children at the follow-up, 13,868 children had the parent SDQ completed. Parents provided teachers' names if the child had started formal schooling by the time of his/

her follow-up visit, and the polyclinic paediatricians distributed the teacher version of the SDQ to the teachers. The SDQ items are identical in the parent and the teacher versions. Of all children seen at follow-up, the teacher SDQ was obtained in 87% (n=12,016); most of the remainder had not yet begun formal schooling at the time of the follow-up. As previously reported,[29] internal consistency and test-retest reliability of the parent and teacher SDQ were assessed. Cronbach's α were 0.82 and 0.73 in the teacher and parent SDQ, respectively, for total difficulties, 0.81 and 0.67 for hyperactivity, 0.69 and 0.51 for conduct problems, 0.69 and 0.60 for emotional symptoms, 0.49 and 0.34 for peer problems, and 0.81 and 0.62 for prosocial behaviour.

Weight (g), length (cm), head circumference (cm), and gestational age in completed weeks at birth were obtained from obstetric records during the maternity stay. Gestational age was confirmed by ultrasound dating for 93.9% of the children. In only 3.8% was the gestational age estimate based solely on maternal report of the last menstrual period and in 2.3% by obstetric and/or paediatric clinical estimates. Birthweight, length and head circumference were standardized (z-scores) for gestational age and sex. The birthweight standardization was based on the Canadian sex-specific reference for birthweight for gestational age,[30] because no Belarusian reference is available. Birth weight for gestational age was also categorized into the sex-specific weight <10th percentile (small for gestational age, SGA), 10th–90th percentile (appropriate for gestational age, AGA), and >90th percentile (large for gestational age, LGA) based on the Canadian reference. Birth length and head circumference were internally standardized within the sample for each sex and gestational age because there is no comparable external reference data available. Potentially confounding maternal and family characteristics included maternal and paternal age at birth of the child, maternal height, maternal smoking and drinking during pregnancy, marital status, number of other children in the household at the time of birth, and parental education and occupation ascertained by maternal report at enrolment.

Statistical Analysis

Mean differences in SDQ scores by birth size measures and gestational age were estimated by multiple linear regression models based on generalized estimating equations (GEE) to take into account clustering of variables by polyclinics and teachers. Crude associations between total difficulties, conduct problems, hyperactivity, peer problems, emotional symptoms, and prosocial behaviour and birthweight, length, and head circumference z-scores were separately estimated for the parent and teacher SDQs. Subsequent adjusted models controlled for potential confounding factors.

RESULTS

Children who were lost to follow-up were not different from those followed up with respect to mean gestational age, but the proportion of children born at 41 weeks was slightly higher in those lost to follow-up (8% vs. 6%). There was no difference in mean birthweight, but children who were lost to follow-up had shorter in birth length (51.7 cm vs. 51.9 cm) and smaller head size (34.8 cm vs. 34.9 cm). Those lost to follow-up also included more first-born children (63% vs. 56%), children from cohabiting or unmarried couples (15% vs. 11%), children whose father was a university graduate (18% vs. 12%), and children whose mother smoked during pregnancy (3% vs. 2%).

Table 1 describes the study children according to birth size measures, gestational age, SDQ scores, and maternal and family characteristics. Boys were heavier, longer, and had larger head circumferences at birth and showed better behavioural profiles on both the parent and teacher SDQ. However, no interaction was observed between sex and birth size measures or gestational age on SDQ scores (all p-values > 0.10). Thus, we present sex-adjusted associations. Correlations between the parent and the teacher SDQ scores were modest: 0.28 for total difficulties, 0.29 for conduct problems, 0.36 for hyperactivity, 0.19 for emotional symptoms, 0.19 for peer problems and 0.19 for prosocial behaviour.

Behaviour Scores by Gestational Age in Completed Weeks

Table 2 presents the mean differences in parent and teacher SDQ results by gestational age, with 40 completed weeks as reference. For both the parent and teacher SDQ, mean scores for total difficulties, conduct problems and hyperactivity among children born at 37 or 38 weeks were slightly higher than those born at 40 weeks of gestation, but the differences were not statistically significant. Children born at 43 weeks showed significantly greater scores for behavioural problems than those born at 40 weeks on the parent SDQ, but not on the teacher SDQ.

