

Post-term birth and the risk of behavioural and emotional problems in early childhood

Hanan El Marroun,^{1,2*} Mijke Zeegers,^{1,3} Eric AP Steegers,⁴ Jan van der Ende,¹ Jacqueline J Schenk,⁵ Albert Hofman,⁶ Vincent WV Jaddoe,^{2,6,7} Frank C Verhulst¹ and Henning Tiemeier^{1,6,8}

¹Department of Child and Adolescent Psychiatry, Erasmus MC—Sophia, Rotterdam, The Netherlands, ²The Generation R Study Group, Erasmus MC, Rotterdam, The Netherlands, ³Pallas Health Research and Consultancy, Rotterdam, The Netherlands, ⁴Department of Obstetrics and Gynecology, Erasmus MC, Rotterdam, The Netherlands, ⁵Department of Psychology, Erasmus University Rotterdam, The Netherlands, ⁶Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands, ⁷Department of Pediatrics, Erasmus MC, Rotterdam, The Netherlands and ⁸Department of Psychiatry, Erasmus MC, Rotterdam, The Netherlands

*Corresponding author. Department of Child and Adolescent Psychiatry, Erasmus MC—Sophia, P.O. Box 2060, 3000 CB Rotterdam, The Netherlands. Email: h.marrounel@erasmusmc.nl

Accepted 23 February 2012

Background Post-term birth, defined as birth after pregnancy duration of 42 weeks, is associated with increased neonatal morbidity and mortality. The long-term consequences of post-term birth are unknown. We assessed the association of post-term birth with problem behaviour in early childhood.

Methods The study was performed in a large population-based prospective cohort study in Rotterdam, The Netherlands. Pregnant mothers enrolled between 2001 and 2005. Of a cohort of 5145 children, 382 (7%) were born post-term, and 226 (4%) were born preterm. Parents completed a standardized and validated behavioural checklist (Child Behavior Checklist, CBCL/1.5–5) when their children were 1.5 and 3 years old. We examined the relation between gestational age (GA) at birth, based on early fetal ultrasound examination, and problem behaviour with regression analyses, adjusting for socio-economic and pregnancy-related confounders.

Results A quadratic relationship between GA at birth and problem behaviour indicates that both preterm and post-term children have higher behavioural and emotional problem scores than the term born children. Compared with term born children, post-term born children had a higher risk for overall problem behaviour [odds ratio (OR) = 2.10, 95% confidence interval (CI) = 1.32–3.36] and were almost two and a half times as likely to have attention deficit / hyperactivity problem behaviour (OR = 2.44, 95% CI = 1.38–4.32).

Conclusions Post-term birth was associated with more behavioural and emotional problems in early childhood, especially attention deficit / hyperactivity problem behaviour. When considering expectant management, this aspect of post-term pregnancy should be taken into account.

Keywords Post-term birth, preterm birth, behavioural and emotional problems, childhood

Introduction

Timely onset of labour is important for peri- and post-natal health. Both preterm (<37 weeks of gestation) and post-term birth (≥ 42 weeks of gestation) are associated with neonatal morbidity and mortality.^{1–3} Local management protocols with regard to elective caesarean delivery and labour induction affect the prevalence of post-term birth. Overall, labour induction before or at 42 weeks of gestation has increased,¹ but post-term births still occur relatively frequently (up to 5–10%), even in industrialized countries.^{3,4} Accurate pregnancy dating is critical to the diagnosis of post-term births.^{3,4} Routine use of ultrasound to confirm pregnancy dating can decrease occurrence of post-term birth.⁵ Common risk factors for post-term birth include obesity, nulliparity and prior post-term birth and rare causes include placental sulphatase deficiency (an X-linked recessive disorder characterized by low estriol levels), fetal adrenal hypoplasia or insufficiency and trisomy 16 and 18.^{1,2,6,7}

The long-term problems associated with preterm birth, such as increased incidence of cerebral palsy, sensory impairments and behavioural problems are well known.⁸ The studies investigating effects of post-term birth have focused on the risks during pregnancy and delivery.⁹ Post-term birth increased the risk of neonatal encephalopathy and death during the first year of life,^{5,10} but the long-term consequences are unclear. One of the few studies performed found that post-term born infants did not differ from controls at age 2 years regarding general intelligence, physical milestones and illnesses.¹¹ However, a recent study using referral to a neurologist or psychologist as indicator of developmental problems found that 13% of children born post-term had a neurological or developmental disorder at the age of 5 years.¹²

In this population-based prospective study, we hypothesize that post-term birth is related to behavioural and emotional problems in preschool children. In order to examine the specificity of the association between post-term birth and problem behaviour, we examined specific behavioural and emotional problems including attention deficit / hyperactivity disorder problems (ADHD), affective problems and pervasive developmental problems.

