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Preterm birth is associated with depression from childhood to early adulthood

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Table S1: Relationship between covariates and gestational age, and between weight for gestational age for the controls

Table S2: Relationship between covariates and depression in cases and controls

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Figure S1: Predicted ORs for depression with an interaction between gestational age and sex

Lay summary:

National health care registers were used to identify 37,682 cases of depression and 148,795 matched controls from the source population of 1,240,062 singleton children born in Finland in 1987-2007. Preterm infants born before 28 weeks of gestation and full-term infants with poor fetal growth had an increased risk of depression during childhood and adolescence. This study provides one additional reason to support parents' mental wellbeing during pregnancy and neonatal care as parent's depression increases the risk of the psychopathology of the child. Screening and supporting the mental health of both the child and the parent should be included in the follow up of high-risk infants.

Clinical guidance:

- Clinicians should pay special attention to supporting parental mental health during pregnancy and during neonatal care, especially in case of extremely preterm infants and growth retarded full term infants.

- Follow-up of high-risk infants should include screening of depression of both the child and the parents, as well as appropriate mental health support.

- Research on the impact of family centered neonatal care on later risk of childhood depression is needed.

ABSTRACT

Objective There have been inconsistent findings on the associations between prematurity, poor fetal growth and depression. We examined the associations between gestational age, poor fetal growth and depression in individuals aged 5 to 25 years.

Methods We identified 37,682 cases based on ICD-9 code 2961 and ICD-10 codes F32.0-F32.9 and F33.0-F33.9 from the Care Register for Health Care, and 148,795 matched controls from the Finnish Central Population Register. Conditional logistic regression examined the associations between gestational age by each gestational week, poor fetal growth and depression. The associations were adjusted for parental age and psychopathology, paternal immigrant status, maternal substance abuse, depression, number of previous births, marital status, socio-economic status, smoking during pregnancy and the infant's birthplace.

Results In the adjusted models, increased risk of depression was found in children born ≤ 25 weeks (1.89, 1.08-3.31), at 26 weeks (2.62, 1.49-4.61), at 27 weeks (1.93, 1.05-3.53) and ≥ 42 weeks (1.11, 1.05-1.19). In girls, extremely preterm birth was associated with depression diagnosed at 5 to 12 years (2.70, 1.83-3.98) and 13 to 18 years (2.97, 1.84-4.78). In boys, post-term birth (≥42 weeks) was associated with depression diagnosed at 19 to 25 years (1.28, 1.07-1.54). Poor fetal growth was associated with an increased risk of depression in full-term infants (1.06, 1.03-1.10) and post-term infants (1.24, 1.08-1.43).

Conclusion Preterm birth before 28 weeks of gestation appeared to play a role in the development of childhood depression. Smaller effects were also seen in post-term births, especially in boys.

Keywords: fetal growth, SGA, prematurity, epidemiology, mental disorders

INTRODUCTION

Depression is a common psychiatric disorder that has been reported to affect 1-2% of preschool and prepubertal children and 3-8% of adolescents.[1,2] It has been reported to have a significant effect on social and occupational functioning and it can be disabling. Suicides, associated with depression, are the second leading cause of death among adolescents and young adults. [3]

The etiology of depression is multifactorial, and it has been suggested that an interaction between genes and the environment play a role in its development.[4] The environmental risk factors that have been identified for depression among children and adolescents include parental depression, parental divorce, low maternal socio-economic status (SES) and maternal smoking during pregnancy.[5,6] It is important to investigate potential risk factors to help us develop a better understanding of the etiology of depression and to identify at-risk individuals at an early stage, so that they can benefit from closer monitoring or early interventions.

Preterm birth, before 37 weeks of gestation, is a common public health concern with many consequences. It occurs in 5-18% of all births.[7] Increased survival rates due to advances in perinatal and neonatal care have led to growing number of adults born preterm. Individuals born preterm are more susceptible to long-term developmental and neurological issues and other health problems than their term-born counterparts.[8]

Studies linking preterm birth and depression have produced inconsistent findings. Some have reported that preterm birth was associated with an increased risk of depression,[9-11] while others did not find any association.[12-14] Most of these studies focused on very preterm infants,

born before 32 weeks of gestation. Only two[13,14] examined the risk of depression among post-term infants, born after 42 weeks of gestation, but the findings were not significant. No previous studies have reported the risk of depression by each gestational week.

There are several potential pathways from prematurity to depression. The increased risk of depression among very preterm infants may be due to antenatal conditions contributing to preterm delivery and compromising the in utero environment, thereby affecting brain growth and the development and functioning of the hypothalamic-pituitary-adrenal (HPA) axis.[15] In addition, there might be shared genetic predispositions for preterm birth and depression.[16] Very preterm birth also alters the postnatal environment in ways that can increase psychosocial risks. [17]

Poor fetal growth, defined as being born small for gestational age (SGA), has also been studied as a possible risk factor for depression, but the findings have been contradictory.[10,12,13,18-21] Interestingly, Räikkönen et al., found that very low birth weight infants who were also SGA had a higher risk of depression than full-term controls. However, low birth weight infants who displayed normal growth during pregnancy later developed a lower rate of depression than their full-term controls highlighting poor fetal growth as a risk factor.[21] A suboptimal in utero environment that affects fetal growth can increase later psychosocial risks even without prematurity.[22] One register-based study found an association between SGA and depression.[20]

To our knowledge, there have been no population-based studies on depression that have used birth weight for gestational age to differentiate between the roles of antenatal growth and prematurity. The overall aim of this Finnish nested case-control study was to examine the

associations between preterm birth and fetal growth in relation to depression diagnosed by specialized health care services. The first aim was to examine the association between gestational age and depression by each gestational week. The second aim was to study the association between birth weight for gestational age and depression. We hypothesized that preterm birth and poor fetal growth would be associated with depression in a dose-response manner. In addition, we examined whether the associations between preterm birth and depression differed by sex and the age of depression diagnosis.

METHODS

This Finnish nationwide population-based study had a nested case-control design and used national registers to identify cases, controls and their parents. The source population comprised 1,240,062 singleton children born from 1987-2007.

The nationwide registers

The Care Register for Health Care includes all inpatient diagnoses since 1969 and outpatient diagnoses from specialized services since 1998. It provided the patients' personal identity codes, date of birth, sex, the dates of any medical admissions and discharges, the primary diagnoses at discharge and any diagnoses of maternal and paternal psychopathology. Psychiatric diagnoses were based on the International Classification of Diseases: ICD-8 (1969-1986), ICD-9 (1987-1995) and ICD-10 (1996 onwards). The demographic characteristics of the cases and controls were retrieved from the Finnish Central Population Register. The Finnish Maternal Birth Register, available since 1987, provided the child's birthplace, maternal marital status, smoking during pregnancy, SES, gestational age and birthweight. These registers, and their linkages, have previously been described in detail. [23]

Cases and controls

The cases were born between January 1987 and December 2007 and their diagnosis of a depressive episode or recurrent depression was registered in the Care Register before December 2012, when they were at least five years old. The diagnoses were based on ICD-9 code 2961 and ICD-10 codes F32.0-F32.9 and F33.0-F33.9. Mild, moderate and severe depressive episodes as well as depression with psychotic features were all included. Each case was matched with four controls, without depression, by their date of birth (±30 days), sex, birthplace and where they lived when the case was diagnosed. We excluded cases and controls with severe or profound mental disabilities, i.e. ICD-9 codes 3181 and 3182 and ICD-10 codes F72 and F73, as these conditions make it challenging to diagnose depression. After exclusions, we had 37,682 cases and 148,795 controls.