Behaviour Scores by Sex- and Gestational Age-Specific Birth Size

Table 3 presents crude and adjusted mean differences in parent SDQ scores per standard deviation (SD) of each of the birth size z-scores. In the crude analysis, higher birthweight z-scores were associated with lower scores for total difficulties, conduct problems, and hyperactivity and higher scores for prosocial behaviour. After adjusting for all confounding factors, a 1-SD (approximately 400 g) increase in birthweight for gestational age was associated with 0.03 [95% CI: −0.05, −0.01] and 0.09 [95% CI: −0.13, −0.05] lower scores for conduct problems and hyperactivity, respectively, but nonsignificantly with total difficulties [−0.09, 95% CI: −0.19, 0.00]. The association with prosocial behaviour was no longer statistically significant after adjustment for confounders. Similarly, a 1-SD (approximately 2 cm) in birth length z-score remained significantly associated with lower hyperactivity scores [−0.05, 95% CI: −0.09, −0.01] after adjustment for potential confounders. For head circumference, a 1-SD (approximately 1.5 cm) increase in z-score was negatively associated with total difficulties [−0.11, 95% CI: −0.22, −0.01], conduct problems [−0.04, 95% CI: −0.06, −0.01], and hyperactivity [−0.08, 95% CI: −0.12, −0.03] after adjusting for potential confounders.

Table 4 presents the results for the teacher SDQ. Consistent with the parent SDQ, foetal growth measures were associated with the teacher SDQ, although the magnitude of association was even larger. After adjustment for potential confounders, a 1-SD increase in birthweight z-score was associated with lower scores for total difficulties [−0.31, 95% CI: −0.43, −0.19], hyperactivity [−0.16, 95% CI: −0.21, −0.10], emotional symptoms [−0.07, 95% CI: −0.10, −0.03], and peer problems [−0.05, 95% CI: −0.09, −0.02]. Birth length and head circumference z-scores showed similar associations.

When we examined the associations after simultaneously adjusting for foetal growth measures—birthweight z-score in estimating the effects of birth length or head circumference z-score and birth length or head circumference z-score in estimating the effects of birthweight z-score, the associations with birth length and head circumference were substantially attenuated, while the association with birthweight remained statistically significant. For example, mean differences in total difficulties scores in the teacher SDQ were −0.26 [95% CI: −0.41, −0.11] per 1-SD increase in birthweight z-score, −0.07 [95% CI: −0.20, 0.07] per 1-SD increase in birth length z-score, and −0.18 [95% CI: −0.30, −0.06] per 1-SD increase in birth head circumference z-score.

Similar patterns of association were observed in the analysis of SGA, AGA, and LGA. For example, compared to children born AGA, those born SGA had higher scores in total difficulties [0.55, 95% CI: 0.18, 0.92], conduct problems 0.05 [95% CI: −0.06, 0.17], hyperactivity [0.21, 95% CI: 0.05, 0.38], emotional symptoms [0.10, 95% CI: −0.03, 0.22], and peer problems [0.18, 95% CI: 0.07, 0.29] in the teacher SDQ. The corresponding figures for the parent SDQ were 0.24 [95% CI: 0.05, 0.53], 0.08 [95% CI: 0.01, 0.16], 0.15 [95% CI: 0.04, 0.25], −0.01 [95% CI: −0.13, 0.11], and 0.02 [−0.07, 0.10]. Consistent with the main analysis, children born LGA had lower scores in total difficulties [−0.24, 95% CI: −0.06, 0.11 in the parent SDQ and −0.40, 95% CI: −0.77, −0.02 in the teacher SDQ], conduct problems [−0.08, 95% CI: −0.18, 0.01 in the parent; −0.03, 95% CI: −0.14, 0.08 in the teacher SDQ], hyperactivity [−0.21, 95% CI: −0.33, −0.10 in the parent; −0.29, 95% CI: −0.46, −0.12 in the teacher SDQ], emotional symptoms [0.01, 95% CI: −0.14, 0.16 in the parent; −0.07, 95% CI: −0.20, 0.05], and peer problems [0.04, 95% CI: −0.07, 0.14 in the parent; −0.01, 95% CI: −0.12, 0.12 in the teacher SDQ].

Sensitivity Analysis

Associations with gestational age and birth sizes for gestational age remained unchanged after excluding children with delivery complications (N=2,741), children whose gestational age was not confirmed by ultrasound (N=849), or nonspontaneous births (N=1,613) (data not shown). The associations of birthweight z-scores based on internal standardization within our sample, as done for birth length and head circumference, were substantially identical with the results presented. We also examined associations using a dichotomized behaviour score at the 85th or at 90th percentile (i.e., top 10 or 15 percent defined as 'behaviour problem' for total difficulty scores and 4 subscales and the lowest 10 or 15 percent for prosocial behaviour), and the results were essentially unchanged from those with continuous outcomes (data not shown). We also observed that the associations presented did not vary by parental socioeconomic factors (all p-values for the interactions >0.1, data not shown).