Materials and methods

This study was embedded within the Generation R Study, a population-based cohort from fetal life onwards.¹³ Briefly, pregnant women who were resident in Rotterdam, The Netherlands, and whose delivery dates were between April 2002 and January 2006, were asked by their midwives and gynaecologists to participate. In the post-natal follow-up of the Generation R cohort, 7484 live born children and

their prenatally recruited mothers participated. Post-natally, 38 children died. The remaining 7446 children were eligible for the study. Mothers of 477 children withdrew consent, and mothers of 410 children gave restricted consent (i.e. no participation in questionnaire studies). The remaining mothers of 6559 children gave full consent for post-natal follow-up. We excluded twin pregnancies, leaving 6422 children who could be contacted. Information on child behavioural and emotional problems at 18 and/or 36 months was available for 5145 children (response rate of 78%). Maternal report at both 18 and 36 months was available for 3840 children, 812 mothers reported at 18 months only and 493 mothers reported at 36 months only. The Medical Ethical Review Board of the Erasmus Medical Centre, Rotterdam approved the study protocol. All parents of participating children gave written informed consent.

Ultrasound during the first visit determined gestational age (GA) to the nearest day, which will be expressed in our analyses in weeks. In total, 4132 women (80%) had their first ultrasound examination in early pregnancy (median 13.1 weeks, range 5.1–18.0), 868 women (17%) had it in mid-pregnancy (20.4 weeks, 18.1–25.0) and only 145 women (3%) had their first ultrasound examination in late pregnancy (30.2 weeks, 25.1–39.2). Crown–rump length was used for pregnancy dating until a GA of 12 weeks and 5 days (crown–rump length <65 mm), and biparietal diameter was used for pregnancy dating thereafter (GA from 12 weeks and 5 days onwards, biparietal diameter >23 mm). Methods for establishing GA and standard ultrasound planes for fetal measurements have been described previously.¹⁴ Inter- and intra-observer intra-class correlation coefficients were all >0.98.¹⁴

Preterm birth was defined as birth before 37 weeks gestation ($N=226$) and post-term birth was defined as birth after ≥ 42 weeks gestation ($N=382$). As an additional comparison group, we defined a group of children born before 35 weeks of gestation ($N=78$) which is normally included in cohorts of preterm babies.

The Child Behavior Checklist for toddlers (CBCL/1.5–5) was used to obtain standardized parental reports of children's behavioural and emotional problems.^{15,16} The CBCL was a postal questionnaire and sent to be filled out by the mother when the child was 18 months old and again when the child was 36 months old. At 36 months of age, we also asked the father to fill out the CBCL. Each item (99 items in total) is scored on a three-point scale (0=not true, 1=somewhat or sometimes true and 2=very true or often true), based on the child's behaviour during the preceding 2 months. The sum of all problem items is the Total Problems score. There are five Diagnostic and Statistical Manual of Mental Disorders (DSM)-oriented scales: anxiety problems, affective problems,

pervasive developmental problems, ADHD and oppositional defiant problems. It has been shown that these DSM-oriented scales provide accurate and supplementary information on clinical diagnoses.¹⁷ Also, good reliability and validity have been reported for the CBCL.¹⁶ We used the clinical cut-off scores (91st percentile for the Total Problems score and 98th percentile for the syndrome scales) to classify children as having behavioural problems in the clinical range.¹⁷ When parents filled out the questionnaire, they were not aware of our research question exploring the relation between post-term birth and behavioural problems, but parents generally are aware of the GA of their child and the risks associated with preterm birth. The maternal CBCL Total Problems ratings at 18 months and 36 months were correlated ($r=0.58$, $P<0.001$). Maternal and paternal CBCL Total Problems ratings at 36 months were correlated ($r=0.56$, $P<0.001$).

Several covariates were considered in the analyses and were chosen based on the existing literature and effect estimate changes. Maternal weight and height were measured at intake. We used postal questionnaires to obtain information on mother's parity, ethnicity and family income. Maternal ethnicity was defined according to the classification of Statistics Netherlands.¹⁸ Educational level was categorized into three levels: primary, secondary and higher education.¹⁹ Information about maternal smoking and alcohol use was obtained by questionnaires in each trimester. Based on these questionnaires, maternal smoking or drinking were categorized into 'no', 'until pregnancy was known' and 'continued during pregnancy' as described previously.²⁰ The Brief Symptom Inventory (BSI) was used to assess maternal psychopathology in mid-pregnancy; the BSI is a validated self-report questionnaire, which defines a spectrum of psychiatric symptoms.²¹ Registries provided information on obstetric variables such as induction, birthweight, mode of delivery, umbilical artery pH and Apgar scores after 1 and 5 min. The post-natal questionnaire administered at age 6 and 12 months was used to gather information on breastfeeding and frequency of day care use.

