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Maternal Pre-pregnancy Overweight and Child Cognition and Behavior: Exploring Intrauterine Effects in Two Pregnancy Cohorts

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Abstract

Objective—Maternal greater pre-pregnancy adiposity has been associated with behavioral problems, such as ADHD, and lower intellectual function in offspring. However, few human studies have explored this and it is unclear if intrauterine mechanisms or confounding factors drive these associations.

Patients and Methods—Parental BMI and offspring verbal skills, non-verbal skills and behavioral problems were assessed in the British ALSPAC (N~5000) and Dutch Generation R (N~ 2500) cohorts. We aimed to determine the plausibility of intrauterine effects by (i) adjusting for multiple confounders, (ii) comparing associations between maternal and paternal BMI with offspring cognition/ behaviors, and (iii) searching for cross-cohort consistency.

Results—Maternal pre-pregnancy overweight was associated with reduced child verbal skills (unadjusted). However, after adjusting for confounders, this was not consistently observed in both cohorts. Maternal overweight was also associated with child total behavior problems and externalising problems, even after adjusting for confounders. However, this was observed in Generation R only and was not replicated in ALSPAC. No associations of maternal overweight with child attention problems, emotional/internalising problems, or non-verbal skills were observed in either cohort. Paternal overweight was not associated with any of the child outcomes, but was also less strongly related to potential confounding factors than was maternal overweight.

Conclusions—Overall, we find little consistent evidence of intrauterine effects of maternal pre-pregnancy overweight on child cognition and behavior. Some associations initially observed were not consistently replicated across cohorts or robust to adjustment for confounding factors and are thus likely to reflect confounding by socioeconomic or postnatal factors.

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Conflicts of interest: Dr. Verhulst is director at the Department of Child and Adolescent Psychiatry, Erasmus University Medical Center-Sophia Children's Hospital, which publishes the Dutch translations of the Achenbach System of Empirically Based Assessment and from which he receives remuneration.

Keywords

ALSPAC; behavioral problems; cognitive function; cohort; Generation R; intrauterine exposure; obesity; pregnancy

INTRODUCTION

There is some evidence from human and animal studies that maternal overweight and obesity pre-pregnancy is associated with reduced offspring cognitive abilities and greater risk of behavioral problems. A recent study of around 12,000 children from 3 Nordic cohorts reported an association between maternal pre-pregnancy overweight or obesity and core symptoms of attention deficit hyperactivity disorder (ADHD) in school-age children ¹. This was replicated and extended in a follow-up study of around 1700 five year-old Finnish children which reported associations with child attention and emotional problems ². For cognitive development, in two Finnish cohorts initiated in 1966 and 1986, studied concurrently, maternal pre-pregnancy obesity was associated with increased risk of mild intellectual disability in offspring. However, this was only found in the latter more contemporary cohort ³, suggesting that an association may be only apparent in more contemporary cohorts who are experiencing the obesity epidemic. There is also evidence from animal studies that maternal diet-induced obesity pre-pregnancy results in alterations in offspring brain development ⁴.

Few replication studies exist exploring these reported associations of maternal pre-pregnancy overweight with child cognitive function and behavioral problems. Furthermore, it is not clear if associations involve intrauterine mechanisms or reflect confounding by familial socioeconomic position or other postnatal risk factors. The aim of this study was to investigate maternal pre-pregnancy overweight and offspring cognition and behavior in two pregnancy cohorts; The Avon Longitudinal Study of Parents and Children (ALSPAC), based in Britain, and the Generation R Cohort, based in the Netherlands. We aimed to determine the plausibility of intrauterine effects by adjustment for multiple indicators of socioeconomic position, by comparing associations between maternal and paternal BMI with offspring cognition and behaviors and by searching for cross-cohort consistency. The rationale for comparing maternal to paternal associations is based on the assumption that maternal exposures in pregnancy directly affecting fetal development will produce a considerably stronger association than paternal exposures at the same time, which would not generally be expected to affect fetal development.⁵ Associations driven by shared familial, social, genetic and environmental factors will be likely to produce similar maternal-paternal associations. This approach is validated by markedly discordant associations of maternal and paternal smoking in pregnancy with offspring birth weight, which is known to be directly affected by maternal smoking in pregnancy (5).

METHODS

Participants

ALSPAC—ALSPAC is a geographically-based prospective cohort study investigating the health and development of children ⁶. Pregnant women residing in three health districts in the South West of England with an expected date of delivery between 1st April 1991 and 31st December 1992 were eligible to enrol. 14,541 pregnant women were recruited and 13,678 had a live-born, singleton child. For this study we excluded parents and children of multiple births. Data on both maternal and paternal BMI is available in 7641 mother-partner pairs. Data on nonverbal skills at 8 years are available in 6353 children, verbal skills was assessed in 9731 (sentence length) and 9901 (word production) children at 38 months, and

behavioral problems in 9314 children at 47 months. Analyses of nonverbal skills, sentence length, word production and behavioral problems were carried out on 3221, 4658, 4712 and 4873 children, respectively, with complete data on both maternal and paternal BMI, all confounders and child outcomes. Ethical approval of the study was obtained from the ALSPAC Law and Ethics Committee (IRB00003312) and three Local Research Ethics Committees.

