Published in final edited form as:

Paediatr Perinat Epidemiol. 2010 January ; 24(1): 79–87. doi:10.1111/j.1365-3016.2009.01073.x.

Maternal Smoking During Pregnancy and Intellectual Performance in Young Adult Swedish Male Offspring

Frida Lundberg^a, Sven Cnattingius^a, Brian D'Onofrio^b, Daniel Altman^a, Mats Lambe^a, Christina Hultman^a, and Anastasia Iliadou^a

^aDepartment of Medical Epidemiology and Biostatistics, Karolinska Institutet

^bDepartment of Psychological and Brain Sciences, Indiana University

SUMMARY

Smoking during pregnancy has been linked to an increased risk of several adverse birth outcomes. Associations with deficits in cognitive development have also been suggested. It is unclear if these associations are due to genetic and/or environmental confounding. In a population-based Swedish cohort study on 205 777 singleton males born to Nordic mothers between 1983 and 1988, we examined the association between maternal smoking during pregnancy and the risk of poor intellectual performance in young adult male offspring. In the cohort analyses, the risk of poor intellectual performance was increased in sons of smoking mothers compared to sons of non-smokers. Stratifying for maternal smoking habits across two pregnancies, there was an increased risk of poor intellectual performance for both sons if the mother was only smoking in the first pregnancy, but in neither son if the mother was only smoking in the second pregnancy. The effect of smoking during pregnancy on intellectual performance was not present when the association was evaluated within sibling pairs. Thus, the association between prenatal smoking exposure and offspring risk of low intellectual performance appears to be completely confounded by familial (genetic and early environmental) factors.

INTRODUCTION

Maternal smoking during pregnancy has been causally linked to fetal growth restriction, and probably also with placental abruption, preterm birth, stillbirth and sudden infant death syndrome (SIDS).^{1–3} Several studies have found evidence of associations between prenatal exposure to smoking and subsequent deficits in childhood, including cognitive development, school achievement and behavioral adjustment.^{4–10} An association between smoking during pregnancy and offspring adult intelligence has also been suggested.¹¹

Smoking during pregnancy is correlated with low parental education and socioeconomic status, poor parenting, early age at childbearing and use of other drugs during pregnancy, all potential risk factors for poor outcomes in children.^{6, 8, 12–15} Two U.S studies, using retrospectively collected information about smoking during pregnancy, found that the association between prenatal smoking exposure and offspring intellectual abilities was substantially or entirely confounded by maternal factors, foremost maternal IQ and education.^{14, 15}

Sibling studies is an alternative approach to reduce confounding when investigating effects of prenatal smoking exposure in offspring. Since siblings share childhood environment and

half of their segregating genes, sibling analyses adjust for unmeasured familial (common genetic and shared environmental) factors. Importantly, studies of successive pregnancies also allow us to investigate how change of smoking habits between pregnancies influence intellectual performance in offspring.

We investigated the association between exposure to maternal smoking during pregnancy and subsequent risk of poor intellectual performance in young adult Swedish males, taking both parental and birth characteristics into account. Further, to investigate if the association was confounded by unmeasured familial factors (shared environment and common genes), we studied maternal smoking habits across two pregnancies.

METHODS

Five Swedish population-based registers were used to obtain data for the study: the Medical Birth Register, the Multigeneration Register, the Population and Housing Census of 1990, the Education Register of 2000 and the Swedish Conscript Register. The records were linked using the unique national registration number assigned to each Swedish citizen at birth and included in each register.

The Swedish Medical Birth Register was used to obtain data on maternal characteristics (age at delivery, parity, smoking, pre-pregnancy weight and height) and birth characteristics (gestational age, birthweight and head circumference). This register contains data on more than 99% of all births in Sweden since 1973.¹⁶ During pregnancy and delivery, information is prospectively recorded in standardized records. More than 95% of pregnant women in Sweden attend prenatal care before gestational week 15.¹⁷ A previous study on the Birth Register has found that the quality of the variables included in this study is high.¹⁶

