

# Widespread covariation of early environmental exposures and trait-associated polygenic variation

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Although gene–environment correlation is recognized and investigated by family studies and recently by SNP-heritability studies, the possibility that genetic effects on traits capture environmental risk factors or protective factors has been neglected by polygenic prediction models. We investigated covariation between trait-associated polygenic variation and parental behavior and characteristics relevant to children's developmental outcomes—independently of population stratification. For instance, offspring genetic risk for schizophrenia was associated with paternal age ( $R^2 = 0.002$ ;  $P = 1e-04$ ), and offspring education-associated variation was associated with variance in breastfeeding ( $R^2 = 0.021$ ;  $P = 7e-30$ ), maternal smoking during pregnancy ( $R^2 = 0.008$ ;  $P = 5e-13$ ), parental smacking ( $R^2 = 0.01$ ;  $P = 4e-15$ ), household income ( $R^2 = 0.032$ ;  $P = 1e-22$ ), watching television ( $R^2 = 0.034$ ;  $P = 5e-47$ ), and maternal education ( $R^2 = 0.065$ ;  $P = 3e-96$ ). Education-associated polygenic variation also captured covariation between environmental exposures and children's inattention/hyperactivity, conduct problems, and educational achievement. The finding that genetic variation identified by trait GWASs partially captures environmental risk factors or protective factors has direct implications for risk prediction models and the interpretation of GWAS findings.

environmental risk | polygenic scores | gene–environment correlation | human complex traits | prediction

Environmental exposures are among the best early predictors of developmental outcomes. For instance, maternal smoking during pregnancy, socioeconomic deprivation, and time spent watching television and playing video games are associated with lower academic achievement (1–9). Harsh parental physical discipline such as hitting has been linked to increased emotional and behavioral problems including aggression in adolescence (10–14). Paternal age is a risk factor for a range of disorders and subclinical phenotypes including low academic achievement (15), with the link to autism spectrum disorders and schizophrenia most robustly replicated (16–21). Breastfeeding and higher parental socioeconomic status (education, income, occupation) are protective factors for a range of outcomes including educational achievement (7, 8, 22).

Evidence from many family, twin, and adoption studies converges in showing that individuals' exposure to environments partially depends on their genotype (i.e., genotype–environment correlation). This includes both parenting characteristics and broad socioeconomic variables; all are partially heritable (23–28). In the past decade, quantitative genetic research of this type has been extended to explore genetic and environmental contributions to

correlations between environmental factors and children's outcomes (29–32). Some new designs such as the children-of-twins designs make it possible to tease apart different types of genotype–environment correlation and identify environmental influences free of genetic confounds (33–37). These designs are limited by the extent to which environmental variables differ between close relatives.

Converging evidence for gene–environment correlation comes more recently from “single nucleotide polymorphism (SNP)-heritability” studies that estimate overall genetic influences from genome-wide DNA differences in unrelated individuals. These studies have shown that variation in individuals' social deprivation, household income, stressful life events, and family socioeconomic status partially reflects individuals' differences across genome-wide common genetic variants measured on SNP arrays (38–44). There have also been a few reports of extending SNP heritability analysis to estimate genetic correlations between environmental measures and measures of children's developmental outcomes (38–40).

Gene–environment correlation is recognized and investigated by family studies and recently by SNP-heritability studies. However, the possibility that genetic effects on traits capture environmental risk factors or protective factors has been neglected by polygenic prediction models, which use trait-associated genetic

## Significance

Environmental exposures are among the best predictors of health and educational outcomes. Models that estimate the effect of environmental exposures on developmental outcomes typically ignore genetic factors or focus on gene–environment interaction (whether individuals' response to environmental exposures depends on their genotype). Here we test gene–environment correlation (whether individuals' exposure to environments depends on their genotype). Using a method that tests specific genetic effects while controlling for background genetic effects, we estimate covariation between children's genetic liability/propensity for core developmental outcomes and a wide range of environmental exposures. Findings suggest that genetic variants associated with traits, such as educational attainment, body mass index, and schizophrenia, also capture environmental risk and protective factors.

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variants identified by genome-wide association studies (GWASs) to estimate individual-level genetic trait propensities for trait prediction.

Here we tested whether genetic variation identified by trait GWASs captures variation in environmental risk factors or protective factors. Specifically, as children's environments and genetic propensities are both "provided by" their parents, these are expected to correlate because parents pass on genetic variants to their offspring that influence parents' environment-providing behaviors. Therefore, we examine to what extent offspring trait-associated alleles covary with parental traits and behaviors previously reported to be environmental risk or protective factors for important child outcomes. We also tested to what extent offspring genetic trait propensities contribute to the correlation between parenting characteristics and children's developmental outcomes.