Gestational age and birth weight for gestational age

Information on gestational age and birth weight was obtained from the Birth Register. First, each gestational week was used separately. In the stratifications for sex, age of the diagnosis, and poor fetal growth, five categories of completed gestational weeks were used (< 28 weeks, 28-31 weeks, 32-36 weeks, 37-41 weeks and ≥ 42 weeks). Gestational age was based on the last menstrual period, corrected by a first trimester ultrasound if needed.[24]

The birth weight for gestational age was calculated using national sex-specific birth weight distribution standards at a given gestational age for singletons.[25] The birth weight standard deviation scores, or z-scores, were divided into nine categories that used 0.5 intervals from below -2.0 to above 2.0 (Table 2).

Covariates

Various covariates were examined as potential confounders. Factors related to both parents were age, psychopathology, depression and immigrant status. Maternal factors were maternal substance abuse, number of previous births, marital status, SES, smoking during pregnancy and the infant's birthplace.

Parental age was a continuous variable. Parental psychopathology was a history of any psychiatric disorder (ICD-10 F10-99, ICD-9 291-316 and ICD-8 291-308). Psychopathology was dichotomized as 'yes' or 'no' for mothers and fathers. Parental depression was dichotomized as 'yes' or 'no' (ICD-10 F32 and F33, ICD-9 2961 and ICD-8 296.00, 298.00, 300.40 and 300.41). Maternal substance abuse was dichotomized as 'yes' or 'no' (ICD-10 F10-F19, ICD-9 291, 292, 303, 304 and 305 and ICD-8 291, 303 and 304). Parental psychopathology included all other psychopathology except for parental depression and maternal substance use. We also dichotomized previous births as 'none' or 'one or more' and marital status as being 'single' or 'married or in a relationship'. Maternal SES was divided into four categories based on their occupation and educational background. The first category included 'managers and professionals' such as experts in their field, teachers, physicians and lawyers. The second category included 'clerical support workers' such as secretaries and people doing office work who did not fall into the previous category. The third category included 'manual workers' such as cooks and cleaners, and the final category included 'other' unclassifiable occupations such as entrepreneurs, students, unemployed persons and housewives. Women who reported they were in education, rather than doing a job, were included in the first category if they graduated from university and to the second category if they had a vocational degree, which was lower than a university degree. Maternal smoking during pregnancy was dichotomized as 'yes' or 'no'. The infant's place of birth was divided

into 'urban', 'semi-urban' and 'rural' and the parents were divided into 'immigrants' and 'non-immigrants' based on the country of birth.

Statistical analyses

We analyzed the associations between 1) covariates and prematurity and fetal growth and 2) covariates and depression. Potential covariates were tested using Pearson's chi-square test for the association with gestational age and birth weight for gestational age among the controls. Conditional logistic regression was used to examine the associations between the potential covariates and depression. The covariates that were associated with gestational age, fetal growth and depression were included in the adjusted model if the significance level was $p<0.1$. All of the tested potential covariates were adjusted for in the final model, with the exception of paternal depression and maternal immigrant status, which were not associated with gestational age or with birth weight for gestational age (see Tables S1 and S2, available online).

Conditional logistic regression models were used to examine the associations between exposures and outcomes. The first model estimated unadjusted odds ratios (ORs) and two-sided 95% confidence intervals (95% CIs) for each week of gestation and for birth weight z-scores. In the final model, adjustments were made for the covariates listed above.

We examined the associations between combined prematurity and fetal growth categories and depression. The categories for gestational age were < 28 weeks, 28-31 weeks, 32-36 weeks, 37-41 weeks and ≥ 42 weeks and for birth weight z-scores below -1.0, between -1.0 to 1.0, and above 1.0. In addition, the associations between gestational age categories and depression were studied by sex and by age at the diagnosis of depression. The associations were adjusted

for the covariates mentioned above and reported as adjusted ORs (aORs) and two-sided 95%

confidence intervals (CIs). We used linear quadratic model to test for sex-by-gestational age

interaction effect (χ_1^2=9.82, p=0.002).

A two-sided *p*-value of <0.05 was statistically significant. The statistical analyses were

performed with SAS statistical software, version 9.4 (SAS Institute Inc, Cary, NC, USA).

RESULTS

There were 37,682 singleton children (65.5% girls), born between 1 January 1987 and 31

December 2007, diagnosed with a depressive episode or recurrent depression before

December 2012. The mean age at diagnosis was 16.2 ± 3.5 years (range 5-25 years). They

were compared with 148,795 matched controls without depression.

The associations between each week of gestation and depression are shown in Table 1,

including both unadjusted and adjusted models. In the unadjusted models, the OR for

depression was about two-fold for children born below 29 gestational weeks. After adjusting

for covariates, an increased risk was observed in children born ≤25 gestational weeks (aOR

1.89, 95% CI 1.08-3.31, p=0.02), at 26 gestational weeks (aOR 2.62, 95% CI 1.49-4.61, p

<0.001), at 27 gestational weeks (aOR 1.93, 95% CI 1.05-3.53, p=0.03) and ≥42 gestational

weeks (aOR 1.11, 95% CI 1.05-1.19, p=<0.001). Moderate or late preterm children did not

show an increased risk for depression.

Insert Table 1 here

The associations between birth weight for gestational age and depression are shown in Table 2, including both unadjusted and adjusted models. A birth weight z-score below -1.0 was associated with an increased risk for depression. The risk for depression increased as the z-scores decreased, with ORs ranging from 1.1 to 1.23 in the unadjusted analyses. After adjustment for covariates, the aORs were 1.07 (95% CI 0.99-1.15, p=0.07) for a z-score below -2.0, 1.06 (95% CI 1.00-1.13, p=0.05) for z-score -2.0 to -1.5, and 1.05 (95% CI 1.008-1.10, p=0.02) for a z-score of -1.5 to -1.0. The associations between birth weight z-scores and depression are shown separately for both sexes (see Table S3, available online).