In addition, further adjustment for child cognitive ability (as measured by the Wechsler Abbreviated Scales of Intelligence at the 6.5-year follow-up) did not alter the results; a 1-SD increase in birthweight z-score was associated with lower scores for total difficulties [−0.22, 95% CI: −0.37, −0.07], hyperactivity [−0.11, 95% CI: −0.18, −0.04], peer problems [−0.06, 95% CI: −0.10, −0.01], and emotional symptoms [−0.06, 95% CI: −0.11, −0.01] on the teacher SDQ after adjusting for confounders, birth length z-score, and cognitive ability. Cognitive ability was associated with all behaviour scores independent of birth size for gestational age and other covariates in our study. For example, a 1-point increase in the full-scale IQ was associated with 0.06 [95% CI: −0.07, −0.05] lower scores for total difficulties and with 0.02 [95% CI: 0.01, 0.02] higher scores for prosocial behaviour on the teacher SDQ. Similarly, additional adjustment for cognitive ability did not change the associations of birth length and birth head circumference with behaviour scores presented in our main analysis (data not shown).

DISCUSSION

We observed that increased size at birth is associated with less problem behaviour at age 6.5 years among children who had been born at or after term. Although larger birth size was associated with lower behavioural problem scores in both the parent and teacher assessments, the magnitude of association was stronger in the teacher assessments. With simultaneous adjustment for measures of birth size, birthweight for gestational age was most consistently associated with behavioural problems at age 6.5 years, while the associations with birth length and head circumference were substantially attenuated.

Gestational age was not associated with child behaviour among term births. Although we observed slightly greater behavioural problems among children born at early term (37–38 weeks), the differences did not reach statistical significance. The significantly higher behavioural problem scores observed on the parent SDQ among children born at 43 weeks require confirmation, since only 10 children were born at that gestational age in our study. Moreover, higher scores were not observed on the teacher assessment, and teachers have been reported to more accurately identify problem behaviours such as hyperactivity and conduct problems than parents.[27]

Comparisons with other studies

Although many studies have reported associations between small size at birth and behavioural problems in childhood, most have been based on small, selected samples.[3, 4, 7] Moreover, they have not accounted for gestational age to separate the effects of preterm birth and restricted foetal growth.[11] Few studies have restricted their analysis to children born at or after term,[16–19] and their results have been inconsistent. Some reported smaller size at birth to be associated with increased emotional or behavioural problems,[16, 17, 19] but others[18] showed no such differences. The inconsistent results would be owing to variation in child behaviour measures, different treatment of birth size and behaviour measures (binary vs. continuous), and population differences. Compared to other studies, the effect sizes associated with birth size in our study are smaller; studies using continuous scale of behavior[16, 17] reported the associations with the size of 10–15% of standard deviation (SD) of behavioural outcome, while our results show 2–6% of SD. This smaller effect size would be due to our study inclusion criterion on birthweight ≥2500 g.

All three indicators of foetal “growth” included in our study were predictive of child behavioural problems after controlling for maternal and family characteristics. When we assessed the independent effect of each birth size measure by simultaneous adjustment, birthweight z-score was a better predictor than birth length or head circumference. Birthweight reflects two important aspects of body size—longitudinal (skeletal) growth and growth of the soft tissues. The effects of birthweight adjusted for birth length thus reflect the effects of the soft tissue (except brain) mass, while estimates of birth length or head circumference adjusted for birthweight reflect the effects of the skeletal and brain growth. The more consistently observed association of birthweight might indicate that birthweight is a better measure of foetal ‘growth’ as birthweight is more sensitive to maternal diet and lifestyles as observed by the occurrence of skeletal ‘sparing’ under growth restriction.[31] Alternatively, more robust associations of birth weight might indicate that measurement of birth length and head circumference is more prone to error than that of birthweight. Few studies have simultaneously examined the effects of multiple measures of birth size,[16, 17, 19] and even fewer examined the independent associations of those measures. The study by Wiles et al[19] is the only large population-based study that examined associations of birthweight and birth length with behavioural problems. They observed that birth length, but not birthweight, was negatively associated with behavioural problems among children at age 7 years. The reasons for differences in results from our study are unclear but may reflect differences in study populations or measurement errors in birth size between the two studies., and measures of birth length or head circumference are also likely to vary to a greater degree across study sites. Birth length in Wiles et al’s study[19] was standardized and measured by research staff, while it was not standardized across study sites in our study.