For descriptive analyses, children were categorized in three groups based on GA: (i) born after 37 weeks of gestation up to and including 41 weeks and 6 days (term, reference group); (ii) born after <37 weeks of gestation (preterm); and (iii) born after 42+0 weeks of gestation or more (post-term). Chi-square and *t*-tests were used to compare maternal and child characteristics. To test the associations between GA and behavioural problems, we used linear regression models with GA as a continuous variable. We used the generalized estimating equation (GEE) to analyse the relation of GA with the behavioural and emotional outcomes measured at different time points. GEE adjusts for auto-correlation within the same subject. We used an unstructured correlation matrix,

and thus no assumptions were made about the correlations. The GEE procedure provides a more precise effect estimate and reduces the error derived from multiple comparisons (Type I error). A quadratic term was added to the linear regression models to test whether the associations between GA and behavioural problems were curvilinear. We conducted the primary analyses in all children, thus also including the children whose GA was assessed in the second and third trimester. This was done to reduce the risk of potential selection bias. Furthermore, we reran the analyses including only those children with a GA dating in early pregnancy ($N=4132$), because GA dating by ultrasound is assumed to be more accurate in early pregnancy.⁵

Moreover, we performed linear regression analyses for maternal ratings at 18 and 36 months separately to assess whether the quadratic association between GA at birth and child total problems was present at both ages. We also performed the same linear regression analyses for paternal ratings at 36 months. The results of these analyses can be found in the [Supplementary data](#), available at *IJE* online.

Both linear and quadratic analyses were rerun after exclusion of the preterm children, to ascertain that the relationship between GA and behavioural problems was not solely driven by the preterm children. In addition, we restricted the analyses to the children born after 39 weeks of gestation. To check whether results were not unduly influenced by ethnicity, we reran analyses regarding the Total Problems score including only the indigenous Dutch children. Gender-specific estimates for the quadratic association between GA at birth and child behavioural problems are provided in the [Supplementary Table S1](#), available as [Supplementary data](#) at *IJE* online.

For logistic regression analyses, scales were dichotomized using the clinical cut-offs. We further explored the nature of the association between GA and behavioural problems with the GEE approach, and calculated the odds ratios (ORs) of clinical problem behaviour for pre- and post-term born children. We analysed only those scales on which >0.5% of the participants were classified as having clinical problems; these were the ADHD, affective problems and pervasive developmental problems scales.

Potential confounders were chosen based on the literature and effect estimate changes. Both linear and logistic regression models were adjusted for child gender, maternal age, education, ethnicity, psychopathology, smoking and drinking during pregnancy, family income and age of the child at the time of assessments of the CBCL. Maternal weight, height, parity, breastfeeding and day care did not change the effect estimates (<5%). Maternal age, psychopathology and age of the child were used as continuous variables. Maternal education, ethnicity, smoking, drinking and family income were used as categorical variables in the analyses.

Several post-hoc analyses were performed, including only post-term children without induction, without assisted extraction or no high birthweight (>4000 g) to test if effects were driven by these birth characteristics.

Not all variables were available for each participant, the mean proportion of missing values was 5.1% and these were imputed. Variables were centred and missing data were imputed with the mean or, for categorical variables, dummy variables were made. The association between GA at birth and child behaviour problems of the imputed and non-imputed data set were compared, and these associations were similar. Therefore, we only report results of analyses with the imputed data.

For the non-response analysis, we compared maternal and child characteristics of included participants with participants from whom we did not obtain behavioural data. Non-responders were lower educated (14.7% primary education vs 6.3%, $P < 0.001$), younger (maternal age 28.1 vs 31.2 years, $P < 0.001$), more likely to be non-Dutch (62.0 vs 35.4%, $P < 0.001$). Excluded infants had a lower birthweight (3313 vs 3431 g, $P < 0.001$) and were born after a shorter period of gestation (39.5 vs 39.8 weeks, $P < 0.001$), compared with included infants. The proportion of children born post-term was lower in the non-response group than in the response group (5.8 vs 6.9%, $P < 0.001$).

Results

Table 1 compares demographic and birth characteristics of 5145 children of whom 4537 (88.2%) were born at term, 382 were born post-term (7.4%) and 226 were born preterm (4.4%).

In Figure 1, the unadjusted associations between the Total Problems scale and GA at age 18 and 36 months are shown. The curves show a nadir of the Total Problems score in children born with a GA around 40 weeks, whereas the mean problem scores are higher in children who are born more preterm or more post-term. In addition, we present a scatterplot of the correlation between GA at birth and Total Problems score in the [Supplementary data](#), available at *IJE* online.