Generation R—The Generation R Study is a population-based pregnancy cohort ^{7,8}. Pregnant women resident in the city of Rotterdam, the Netherlands, with delivery dates April 2002 to January 2006, were approached by their midwives to participate. The parents of a total of 7295 children gave consent for the postnatal period. Data on maternal and paternal BMI are available in 4142 mother-partner pairs. Nonverbal skills at 30 months is available 4339 children, verbal skills (word production, sentence length) at 30 months in 4674 children, and behavioral problems at 36 months in 3922 children. Analyses of nonverbal skills, sentence length, word production and behavioral problems were carried out on 2258, 2398, 2385 and 2046 children, respectively, with complete data on both maternal and paternal BMI, all confounders and child outcomes. The cohort study protocol was approved by the Medical Ethical Review Board of the Erasmus Medical Center, Rotterdam. All parents of participating children gave written informed consent.

Maternal and Paternal Overweight

ALSPAC—At initial enrolment, mothers provided their height and pre-pregnancy weight, from which pre-pregnancy BMI was calculated (kg/m^2). Paternal BMI was derived from self-reported height and weight from a questionnaire sent to partners at 12 weeks gestation. Maternal weight was also measured at the first antenatal clinic visit (median gestational age: 10 completed weeks (IQR 8, 14)). Since measured gestational weight and self-reported pre-pregnancy weight were highly correlated ($r=0.97$ $p<0.0001$), self-reported pre-pregnancy weight was used due to the higher numbers available. Maternal and paternal BMI were grouped according to the World Health Organization categories for underweight (<18.50), normal ($18.50 - 24.99$), overweight (≥ 25.00) and obese (≥ 30.00). These were used to generate two binary variables: overweight/obese vs normal BMI, and obese vs normal BMI.

Generation R—Maternal pre-pregnancy weight, analysed in this study, was obtained by questionnaire at enrolment. In addition, weight (kg) and height (cm) were measured at enrolment, in light clothing without shoes, and were used to calculate maternal BMI (kg/m^2). In this study sample, 47% and 71% of all women were enrolled before a gestational age of 14 and 18 weeks, respectively. Correlation of pre-pregnancy weight obtained by questionnaire and weight measured at enrolment was 0.96 ($P < 0.001$). Paternal BMI was derived from self-reported height and weight from a questionnaire sent to partners at 12 weeks gestation. Maternal and paternal BMI were grouped into overweight, obese and normal BMI categories as described above for ALSPAC.

Child Cognition and Behavior

ALSPAC—Vocabulary and word combination levels were assessed using questions adapted from the MacArthur Toddler Communication questionnaire ⁹. These were included in maternal questionnaires sent at 38 months postnatal. Vocabulary scores were based on 123 items and word combination scores were derived from a list of two- and three-word phrases. Nonverbal skills were assessed using the faces subtest of the Diagnostic Analysis of Nonverbal Accuracy test (DANVA) ¹⁰ administered at the 8-year clinic, based on recognition of emotion. Child behavioral problems were assessed at 4 years by maternal report using the Strengths and Difficulties Questionnaire (SDQ) ¹¹. The SDQ comprises 25 questions which generate scores for Inattention-Hyperactivity, Emotional Symptoms, Peer

Problems, Conduct Problems and Prosocial Behavior, as well as a Total Behavioral Problems. Scores analysed and used for comparison with Generation R's CBCL (Child Behavior Checklist) measures, are based on those previously compared by Goodman ¹² [i.e. Total Behavioral Problems scores (both), SDQ Inattention-Hyperactivity and CBCL Attention Problems; SDQ Emotional Symptoms and CBCL Internalising Problems; SDQ Conduct Problems and CBCL Externalising Problems]. Psychologist-assessed general intelligence was also explored based on a short form (using alternate items) of the Wechsler Intelligence Scale for Children (WISC-III UK ¹³) at 8 years. Teacher-rated behavioral problems at 8 years were also assessed using the SDQ.

Generation R—Verbal skills at 30 months was assessed using parent report on a Dutch translation of the Language Development Survey (LDS; ¹⁴). The LDS contains a 310-word vocabulary checklist and also asks the parent to write down five of their child's best sentences. Nonverbal skills were assessed using the Dutch version of the Parent Report of Children's Abilities (PARCA; ¹⁵) at 30 months. The PARCA comprises parent-administered subtests for: (a) matching-to-sample; (b) block building and (c) imitation, and parental-report of quantitative skills, spatial abilities, symbolic play, planning and organizing, adaptive behaviors, and memory. An overall PARCA score was derived from the sum of the parent-administered and parent-reported sections.