Insert Table 2 here

The associations between poor fetal growth and the risk of depression was seen in full-term infants and post-term infants, but not in extremely and very preterm infants. In the unadjusted models, the associations between prematurity and depression was significant among infants born extremely preterm with normal fetal growth (OR 3.20, 95% CI 2.16-4.74, p <0.001), extremely preterm with excess fetal growth (OR 1.76 , 95% CI 1.05-2.94, p=0.03), very preterm with normal fetal growth (OR 1.43, 95% CI 1.11-1.86, p=0.005), moderately preterm with normal fetal growth (OR 1.11, 95% CI 1.03-1.21, p=0.008), full-term with poor fetal growth (OR 1.16, 95% CI 1.13-1.20, p <0.001), full-term with excess fetal growth (OR 0.95, 95% CI 0.91-0.98, p=0.002), post-term with poor fetal growth (OR 1.32, 95% CI 1.17-1.49, p <0.001) and post-term with normal fetal growth (OR 1.10, 95% CI 1.03-1.17, p=0.003). After adjusting for the covariates, the associations remained significant for infants born extremely preterm with normal fetal growth (aOR 2.99, 95% CI 1.87-4.78), p <0.001), full-term with poor fetal growth (aOR 1.06, 95% CI 1.03-1.10, p <0.001), post-term with poor fetal growth

(aOR 1.24, 95% CI 1.08-1.43, p=0.002) and post-term with normal fetal growth (aOR 1.09, 95% CI 1.02-1.18, p=0.01). Table 3 shows both the unadjusted and adjusted models.

Insert Table 3 here

The association between preterm birth and depression was only present in girls, whereas the association between post-term birth and depression was present in both sexes. In girls, the aOR for depression was 2.27 (95% CI 1.19-4.32, p=0.01) in children born at or below 25 gestational weeks, 3.22 (95% CI 1.66-6.24, p <0.001) at 26 gestational weeks, 3.00 (95% CI 1.46-6.15, p=0.002) at 27 gestational weeks and 1.09 (95% CI 1.01-1.19, p=0.01) at or after 42 gestational weeks. In boys, the aOR for post-term birth was 1.15 (95% CI 1.03-1.28, *p*=0.009) (Table 4). The sex by gestational age interactions showed significant associations with depression (p=0.002) (see Figure S1, available online).

Insert Table 4 here

Additional analyses were conducted that stratified the children according to sex and the age when they were diagnosed with depression. The risk of a diagnosis of depression was increased in extremely preterm girl infants when they were 5 to 12 years (aOR 2.70, 95% CI 1.83-3.98, p=<0.001) and 13 to 18 years of age (aOR 2.97, 95% CI 1.84-4.78, p <0.001). The risk of a diagnosis of depression was increased in post-term boys when they were 19 to 25 years of age (aOR 1.28, 95% CI 1.07-1.54, p=0.006) (Table 5).

Insert Table 5 here

DISCUSSION

This population-based study showed that extremely preterm and post-term birth were both risk factors for depression among children and young adults. Extremely preterm birth was only a risk factor for depression among girls, whereas post-term birth was a risk factor in both sexes. Poor fetal growth was associated with depression and the impact rose as the gestational weeks increased.

The link between extremely preterm birth and depression was also shown in a Swedish register-based study of 2,333 young adults. [10] Both studies found that the risk increased as gestational age decreased, but the Swedish study also reported a significant association with moderately preterm birth at 32 to 36 weeks. Many smaller studies have been performed with conflicting results: associations between preterm birth and depression have been shown in some studies,[11,26,27] while others have reported no associations.[12-14] There have also been conflicting results regarding fetal growth and later depression. A Danish register-based study showed a significant association between being born SGA and depression,[20] but others have not reported any associations between birth weight for gestational age and depression.[10,12,13] Räikkönen *et al* found that poor fetal growth was a stronger underlying factor for depression than prematurity.[21] In our study, extreme prematurity was a stronger risk factor than poor fetal growth. Our study suggests that prematurity and poor fetal growth affect the risk of depression independently, as the effects of poor fetal growth become more evident with increasing gestational age. The increased risk of depression was seen in full-term and post-term infants with poor fetal growth. In extremely preterm infants, poor fetal growth did not increase the risk of depression, but the risk was highest in extremely preterm infants with normal growth.

Our study observed sex-specific differences in the associations between gestational age and depression. Extreme preterm birth was only associated with depression among girls. Post-term birth was associated with depression among both sexes. Our sex-specific findings differed from the findings of a Finnish questionnaire study of adults aged 57 to 71 years, which did find an interaction between sex and depression.[11] Our cases with depression had been clinically diagnosed by healthcare professionals working in specialized health care services. Therefore, the cases in our study may have had more severe depression than the questionnaire study. As depression manifests earlier in girls, it was important to investigate whether preterm birth was associated with an increased risk of depression differently in different age groups. Extremely preterm birth increased the risk for depression in girls in the age groups before 19 years of age, while there were no associations between depression and prematurity in any age groups in boys.

The potential mechanisms underlying depression in extremely preterm children and adolescents may be related to the causes of preterm birth, including genetic predispositions, pathologies during pregnancy, immature brain development in infants born extremely preterm and psychosocial risks related to the postnatal hospital environment and later growth environment of preterm infants.[15]

We have recently learned about candidate genes related to prematurity. [16] However, there is a lot to be learned about their potential relation to later outcomes. It is clear that the majority of preterm infants are exposed to a variety of pathologies before birth leading to prematurity and/or poor fetal growth. [15] Pre-eclampsia and intrauterine inflammation/infections are common pathologies underlying preterm birth. Other antenatal factors associated with preterm birth and poor fetal growth include maternal smoking and stress.[28] It is interesting to

speculate how all these pathologies and risk factors affect the HPA axis, which activates the normal labor process. This hormonal system, a key component in tuning the symbiotic relationship between the mother and fetus, [29] might be affected by glucocorticoids induced by different types of stress. [30] These perturbations might increase the risk of later psychopathologies. The administration of glucocorticoids to a pregnant mother has been shown to increase mental and behavioral disorders in the offspring. [31]

The development of oligodendroglial lineage and cortical connectivity of the brain is different in developing preterm infants than to full term infants. [32] The underlying factors for altered brain development include potential genetic predispositions, abnormal fetal growth environment during the second trimester, when the cortical subplate and neocortex are formed, [33] and the effects of the non-physiological hospital environment after birth. It is possible that the differences in brain development play a role in predisposing extremely preterm infants to later depression.[34] It is also possible that stressful experiences, during the hospital stay and beyond, alter the infant's HPA axis, [35] which has been suggested by increased cortisol reactivity in infancy, childhood and adulthood in individuals born preterm. [36,37] Elevated cortisol levels have been associated with poor stress management, reduced resiliency [38] and depression. [39]

Later depression in individuals born extremely preterm might also have roots in their psychosocial environment. Long neonatal hospital stays and separation may affect the development of parent-infant relationships after extremely preterm birth[17] and these often lead to depressive symptoms in parents. [40] It is known that parental depression is associated with an increased risk of depression in their children. [41] The psychosocial environment of the

extremely preterm child might also be affected by his/her health problems, challenges in socio-emotional and cognitive development, and problems in peer-relationships.[42,43]