First, we conducted a systematic investigation of covariation between children's genetic propensities for specific developmental outcomes and a wide range of environmental exposures previously shown to be risk or protective factors for these outcomes (*SI Appendix, Methods S3*). We focus on genetic propensities—that is, individual-specific genomic profiles of trait-associated alleles—for three core developmental outcomes: educational attainment (45), body mass index (BMI) (46), and schizophrenia (47). These traits from three important domains of child development—social-cognitive, mental health, and physical health—each are robust predictors of mortality and life expectancy, with substantial associated societal and personal burden (48–55). They were chosen because of the availability of statistically powerful GWAS summary statistics for these traits (56).

Second, we tested whether the environmental exposures predicted children's developmental outcomes (as would be expected based on previous literature) and to what extent these associations are captured by children's polygenic propensities for education, BMI, and schizophrenia. For this, we examined associations between the environmental exposures and three developmental outcomes assessed at age 16 in our sample: educational achievement, inattention-hyperactivity symptoms, and conduct problems (*SI Appendix, Methods S3*).

We used a sample of 6,710 unrelated individuals, drawn from the Twins Early Development Study (TEDS), for whom genotype data and a wide range of specific environmental exposure measures and developmental outcomes from birth to adolescence are available. TEDS is a multivariate longitudinal study that recruited over 11,000 twin pairs born in England and Wales in 1994, 1995, and 1996 (57, 58), shown to be representative of the UK population (38, 59).

We created genome-wide polygenic scores for trait-associated genetic variants for each individual in the sample using summary statistics from the independent GWAS of years of education (EDU) (45), BMI (46), and schizophrenia (SCZ) (47). We used a Bayesian approach (60) that estimates posterior mean effect size of each marker by using a point-normal mixture prior on effect sizes and linkage disequilibrium (LD) information (*Materials and Methods*).

Because of the salience of possible population stratification when investigating the genetic effect on differences in environmental exposures, we estimated the effect of the polygenic scores while controlling for overall genetic relatedness in the form of a genomic relatedness matrix restricted maximum likelihood model. Specifically, we fit the effects of all SNPs as random effects, while estimating the fixed effects of the polygenic scores (*Materials and Methods*).

## Results

To estimate the univariate effect of each polygenic score on the environmental exposures, we fit a series of single-score models, which reveal significant trait-associated polygenic effects across a wide range of environmental exposures. Fig. 1, *Left* (and *SI Appendix, Table S1*) shows the estimated variance explained by each polygenic score for each of the environmental measures.

Environmental factors varied significantly as a function of trait-associated polygenic variation, independently of population stratification. This provides evidence for trait-associated genotype–environment correlation. However, given the robust evidence for extensive pleiotropy across complex traits (61), we aimed to isolate the effects of each trait-associated polygenic score using a multi-score model. To test the trait specificity of the polygenic effects on environmental exposures, we jointly modeled the three scores for years of education, BMI, and schizophrenia, allowing us to estimate the effects of each polygenic score while statistically adjusting for the effects of the others. Fig. 1, *Right* (and *SI Appendix, Table S2*) shows that the multiscore models revealed some attenuation of the polygenic score effects compared with the single-score models, suggesting that the effects of the three scores on environmental exposures are nonindependent. Specifically, the effects of BMI-associated polygenic variation on several environmental measures (including watching television and parental education) were no longer significant.

Breastfeeding duration was positively associated with offspring education polygenic score, adjusted for BMI and schizophrenia polygenic scores ( $R^2 = 0.021$ ,  $\beta = 0.144$ ;  $P = 7\text{e-}30$ ). Fig. 2*A* displays children's adjusted education polygenic score as a function of whether and for how long they were breastfed. Children who were breastfed had, on average, an education polygenic score approximately one third SD higher (Hedges'  $g = 0.30$ ) than children who were not breastfed ( $t = -11.55$ ,  $df = 5,664.2$ ,  $P = 1.6\text{e-}30$ ).

Maternal smoking during pregnancy was negatively associated with offspring education polygenic score adjusted for BMI and schizophrenia polygenic scores ( $R^2 = 0.008$ ,  $\beta = -0.090$ ;  $P = 5\text{e-}13$ ; Fig. 2*B*). Children exposed to maternal smoking prenatally had, on average, an education polygenic score approximately one quarter SD lower (Hedges'  $g = 0.26$ ) than children whose mothers did not smoke ( $t = 7.93$ ,  $df = 1,556.3$ ;  $P = 4\text{e-}15$ ).