At the first prenatal care visit, women report whether they are daily smokers (categorized as moderate [1–9 cigarettes per day] or heavy smokers [≥ 10 cigarettes per day]) or not. Maternal body mass index (BMI) before pregnancy was calculated as the ratio between weight in kilograms and the square of the height in meters (kg/m^2), and was categorized according to the WHO recommendations.¹⁸ Family situation was categorized into parents living or not living together in early pregnancy. Birthweight and head circumference for gestational age were expressed in standard deviation scores for gestational age according to Swedish standard curves.¹⁹

The Multigeneration Register was used to identify the biological father of each son. Data on the parents' socioeconomic status (SES) was collected from the Population and Housing Census of 1990 and classified according to the recommendations by Statistics Sweden.²⁰ The Education Register of 2000 was used to establish the educational level of the parents. A validation study has shown that the highest level of formal education is correctly reported for 83% of the population.²¹

The Swedish Conscript Register includes information about Swedish males conscripted for military service. Intellectual performance and age at conscription were obtained at conscription. The only information obtained from the Conscript Register regarding intellectual performance (IP) is that it is tested in 4 dimensions: logical/inductive, verbal, spatial and theoretical/technical. The time-limited test consists of 40 questions for each dimension. Results are presented as a combined standard nine (stanine) score with mean 5 and standard deviation 2. Poor intellectual performance in the current study was defined as a score of ≤ 2. These individuals can be expected to have difficulties coping with basic educational programs. While there was no formal evaluation of the data quality available, data from the Conscript Register has been successfully used in previous studies on intellectual performance.^{22, 23}

Sample and subsets

Data on 232 378 Swedish live-born males born between 1983 and 1988 and conscripted between 2000 and 2006 was obtained from the Swedish Birth Register linked with the Swedish Conscript Registry. In order to obtain a more homogeneous study population, we excluded 13 240 males born to non-Scandinavian mothers, 4 260 males born in multiple births and 9 101 males with congenital malformations. Fewer non-Scandinavian mothers smoked during pregnancy, but the frequency of poor intellectual performance was higher in this group, indicating that these offspring may be exposed to other risk factors. For males born in multiple births and with congenital malformations, the frequency of maternal smoking and of low intellectual performance did not differ significantly from those in the cohort. Of the remaining 205 777 males, we obtained data on intellectual performance from 172 182 individuals. Information on maternal smoking habits during pregnancy was available for 94% of the study population.

The sibling subset included 14 722 full sibling pairs. The first two sons with data on intellectual performance were selected from each family with more than one child in the cohort. The small sample size of half siblings (N=386 pairs) limited our statistical power to investigate the association within these pairs. Complete information on maternal smoking during pregnancy was available for 88% of the sibling pairs. In order to get an estimate from the unrelated individuals, one son per mother was randomly selected from the total sample to represent the unrelated group (N=156 663), where 94% had information on maternal smoking during pregnancy.

Analyses

We used generalized estimating equation models²⁴ to estimate risks of poor intellectual performance in early adulthood in relation to maternal smoking during pregnancy, other parental characteristics and birth characteristics. A correlation matrix was specified in order to control for the dependence between siblings. Analyses were performed using Proc Genmod in SAS (SAS Institute, Inc, Cary, NC) and risks were presented as odds ratios (OR) with 95% confidence intervals [CI]. Associations between smoking during pregnancy and intellectual performance were estimated using both univariate and multivariable analyses. Risks of poor intellectual performance associated with smoking during pregnancy were investigated in three multivariable models. In the first model, we adjusted for parental characteristics (mother's age, parity, height and BMI, family situation in early pregnancy, parents' educational level and socioeconomic status) and age at conscription of the son. In the second model, we adjusted for birth characteristics (gestational age, birthweight and head circumference for gestational age), and in the third model, we adjusted for both parental and birth characteristics simultaneously. The final models only included variables that significantly influenced the risk of poor intellectual performance.

To examine whether the effect was influenced by unmeasured familial factors, we proceeded in two ways. First, we estimated the risks of poor intellectual performance in first- and second-born sons, stratified by maternal smoking habits across pregnancies. Risks of poor intellectual performance by changes in maternal smoking habits (non-smoker, continuous smoker, starting or quitting smoking between pregnancies) were estimated in first- and second born siblings separately using logistic regression models.