For continuous scores on the total problems, ADHD, affective problems scales and pervasive developmental problems, linear regression analyses showed a curvilinear relation between GA and behavioural problems, indicating that children with shorter or longer gestation had higher behavioural problem scores compared with children born at term (Table 2). After exclusion of the preterm born children, the curvilinear relations between GA and behavioural problems remained, showing that mean problem scores were higher in children with a longer GA [Total Problems score β GA² = 0.34, 95% confidence interval (CI) = 0.14–0.54]. When we restricted the analyses to the

children born after 39 weeks of gestation ($n = 4115$), we still observed a linear association between GA at birth and total child behavioural and emotional problems (data not shown).

Supplementary analyses demonstrated that results were similar when children with second or third trimester GA dating were excluded (Total Problems score β GA² = 0.12, 95% CI = 0.06–0.18). Moreover, analyses on the Total Problems score were rerun in a smaller subset of Dutch children; the results were somewhat similar (β GA² = 0.08, 95% CI = 0.01–0.12). In addition, there was no interaction between GA and the two time points of CBCL measurement indicating that effects remained stable over early childhood (data not shown).

Separate linear regression analyses using the two maternal ratings each demonstrated that the quadratic association between GA at birth and child behavioural problems was present at 18 and 36 months (Supplementary Table S2, available as [Supplementary data](#) at *IJE* online). Analyses using the paternal ratings of child behavioural and emotional problems also demonstrated a quadratic relationship between GA at birth and child emotional and behavioural outcomes (Supplementary Table S3, available as [Supplementary data](#) at *IJE* online).

Table 3 shows that post-term children were almost twice as likely as term born children to have clinical problem behaviour on the Total Problems scale and were more likely to have problems in the clinical range on the ADHD scale. Compared with term born children, post-term children did not have higher ORs on the affective problems or pervasive developmental problems scales.

The preterm group showed considerably more behavioural or emotional problems compared with the term group; this group was more likely to develop problems on the Total Problems scale and the ADHD scale. With a more stringent cut-off for preterm birth (<35 weeks), we found that these children were more likely to have problems in the clinical range on the Total Problems scale, ADHD scale and the pervasive developmental problems scale.

In addition, some groups of children were excluded from the analyses. These exclusions did not change the results. The risk for developing total problems in children born post-term remained present after excluding children with induction (OR = 1.77, 95% CI = 1.01–3.10) or after excluding children >4000 g of birth weight (OR = 1.83, 95% CI = 1.06–3.15).

Discussion

Our study demonstrated that children born post-term were more likely than their term born peers to have emotional and behavioural problems at both 18 and 36 months after birth.

Post-term delivery and behavioural problems could be explained in several pathways. First, a larger baby

Table 1 Maternal and child characteristics in the study population

	Term ^a N = 4537	Post-term ^a N = 382		Preterm ^a N = 226	
	Mean (SD) or %	Mean (SD) or %	P (to ref)	Mean (SD) or %	P (to ref)
Maternal characteristics					
Age, mean years (SD)	31 (5)	31 (5)	0.34	31 (5)	0.55
Education level, %					
Primary education	6.9	5.8	0.46	7.1	0.89
Secondary education	37.8	31.4	0.01	39.8	0.57
Higher education	52.0	59.2	<0.01	47.3	0.20
Ethnicity, %					
Dutch	59.3	63.4	0.13	52.7	0.05
Other Western	8.6	10.5	0.22	8.0	0.90
Turkish, Moroccan	11.1	11.5	0.80	10.6	0.91
Surinamese, Antillean	8.1	5.9	<0.01	10.6	0.17
Psychopathology, mean score (SD)	0.25 (0.3)	0.23 (0.3)	0.43	0.28 (0.4)	0.15
Marital status, % single	9.4	7.8	0.35	14.8	0.01
Parity >1, %	12.2	10.2	0.15	8.4	0.09
Family income, %					
<€1200	11.5	10.5	0.62	18.1	<0.01
>€1200 and <€2000	14.7	12.0	0.17	14.6	1.00
>€2000	63.4	67.5	0.11	53.5	<0.01
Smoking throughout pregnancy %	14.6	14.4	1.0	18.6	0.15
Alcohol use throughout pregnancy, %	46.8	52.9	0.03	44.9	0.62
Breastfeeding at 2 months, %	68.8	71.5	0.31	63.5	0.12
Child characteristics					
GA, mean weeks (SD)	40.0 (1.1)	42.3 (0.3)	<0.001	35.0 (2.0)	<0.001
Range	37.0–41.9	42.0–43.4		26.7–36.9	
Birthweight, mean grams (SD)	3481 (486)	3819 (456)	<0.001	2403 (604)	<0.001
Boys, %	49.1	58.4	<0.001	46.0	0.15
Suspected fetal distress, %	6.9	15.2	<0.001	13.5	<0.001
Hospital delivery, %	79.1	89.5	<0.001	96.4	<0.001
Labour induction, %	9.7	37.1	<0.001	12.9	0.16
Meconium in amniotic fluid, %	15.8	18.0	0.15	0.9	<0.001
Assisted delivery, %	8.6	30.6	<0.001	13.4	0.033
Caesarean delivery, %	11.6	18.2	<0.001	25.3	<0.001
Apgar 5 min <7, %	1.0	0.8	0.51	0.9	1.00
pH umbilical artery <7.1, %	3.8	3.3	0.45	2.9	0.68
Behavioural scores measured with CBCL ^b					
Total problems					
Score at 18 months	23.53 (15.66)	24.47 (16.71)	0.29	28.35 (17.73)	<0.001
Score at 36 months	20.52 (15.07)	22.29 (15.02)	0.04	24.10 (17.34)	0.002
ADHD					
Mean score (SD) at 18 months	3.86 (2.45)	4.00 (2.45)	0.33	4.51 (2.56)	<0.001
Mean score (SD) at 36 months	2.95 (2.32)	3.08 (2.31)	0.36	3.43 (2.63)	0.007
Affective problems					
Mean score (SD) at 18 months	1.56 (1.69)	1.73 (1.90)	0.12	2.09 (1.91)	<0.001
Mean score (SD) at 36 months	1.41 (1.58)	1.55 (1.62)	0.12	1.78 (1.76)	0.002
Pervasive developmental problems					
Mean score (SD) at 18 months	1.73 (2.05)	1.86 (2.15)	0.28	2.27 (2.67)	<0.001
Mean score (SD) at 36 months	1.99 (2.26)	2.23 (2.32)	0.06	2.46 (2.87)	0.006