Maternal-reported child behavioral problems were assessed using the Child Behavior Checklist for toddlers (CBCL/1.5-5) ¹⁶ at 36 months. The CBCL contains 99 items, each 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 behavior during the preceding two months. These result in a total problems score, plus various subscales of behavior, of which attention, internalising problems and externalising problems are analysed in this study.

Confounders and Mediators

ALSPAC—In a questionnaire sent at 32-weeks gestation, mothers recorded their own and their partner's highest education level. Mothers also recorded their occupation and their partner's occupation, which were used to allocated them to social categories according to the 1991 Office and Populations Censuses and Surveys standard ¹⁷. A single variable (head of household) was derived from the highest social class of either parent. Family income per week was assessed at 47 months after delivery. Maternal smoking in each of the three trimesters is available from questionnaires sent at 18- and 32-weeks gestation. Smoking at any time during pregnancy was used in this study. Breastfeeding was assessed repeatedly during infancy and was categorised as 'never breastfed', 'partially breastfed' and 'exclusively breastfed', as reported at 2 months of age. Infant size was calculated by converting weight and height, from health visitor records (at median age 3.7 years), into age-specific weight-for-height z-scores.

Generation R—Postal questionnaires were used to obtain information on educational level and family income. Maternal smoking during pregnancy was assessed using three prenatal questionnaires. Maternal smoking in the present study was taken as smoking at any stage during pregnancy. Breastfeeding (yes/no) at 2 months of age was assessed by postal questionnaire at 2 and 6 months of age. Infant size at 30 and 36 months was assessed using data from child health care centres and variables for weight-for-height z-scores were created.

Statistical Analysis

Confounder associations of maternal / paternal overweight / child outcomes with indicators of socioeconomic position were explored using logistic regression (parental overweight) and ordinal logistic regression (quintile for child outcomes), with dichotomised indicators of

socioeconomic position. Associations of maternal/paternal overweight with child verbal skills, non-verbal skills and behavioral problems were explored with child outcome scores divided into quintiles and analysed using ordinal logistic regression with the following statistical models: i) maternal/paternal overweight individual models unadjusted for confounders, ii) maternal/paternal overweight individual models adjusted for confounders, iii) maternal/paternal overweight mutually adjusted without confounders, iv) maternal/paternal overweight mutually adjusted and with confounder-adjustment. Where persisting associations are observed, a fifth model additionally adjusting for mediators (infant size, breastfeeding) is also carried out. Complete case analyses were carried out for all models, however, to address the missing data issues, multivariate multiple imputation was carried out (presented as supplementary data). All analyses were performed using STATA 10.

RESULTS

Sample characteristics for each cohort are displayed in Table 1. Associations of socioeconomic position with parental overweight / offspring outcomes are displayed in Tables 2 and 3. Lower maternal and paternal education, income and social class were associated with greater odds of maternal and paternal pre-pregnancy overweight / obesity. Maternal overweight was more strongly associated with socioeconomic factors than paternal overweight. Lower socioeconomic position was associated with reduced sentence length scores and total behavioral problems, but was not associated with non-verbal skills or word production scores.

In unadjusted models, maternal pre-pregnancy overweight was consistently (in both cohorts) associated with sentence formation (Table 4). However, after adjusting for confounders, there was little persisting evidence in Generation R, and in ALSPAC, although the association persisted it was substantially attenuated compared to the unadjusted association. The persisting ALSPAC association between maternal pre-pregnancy overweight and offspring sentence length was not altered by additional adjustment for infant size (OR=0.84, 95% CI: 0.72 to 0.98, $p=0.02$, adjusted for weight-for-height age-specific infant z-score, paternal overweight and confounders), but was partially accounted for by breastfeeding (OR=0.90, 95% CI: 0.79 to 1.03, $p=0.1$). There were no associations (unadjusted or adjusted) observed with nonverbal skills or word production in either cohort.

Maternal overweight was associated with increased child total behavioral problems in Generation R, both unadjusted and adjusted for confounders (Table 5). However, no such associations were observed in ALSPAC in either model. For the behavioral subscales in Generation R (attention, internalising, externalising), associations persisted with child externalising problems when adjusting for confounders, but with no strong evidence of associations with child attention or internalising problems. No associations were observed with the equivalent behavioral subscales in ALSPAC. The observed association in Generation R with child total behavioral problems was not substantially altered by additional adjustment for infant size (OR=1.21, 95% CI: 0.97 to 1.50, $p=0.09$). The confounder-adjusted association also persisted following additional adjustment for breastfeeding (OR=1.22, 95% CI: 0.97 to 1.50, $p=0.05$).