Second, to further examine the importance of familial confounding, we estimated the effects of smoking during pregnancy on intellectual performance in unrelated individuals and within sibling pairs. The effects of smoking during pregnancy on offspring intellectual performance within and between families were estimated using Proc Mixed in SAS. In these analyses, the exposure was decomposed into between- and within-family components.²⁵ The

between-family component was measured by the maternal mean of smoking across pregnancies, and the within-family component was centered on the family-mean for each son. The within-family component estimates the difference in intellectual performance between two siblings.²⁵ For comparison, the effect of smoking on the continuous measure of intellectual performance was also estimated in an unrelated subset of the cohort. If familial confounding is present one should expect the estimate of the within component to decrease compared to the effect seen between unrelated males. Due to the complexity of these analyses we treated smoking during pregnancy as a dichotomous variable (smokers vs non-smokers). The stanine scale of intellectual performance was used as outcome in these models.

RESULTS

Parental and birth characteristics in relation to offspring risk of poor intellectual performance are presented in Table 1. Risks of poor intellectual performance increased with declining maternal age and height. Sons of overweight (BMI 25–29) and obese (BMI ≥ 30) mothers also showed increased risks of low test scores. The risks were also highly influenced by socially related factors, including lower education and socioeconomic status of mothers and fathers, and single motherhood.

Males with a low birthweight or a small head circumference for gestational age were at higher risks of poor intellectual performance than males born with a normal birthweight or head circumference, respectively. Compared with males born at term (37–41 weeks), the risk of a low score on the general intellectual performance test was slightly higher for those born moderately preterm (32–36 weeks) and substantially higher for very preterm (< 32 weeks) born individuals.

Maternal smoking habits during pregnancy were closely associated with parental socioeconomic and educational status. More than half of the teenage mothers were smokers in contrast to less than 25% of mothers aged 30 years or more. Mothers of low education level (49%) and low socioeconomic status (39%) were more likely to smoke than mothers with the highest level of education and high-level white collar workers (14% in both groups). Maternal smoking habits during pregnancy were similarly associated to lower paternal educational level and socioeconomic status. More than half of mothers not living with the father of the child were smokers. Males with a low birthweight for gestational age and males born preterm were far more likely to have smoking mothers (51 % and 44%, respectively) than males born with a normal birthweight or born at term (29% in both groups).

Table 2 displays the association of smoking during pregnancy and intellectual performance as crude odds ratios and odds ratios adjusted for parental and birth characteristics. In the crude analysis, sons of moderate and heavy smokers were at increased risks of having a low score on the intellectual performance test (OR = 1.70 [95% CI 1.63, 1.78] and 1.91 [95% CI 1.81, 2.00], respectively). After adjusting for parental characteristics, corresponding odds ratios were decreased, but remained significant (OR = 1.27 [95% CI 1.19, 1.34] and 1.22 [95% CI 1.14, 1.31], respectively). While all parental characteristics were significantly associated with the outcome, the reduction in the smoking-related risk was primarily attributed to adjustment for mother's and father's educational level. Next, to examine whether the effects on intellectual performance were mediated by fetal growth restriction, adjustments were made for birth characteristics. The decrease in risk was negligible, although birthweight and head circumference were found to be significantly and independently associated with poor intellectual performance. When we in the final model adjusted for both birth and parental characteristics, smoking during pregnancy was still

significantly associated with increased risk of poor intellectual performance (OR = 1.25 [95% CI 1.18, 1.33] for sons of moderate smokers and 1.21 [95% CI 1.12, 1.30] for sons of heavy smokers).

Analyzing intellectual performance as a continuous variable showed the same increase in risk of low intellectual performance with increasing level of smoking (data not shown). Similar effects on intellectual performance could also be seen in the original dataset (including males born to non-Scandinavian mothers, in multiple births and with congenital malformations) and in complete case analyses (data not shown).

We also investigated possible interactions of smoking with maternal age, education and socioeconomic index. None of the tested interactions were significant in the adjusted analysis (data not shown).