P-values are derived from *t*-tests for continuous variables and chi-square tests for categorical variables.

^aCategorization was based on GA at birth, term (GA from 37 weeks up to 42 weeks), preterm (GA <37 weeks) and post-term (GA of 42 weeks or more).

^bBehavioural and emotional problem scores were measured using the CBCL reported by mother at 18 and 36 months.

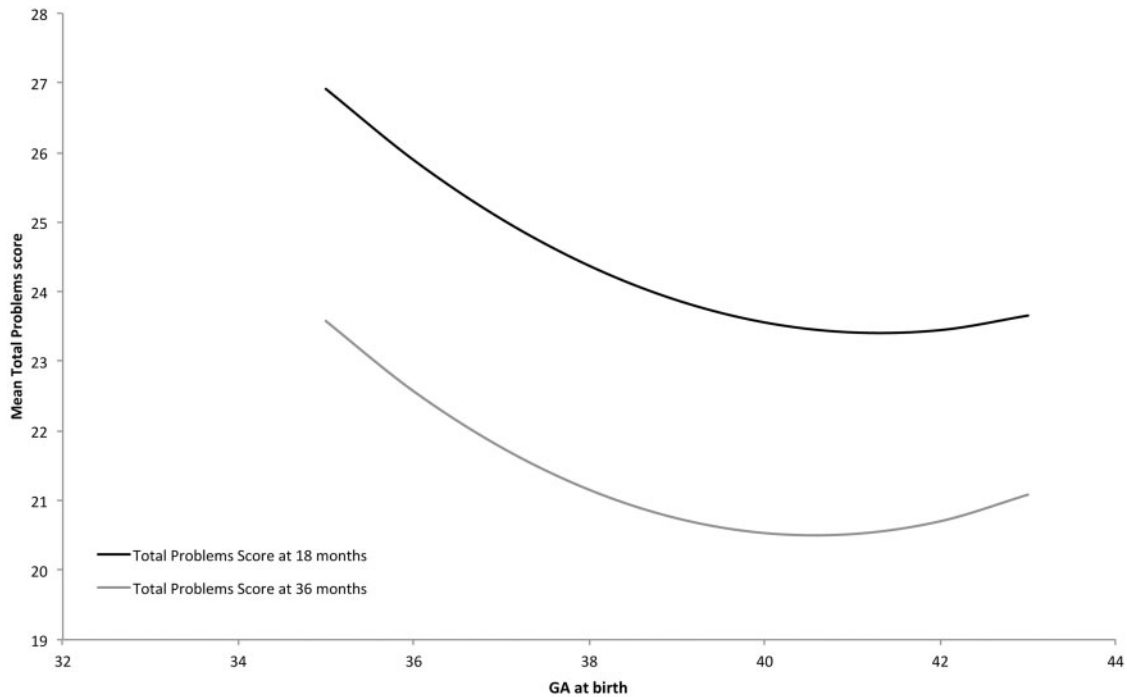


Figure 1 The unadjusted association between GA at birth and total behavioural and emotional problem score

Table 2 Association between GA at birth and behavioural and emotional problem score (continuous)