Maternal overweight/obesity was strongly associated with greater psychologist-assessed child general intelligence (IQ), even after adjusting for confounders (Table 6). For teacher-reported behavioral problems, results were not materially different to those based on maternal-report, although with slightly stronger effect sizes for unadjusted associations (Table 7). None of the associations were substantially altered following adjustment for child BMI (data not shown).

Paternal overweight was not associated with any of the child outcomes in most models. Maternal-paternal overweight associations with child outcomes were similar to one another, except for stronger maternal associations observed with child sentence length (ALSPAC), behavior problems (Generation R) and psychologist-administered IQ (ALSPAC). Additional adjustment of maternal overweight associations for paternal overweight did not materially alter observed associations.

Main analyses repeated using imputed datasets for missing data are provided as online supplementary data (Generation R N=5420; ALSPAC N=10,874). These results were very similar to those presented here using samples excluding participants with any missing data. Specifically, results for ALSPAC were essentially the same; with effect sizes in fully adjusted analyses in Generation R somewhat weaker than those presented here, meaning that they were more consistent with the overall null findings in ALSPAC.

DISCUSSION

Based on two European pregnancy cohorts - ALSPAC (UK) and Generation R (Netherlands) - we find little consistent evidence of intrauterine effects of maternal pre-pregnancy overweight on offspring cognitive development and behavioral problems. Of a wide range of measures explored – nonverbal skills, verbal skills, total behavioral problems, attention-hyperactivity problems, emotional-internalising problems and conduct-externalising problems – there were no associations with maternal overweight that, for both cohorts, persisted following adjustment for confounders.

In Generation R, maternal overweight was associated with greater child total behavioral problems and externalising behavior. However, statistical evidence for these associations was modest after adjusting for socioeconomic factors ($p=0.05$ for both), replication was not observed in ALSPAC, and these associations attenuated to the null in analyses using imputed datasets for missing data. Thus, it is unlikely that the observed associations are due to intrauterine mechanisms and are likely to reflect residual confounding by factors not completely controlled for by the variables included in the analysis. As mentioned in the introduction, maternal pre-pregnancy overweight has been found to be associated with child attention problems in three Nordic cohorts. However, this was not supported by the present study; No association was observed with child attention/hyperactivity problems in either ALSPAC or Generation R. Since the previous study was based on teacher-rated behavior and maternal-report was used in the present study, it is possible that maternal reporting bias may be diluting an association. Indeed, a recent study showed that robust associations with teacher-rated child behavior problems (inattention and emotionality) were weak/null when maternal-rated behavior was analysed². However, analyses repeated in ALSPAC using teacher-rated behavioral problems were not materially different to those based on maternal report. Thus, it is possible that the findings from the previous studies reflect residual confounding. This might occur, for example, if being overweight led to more adverse behavioral ratings by teachers. In the present study teacher-rated associations were not, however, substantially altered by adjustment for child BMI.

Strengths and Limitations

Key strengths of this study are the inclusion of two similar pregnancy cohorts, incorporating a means of cross-population replication and, additionally, exploring paternal pre-pregnancy overweight together with multiple indicators of socioeconomic position as measures of residual confounding. A limitation, as mentioned above, is the reliance on maternal report for the behavioral and cognitive measures, which may have resulted in maternal response bias. Whilst repeated analyses in ALSPAC using psychologist-administered and teacher-rated assessments suggest that this is unlikely for the behavioral outcomes, it is possible that

maternal response bias may have affected the analyses of infant verbal skills. Additionally, we aimed to compare the same measures across the cohorts; however, different instruments were applied in each cohort for the cognitive and behavioral measures. Despite this, the fact that consistent results were observed even when using different instruments is particularly reassuring. Furthermore, for the behavioral measures, the SDQ (implemented in ALSPAC) and the CBCL (implemented in Generation R) have been compared to one another previously¹². Equivalent validity has been observed between the two instruments with scores from the SDQ and CBCL being both highly correlated and equivalent at detecting inattention and hyperactivity, internalizing problems and externalizing problems¹².

Whilst the maternal-paternal comparisons were carried out to explore the likelihood of intrauterine mechanisms, in this particular context these comparisons and the additional adjustment for paternal overweight may not capture shared confounding factors as well as in previous analyses (e.g. maternal/paternal smoking)⁵. In this case, maternal overweight appears much more strongly associated with socioeconomic factors than paternal overweight. Hence some of the stronger maternal (versus paternal) associations are likely to reflect residual confounding rather than intrauterine effects.