The results from comparing the risk of poor intellectual performance between full brothers in relation to the mothers' smoking across pregnancies are shown in Table 3. In the crude analysis, the risk of a low score on the intellectual performance test was nearly doubled among sons of mothers who smoked in both pregnancies, compared with sons of mothers who did not smoke in any pregnancy (OR = 1.85 [95% CI 1.57, 2.18] for the first son and 1.89 [95% CI 1.65, 2.17] for the second son). If the mother smoked in first but not in second pregnancy, the risk of poor intellectual performance was similarly increased in both sons. If the mother had started smoking after the first pregnancy, both sons also seemed to have an increased risk of a low score. In the adjusted analyses, all smoking-related risks were decreased. However, not only smoking in both pregnancies but also smoking in first but not in second pregnancy was still associated with increased risks of poor intellectual performance in both sons (OR = 1.40 [95% CI 1.03, 1.91] for the first son and 1.39 [95% CI 1.08, 1.79] for the second son). Compared to mothers not smoking in either pregnancy, maternal smoking only in the second pregnancy was not associated with an increased risk of poor intellectual performance in either son.

Finally, to investigate the importance of familial factors, we studied the effect of smoking during pregnancy on intellectual performance between unrelated sons and within siblings (Figure 1). Along the lines of preceding results, sons of mothers who had smoked during pregnancy scored approximately 0.65 points less than sons of non-smoking mothers in the unrelated subset [95% CI -0.67, -0.63]. Adjusting for parental characteristics decreased this difference to 0.24 points [95% CI -0.27, -0.22]. In the sibling subset, there was a small but significant increase in intellectual performance for the sons exposed to smoking during pregnancy (regression coefficient β = 0.22 [95% CI 0.10, 0.34]). However, after adjustment for birth order and maternal age, this effect was no longer significant (β = 0.06 [95% CI -0.06, 0.18]).

Analyzing the complete dataset without exclusions showed virtually the same results (data not shown).

DISCUSSION

We found that the association between maternal smoking during pregnancy and poor intellectual performance in young adult male offspring can be explained partly by parental education but also by unmeasured familial factors, such as common genes and shared environment.

In the cohort analyses, more than half of the smoking-related increased risk was accounted for by parental educational level, indicating that the association largely depends on familial factors. Two recent studies reported that the association between maternal smoking and

offspring intellectual performance was diminished after adjusting for maternal education and IQ.^{14, 15} Our results in relation to these studies indicate that other familial effects besides education are of importance for the association. In the current study, smoking-related birth outcomes did not mediate the association between smoking during pregnancy and poor intellectual performance in the offspring. This indicates that any effect of prenatal smoking exposure on intellectual performance in offspring is independent of fetal growth or gestational age.

In the sibling subset of the studied cohort, we found an increased risk of poor intellectual performance for both sons if the mother was smoking in the first pregnancy, regardless of her smoking habits during the second pregnancy. In contrast, if the mother was only smoking in the second pregnancy there was no increase in risk for either son. The finding that change of exposure to maternal smoking across pregnancies seems to be unrelated to offspring risk of poor intellectual performance does not support the hypothesis that prenatal smoking exposure influence intellectual performance in offspring.

The effect of maternal smoking on offspring intellectual performance could not be seen within full sibling pairs, suggesting that the association seen in the cohort is confounded by unmeasured familial (genetic or environmental) factors. Similarly, a recent study on siblings from the Collaborative Perinatal Project found no effect of maternal smoking during pregnancy on twelve different outcomes of cognitive and physical development within 2064 sibling sets where the mother's had changed smoking habits between pregnancies.²⁶ In the current study, the apparent positive effect of prenatal smoking exposure on intellectual performance within siblings was lost after adjusting for birth order. Though debated, intellectual performance has been negatively associated with increasing birth order within families in previous studies.^{27, 28}

The data on maternal smoking during pregnancy was collected at the first prenatal care visit. The proportion of women who stop smoking during pregnancy has been reported to be around 30% in previous Swedish studies. In these studies, women with a higher level of education and a higher age at the initiation of smoking were more likely to stop smoking when pregnant, while women not living with the father of the child, heavy smokers and women exposed to daily passive smoking at home were more likely to continue smoking throughout the pregnancy.^{29, 30} Thus, misclassification of smoking exposure during pregnancy may have influenced the obtained risk estimates. Finally, most pregnant smokers continue to smoke after pregnancy, and we cannot distinguish between the effects of prenatal and postnatal smoking exposure.