The finding that preterm birth was only a risk for depression in girls could be explained by the sex-specific programming of the HPA axis.[44] In primates, exposure to longer courses of antenatal glucocorticoids resulted in reduced plasma cortisol levels in boys, but higher plasma cortisol levels in girls in adulthood.[45] Puberty and sex hormones play important roles in adolescent psychiatric morbidity as girls undergo puberty earlier than boys and they manifest depression at an earlier age. [46] The lifetime prevalence of depression is two times higher in girls than in boys.[47] On the other hand, girls are more likely to seek help for depression than boys, which may lead to overestimation of the prevalence in girls.[48]

We analyzed the associations by each gestational week and used extensive adjustments for covariates. In addition, we had a large sample size, links between national registers, and a prospective design that prevented recall bias. Previous nationwide population-based studies from other Nordic countries have reported associations between gestational age, fetal growth and depression without adjustments for parental depression, parental psychiatric illness and maternal substance abuse.

We acknowledge that our study had limitations. First, the depression diagnoses were derived from the Care Register, which included diagnoses from hospital services. This might have missed milder cases of depression diagnosed in primary care settings or in the private clinics. Second, the diagnoses were based on clinical evaluations or diagnostic interviews by psychiatrists rather than standardized interviews. Third, specific data on the accuracy of the Care Register for depression was not available, but register data have demonstrated good

accuracy for diagnosing mental disorders in general.[49,50] Finally, the limited age range of 5 to 25 years may have skewed the case mix to early onset depression and underestimate depression in boys, who manifest their depression later than girls.

There are emerging remedies for maternal depression after preterm birth. For example, single family rooms increase parent-infant bonding and skin-to-skin contact. [51] In addition, parenting interventions in neonatal units have decreased parental depression, [52] which could reduce psychiatric problems, including depression, among children born preterm.

In conclusion, this national population-based birth cohort demonstrated an increased risk for depression among girls born extremely preterm. Poor fetal growth only increased the risk for depression when the pregnancy had lasted longer. Preventive interventions should be targeted to at-risk individuals especially those born extremely preterm.

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Table 1: Unadjusted and adjusted models, with ORs (95% CIs), for the associations between gestational age and depression

	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	P value	Adjusted[b] OR (95% CI)	P value
Gestational age (weeks)[a]						
≤25	26 (0.07)	53 (0.04)	1.93 (1.20-3.09)	0.006	1.89 (1.08-3.31)	0.024
26	29 (0.08)	39 (0.03)	3.04 (1.87-4.93)	<0.001	2.62 (1.49-4.61)	<0.001
27	24 (0.06)	46 (0.03)	2.10 (1.28-3.44)	0.003	1.93 (1.05-3.53)	0.03
28	34 (0.09)	79 (0.05)	1.75 (1.16-2.62)	0.006	1.12 (0.68-1.85)	0.64
29	24 (0.06)	106 (0.07)	0.92 (0.59-1.44)	0.73	0.94 (0.58-1.52)	0.81
30	48 (0.13)	149 (0.10)	1.31 (0.94-1.82)	0.10	1.27 (0.88-1.84)	0.19
31	47 (0.13)	170 (0.12)	1.09 (0.79-1.51)	0.58	0.96 (0.65-1.40)	0.83
32	79 (0.21)	268 (0.18)	1.19 (0.93-1.54)	0.16	1.18 (0.88-1.58)	0.26
33	110 (0.30)	371 (0.25)	1.21 (0.98-1.50)	0.07	1.04 (0.82-1.33)	0.71
34	180 (0.48)	654 (0.45)	1.11 (0.93-1.31)	0.22	1.02 (0.85-1.24)	0.78
35	344 (0.93)	1213 (0.83)	1.14 (1.01-1.29)	0.03	1.10 (0.96-1.27)	0.16
36	698 (1.88)	2696 (1.84)	1.04 (0.96-1.14)	0.30	0.96 (0.87-1.06)	0.47

37	1719 (4.63)	6567 (4.47)	1.06 (1.00-1.12)	0.04	1.03 (0.96-1.10)	0.37
38	4687 (12.62)	18133 (12.35)	1.04 (1.007-1.08)	0.02	1.03 (0.98-1.07)	0.17
39	9290 (25.02)	37792 (25.73)	0.99 (0.96-1.02)	0.82	0.99 (0.96-1.03)	0.77
40	10854 (29.24)	43940 (29.92)	Reference		Reference	
41	7114 (19.16)	27998 (19.06)	1.02 (0.99-1.06)	0.12	1.03 (0.99-1.07)	0.09
≥42	1819 (4.90)	6594 (4.49)	1.12 (1.05-1.19)	<0.001	1.11 (1.05-1.19)	<0.001

Missing values: [a] 2483. [b] Odd ratios were adjusted for mothers and fathers (age, psychopathology) and just mothers (substance abuse, depression, number of previous births, marital status, SES, smoking during pregnancy and infant's birthplace), and just fathers (immigration status).

Table 2: Unadjusted and adjusted models, with ORs (95% CIs), for the association between birth weight for gestational age and depression

	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	P value	Adjusted[b] OR (95% CI)	P value
Weight for gestational age (z-score)[a]						
Below -2.0	1279 (3.45)	4169 (2.84)	1.23 (1.16-1.32)	<0.001	1.07 (0.99-1.15)	0.07
-2.0 to -1.51	1971 (5.31)	6530 (4.45)	1.20 (1.14-1.27)	<0.001	1.06 (1.00-1.13)	0.05
-1.50 to -1.01	3830 (10.32)	13879 (9.45)	1.10 (1.06-1.15)	<0.001	1.05 (1.008-1.10)	0.02
-1.0 to -0.51	5678 (15.30)	22485 (15.31)	1.01 (0.97-1.04)	0.50	0.97 (0.94-1.01)	0.26
-0.50 to 0.50	13585 (36.60)	54548 (37.15)	Reference		Reference	
0.51 to 1.0	4903 (13.21)	20292 (13.82)	0.97 (0.93-1.00)	0.09	1.00 (0.96-1.04)	0.77
1.01 to 1.50	2925 (7.88)	12640 (8.61)	0.93 (0.88-0.97)	0.001	0.97 (0.92-1.02)	0.22
1.51 to 2.0	1608 (4.33)	6749 (4.60)	0.95 (0.90-1.01)	0.14	1.00 (0.94-1.07)	0.81
Above 2.0	1335 (3.60)	5533 (3.77)	0.97 (0.91-1.03)	0.31	1.03 (0.96-1.11)	0.30

Missing values: [a] 2538. [b] Odd ratios were adjusted for mothers and fathers (age, psychopathology) and just mothers (substance abuse, depression, number of previous births, marital status, SES, smoking during pregnancy and infant's birthplace), and just fathers (immigration status).