Previous studies of other health outcomes in association with birthweight and birth length have also reported inconsistent results. For studies of schizophrenia, for example, some studies observed a negative association with birth length[32] and birthweight,[33] while others showed no association with birth length.[34] Mixed results have also been reported in studies of the associations between different measures of body size at birth and cardiovascular diseases.[35–37]

We observed that smaller birth sizes were more consistently associated with disruptive behaviours, i.e., conduct problems and hyperactivity; the effect size for hyperactivity was

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the largest across birth size measures. Reports of abnormalities in brain and central nervous system functioning observed among children and adolescents with attention-deficit/ hyperactivity disorder[38] support the specific association of birth size with disruptive behaviours, and with hyperactivity in particular, in our study.

It has been widely hypothesized that behavioural problems among preterm or low birthweight children are mediated by intellectual deficits.[39] Given the positive association between foetal growth and cognitive ability across the entire distribution of birthweight[40] and even among term births,[41] the hypothesized mediation is also possible among children born at or after term. However, cognitive ability did not explain the association between foetal growth and behavioural problems in our study, although it was associated with all of the behaviours measured. A recent study of childhood behaviour among children born preterm also failed to confirm mediation by cognitive ability.[42]

Strengths and limitations

Methodological strengths of our study include the large, multi-centre sample and prospective data collection, which enables precise estimates of associations between foetal growth and child behaviours. Gestational age and birth size measures were collected from hospital records rather than maternal recall, thus avoiding potential for recall bias. Both the parents and teachers of the children evaluated child behaviours in our study, instead of relying on the single-informant assessment used in most other studies. The use of multiple informants provides more accurate assessments of behavioural problems. The parent and teacher assessments have been shown to be complementary; teachers are better able to assess externalizing behavioural problems such as conduct and hyperactivity disorders, whereas parents are better at assessing emotional problems.[27] Consistent patterns of association across parent and teacher assessments (except for the difference noted at 43 weeks of gestation) strengthen the results observed in our study. Additionally, we examined the association across the entire distributions of both birth size and behaviours, rather than dichotomizing them at specific cut-offs. Finally, the effects estimated in our study are probably generalisable to other developed country settings, since Belarus resembles Western developed countries, in high literacy rates, readily available basic health care services, good sanitary conditions, and low infant and child mortality.

Although we adjusted for a wide range of important maternal and family characteristics, we did not have direct measures of stress or anxiety during pregnancy, a potential confounder that could theoretically affect both foetal growth and behavioural and emotional problems in the offspring.[43] As family socioeconomic circumstances are associated with both foetal growth and childhood behavioural problems,[11] differences in unmeasured indicators of family socioeconomic circumstances (such as income) could at least partly explain the observed association. In addition, unmeasured parental behaviours may be associated with unreported harmful behaviours during pregnancy and affect child behaviour. Thus, although we controlled for several measures in such family or maternal characteristics, residual confounding cannot be excluded. Another limitation is that measures of birth size in our study were not standardized across study sites. The degree of clustering of birth length and head circumference measures is greater than that of birthweight in our study, as reflected in the intraclass correlation of coefficients of 0.14 for birth length and 0.21 for birth head circumference, as 0.01 for birthweight, indicating 14% of total variance in birth length and 21% of birth head circumference lie between study sites while only 1% of variance of birthweight measure is site-specific. However, the degree of clustering was statistically accounted for in our analysis. Finally, the inclusion criterion of birthweight ≥2500 g is a possible source of selection bias that would have bias our estimated associations toward the null rather than over-estimate the true association.

Conclusions

We observed associations between foetal growth and behavioural problems, i.e., conduct problems and hyperactivity, among children at age 6.5 years who had been born at or after term within normal range of birthweight. The observed effect sizes are small, but these small effects may have public health implications by changing the population distribution,[44] as our results were obtained from a large sample of healthy children born at term, who comprise the majority of live births. Since behavioural problems in childhood often persist and predict health and well-being into adolescence and adulthood,[45] restricted foetal growth may adversely affect long-term psychological and development.

Acknowledgments

This research was supported by a grant from the Canadian Institutes of Health Research.