Conclusion

Based on the findings of two European pregnancy cohorts, we find little consistent evidence for intrauterine effects of maternal pre-pregnancy overweight on child verbal skills, non-verbal skills and behavioral problems. Previously reported findings of associations with child ADHD and intellectual function are not supported by the present study. Although some associations were observed in this study with respect to child verbal skills, total behavioral problems and externalising problems, these were inconsistent between cohorts and generally did not persist in analyses using imputed data. Studies with designs that can further address the issue of confounding using alternative methods may be particularly useful. This could be carried out, for example, using genetic variants that are reliably associated with adiposity as instrumental variables for its causal intrauterine effect (i.e. Mendelian Randomisation studies)^{5,18,19}.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ADHD	attention deficit hyperactivity disorder
ALSPAC	Avon Longitudinal Study of Parents and Children
BMI	body mass index

CBCL	Child Behavior Checklist
CI	confidence interval
DANVA	Diagnostic Analysis of Nonverbal Accuracy test
IQR	interquartile range
LDS	Language Development Survey
OR	odds ratio
PARCA	Parent Report of Children's Abilities
SDQ	Strengths and Difficulties Questionnaire
WISC	Wechsler Intelligence Scale for Children

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Table 1

Sample Characteristics in ALSPAC and Generation R

Characteristic	Total N	Median	(IQR)
Child Characteristics			
<u>ALSPAC</u>			
Child Nonverbal score (DANVA) **	3221	4	3-6
Child Sentence Length (MacArthur)	4658	24	21-26
Child Word Production (MacArthur)	4712	241	229-246
Child Behavioral Problems (SDQ)			
Total	4873	8	5-11
Hyperactivity	4873	4	2-5
Emotional	4873	1	0-2
Conduct problems	4873	2	1-3
<u>Generation R</u>			
Child Nonverbal score (PARCA) *	3187	47.5	43.8-51.0
Child Sentence Length (LDS) *	2398	4.6	2.6-6.2
Child Word Production (LDS) *	2385	259	222-283
Child Behavioral Problems (CBCL) *			
Total Problems	2046	16	9-26
Attention Problems	2483	1	0-2
Internalising	2046	3	1-6
Externalising	2045	7	3-12
Parental Characteristics		Category	N
<u>ALSPAC</u>			
Maternal Overweight/Obesity	4886	Yes	1040
		No	3846
Paternal Overweight/Obesity	4886	Yes	2300
		No	2586
Maternal Education	4886	CSE/none	573
		Vocational	401
		O level	1746
		A level	1283
		Degree	883
Paternal Education	4886	CSE/none	796
		Vocational	373
		O level	1102
		A level	1451
		Degree	1164
Family Weekly Income (Net)	4886	<£100	204
		£100-199	576
		£200-299	1286

Characteristic	Total N		Median	(IQR)
		£300-399	1185	24.3
		>£400	1635	33.5
Family Social Class	4886	IV/V	174	3.6
		IIIM	453	9.3
		IIINM	1195	24.5
		II	2221	45.5
		I	843	17.3
Maternal Prenatal Smoking	4886	Yes	850	17.4
		No	4036	82.6
Breastfeeding	4792	Yes	689	14.4
		No	4103	85.6
<u>Generation R</u>				
Maternal Overweight/Obesity	3187	Yes	704	22.1
		No	2483	77.9
Paternal Overweight/Obesity	3187	Yes	1543	48.4
		No	1644	51.6
Maternal Education *	3187	Primary/none	128	4.0
		Secondary 1	287	9.0
		Secondary 2	856	26.9
		Higher 1	814	25.5
		Higher 2	1102	34.6
Paternal Education *	3187	Primary/none	176	5.5
		Secondary 1	374	11.7
		Secondary 2	789	24.8
		Higher 1	653	20.5
		Higher 2	1195	37.5
Family Monthly Income (Net)	3187	€00 or less	149	4.7
		€00-1400	230	7.2
		€1400-1800	211	6.6
		€1800-2200	349	10.9
		>€2200	2248	70.5
Maternal Prenatal Smoking (Any)	3187	Yes	704	22.1
		No	2483	77.9
Breastfeeding	2967	Yes	2054	69.2
		No	913	30.8

* Secondary 1: lower vocational; intermediate general school; 3 years general secondary school
 Secondary 2: >3 yrs general secondary school; intermediate vocational; 1st year higher vocational
 Higher 1: higher vocational; Bachelors degree
 Higher 2: Higher academic education; PhD

Table 2

Associations of indicators of socioeconomic position with maternal and paternal pre-pregnancy overweight