Table 3: Unadjusted and adjusted models with ORs (95% CIs) for the association between prematurity, fetal growth and depression

Gestational age (weeks) and fetal growth	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	P value	Adjusted[a] OR (95% CI)	P value
<28 weeks and poor fetal growth	13 (0.04)	32 (0.02)	1.64 (0.86-3.14)	0.12	1.86 (0.87-4.01)	0.10
<28 weeks and normal fetal growth	45 (0.12)	57 (0.04)	3.20 (2.16-4.74)	<0.001	2.99 (1.87-4.78)	<0.001
<28 weeks and excess fetal growth	21 (0.06)	48 (0.03)	1.76 (1.05-2.94)	0.03	1.30 (0.69-2.44)	0.40
28-31 weeks and poor fetal growth	39 (0.11)	145 (0.10)	1.09 (0.77-1.56)	0.61	0.97 (0.65-1.45)	0.90
28-31 weeks and normal fetal growth	79 (0.21)	222 (0.15)	1.43 (1.11-1.86)	0.005	1.28 (0.95-1.74)	0.10
28-31 weeks and excess fetal growth	35 (0.09)	135 (0.09)	1.05 (0.72-1.53)	0.77	0.91 (0.59-1.40)	0.66
32-36 weeks and poor fetal growth	364 (0.98)	1318 (0.90)	1.12 (0.99-1.26)	0.05	1.02 (0.89-1.16)	0.78
32-36 weeks and normal fetal growth	764 (2.06)	2782 (1.89)	1.11 (1.03-1.21)	0.008	1.03 (0.93-1.13)	0.55
32-36 weeks and excess fetal growth	283 (0.76)	1100 (0.75)	1.04 (0.91-1.19)	0.51	1.02 (0.87-1.18)	0.78
37-41 weeks and poor fetal growth	6316 (17.02)	22010 (14.99	1.16 (1.13-1.20)	<0.001	1.06 (1.03-1.10)	<0.001
37-41 weeks and normal fetal growth	22035 (59.37)	89665 (61.06)	Reference		Reference	
37-41 weeks and excess fetal growth	5306 (14.30)	22746 (59.37)	0.95 (0.91-0.98)	0.002	1.00 (0.96-1.03)	0.99
≥ 42 weeks and poor fetal growth	348 (0.94)	1073 (0.73)	1.32 (1.17-1.49)	<0.001	1.24 (1.08-1.43)	0.002

≥ 42 weeks and normal fetal growth	1245 (3.35)	4613 (3.14)	1.10 (1.03-1.17)	0.003	1.09 (1.02-1.18)	0.01
≥ 42 weeks and excess fetal growth	221 (0.60)	889 (0.61)	1.01 (0.87-1.17)	0.84	1.09 (0.92-1.28)	0.29

Poor fetal growth: z-score <-1.0; normal fetal growth: z-score between -1.0 to +1.0; excess fetal growth: z-score >1.0

[a] Odd ratios were adjusted for mothers and fathers (age, psychopathology) and just mothers (substance abuse, depression, number of previous births, marital status, SES, smoking during pregnancy and infant's birthplace), and just fathers (immigration status).

Table 4: Sex-specific unadjusted and adjusted models, with ORs (95% CIs), for the association between gestational age and depression

Gestational age (weeks)[a]	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	P value	Adjusted[b] OR (95% CI)	P value
Boys						
≤25	7 (0.05)	16 (0.03)	1.65 (0.68-4.03)	0.26	1.14 (0.37-3.53)	0.81
26	7 (0.05)	13 (0.03)	2.17 (0.85-5.55)	0.10	1.56 (0.50-4.84)	0.43
27	5 (0.04)	20 (0.04)	0.99 (0.37-2.63)	0.98	0.65 (0.18-2.39)	0.52
28	17 (0.13)	36 (0.07)	1.85 (1.03-3.30)	0.03	1.52 (0.79-2.90)	0.20
29	9 (0.07)	33 (0.06)	1.08 (0.52-2.27)	0.82	1.09 (0.48-2.48)	0.83
30	15 (0.12)	56 (0.11)	1.07 (0.60-1.91)	0.79	1.07 (0.58-1.98)	0.82
31	18 (0.14)	69 (0.14)	1.01 (0.60-1.71)	0.94	0.94 (0.51-1.75)	0.86
32	28 (0.22)	112 (0.22)	0.99 (0.65-1.51)	0.98	1.06 (0.65-1.71)	0.81
33	34 (0.27)	159 (0.31)	0.87 (0.60-1.27)	0.48	0.67 (0.43-1.05)	0.08
34	66 (0.52)	239 (0.47)	1.11 (0.84-1.46)	0.46	0.97 (0.70-1.34)	0.85
35	134 (1.05)	457 (0.90)	1.16 (0.95-1.41)	0.13	1.13 (0.90-1.43)	0.26
36	251 (1.96)	1005 (1.97)	1.00 (0.86-1.15)	0.99	0.86 (0.73-1.02)	0.08

37	621 (4.85)	2427 (4.77)	1.02 (0.93-1.12)	0.62	0.96 (0.86-1.07)	0.48
38	1611 (12.58)	6645 (13.05)	0.96 (0.90-1.03)	0.31	0.91 (0.85-0.98)	0.02
39	3176 (24.81)	13056 (25.65)	0.97 (0.92-1.02)	0.26	0.96 (0.90-1.02)	0.22
40	3711 (28.99)	14788 (29.05)	Reference		Reference	
41	2424 (18.93)	94.62 (18.59)	1.02 (0.96-1.08)	0.50	1.01 (0.95-1.08)	0.60
≥42	669 (5.23)	2312 (4.54)	1.15 (1.04-1.26)	0.003	1.15 (1.03-1.28)	0.009
Girls						
≤25	19 (0.08)	37 (0.04)	2.056 (1.18-3.57)	0.01	2.27 (1.19-4.32)	0.01
26	22 (0.09)	26 (0.03)	3.46 (1.96-6.11)	<0.001	3.22 (1.66-6.24)	<0.001
27	19 (0.08)	26 (0.03)	2.97 (1.64-5.37)	<0.001	3.00 (1.46-6.15)	0.002
28	17 (0.07)	43 (0.04)	1.64 (0.93-2.89)	0.08	0.74 (0.33-1.66)	0.47
29	15 (0.06)	73 (0.08)	0.85 (0.48-1.48)	0.57	0.87 (0.48-1.58)	0.66
30	33 (0.14)	93 (0.10)	1.45 (0.97-2.17)	0.06	1.41 (0.89-2.25)	0.14
31	29 (0.12)	101 (0.11)	1.14 (0.75-1.73)	0.52	0.96 (0.69-1.56)	0.89
32	51 (0.21)	156 (0.16)	1.33 (0.97-1.83)	0.07	1.26 (0.87-1.81)	0.21