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Table1

Distributions (mean (sd) or n (%)) of birth size, gestational age, SDQ scores, and covariates in children at 6.5 years of PROBIT

	Boys (n=7,170)	Girls (n=6,698)	Total (n=13,868)
Birth size			
Birth weight, g	3,507(426)	3,369 (402)	3,437 (419)
Birth length, cm	52.3 (2.2)	51.6 (2.0)	51.9 (2.1)
Birth head circumference, cm	35.2 (1.5)	34.8 (1.4)	34.9 (1.5)
Gestational age, weeks: 37	256 (3.6)	214 (3.2)	470 (3.4)
38	1,136 (15.8)	972 (14.5)	2,108 (15.2)
39	2,134 (29.8)	2,069 (30.9)	4,203 (30.3)
40	3,092 (43.1)	2,886 (43.1)	5,978 (43.1)
41	457 (6.4)	469 (7.0)	926 (6.7)
42	89 (1.2)	84 (1.2)	173 (1.2)
43	6 (0.1)	4 (0.1)	10 (0.1)
SDQ scores			
Parent assessments: Total difficulty	11.9 (5.0)	11.1 (4.9)	11.5 (4.9)
Conduct problems	1.8 (1.5)	1.4 (1.4)	1.6 (1.5)
Hyperactivity	5.0 (2.2)	4.5 (2.2)	4.7 (2.2)
Peer problems	2.6 (1.6)	2.5 (1.6)	2.5 (1.6)
Emotional symptoms	2.5 (2.0)	2.7 (2.0)	2.6 (2.0)
Prosocial behaviors	8.1 (1.7)	8.5 (1.5)	8.3 (1.6)
Teacher assessments: Total difficulty	10.7 (6.0)	8.4 (5.3)	9.6 (5.7)
Conduct problems	1.8 (1.9)	0.9 (1.4)	1.3 (1.7)
Hyperactivity	4.5 (2.7)	3.3 (2.4)	3.9 (2.6)
Peer problems	2.4 (1.7)	2.2 (1.7)	2.3 (1.7)
Emotional symptoms	2.0 (1.9)	2.0 (1.9)	2.0 (1.9)
Prosocial behaviors	7.0 (2.3)	7.9 (2.0)	7.4 (2.2)
Covariates			
Maternal age	24.4 (4.9)	24.5 (4.9)	24.4 (4.9)
Paternal age	27.4 (5.1)	27.5 (5.1)	27.4 (5.1)
Maternal height, cm	164.3 (5.6)	164.5 (5.6)	164.4 (5.6)
Smoking during pregnancy, yes	160 (2.2)	132 (2.0)	292 (2.1)
Drinking during pregnancy, yes	171 (2.4)	140 (2.1)	396 (2.3)
Marital status of parents: Married	6,443 (89.9)	5,910 (88.2)	12,353 (89.1)
Cohabitation	466 (6.5)	508 (7.6)	974 (7.0)
Unmarried	261 (3.6)	280 (4.2)	541 (3.9)
No. of older children at home: 0	4,079 (56.9)	3,780 (56.4)	7,859 (56.7)
1	2,465 (34.4)	2,347 (35.0)	4,812 (34.7)
2	626 (8.7)	571 (8.5)	1,197 (8.6)
Maternal education: Less than secondary	256 (3.6)	255 (3.8)	511 (3.7)
Secondary	2,308 (32.2)	2,136 (31.9)	4,444 (32.0)

		Boys (n=7,170)	Girls (n=6,698)	Total (n=13,868)
	Partial university	3,664 (51.1)	3,416 (51.0)	7,080 (51.1)
	University	942 (13.1)	891 (13.3)	1,833 (13.2)
Maternal occupation:	Non-manual	3,101 (43.2)	2,937 (43.9)	6,038 (43.5)
	Manual	2,452 (34.2)	2,232 (33.3)	4,684 (33.8)
	Unemployed	1,617 (22.6)	1,529 (22.8)	3,146 (22.7)
Paternal education:	Less than secondary	164 (2.4)	154 (2.4)	318 (2.4)
	Secondary	2,592 (37.2)	2,407 (37.2)	4,989 (37.2)
	Partial university	3,289 (47.4)	3,084 (47.7)	6,373 (47.6)
	University	902 (13.0)	818 (12.7)	1,720 (12.8)
Paternal occupation:	Non-manual	2,028 (28.3)	1,859 (27.8)	3,887 (28.0)
	Manual	3,863 (53.9)	3,673 (54.8)	7,536 (54.3)
	Unemployed	989 (13.8)	889 (13.3)	1,878 (13.5)
	Unknown	290 (4.0)	277 (4.1)	567 (4.1)