Some strengths of this study are its size, the prospective design and the range of covariates gathered from population-based registers.¹⁶ An advantage of measuring intellectual performance in early adulthood is that it is less affected by postnatal environment than other measures of cognitive ability in early ages. Intelligence measured in children and even more so scholastic achievement are likely to be influenced by motivation and ability to concentrate, and might consequently reflect attention deficits or behavioral problems rather than life-long cognitive ability. A limitation of this study was residual confounding that we could not control for by parental education and SES, such as parental intellectual abilities and behavioral problems, parenting and environmental stimulation, passive smoking and maternal alcohol consumption during pregnancy. We were also unable to control for the duration of breast feeding. However, while breast feeding has been positively linked to intellectual development,³¹ other studies have found no significant advantage of breast feeding on offspring intelligence when adjusting for maternal characteristics and home environment.^{32, 33}

In conclusion, our results support the importance of familial factors to the association between mothers smoking during pregnancy and poor intellectual performance in young adult males. Further research in this field is warranted to clarify the nature of familial risk factors and their potential role in the association between smoking during pregnancy and intellectual performance.

Acknowledgments

This project was supported by grants from the Swedish Research Council (Project number K2007-70P-20518-01-4).

References

1. Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics, and pregnancy outcomes. *Nicotine Tob Res.* 2004; 6 (Suppl 2):S125–140. [PubMed: 15203816]
2. Fleming P, Blair PS. Sudden Infant Death Syndrome and parental smoking. *Early Hum Dev.* 2007; 83:721–725. [PubMed: 17881163]
3. Salihu HM, Wilson RE. Epidemiology of prenatal smoking and perinatal outcomes. *Early Hum Dev.* 2007; 83:713–720. [PubMed: 17884310]
4. Wakschlag LS, Pickett KE, Cook E Jr, Benowitz NL, Leventhal BL. Maternal smoking during pregnancy and severe antisocial behavior in offspring: a review. *Am J Public Health.* 2002; 92:966–974. [PubMed: 12036791]
5. Cornelius MD, Ryan CM, Day NL, Goldschmidt L, Willford JA. Prenatal tobacco effects on neuropsychological outcomes among preadolescents. *J Dev Behav Pediatr.* 2001; 22:217–225. [PubMed: 11530894]
6. Huizink AC, Mulder EJ. Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioral and cognitive functioning in human offspring. *Neurosci Biobehav Rev.* 2006; 30:24–41. [PubMed: 16095697]
7. Olds DL, Henderson CR Jr, Tatelbaum R. Intellectual impairment in children of women who smoke cigarettes during pregnancy. *Pediatrics.* 1994; 93:221–227. [PubMed: 8121734]
8. Noland JS, Singer LT, Short EJ, Minnes S, Arendt RE, Kirchner HL, et al. Prenatal drug exposure and selective attention in preschoolers. *Neurotoxicol Teratol.* 2005; 27:429–438. [PubMed: 15939203]
9. MacArthur C, Knox EG, Lancashire RJ. Effects at age nine of maternal smoking in pregnancy: experimental and observational findings. *BJOG.* 2001; 108:67–73. [PubMed: 11213007]
10. D'Onofrio BM, Hulle CA, Waldman ID, Rodgers JL, Harden KP, Rathouz PJ, et al. Smoking during pregnancy and offspring externalizing problems: An exploration of genetic and environmental confounds. *Dev Psychopathol.* 2008; 20:139–164. [PubMed: 18211732]
11. Mortensen EL, Michaelsen KF, Sanders SA, Reinisch JM. A dose-response relationship between maternal smoking during late pregnancy and adult intelligence in male offspring. *Paediatr Perinat Epidemiol.* 2005; 19:4–11. [PubMed: 15670102]
12. Mattson SN, Calarco KE, Chambers CD, Jones KL. Interaction of maternal smoking and other in-pregnancy exposures: analytic considerations. *Neurotoxicol Teratol.* 2002; 24:359–367. [PubMed: 12009491]
13. Lambe M, Hultman C, Torrang A, Maccabe J, Cnattingius S. Maternal smoking during pregnancy and school performance at age 15. *Epidemiology.* 2006; 17:524–530. [PubMed: 16878043]
14. Batty GD, Der G, Deary IJ. Effect of maternal smoking during pregnancy on offspring's cognitive ability: empirical evidence for complete confounding in the US national longitudinal survey of youth. *Pediatrics.* 2006; 118:943–950. [PubMed: 16950984]
15. Breslau N, Paneth N, Lucia VC, Paneth-Pollak R. Maternal smoking during pregnancy and offspring IQ. *Int J Epidemiol.* 2005; 34:1047–1053. [PubMed: 16085682]
16. Cnattingius S, Ericson A, Gunnarskog J, Kallen B. A quality study of a medical birth registry. *Scand J Soc Med.* 1990; 18:143–148. [PubMed: 2367825]