	Maternal overweight/obesity			Paternal overweight/obesity		
	OR	95% CI	P	OR	95% CI	P
ALSPAC						
Maternal Education nondegree (vs degree)	1.98	1.61, 2.44	<0.001	1.41	1.21, 1.63	<0.001
Paternal Education nondegree (vs degree)	1.77	1.48, 2.12	<0.001	1.43	1.26, 1.64	<0.001
Income lowest quartile (vs higher)	1.47	1.23, 1.75	<0.001	0.92	0.79, 1.08	0.3
Social Class manual (vs nonmanual)	1.74	1.45, 2.10	<0.001	1.12	0.95, 1.33	0.2
Maternal smoking Yes (vs no)	1.22	1.02, 1.45	0.03	0.93	0.80, 1.08	0.4
Breastfeeding Yes (vs no)	0.65	0.54, 0.78	<0.001	0.73	0.63, 0.86	<0.001
Generation R						
Maternal Education nondegree (vs degree)	1.87	1.55, 2.26	<0.001	1.21	1.05, 1.40	0.01
Paternal Education nondegree (vs degree)	1.81	1.50, 2.17	<0.001	1.31	1.13, 1.51	<0.001
Income lower quartile (vs higher)	1.64	1.33, 2.04	<0.001	0.96	0.79, 1.16	0.7
Maternal smoking Yes (vs no)	1.22	1.00, 1.49	0.04	1.03	0.87, 1.22	0.7
Breastfeeding Yes (vs no)	0.58	0.49, 0.70	<0.001	0.82	0.70, 0.96	0.01

ALSPAC N = 4886 with data on parental size and all indicators socioeconomic position

Gen R N=3187 with data on parental size and all indicators of socioeconomic position

Table 3

Associations of indicators of socioeconomic position with child cognition and behavior

	Ordinal odds ratio for being in a higher quintile											
	Non-verbal Skills			Sentence Length			Word Production			Behavioral Problems		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
ALSPAC												
Maternal Education nondegree (vs degree)	1.08	0.93, 1.25	0.3	0.51	0.44, 0.58	<0.001	0.90	0.79, 1.03	0.1	1.50	1.31, 1.71	<0.001
Paternal Education nondegree (vs degree)	1.11	0.97, 1.28	0.1	0.52	0.46, 0.59	<0.001	0.85	0.76, 0.96	0.007	1.46	1.30, 1.64	<0.001
Income lowest quartile (vs rest)	1.03	0.86, 1.24	0.7	0.65	0.57, 0.75	<0.001	0.94	0.81, 1.08	0.4	1.88	1.64, 2.16	<0.001
Social Class manual (vs nonmanual)	1.21	0.99, 1.47	0.06	0.51	0.43, 0.59	<0.001	0.92	0.78, 1.07	0.3	1.59	1.37, 1.84	<0.001
Maternal smoking yes (vs no)	0.96	0.81, 1.15	0.7	0.84	0.73, 0.96	0.01	0.88	0.77, 1.01	0.07	1.61	1.41, 1.84	<0.001
Breastfeeding yes (vs no)	0.81	0.67, 0.97	0.02	1.70	1.47, 1.97	<0.001	1.25	1.08, 1.45	0.003	0.72	0.62, 0.83	<0.001
Generation R												
Maternal Education nondegree (vs degree)	1.07	0.92, 1.24	0.4	0.67	0.57, 0.77	<0.001	0.91	0.79, 1.05	0.2	1.29	1.10, 1.51	0.001
Paternal Education nondegree (vs degree)	1.04	0.90, 1.21	0.6	0.73	0.64, 0.85	<0.001	0.83	0.72, 0.96	0.01	1.29	1.10, 1.51	0.001
Income lowest quartile (vs rest)	1.12	0.90, 1.41	0.3	0.43	0.35, 0.54	<0.001	0.65	0.51, 0.82	<0.001	2.05	1.60, 2.62	<0.001
Maternal smoking Yes (vs no)	1.09	0.90, 1.31	0.4	0.74	0.62, 0.88	0.001	0.90	0.75, 1.08	0.3	1.33	1.10, 1.61	0.003
Breastfeeding Yes (vs no)	1.11	0.94, 1.32	0.2	1.44	1.23, 1.69	<0.001	1.32	1.12, 1.55	0.001	0.81	0.68, 0.96	0.02

ALSPAC N= 3221 (Nonverbal), 4658 (Sentence Length), 4712 (Word Production), 4873 (Behavioral Problems)

Generation R N=2258 (Nonverbal), 2398 (Sentence Length), 2385 (Word Production), 2046 (Behavioral Problems)

Table 4

Associations of parental pre-pregnancy overweight and ordinal odds ratios for offspring cognition