Table 2

Mean differences (95% CI) in parent and teacher SDQ scores according to gestational age (GA) in completed weeks in PROBIT children at age 6.5 years

		Parent SDQ				Teacher SDQ			
	GA	Crude		Adjusted*		Crude		Adjusted*	
Total Difficulties	37	0.28	(−0.05, 0.62)	0.22	(−0.13, 0.57)	0.56	(−0.05, 1.16)	0.34	(−0.24, 0.92)
	38	0.19	(−0.05, 0.42)	0.13	(−0.11, 0.36)	0.24	(−0.08, 0.55)	0.25	(−0.06, 0.56)
	39	−0.09	(−0.26, 0.09)	−0.13	(−0.31, 0.05)	0.11	(−0.13, 0.35)	0.17	(−0.07, 0.41)
	40	reference		reference		reference		reference	
	41	−0.25	(−0.53, 0.03)	−0.26	(−0.58, 0.06)	−0.20	(−0.62, 0.23)	−0.20	(−0.62, 0.22)
	42	−0.07	(−0.67, 0.52)	−0.14	(−0.70, 0.42)	0.11	(−0.99, 1.21)	0.07	(−1.03, 1.16)
	43	4.42	(2.59, 6.26)	3.98	(2.12, 5.84)	−0.12	(−3.57, 3.34)	−0.71	(−4.85, 3.43)
Conduct Problems	37	0.08	(−0.06, 0.22)	0.06	(−0.08, 0.21)	0.14	(−0.05, 0.34)	0.07	(−0.11, 0.25)
	38	0.02	(−0.07, 0.12)	0.01	(−0.06, 0.09)	0.01	(−0.08, 0.11)	0.00	(−0.09, 0.10)
	39	−0.03	(−0.09, 0.04)	−0.02	(−0.09, 0.04)	0.00	(−0.07, 0.08)	0.02	(−0.05, 0.09)
	40	reference		reference		reference		reference	
	41	0.01	(−0.09, 0.10)	0.01	(−0.09, 0.12)	−0.05	(−0.17, 0.07)	−0.06	(−0.18, 0.06)
	42	−0.08	(−0.27, 0.10)	−0.08	(−0.26, 0.11)	0.00	(−0.33, 0.32)	0.00	(−0.32, 0.32)
	43	1.29	(0.39, 2.19)	1.02	(0.21, 1.82)	−0.06	(−1.04, 0.91)	−0.48	(−1.55, 0.59)
Hyperactivity	37	0.17	(−0.01, 0.36)	0.14	(−0.04, 0.32)	0.23	(−0.06, 0.51)	0.11	(−0.17, 0.39)
	38	0.05	(−0.05, 0.15)	0.03	(−0.06, 0.12)	0.11	(−0.04, 0.26)	0.11	(−0.03, 0.26)
	39	−0.02	(−0.10, 0.05)	−0.03	(−0.11, 0.05)	0.01	(−0.10, 0.13)	0.04	(−0.07, 0.15)
	40	reference		reference		reference		reference	
	41	0.00	(−0.15, 0.15)	−0.02	(−0.17, 0.14)	0.00	(−0.20, 0.19)	−0.01	(−0.20, 0.18)
	42	0.09	(−0.23, 0.41)	0.08	(−0.23, 0.40)	0.08	(−0.39, 0.55)	0.05	(−0.41, 0.52)
	43	1.59	(0.58, 2.60)	1.31	(0.17, 2.45)	1.16	(−0.70, 3.03)	0.95	(−1.36, 3.26)
Emotional Symptoms	37	0.05	(−0.11, 0.22)	0.06	(−0.12, 0.24)	0.08	(−0.11, 0.27)	0.10	(−0.10, 0.29)
	38	0.07	(−0.01, 0.15)	0.07	(−0.01, 0.15)	0.05	(−0.05, 0.15)	0.07	(−0.03, 0.18)
	39	−0.01	(−0.06, 0.04)	−0.03	(−0.08, 0.02)	0.05	(−0.03, 0.13)	0.07	(−0.02, 0.15)
	40	reference		reference		reference		reference	