17. Lindmark G, Cnattingius S. The scientific basis of antenatal care. Report from a state-of-the-art conference. *Acta Obstet Gynecol Scand*. 1991; 70:105–109. [PubMed: 1679279]
18. World_Health_Organization. Obesity. Preventing and managing the global epidemic. Geneva: World Health Organization; Jun 3–5. 1998 Contract No.: Document Number]
19. Niklasson A, Ericson A, Fryer JG, Karlberg J, Lawrence C, Karlberg P. An update of the Swedish reference standards for weight, length and head circumference at birth for given gestational age (1977–1981). *Acta Paediatr Scand*. 1991; 80:756–762. [PubMed: 1957592]
20. Statistics_Sweden. Swedish Socioeconomic Classification. 1983.
21. Statistics_Sweden. Reports on Statistical Coordination. 1993. Education in the Swedish population.
22. Bergvall N, Iliadou A, Johansson S, Tuvemo T, Cnattingius S. Risks for low intellectual performance related to being born small for gestational age are modified by gestational age. *Pediatrics*. 2006; 117:e460–467. [PubMed: 16510624]
23. Lundgren M, Cnattingius S, Jonsson B, Tuvemo T. Intellectual performance in young adult males born small for gestational age. *Growth Horm IGF Res*. 2004; 14 (Suppl A):S7–8. [PubMed: 15135769]
24. Cole SR. Analysis of complex survey data using SAS. *Comput Methods Programs Biomed*. 2001; 64:65–69. [PubMed: 11084234]
25. Begg MD, Parides MK. Separation of individual-level and cluster-level covariate effects in regression analysis of correlated data. *Stat Med*. 2003; 22:2591–2602. [PubMed: 12898546]
26. Gilman SE, Gardener H, Buka SL. Maternal smoking during pregnancy and children's cognitive and physical development: a causal risk factor? *Am J Epidemiol*. 2008; 168:522–531. [PubMed: 18653646]
27. Bjerkedal T, Kristensen P, Skjeret GA, Brevik JI. Intelligence test scores and birth order among young Norwegian men (conscripts) analyzed within and between families. *Intelligence*. 2007; 35:503–514.
28. Zajonc RB, Sulloway FJ. The confluence model: birth order as a within-family or between-family dynamic? *Pers Soc Psychol Bull*. 2007; 33:1187–1194. [PubMed: 17586733]
29. Lindqvist R, Aberg H. Smoking habits before, during and after pregnancy among Swedish women and their partners in suburban Stockholm. *Scand J Prim Health Care*. 1992; 10:12–15. [PubMed: 1589656]
30. Cnattingius S, Lindmark G, Meirik O. Who continues to smoke while pregnant? *J Epidemiol Community Health*. 1992; 46:218–221. [PubMed: 1645075]
31. Kramer MS, Aboud F, Mironova E, Vanilovich I, Platt RW, Matush L, et al. Breastfeeding and child cognitive development: new evidence from a large randomized trial. *Arch Gen Psychiatry*. 2008; 65:578–584. [PubMed: 18458209]
32. Der G, Batty GD, Deary IJ. Effect of breast feeding on intelligence in children: prospective study, sibling pairs analysis, and meta-analysis. *BMJ*. 2006; 333:945. [PubMed: 17020911]
33. Zhou SJ, Baghurst P, Gibson RA, Makrides M. Home environment, not duration of breast-feeding, predicts intelligence quotient of children at four years. *Nutrition*. 2007; 23:236–241. [PubMed: 17320351]