33	76 (0.31)	212 (0.22)	1.47 (1.31-1.92)	0.004	1.32 (0.97-1.76)	0.07
34	114 (0.47)	415 (0.43)	1.10 (0.89-1.36)	0.33	1.05 (0.83-1.32)	0.67
35	210 (0.86)	756 (0.79)	1.13 (0.96-1.32)	0.12	1.08 (0.90-1.29)	0.37
36	447 (1.84)	1691 (1.76)	1.07 (0.96-1.32)	0.19	1.02 (0.90- 1.15)	0.72
37	1098 (4.51)	4140 (4.31)	1.08 (1.004-1.15)	0.03	1.06 (0.98-1.15)	0.11
38	3076 (12.65)	11488 (11.97)	1.09 (1.04-1.14)	<0.001	1.09 (1.04-1.15)	<0.001
39	6114 (25.14)	24736 (25.78)	1.01 (0.97-1.05)	0.59	1.01 (0.96-1.05)	0.63
40	7143 (29.37)	29152 (30.38)	Reference		Reference	
41	4960 (19.28)	18536 (19.32)	1.03 (0.99-1.07)	0.15	1.03 (0.99-1.08)	0.11
≥42	1150 (4.73)	4282 (4.46)	1.10 (1.02-1.18)	0.007	1.09 (1.01-1.19)	0.01

Missing values: [a] boys 857, girls 1626. [b] Odd ratios were adjusted for mothers and fathers (age, psychopathology) and just mothers (substance abuse, depression, number of previous births, marital status, SES, smoking during pregnancy and infant's birthplace), and just fathers (immigration status).

Table 5: Association between gestational age categories and depression, stratified by age at diagnosis of depression, for boys and girls. Measured as frequencies of depression cases, controls and ORs with 95% CIs.

	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	P value	Adjusted[a] OR (95% CI)	P value
Boys						
5-12 years	**n=2941**	**n=11740**				
<28 weeks	6 (0.20)	11 (0.09)	2.09 (0.77-5.66)	0.14	1.09 (0.56-2.14)	0.79
28-31 weeks	12 (0.41)	42 (0.36)	1.13 (0.59-2.15)	0.70	1.15 (0.83-1.60)	0.39
32-36 weeks	132 (4.49)	486 (4.14)	1.09 (0.90-1.33)	0.34	0.95 (0.84-1.06)	0.39
37-41 weeks	2633 (89.53)	10667 (90.86)	Reference		Reference	
≥42 weeks	158 (5.37)	534 (4.55)	1.18 (0.98-1.42)	0.07	1.17 (1.06-1.30)	0.001
13-18 years	**n=6193**	**n=24634**				
<28 weeks	6 (0.10)	25 (0.10)	0.97 (0.40-2.40)	0.96	0.76 (0.27-2.16)	0.60
28-31 weeks	26 (0.42)	90 (0.37)	1.13 (0.73-1.75)	0.57	1.11 (0.68-1.82)	0.65
32-36 weeks	229 (3.70)	922 (3.74)	0.99 (0.86-1.15)	0.98	0.94 (0.79-1.11)	0.46

37-41 weeks	5623 (90.80)	22463 (91.19)				
≥42 weeks	309 (4.99)	1134 (4.60)	1.09 (0.95-1.24)	0.18	1.10 (0.94-1.27)	0.21
19-25 years	**n=3669**	**n=14531**				
<28 weeks	7 (0.19)	13 (0.09)	2.05 (0.81-5.17)	0.12	1.26 (0.38-4.12)	0.70
28-31 weeks	21 (0.57)	62 (0.43)	1.38 (0.84-2.27)	0.20	1.32 (0.76-2.29)	0.31
32-36 weeks	152 (4.14)	564 (3.88)	1.09 (0.90-1.31)	0.35	1.00 (0.81-1.24)	0.95
37-41 weeks	3287 (19.88)	13248 (91.17)	Reference		Reference	
≥42 weeks	202 (5.51)	644 (4.43)	1.26 (1.07-1.48)	0.005	1.28 (1.07-1.54)	0.006
Girls						
5-12 years	**n=1494**	**n=5939**				
<28 weeks	5 (0.33)	5 (0.08)	4.10 (1.18-14.17)	0.02	2.70 (1.83-3.98)	<0.001
28-31 weeks	6 (0.40)	25 (0.42)	1.0 (0.41-2.45)	0.99	1.01 (0.77-1.32)	0.93
32-36 weeks	53 (3.55)	190 (3.20)	1.12 (0.82-1.54)	0.46	1.04 (0.95-1.13)	0.32
37-41 weeks	1355 (90.70)	5469 (92.09)	Reference		Reference	
≥42 weeks	75 (5.02)	250 (4.21)	1.21 (0.93-1.57)	0.14	1.07 (0.99-1.15)	0.07
13-18 years	**n= 17027**	**n=67252**				

<28 weeks	43 (0.25)	60 (0.09)	2.84 (1.92-4.21)	<0.001	2.97 (1.84-4.78)	<0.001
28-31 weeks	63 (0.37)	226 (0.34)	1.11 (0.84-1.47)	0.46	0.93 (0.67-1.30)	0.70
32-36 weeks	647 (3.80)	2224 (3.31)	1.15 (1.05-1.26)	0.001	1.09 (0.99-1.21)	0.07
37-41 weeks	15481 (90.92)	61738 (91.80)	Reference		Reference	
≥42 weeks	793 (4.66)	3004 (4.47)	1.06 (0.97-1.14)	0.15	1.05 (0.96-1.15)	0.25
19-25 years	**n=5802**	**n=22772**				
<28 weeks	12 (0.21)	24 (0.11)	1.93 (0.96-3.86)	0.06	1.19 (0.87-4.20)	0.10
28-31 weeks	25 (0.43)	59 (0.26)	1.65 (1.03-2.65)	0.03	1.49 (0.85-2.60)	0.16
32-36 weeks	198 (3.41)	816 (3.58)	0.95 (0.81-1.12)	0.58	0.91 (0.76-1.08)	0.29
37-41 weeks	5285 (91.09)	20845 (91.54)	Reference		Reference	
≥42 weeks	282 (4.86)	1028 (4.51)	1.08 (0.94-1.24)	0.23	1.08 (0.93-1.26)	0.26

[a] Odd ratios were adjusted for mothers and fathers (age, psychopathology) and just mothers (substance abuse, depression, number of previous

births, marital status, SES, smoking during pregnancy and infant's birthplace), and just fathers (immigration status).