Ordinal odds ratio for being in a higher quintile												
Parental	Individual Maternal-Paternal Models						Mutually Adjusted Maternal-Paternal Models					
	Model I *			Model II **			Model I *			Model II **		
Overweight	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Nonverbal Skills												
ALSPAC												
Maternal overweight	0.99	0.85, 1.16	0.9	0.97	0.83, 1.14	0.7	1.00	0.85, 1.16	0.97	0.98	0.84, 1.14	0.8
Paternal overweight	0.98	0.87, 1.11	0.7	0.96	0.85, 1.09	0.6	0.98	0.87, 1.11	0.7	0.97	0.85, 1.09	0.6
Generation R												
Maternal overweight	1.08	0.91, 1.30	0.4	1.08	0.90, 1.30	0.4	1.08	0.90, 1.30	0.4	1.08	0.90, 1.30	0.4
Paternal overweight	1.02	0.88, 1.18	0.8	1.02	0.88, 1.18	0.8	1.01	0.87, 1.17	0.9	1.01	0.87, 1.17	0.9
Language – Sentence Length												
ALSPAC												
Maternal overweight	0.77	0.68, 0.87	<0.001	0.88	0.78, 1.00	0.06	0.76	0.67, 0.87	<0.001	0.88	0.77, 1.00	0.05
Paternal overweight	0.99	0.89, 1.09	0.8	1.04	0.94, 1.16	0.4	1.01	0.91, 1.12	0.9	1.05	0.95, 1.17	0.3
Generation R												
Maternal overweight	0.79	0.67, 0.94	0.007	0.88	0.74, 1.05	0.2	0.81	0.68, 0.96	0.02	0.90	0.75, 1.07	0.2
Paternal overweight	0.85	0.74, 0.98	0.02	0.88	0.76, 1.02	0.09	0.87	0.75, 1.00	0.05	0.90	0.77, 1.03	0.1
Language – Word Production												
ALSPAC												
Maternal overweight	0.91	0.81, 1.04	0.2	0.95	0.84, 1.08	0.5	0.91	0.80, 1.03	0.1	0.94	0.83, 1.07	0.4
Paternal overweight	1.07	0.97, 1.19	0.2	1.09	0.98, 1.21	0.1	1.08	0.98, 1.20	0.1	1.09	0.99, 1.21	0.09
Generation R												
Maternal overweight	0.87	0.73, 1.03	0.1	0.91	0.76, 1.08	0.3	0.87	0.73, 1.04	0.1	0.91	0.76, 1.09	0.3
Paternal overweight	0.97	0.84, 1.12	0.7	0.99	0.85, 1.14	0.9	0.99	0.85, 1.14	0.8	1.00	0.86, 1.15	0.97

Maternal/Paternal overweight or obese versus normal BMI

* Model I: Unadjusted

** Model II: Adjusted for maternal education, paternal education, family income, social class (ALSPAC only), maternal smoking
 Gen R: PARCA at 30m (N=2258), LDS at 30m (sentence length N=2398; Word Production N=2385)
 ALSPAC: Danva at 8 years (N=3221), MacArthur at 38m (Sentence Length N=4658; Word Production N=4712)

Table 5

Associations of parental pre-pregnancy overweight and ordinal odds ratios for offspring behavioral problems

Parental Overweight	Ordinal odds ratio for being in a higher quintile											
	Individual Maternal-Paternal Models						Mutually Adjusted Maternal-Paternal Models					
	Model I *			Model II **			Model I *			Model II **		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Total Behavioral Problems, Quintiles												
ALSPAC												
Maternal overweight	1.11	0.98, 1.25	0.1	1.01	0.89, 1.14	0.9	1.11	0.99, 1.26	0.08	1.01	0.90, 1.15	0.8
Paternal overweight	0.96	0.87, 1.07	0.5	0.94	0.85, 1.04	0.3	0.96	0.86, 1.06	0.4	0.94	0.85, 1.04	0.3
Generation R												
Maternal overweight	1.29	1.07, 1.56	0.008	1.21	1.00, 1.47	0.05	1.29	1.07, 1.57	0.008	1.21	1.00, 1.47	0.05
Paternal overweight	1.01	0.86, 1.17	0.9	1.01	0.86, 1.18	0.9	0.98	0.84, 1.14	0.8	0.99	0.85, 1.16	0.9
Attention/Hyperactivity Problems, Quintiles												
ALSPAC												
Maternal overweight	1.04	0.92, 1.18	0.5	0.92	0.82, 1.05	0.2	1.04	0.92, 1.17	0.6	0.93	0.82, 1.05	0.2
Paternal overweight	1.02	0.92, 1.13	0.7	0.98	0.88, 1.08	0.6	1.02	0.92, 1.13	0.7	0.98	0.89, 1.09	0.7
Generation R												
Maternal overweight	1.14	0.96, 1.35	0.1	1.04	0.88, 1.25	0.6	1.15	0.97, 1.37	0.1	1.06	0.89, 1.27	0.5
Paternal overweight	0.95	0.82, 1.10	0.5	0.92	0.80, 1.06	0.3	0.94	0.81, 1.08	0.4	0.92	0.79, 1.06	0.2
Emotional / Internalising Problems, Quintiles												
ALSPAC												
Maternal overweight	1.00	0.89, 1.13	0.96	0.99	0.88, 1.12	0.9	1.01	0.90, 1.15	0.8	1.00	0.88, 1.13	0.99
Paternal overweight	0.93	0.84, 1.03	0.2	0.93	0.84, 1.03	0.2	0.93	0.84, 1.03	0.1	0.93	0.84, 1.03	0.2
Generation R												
Maternal overweight	1.15	0.96, 1.39	0.1	1.12	0.92, 1.35	0.3	1.16	0.96, 1.41	0.1	1.12	0.93, 1.36	0.2
Paternal overweight	0.97	0.83, 1.13	0.7	0.98	0.84, 1.14	0.8	0.95	0.81, 1.11	0.5	0.97	0.83, 1.13	0.7
Conduct / Externalising Problems, Quintiles												
ALSPAC												
Maternal overweight	1.04	0.92, 1.18	0.5	1.00	0.88, 1.13	0.9	1.05	0.93, 1.19	0.5	1.00	0.88, 1.13	0.98
Paternal overweight	0.97	0.88, 1.07	0.5	0.97	0.88, 1.07	0.6	0.96	0.87, 1.07	0.5	0.97	0.88, 1.08	0.6
Generation R												
Maternal overweight	1.24	1.02, 1.50	0.03	1.21	1.00, 1.46	0.06	1.24	1.03, 1.51	0.02	1.21	1.00, 1.47	0.05
Paternal overweight	0.99	0.85, 1.15	0.9	0.99	0.85, 1.15	0.9	0.97	0.83, 1.13	0.7	0.97	0.83, 1.13	0.7