	Total problems β (95% CI)	ADHD β (95% CI)	Affective problems β (95% CI)	Pervasive developmental problems β (95% CI)
Model I				
Linear model; GA	-0.24 (-0.48 to 0.01)	-0.04 (-0.08 to 0.01)	-0.04 (-0.06 to 0.10)	-0.05 (-0.09 to -0.02)
Quadratic model; GA	0.05 (-0.21 to 0.32)	-0.01 (-0.05 to 0.04)	0.00 (-0.03 to 0.06)	-0.03 (-0.06 to 0.01)
GA ²	0.13 (0.06 to 0.20)	0.01 (0.00 to 0.03)	0.02 (0.01 to 0.02)	0.01 (0.00 to 0.03)
Model II				
Linear model; GA	0.15 (-0.16 to 0.46)	0.01 (-0.05 to 0.06)	0.08 (-0.03 to 0.04)	-0.02 (-0.06 to 0.02)
Quadratic model; GA	-0.06 (-0.39 to 0.28)	0.02 (-0.08 to 0.03)	-0.01 (-0.05 to 0.02)	-0.05 (-0.09 to -0.01)
GA ²	0.34 (0.14 to 0.54)	0.05 (0.02 to 0.08)	0.03 (0.01 to 0.05)	0.04 (0.02 to 0.07)

Behavioural and emotional problem scores were measured using the CBCL reported by mother at 18 and 36 months.

Model I: included all children.

Model II: included all children born after 37 weeks.

All models were adjusted for maternal age, education, ethnicity, psychopathology, smoking and drinking during pregnancy, family income, gender of the child and age of the child at the assessment of the CBCL.

β gives the estimate of increase in CBCL score per week increase of the centred GA. Bold values represent findings that were considered statistically significant ($P < 0.05$).

typically has a higher risk for perinatal problems. Prolonged labour, cephalopelvic disproportion and shoulder dystocia are increased in post-term children.² A perinatal lack of oxygen has been associated with behavioural problems.²² However, our results did not suggest increased fetal stress in the post-term children, as indicated by low Apgar score, low umbilical pH or meconium-stained amniotic fluid. We controlled for several birth characteristics. Moreover, exclusion of post-term children with induction and

>4000 g of birth weight did not change results. A second explanation is uteroplacental insufficiency: a non-optimal 'old' placenta offers fewer nutrients and less oxygen than a full term fetus requires.¹ The lack of nutrients and oxygen may predispose to abnormal fetal development and this may lead to abnormal emotional and behavioural development.²³ In our study, we could not distinguish possible effects of uteroplacental insufficiency from perinatal problems. Thirdly, it is possible that a disturbance of the

Table 3 Association between GA at birth and behavioural and emotional problems (clinical cut-off)

	N	Total problems	ADHD	Affective problems	Pervasive developmental problems
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Term birth	N = 4537	1.0	1.0	1.0	1.0
Post-term birth	N = 382	1.83 (1.17–2.85)	2.04 (1.18–3.55)	1.48 (0.88–2.51)	1.84 (0.95–3.55)
Preterm birth <37 weeks	N = 226	2.35 (1.43–3.88)	2.28 (1.21–4.28)	1.51 (0.83–2.76)	1.83 (0.84–3.97)
Preterm birth <35 weeks	N = 78	3.00 (1.48–6.09)	3.42 (1.41–8.32)	1.92 (0.74–4.99)	3.95 (1.47–10.6)
Prevalence of behavioural and emotional problems					
		Total problems (%)	ADHD (%)	Affective problems (%)	Pervasive developmental problems (%)
Problems at 18 months		4.2	2.5	3.5	1.8
Problems at 36 months		3.1	1.2	2.5	2.0

Behavioural and emotional problem scores were measured using the CBCL reported by mother at 18 and 36 months.

All models were adjusted for maternal age, education, ethnicity, psychopathology, smoking and drinking during pregnancy, family income, gender of the child and age of the child at the assessment of the CBCL.

Categorization was based on GA at birth, term (GA from 37 weeks up to 42 weeks), post-term (GA of 42 weeks or more) and preterm (GA <37 weeks or <35 weeks). Bold values represent findings that were considered statistically significant ($P < 0.05$).

'placental clock', which controls the length of pregnancy, is involved. A marker of this clock is the placental secretion of corticotrophin-releasing hormone (CRH), which is lower in women who deliver post-term than in women delivering at term.²⁴ CRH is the principal regulator of the maternal and fetal hypothalamic–pituitary–adrenal (HPA) axis.²⁵ It has been suggested that placental endocrine malfunctioning or maternal stress at critical times during fetal development may influence the fetal HPA axis, leading to neuroendocrine abnormalities that could increase the child's vulnerability to emotional and behavioural problems later in life.²⁶ Finally, the association between post-term birth and childhood behavioural problems could be explained by underlying causes of being born post-term. In other words, the cause for post-term could also be the cause for having behavioural problems, for example neurodevelopmental factors related to behavioural problems could be involved in the complex process of birth.