Figure 1.
Effect of smoking on intellectual performance

Table 1

Birth and parental characteristics and the risk of poor intellectual performance in the offspring

Parental characteristics	Low IP			OR	Crude [95% CI]
	N	n	%		
Mother's age (yrs)					
0–19	4808	764	15.9	2.01	[1.85, 2.18]
20–24	39954	4493	11.2	1.36	[1.31, 1.42]
25–29	64647	5472	8.5	1.00	Reference
30–34	43773	3079	7.0	0.82	[0.78, 0.86]
35	19000	1337	7.0	0.82	[0.77, 0.87]
Maternal parity					
Primipara	72109	5853	8.1	1.00	Reference
Multipara	100073	9292	9.3	1.16	[1.13, 1.20]
Mother's height (cm)					
<155	2765	311	11.2	1.42	[1.25, 1.60]
155–164	50384	4789	9.5	1.18	[1.13, 1.23]
165–174	75706	6184	8.2	1.00	Reference
175	10865	777	7.2	0.87	[0.80, 0.94]
Missing	32462	3084	9.5		
Mother's BMI (kg/m ²)					
<18.5	9389	841	9.0	1.12	[1.04, 1.21]
18.5–24	100553	8093	8.0	1.00	Reference
25–29	15333	1646	10.7	1.38	[1.30, 1.45]
30	2525	349	13.8	1.83	[1.63, 2.05]
Missing	44382	4216	9.5		
Mother's education					
9-year compulsory	21494	3461	16.1	1.55	[1.48, 1.62]
Secondary school 1–2 years	68483	7536	11.0	1.00	Reference
Secondary school 3 years	20773	1569	7.6	0.66	[0.62, 0.70]
Higher education < 3 years	31033	1532	4.9	0.42	[0.40, 0.45]
Higher education 3 years	30040	1005	3.3	0.28	[0.26, 0.30]

Parental characteristics	Low IP			OR	Crude [95% CI]
	N	n	%		
Missing	359	42	11.7		
Maternal socioeconomic category					
Unskilled blue collar worker	46721	5980	12.8	3.23	[3.04, 3.43]
Skilled blue collar worker	19743	1853	9.4	2.27	[2.12, 2.44]
Low-level white collar worker	26202	1877	7.2	1.70	[1.58, 1.82]
Intermediate-level white collar worker	32943	1436	4.4	1.00	Reference
High-level white collar worker	11726	310	2.6	0.60	[0.53, 0.68]
Self-employed	4854	363	7.5	1.77	[1.56, 1.99]
Employed, uncategorized	9870	1022	10.4	2.53	[2.33, 2.76]
Missing	20123	2304	11.4		
Father's education					
9-year compulsory	35474	4902	13.8	1.29	[1.24, 1.34]
Secondary school 1–2 years	61091	6767	11.1	1.00	Reference
Secondary school 3 years	21767	1336	6.1	0.53	[0.50, 0.56]
Higher education < 3 years	23336	1057	4.5	0.38	[0.36, 0.41]
Higher education 3 years	28359	858	3.0	0.25	[0.23, 0.27]
Missing	2155	225	10.4		
Paternal socioeconomic category					
Unskilled blue collar worker	32745	4194	12.8	2.73	[2.57, 2.90]
Skilled blue collar worker	36569	4095	11.2	2.34	[2.20, 2.49]
Low-level white collar worker	14915	1115	7.5	1.50	[1.39, 1.63]
Intermediate-level white collar worker	29222	1490	5.1	1.00	Reference
High-level white collar worker	25676	852	3.3	0.64	[0.59, 0.70]
Self-employed	13162	1232	9.4	1.92	[1.78, 2.08]
Employed, uncategorized	8882	919	10.3	2.15	[1.97, 2.34]
Missing	11011	1248	11.3		
Family situation					
Parents living together	157657	13566	8.6	1.00	Reference
Parents not living together	8187	1014	12.4	1.48	[1.39, 1.59]
Missing	6338	565	8.9		