		Parent SDQ				Teacher SDQ			
	GA	Crude		Adjusted*		Crude		Adjusted*	
	41	−0.20	(−0.31, −0.08)	−0.20	(−0.31, −0.08)	−0.08	(−0.22, 0.06)	−0.07	(−0.21, 0.07)
	42	0.03	(−0.15, 0.22)	0.01	(−0.20, 0.21)	0.03	(−0.29, 0.34)	0.02	(−0.29, 0.34)
	43	0.95	(−0.08, 1.97)	0.93	(−0.19, 2.06)	−0.71	(−2.23, 0.81)	−0.47	(−2.17, 1.23)
Peer	37	−0.01	(−0.13, 0.11)	−0.04	(−0.17, 0.10)	0.11	(−0.06, 0.28)	0.06	(−0.11, 0.23)
Problems	38	0.04	(−0.04, 0.12)	0.02	(−0.06, 0.11)	0.05	(−0.04, 0.14)	0.05	(−0.04, 0.14)
	39	−0.03	(−0.09, 0.04)	−0.05	(−0.12, 0.02)	0.03	(−0.04, 0.10)	0.03	(−0.04, 0.11)
	40	reference		reference		reference		reference	
	41	−0.06	(−0.19, 0.08)	−0.06	(−0.20, 0.08)	−0.05	(−0.18, 0.07)	−0.05	(−0.18, 0.08)
	42	−0.10	(−0.25, 0.05)	−0.14	(−0.29, 0.01)	−0.03	(−0.32, 0.26)	−0.04	(−0.34, 0.25)
	43	0.60	(−0.33, 1.54)	0.74	(−0.30, 1.79)	−0.40	(−1.20, 0.41)	−0.58	(−1.48, 0.32)
Prosocial	37	−0.07	(−0.20, 0.06)	−0.05	(−0.19, 0.08)	−0.06	(−0.29, 0.16)	0.03	(−0.19, 0.25)
Behaviour	38	−0.02	(−0.12, 0.09)	−0.01	(−0.10, 0.09)	−0.05	(−0.17, 0.07)	−0.02	(−0.14, 0.10)
	39	0.00	(−0.08, 0.07)	0.00	(−0.09, 0.09)	−0.05	(−0.14, 0.04)	−0.06	(−0.15, 0.03)
	40	reference		reference		reference		reference	
	41	−0.03	(−0.12, 0.06)	−0.04	(−0.13, 0.06)	0.09	(−0.06, 0.25)	0.10	(−0.06, 0.26)
	42	0.01	(−0.28, 0.30)	0.07	(−0.21, 0.36)	0.08	(−0.25, 0.41)	0.12	(−0.22, 0.45)
	43	−1.10	(−1.45, −0.75)	−0.99	(−1.39, −0.60)	0.12	(−1.43, 1.67)	0.84	(−0.31, 1.98)

*Adjusted for sex, birth weight for gestational age, maternal and paternal age, maternal height, smoking and drinking during pregnancy, number of children at home, marital status of parents, maternal and paternal education and occupation

Table 3

Mean differences (95% CI) in parent SDQ scores according to birth size z-scores in PROBIT children at age 6.5 years

	Birth weight z-score					
	Crude		**Adjusted 1**		**Adjusted 2**	
Total difficulties	−0.21	(−0.31, −0.11)	−0.15	(−0.26, −0.05)	−0.09	(−0.19, 0.00)
Conduct problems	−0.06	(−0.08, −0.03)	−0.04	(−0.06, −0.01)	−0.03	(−0.05, −0.01)
Hyperactivity	−0.13	(−0.17, −0.09)	−0.11	(−0.15, −0.08)	−0.09	(−0.13, −0.05)
Emotional symptoms	−0.01	(−0.06, 0.04)	−0.001	(−0.05, 0.05)	0.02	(−0.03, 0.07)
Peer problems	−0.01	(−0.04, 0.02)	−0.001	(−0.03, 0.03)	0.004	(−0.02, 0.03)
Prosocial behaviors	0.03	(0.003, 0.06)	0.02	(−0.01, 0.05)	0.01	(−0.02, 0.04)
	Birth length z-score					
	Crude		Adjusted 1		Adjusted 2	
Total difficulties	−0.14	(−0.25, −0.03)	−0.09	(−0.20, 0.02)	−0.04	(−0.15, 0.07)
Conduct problems	−0.04	(−0.07, −0.01)	−0.03	(−0.06, 0.004)	−0.02	(−0.05, 0.01)
Hyperactivity	−0.09	(−0.12, −0.05)	−0.07	(−0.11, −0.03)	−0.05	(−0.09, −0.01)
Emotional symptoms	−0.01	(−0.04, 0.03)	0.002	(−0.04, 0.04)	0.02	(−0.02, 0.05)
Peer problems	−0.01	(−0.04, 0.02)	0.002	(−0.03, 0.03)	0.01	(−0.02, 0.04)
Prosocial behaviors	0.00	(−0.03, 0.03)	−0.005	(−0.04, 0.03)	−0.02	(−0.05, 0.01)
	Head circumference z-score					
	Crude		Adjusted 1		Adjusted 2	
Total difficulties	−0.19	(−0.30, −0.08)	−0.16	(−0.28, −0.05)	−0.11	(−0.22, −0.004)
Conduct problems	−0.05	(−0.08, −0.02)	−0.04	(−0.07, −0.02)	−0.04	(−0.06, −0.01)
Hyperactivity	−0.10	(−0.14, −0.06)	−0.09	(−0.14, −0.05)	−0.08	(−0.12, −0.03)
Emotional symptoms	−0.004	(−0.06, 0.05)	0.00	(−0.05, 0.05)	0.02	(−0.04, 0.07)
Peer problems	−0.03	(−0.05, 0.001)	−0.02	(−0.05, 0.003)	−0.01	(−0.04, 0.01)
Prosocial behaviors	0.02	(−0.01, 0.06)	0.02	(−0.02, 0.05)	0.01	(−0.03, 0.04)