This is a population-based study including many post-term children. We measured problem behaviour with the same validated instrument (CBCL/1.5–5) at two time points. As ultrasound gestational dating is thought to be superior to last menstrual period-based gestational dating,⁵ we decided to use primarily ultrasound dating. Eighty percent of our sample was dated with ultrasound assessment in early pregnancy. However, some limitations must be discussed. Firstly, mothers were not formally blinded for the GA of their children and they might perceive more behavioural problems in post-term children. However, the notion that a post-term birth may signal at-risk babies is largely non-existent in the medical profession and absent in the public debate. Secondly, in the current study, we relied on the CBCL,

as it was not feasible to obtain clinical diagnoses in such a large number of children. Moreover, these children were too young to be assessed by teachers or other informants, thus we had to rely on parental ratings that may be biased. Moreover, the CBCL is not a clinical instrument and cannot provide diagnoses, but addresses continuous traits in children. However, the DSM-oriented scales provide accurate information¹⁷ and good reliability and validity have been reported.¹⁶

Finally, although we controlled for a large number of confounders, including maternal smoking, psychopathology and socio-economic characteristics, residual confounding, for example maternal malnutrition during pregnancy, cannot be ruled out.

Management of prolonged pregnancy follows two approaches: proposing induction before 42 weeks of gestation or close monitoring of pregnancy after 41 weeks with selective induction in case of fetal distress or a favourable Bishop score.⁴ Pregnancy and perinatal care are criticized in The Netherlands, as perinatal mortality ranks as the third worst in Europe.²⁷ Until mid-2008, a woman with a low-risk pregnancy at 42 weeks was referred to a gynaecologist for close monitoring only. The current revised policy requires a referral at 41 weeks. Although the rate of post-term births went down after introducing first trimester ultrasound dating of GA,⁵ post-term delivery remains common.⁴

In conclusion, post-term children have a considerably higher risk of clinically relevant problem behaviour. They are more than twice as likely as term born children to have clinical ADHD. Further research is needed to determine the causes of post-term birth to reduce post-term birth rates and to minimize long-term consequences. Also, longer follow-up is

necessary to establish whether the relationship between post-term birth and behavioural problems will persist.

Supplementary Data

Supplementary Data are available at *IJE* online.

Funding

The Sophia Children's Hospital Fund (project number 553) and the WH Kröger Foundation. The first phase of the Generation R Study is made possible by financial support from the Erasmus Medical Centre, the Erasmus University and The Netherlands Organization for Health Research and Development (Zon MW, grant ZonMW Geestkracht 10.000.1003).

Acknowledgments

The Generation R Study is conducted by the Erasmus Medical Centre in close collaboration with the School

of Law and Faculty of Social Sciences of the Erasmus University Rotterdam, the Municipal Health Service Rotterdam area, the Rotterdam Homecare Foundation and the Stichting Trombosedienst & Artsenlaboratorium Rijnmond (STAR), Rotterdam. We gratefully acknowledge the contribution of general practitioners, hospitals, midwives and pharmacies in Rotterdam. H.E.M. checked the references used in this article for accuracy and completeness. H.T. will act as guarantor for the article. Someone with an excellent mastery of the English language has carefully edited the article. This article represents original material and has not been published previously in whole or in part. In addition, no similar paper is in press or under review elsewhere.

Conflict of interest: F.C.V. is author and head of the Department of Child and Adolescent Psychiatry at Erasmus MC, which publishes the Achenbach System of Empirically Based Assessment (ASEBA) and from which he receives remuneration. All other authors report no conflicts of interest.

KEY MESSAGES

- GA at birth and behavioural and emotional problems in early childhood show a non-linear quadratic relation indicating that both preterm and post-term children are at higher risk for problems.
- Children born post-term were twice as likely as their term-born peers to have ADHD in early childhood.
- Our results suggest that children born post-term have a neurodevelopmental delay. However, further research is needed to demonstrate a causal relation.