Maternal/Paternal overweight or obese versus normal BMI

* Model I: Unadjusted

** Model II: Adjusted for maternal education, paternal education, family income, social class (ALSPAC only) maternal smoking
Gen R: CBCL total problems at 36m, internalising, externalising (N=2046); attention (N=2483)

ALSPAC: SDQ total problems at 47m, emotional, conduct and attention problems (N=4873)

Table 6

Psychologist-administered child IQ at 8 years and maternal pre-pregnancy overweight in ALSPAC

Ordinal odds ratio of higher child IQ quintile						
Parental Overweight / obesity	Mutually-Adjusted Maternal-Paternal Models					
	Unadjusted *			Confounder-Adjusted**		
	OR	95% CI	P	OR	95% CI	P
Maternal overweight/obese [¶]	0.68	0.59, 0.79	<0.001	0.84	0.73, 0.98	0.03
Paternal overweight/obese [¶]	0.87	0.77, 0.98	0.02	0.96	0.85, 1.08	0.5

[¶]Versus normal BMI; N=3480

* unadjusted for confounders

** adjusted for maternal and paternal education, family income, social class, maternal smoking. Maternal and paternal obesity mutually adjusted for one another in all models.

Table 7

Teacher-rated behavioral problems at 8 years and maternal pre-pregnancy overweight in ALSPAC

Ordinal odds ratio for being in a higher quintile												
Parental Overweight	Individual Maternal-Paternal Models						Mutually Adjusted Maternal-Paternal Models					
	Model I *			Model II**			Model I *			Model II**		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Total Behavioral Problems, Quintiles												
Maternal overweight	1.19	1.00, 1.42	0.05	1.19	1.00, 1.42	0.05	1.18	0.98, 1.41	0.07	1.10	0.92, 1.32	0.3
Paternal overweight	1.14	0.99, 1.32	0.07	1.14	0.99, 1.32	0.08	1.13	0.98, 1.30	0.1	1.13	0.98, 1.31	0.09
Attention Problems, Quintiles												
Maternal overweight	1.18	0.99, 1.41	0.07	1.07	0.89, 1.28	0.5	1.16	0.97, 1.39	0.1	1.06	0.89, 1.27	0.5
Paternal overweight	1.15	0.99, 1.33	0.06	1.12	0.97, 1.30	0.1	1.14	0.98, 1.32	0.08	1.12	0.96, 1.30	0.1
Emotional Problems, Quintiles												
Maternal overweight	1.16	0.97, 1.40	0.1	1.13	0.94, 1.36	0.2	1.15	0.95, 1.38	0.1	1.12	0.92, 1.35	0.3
Paternal overweight	1.13	0.97, 1.31	0.1	1.14	0.98, 1.33	0.09	1.12	0.96, 1.30	0.2	1.13	0.97, 1.32	0.1
Conduct Problems, Quintiles												
Maternal overweight	1.03	0.83, 1.29	0.8	0.95	0.76, 1.19	0.7	1.03	0.83, 1.28	0.8	0.95	0.76, 1.19	0.7
Paternal overweight	1.04	0.87, 1.24	0.7	1.01	0.84, 1.21	0.9	1.03	0.86, 1.24	0.7	1.01	0.84, 1.22	0.9

N=2325 (total problems), 2349 (attention), 2358 (emotional problems), 2355 (conduct)