Table S1: Relationship between covariates and gestational age, and between weight for gestational age for the controls

	Gestational age (in weeks)					*p*	Weight for gestational age (z score)			*p*
	<28	28-31	32-36	37-41	≥42		<-2	-2-(+2)	>+2	
n=148795	Mean (SD)						Mean (SD)			
Maternal age	29.78 (6.12)	29.64 (5.58)	29.10 (5.68)	28.81 (5.11)	28.27 (4.98)	<0.001	28.71 (5.58)	28.75 (5.10)	30.13 (5.20)	<0.001
Paternal age	32.18 (6.19)	31.77 (6.24)	31.44 (6.30)	31.16 (5.73)	30.82 (5.79)	<0.001	31.06 (6.21)	31.10 (5.72)	32.51 (5.98)	<0.001
	n (%)						n (%)			
Maternal psychopathology[a]										
Yes	16 (11.59)	67 (13.29)	602 (11.58)	12309 (9.16)	620 (9.40)	<0.001	434 (10.41)	12603 (9.19)	573 (10.36)	<0.001
No	122 (88.41)	437 (86.71)	4598 (88.42)	122117 (90.84)	5974 (90.60)		3734 (89.59)	124515 (90.81)	4960 (89.64)	
Paternal psychopathology[b]										
Yes	17 (12.50)	92 (18.55)	714 (13.93)	15564 (11.68)	807 (12.41)	<0.001	617 (15.13)	15966 (11.75)	603 (10.98)	<0.001
No	119 (87.50)	404 (81.45)	4413 (86.07)	117708 (88.32)	5696 (87.59)		3460 (84.87)	119955 (88.25)	4891 (89.02)	
Maternal Substance use[a]										
Yes	6 (4.35)	29 (5.75)	210 (4.04)	3290 (2.45)	208 (3.15)	<0.001	227 (5.45)	3412 (2.49)	103 (1.86)	<0.001
No	132 (95.65)	475 (94.25)	4990 (95.96)	131136 (97.55)	6386 (96.85)		3941 (94.55)	133706 (97.51)	5430 (98.14)	
No. of previous births[c]										
Yes	95 (68.84)	351 (69.78)	3358 (64.55)	93752 (69.78)	4015 (60.94)	<0.001	2317 (55.67)	94557 (69.00)	4669 (84.40)	<0.001
No	43 (31.16)	152 (30.22)	1844 (35.45)	40593 (30.22)	2573 (39.06)		1845 (44.33)	42482 (31.00)	863 (15.60)	
Maternal marital status[d]										
Single	2 (1.68)	10 (2.21)	85 (1.78)	1545 (1.22)	99 (1.63)	<0.001	84 (2.23)	1606 (1.25)	50 (0.95)	<0.001
Married/in a relationship	117 (98.32)	443 (97.79)	4680 (98.22)	124798 (98.78)	5959 (98.37)		3685 (97.77)	127058 (98.75)	5214 (99.05)	
Maternal SES[e]										
Managers and professionals	11 (7.97)	37 (7.34)	411 (7.90)	11702 (8.70)	588 (8.92)	0.03	317 (7.60)	11979 (8.74)	445 (8.04)	<0.001
Clerical support workers	42 (30.43)	160 (31.75)	1440 (27.68)	37861 (28.16)	1891 (28.68)		1181 (28.33)	38626 (28.27)	1573 (28.43)	
Manual workers	13 (9.42)	56 (11.11)	622 (11.96)	15288 (11.37)	826 (12.53)		565 (13.55)	15637 (11.40)	600 (10.84)	
Others	16 (11.59)	49 (9.72)	486 (9.34)	12035 (8.95)	599 (9.08)		357 (8.56)	12314 (8.98)	511 (9.24)	
Missing	56 (40.58)	202 (40.08)	2243 (43.12)	57544 (42.81)	2690 (40.79)		1749 (41.95)	58567 (42.71)	2404 (43.45)	

Table S1: Relationship between covariates and gestational age, and between weight for gestational age for the controls (continued)

	Gestational age (in weeks)					p	Weight for gestational age (z score)			p
n=148795	<28	28-31	32-36	37-41	≥42		<-2	-2-(+2)	>+2	
	n (%)						n (%)			
Maternal smoking[f]										
Yes	30 (22.73)	97 (19.80)	963 (18.87)	19459 (14.76)	1099 (17.01)	<0.001	1201 (29.46)	19960 (14.85)	479 (8.84)	<0.001
No	102 (77.27)	393 (80.20)	4139 (81.13)	112337 (85.24)	5362 (82.99)		2876 (70.54)	114485 (85.15)	4939 (91.16)	
Municipality of birth place[g]										
Rural	28 (20.44)	116 (23.02)	1217 (23.41)	31863 (23.72)	1465 (22.23)	<0.001	909 (21.81)	32162 (23.47)	1611 (29.13)	<0.001
Semi-urban	26 (18.98)	80 (15.87)	910 (17.50)	24577 (18.29)	1081 (16.41)		667 (16.01)	24961 (18.21)	1035 (18.71)	
Urban	83 (60.58)	308 (61.11)	3072 (59.09)	77911 (57.99)	4043 (61.36)		2591 (62.18)	79916 (58.32)	2885 (52.16)	
Mother immigrant[a]										
Yes	2 (1.45)	6 (1.19)	86 (1.65)	1795 (1.34)	104 (1.58)	0.17	67 (1.61)	1876 (1.37)	47 (0.85)	0.001
No	136 (98.55)	498 (98.81)	5114 (98.35)	132631 (98.66)	6490 (98.42)		4101 (98.39)	135242 (98.63)	5486 (99.15)	
Father immigrant[b]										
Yes	1 (0.74)	9 (1.81)	123 (2.40)	2312 (1.73)	126 (1.94)	0.005	105 (2.58)	2407 (1.77)	58 (1.06)	<0.001
No	135 (99.26)	487 (98.19)	5004 (97.60)	130960 (98.27)	6377 (98.06)		3972 (97.42)	133514 (98.23)	5436 (98.98)	
Maternal depression[a]										
Yes	17 (12.32)	45 (8.93)	460 (8.85)	9400 (6.99)	478 (7.25)	<0.001	344 (8.25)	9590 (6.99)	463 (8.37)	<0.001
No	121 (87.68)	459 (91.07)	4740 (91.15)	125026 (93.01)	6116 (92.75)		3824 (91.75)	127528 (93.01)	5070 (91.63)	
Paternal depression[b]										
Yes	12 (8.82)	33 (6.65)	319 (6.22)	7437 (5.58)	370 (5.69)	0.10	248 (6.08)	7612 (5.60)	306 (5.57)	0.41
No	124 (91.18)	463 (93.35)	4808 (93.78)	125835 (94.42)	6133 (94.31)		3829 (93.92)	128309 (94.40)	5188 (94.43)	

Missing values: [a] 1933 for gestational age and 1976 for WGA. [b] 3261 for gestational age and 3303 for WGA. [c] 2019 for gestational age and 2062 for WGA. [d] 11057 for gestational age and 11098 for WGA. [e] 1927 for gestational age and 1970 for WGA. [f] 4814 for gestational age and 4855 for WGA. [g] 2015 for gestational age and 2058 for WGA.WGA, weight for gestational age.