Adjusted1: adjusted for maternal and paternal age, maternal height, smoking and drinking during pregnancy;
Adjusted2: adjusted1+ number of children at home, marital status of parents, maternal and paternal education and occupation.

Table 4

Mean differences (95% CI) in teacher SDQ scores according to birth size z-scores in PROBIT children at 6.5 years

	Birth weight z-score					
	Crude		**Adjusted 1**		**Adjusted 2**	
Total difficulties	−0.37	(−0.49, −0.26)	−0.34	(−0.46, −0.23)	−0.31	(−0.43, −0.19)
Conduct problems	−0.06	(−0.09, −0.02)	−0.04	(−0.08, −0.01)	−0.03	(−0.07, 0.00)
Hyperactivity	−0.19	(−0.24, −0.14)	−0.17	(−0.23, −0.12)	−0.16	(−0.21, −0.10)
Emotional symptoms	−0.07	(−0.11, −0.03)	−0.07	(−0.11, −0.03)	−0.07	(−0.10, −0.03)
Peer problems	−0.06	(−0.09, −0.03)	−0.06	(−0.09, −0.02)	−0.05	(−0.09, −0.02)
Prosocial behaviors	0.06	(0.02, 0.10)	0.05	(0.01, 0.09)	0.04	(−0.01, 0.08)
	Birth length z-score					
	Crude		Adjusted 1		Adjusted 2	
Total difficulties	−0.30	(−0.41, −0.19)	−0.28	(−0.39, −0.16)	−0.24	(−0.35, −0.13)
Conduct problems	−0.05	(−0.08, −0.02)	−0.04	(−0.07, −0.01)	−0.04	(−0.07, −0.01)
Hyperactivity	−0.14	(−0.19, −0.10)	−0.14	(−0.18, −0.09)	−0.12	(−0.17, −0.07)
Emotional symptoms	−0.05	(−0.09, −0.02)	−0.04	(−0.08, −0.01)	−0.04	(−0.08, −0.01)
Peer problems	−0.05	(−0.09, −0.02)	−0.05	(−0.09, −0.01)	−0.02	(−0.06, 0.01)
Prosocial behaviors	0.05	(0.01, 0.10)	0.05	(−0.002, 0.10)	0.03	(−0.01, 0.07)
	Head circumference z-score					
	Crude		Adjusted 1		Adjusted 2	
Total difficulties	−0.34	(−0.44, −0.24)	−0.33	(−0.44, 0.22)	−0.30	(−0.41, −0.17)
Conduct problems	−0.05	(−0.08, −0.02)	−0.05	(−0.08, −0.02)	−0.04	(−0.07, −0.01)
Hyperactivity	−0.15	(−0.18, −0.11)	−0.14	(−0.18, −0.11)	−0.13	(−0.16, −0.10)
Emotional symptoms	−0.06	(−0.11, −0.02)	−0.06	(−0.11, −0.01)	−0.06	(−0.11, −0.02)
Peer problems	−0.07	(−0.11, −0.03)	−0.07	(−0.11, −0.03)	−0.07	(−0.11, −0.03)
Prosocial behaviors	0.06	(0.01, 0.10)	0.06	(0.01, 0.11)	0.05	(0.004, 0.09)

Adjusted1: adjusted for maternal and paternal age, maternal height, smoking and drinking during pregnancy;

Adjusted2: adjusted1+ number of children at home, marital status of parents, maternal and paternal education and occupation.