Parental characteristics	Low IP			
	N	n	%	OR Crude [95% CI]
Age at conscription				
<17.5	1516	150	9.9	1.21 [1.02, 1.43]
17.5 – 18.5	144098	11959	8.3	1.00 Reference
>18.5	26568	3036	11.4	1.42 [1.36, 1.48]
Birth characteristics				
Birthweight for gestational age (SDS)				
<-2	3770	449	11.9	1.40 [1.27, 1.55]
-2 to 2	162704	14198	8.7	1.00 Reference
>2	4213	354	8.4	0.96 [0.86, 1.08]
Missing	1495	144	9.6	
Head circumference for gestational age (SDS)				
<-2	6717	749	11.2	1.32 [1.22, 1.42]
-2 to 2	157871	13751	8.7	1.00 Reference
>2	4186	300	7.2	0.81 [0.72, 0.91]
Missing	3408	345	10.1	
Gestational age (weeks)				
28–31	495	71	14.3	1.74 [1.36, 2.24]
32–36	6262	591	9.4	1.08 [0.99, 1.18]
37–41	142571	12477	8.8	1.00 Reference
41	22218	1922	8.7	0.99 [0.94, 1.04]
Missing	636	84	13.2	

Men born 1983–1988 and conscripted for military service 2000–2006. IP indicates intellectual performance. Low IP was defined as an IP test score at conscription of 2. All analyses accounted for the clustered data structure.

Table 2

Maternal smoking and the risk of poor intellectual performance in the offspring

Mother's smoking (no. of cigarettes per day)	N	Low IP %	OR [95% CI]			
			Crude	Adj. for parental Characteristics ^a	Adj. for birth Characteristics ^b	Fully adjusted ^c
0	115159	7.4	Reference	Reference	Reference	Reference
1–9	28568	12	1.70 [1.63, 1.78]	1.27 [1.19, 1.34]	1.69 [1.62, 1.76]	1.25 [1.18, 1.33]
10 or more	17321	13.2	1.91 [1.81, 2.00]	1.22 [1.14, 1.31]	1.88 [1.79, 1.98]	1.21 [1.12, 1.30]
Missing	11134	8.8				

Men born 1983–1988 and conscripted for military service 2000–2006. IP indicates intellectual performance. Low IP was defined as an IP test score at conscription of 2. All analyses accounted for the clustered data structure.

^a Adjusted for maternal age, height and BMI, maternal and paternal education and socioeconomic category, family situation, birth order and age at conscription.

^b Adjusted for birthweight and head circumference for gestational age.

^c Adjusted for significant birth- and parental characteristics listed above.

Table 3
Maternal smoking in first and second pregnancy and the risk of poor intellectual performance in the sons

Maternal smoking		First Son			Second Son		
First pregnancy	Second pregnancy	N	Low IP %	OR [95% CI]	Low IP%	Crude	Adjusted ^a
no	no	9346	5.2	1.00	Reference	1.00	Reference
no	yes	356	6.2	1.21 [0.78, 1.87]	9.3 [0.56, 1.55]	1.24 [0.86, 1.78]	0.91 [0.60, 1.39]
yes	no	813	8.1	1.62 [1.24, 2.11]	1.40 [1.03, 1.91]	1.64 [1.31, 2.06]	1.39 [1.08, 1.79]
yes	yes	2482	9.2	1.85 [1.57, 2.18]	1.25 [1.02, 1.53]	1.89 [1.65, 2.17]	1.24 [1.05, 1.46]
missing	missing	1725	5.9		8.4		

Brothers born 1983 – 1988. IP indicates intellectual performance. Low IP was defined as an IP test score of 2.

^a Adjusted for parental education level and socioeconomic status, birth order (first son only) and age at conscription.