References

- 1 Caughey AB, Snegovskikh VV, Norwitz ER. Postterm pregnancy: how can we improve outcomes? *Obstet Gynecol Surv* 2008;**63**:715–24.
- 2 Norwitz ER, Snegovskikh VV, Caughey AB. Prolonged pregnancy: when should we intervene? *Clin Obstet Gynecol* 2007;**50**:547–57.
- 3 Shea KM, Wilcox AJ, Little RE. Postterm delivery: a challenge for epidemiologic research. *Epidemiology* 1998;**9**:199–204.
- 4 Zeitlin J, Blondel B, Alexander S, Breart G. Variation in rates of postterm birth in Europe: reality or artefact? *BJOG* 2007;**114**:1097–103.
- 5 Savitz DA, Terry JW Jr, Dole N, Thorp JM Jr, Siega-Riz AM, Herring AH. Comparison of pregnancy dating by last menstrual period, ultrasound scanning, and their combination. *Am J Obstet Gynecol* 2002;**187**:1660–66.
- 6 Caughey AB, Stotland NE, Washington AE, Escobar GJ. Who is at risk for prolonged and postterm pregnancy? *Am J Obstet Gynecol* 2009;**200**:683.e1–e5.
- 7 Roos N, Sahlin L, Ekman-Ordeberg G, Kieler H, Stephansson O. Maternal risk factors for postterm pregnancy and cesarean delivery following labor induction. *Acta Obstet Gynecol Scand* 2010;**89**:1003–10.
- 8 Allen MC. Preterm outcomes research: a critical component of neonatal intensive care. *Ment Retard Dev Disabil Res Rev* 2002;**8**:221–33.
- 9 Olesen AW, Westergaard JG, Olsen J. Perinatal and maternal complications related to postterm delivery: a national register-based study, 1978–1993. *Am J Obstet Gynecol* 2003;**189**:222–27.
- 10 Mogren I, Stenlund H, Hogberg U. Recurrence of prolonged pregnancy. *Int J Epidemiol* 1999;**28**:253–57.
- 11 Shime J, Librach CL, Gare DJ, Cook CJ. The influence of prolonged pregnancy on infant development at one and two years of age: a prospective controlled study. *Am J Obstet Gynecol* 1986;**154**:341–45.
- 12 Lindstrom K, Fernell E, Westgren M. Developmental data in preschool children born after prolonged pregnancy. *Acta Paediatr* 2005;**94**:1192–97.
- 13 Jaddoe VW, van Duijn CM, van der Heijden AJ *et al*. The Generation R Study: design and cohort update 2010. *Eur J Epidemiol* 2010;**25**:823–41.
- 14 Verburg BO, Mulder PG, Hofman A, Jaddoe VW, Witteman JC, Steegers EA. Intra- and interobserver reproducibility study of early fetal growth parameters. *Prenat Diagn* 2008;**28**:323–31.
- 15 Reijneveld SA, de Kleine MJ, van Baar AL *et al*. Behavioural and emotional problems in very preterm

- and very low birthweight infants at age 5 years. *Arch Dis Child Fetal Neonatal Ed* 2006;**91**:F423–28.
- ¹⁶ Achenbach TM, Rescorla LA. *Manual for the ASEBA Pre-School Forms and Profiles*. Burlington, VT: Research Center for Children, Youth and Families, University of Vermont, 2000.
- ¹⁷ Nakamura BJ, Ebesutani C, Bernstein A, Chorpita BF. A psychometric analysis of the child behavior checklist DSM-oriented scales. *J Psychopathol Behav* 2009;**31**:178–89.
- ¹⁸ Statistics Nederland. *Allochtonen in Nederland 2004*. Heerlen: Voorburg, 2004.
- ¹⁹ Statistics Nederland. *Standaard onderwijsindeling 2003*. Heerlen: Voorburg, 2004.
- ²⁰ Roza SJ, Verburg BO, Jaddoe VW *et al.* Effects of maternal smoking in pregnancy on prenatal brain development: the Generation R Study. *Eur J Neurosci* 2007;**25**:611–17.
- ²¹ Derogatis LR. *Brief Symptom Inventory (BSI): Administration, Scoring and Procedures Manual*. 3rd edn. Minneapolis, MN: National Computer Systems, 1993.
- ²² van Handel M, Swaab H, de Vries LS, Jongmans MJ. Long-term cognitive and behavioral consequences of neonatal encephalopathy following perinatal asphyxia: a review. *Eur J Pediatr* 2007;**166**:645–54.
- ²³ Courchesne E, Townsend J, Chase C. Neurodevelopmental principles guide research on developmental psychopathologies. In: Cicchetti D, Cohen DJ (eds). *Developmental Psychopathology*. New York: Wiley, 1995, pp. 195–220.
- ²⁴ McLean M, Bisits A, Davies J, Woods R, Lowry P, Smith R. A placental clock controlling the length of human pregnancy. *Nat Med* 1995;**1**:460–63.
- ²⁵ Smith R. Parturition. *N Engl J Med* 2007;**356**:271–83.
- ²⁶ Austin MP, Leader LR, Reilly N. Prenatal stress, the hypothalamic–pituitary–adrenal axis, and fetal and infant neurobehaviour. *Early Hum Dev* 2005;**81**:917–26.
- ²⁷ Sheldon T. Perinatal mortality in Netherlands third worst in Europe. *BMJ* 2008;**337**:a3118.