Table S2: Relationship between covariates and depression in cases and controls

	Cases (n=37682)	Controls (n=148795)	Point estimate (95% CI)	*p* for covariate and depression
	Mean (SD)	Mean (SD)		
Maternal age	28.24 (5.58)	28.80 (5.13)	0.98 (0.97-0.98)	<0.001
Paternal age	30.86 (6.31)	31.16 (5.75)	0.99 (0.98-0.99)	<0.001
	n (%)	n (%)		
Maternal psychopathology[a]				
Yes	8236 (21.86)	13782 (9.26)	2.73 (2.65-2.81)	<0.0001
No	29445 (78.14)	135001 (90.74)	Reference	
Paternal psychopathology[b]				
Yes	8369 (22.65)	17400 (11.81)	2.19 (2.13-2.25)	<0.001
No	28583 (77.35)	129910 (88.19)	Reference	
Maternal Substance use[a]				
Yes	2708 (7.19)	3791 (2.55)	2.95 (2.80-3.10)	<0.001
No	34973 (92.81)	144992 (97.45)	Reference	
No. of previous births[c]				
Yes	26022 (69.87)	101952 (69.22)	1.03 (1.006-1.05)	0.01
No	11223 (30.13)	45338 (30.78)	Reference	
Maternal marital status[d]				
Single	824 (2.44)	1754 (1.27)	1.95 (1.79-2.12)	<0.001
Married/in a relationship	32999 (97.56)	136318 (98.73)	Reference	
Maternal SES				
Managers and professionals	2605 (6.91)	12773 (8.58)	Reference	<0.001
Clerical support workers	9444 (25.06)	41486 (27.88)	1.11 (1.06-1.17)	
Manual workers	4864 (12.91)	16849 (11.32)	1.41 (1.34-1.49)	
Others	4153 (11.02)	13219 (8.88)	1.50 (1.39-1.62)	
Missing	16616 (44.10)	64468 (43.33)	1.54 (1.45-1.62)	

Table S2: Relationship between covariates and depression in cases and controls (continued)

	Cases (n=37682)	Controls (n=148795)	Point estimate (95% CI)	*p* for covariate and depression
	n (%)	n (%)		
Maternal smoking[e]				
Yes	8818 (24.18)	21709 (15.04)	1.80 (1.75-1.85)	<0.001
No	27655 (75.82)	122599 (84.96)	Reference	
Municipality of birth place[f]				
Rural	7465 (19.93)	34983 (22.63)	1.06 (1.02-1.10)	<0.001
Semi-urban	6077 (16.22)	26887 (18.16)	1.30 (1.26-1.34)	
Urban	23915 (63.85)	86165 (58.21)	Reference	
Mother immigrant[a]				
Yes	465 (1.23)	2214 (1.42)	0.86 (0.78-0.96)	0.006
No	37216 (98.77)	146669 (98.58)	Reference	
Father immigrant[b]				
Yes	826 (2.24)	2716 (1.84)	1.21 (1.12-1.31)	<0.001
No	36126 (97.76)	144594 (98.16)	Reference	
Maternal depression[a]				
Yes	7333 (19.46)	10536 (7.08)	3.17 (3.07-3.27)	<0.001
No	30348 (80.54)	138247 (92.92)	Reference	
Paternal depression[b]				
Yes	4516 (12.22)	8271 (5.61)	2.35 (2.26-2.44)	<0.001
No	32436 (87.78)	139039 (94.39)	Reference	

Missing values: [a] 1 case and 12 controls; [b] 730 cases and 1485 controls; [c] 437 cases and 1505 controls; [d] 3859 cases and 10723 controls; [e] 1209 cases and 4487 controls; [f] 225 cases and 760 controls.

Table S3: Sex-specific unadjusted and adjusted models, with ORs (95% CIs), for the association between birth weight for gestational age and depression

Weight for gestational age (z score)[a]	Cases n (%)	Controls n (%)	Unadjusted OR (95% CI)	P value	Adjusted[b] OR (95% CI)	P value
Boys						
Below -2.0	461 (3.60)	1455 (2.86)	1.28 (1.15-1.43)	<0.001	1.09 (0.95-1.24)	0.19
-2.0 to -1.51	644 (5.03)	2267 (4.45)	1.14 (1.04-1.25)	0.005	1.01 (0.91-1.13)	0.79
-1.50 to -1.01	1377 (10.76)	4788 (9.41)	1.16 (1.08-1.24)	<0.001	1.10 (1.02-1.19)	0.01
-1.0 to -0.51	1912 (14.94)	7783 (15.29)	0.98 (0.93-1.05)	0.68	0.96 (0.89-1.02)	0.23
-0.50 to 0.50	4686 (36.61)	18904 (37.15)	Ref	Ref	Ref	Ref
0.51 to 1.0	1754 (13.70)	7187 (14.12)	0.98 (0.92-1.04)	0.57	1.03 (0.96-1.11)	0.28
1.01 to 1.50	1027 (8.02)	4408 (8.66)	0.93 (0.87-1.01)	0.09	0.97 (0.90-1.06)	0.62
1.51 to 2.0	520 (4.06)	2224 (4.37)	0.94 (0.85-1.04)	0.24	0.97 (0.86-1.08)	0.60
Above 2.0	418 (3.27)	1871 (79.90)	0.90 (0.80-1.00)	0.06	0.96 (0.84-1.08)	0.51
Girls						
Below -2.0	818 (3.36)	2714 (2.83)	1.21 (1.11-1.31)	<0.001	1.06 (0.96-1.16)	0.21
-2.0 to -1.51	1327 (5.46)	4263 (4.44)	1.24 (1.16-1.32)	<0.001	1.09 (1.01-1.17)	0.02
-1.50 to -1.01	2453 (10.09)	9091 (9.48)	1.08 (1.02-1.13)	0.002	1.03 (0.97-1.09)	0.33
-1.0 to -0.51	3766 (15.49)	14702 (15.32)	1.02 (0.98-1.07)	0.26	0.98 (0.94-1.03)	0.58
-0.50 to 0.50	8899 (36.60)	35644 (37.15)	Ref	Ref	Ref	

0.51 to 1.0	3149 (12.95)	13105 (13.66)	0.96 (0.92-1.00)	0.09	0.98 (0.94-1.04)	0.64
1.01 to 1.50	1898 (7.81)	8232 (8.58)	0.92 (0.87-0.97)	0.005	0.96 (0.90-1.02)	0.25
1.51 to 2.0	1088 (4.47)	4525 (4.72)	0.96 (0.90-1.03)	0.32	1.02 (0.94-1.10)	0.56
Above 2.0	917 (3.77)	3662 (3.82)	1.00 (0.93-1.08)	0.94	1.07 (0.98-1.16)	0.09

Missing values: [a] boys 879, girls 1659. [b] Odd ratios were adjusted for mothers and fathers (age, psychopathology) and just mothers (substance abuse, depression, number of previous births, marital status, SES, smoking during pregnancy and infant's birthplace), and just fathers (immigration status).