Other effects of education-associated polygenic variation on environmental exposures included 3.3% in household income ( $\beta = 0.181$ ,  $P = 1\text{e-}22$ ), 6.5% in maternal education level ( $\beta = 0.255$ ,  $P = 3\text{e-}96$ ), 1% in parental smacking ( $\beta = -0.10$ ,  $P = 4\text{e-}15$ ), and 3.4% in television watching in the household ( $\beta = -0.184$ ,  $P = 5\text{e-}47$ ).

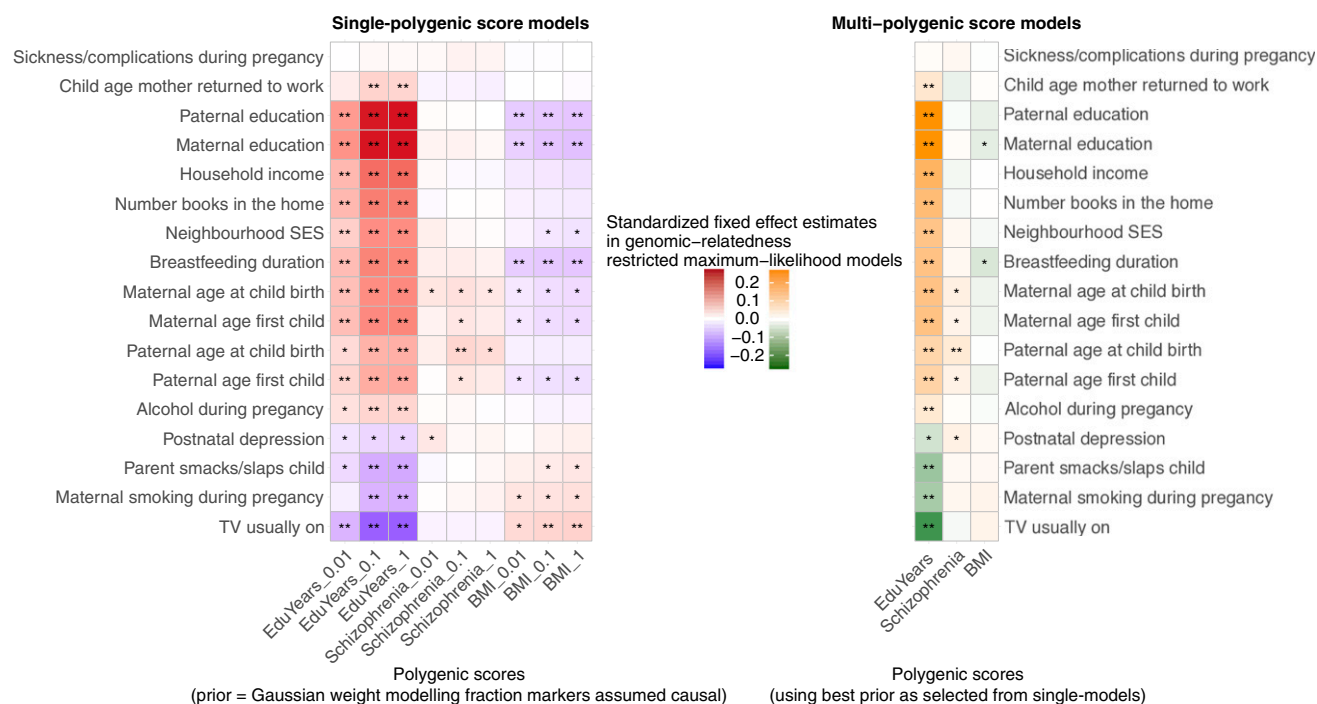
Offspring genetic risk for schizophrenia was positively associated with paternal age, even when adjusting for education and BMI-associated polygenic variation ( $R^2 = 0.002$ ,  $\beta = 0.049$ ;  $P = 1\text{e-}04$ ). Fig. 2*C* shows children's adjusted genetic risk for schizophrenia as a function of paternal age. Children whose father was aged over 45 at their birth had, on average, a genetic risk score for schizophrenia over one quarter SD (Hedges'  $g = 0.26$ ) higher than children whose father was under the age of 26 at their birth ( $t = -3.01$ ,  $df = 411.91$ ;  $P = 3\text{e-}03$ ).

Next, we examined the extent to which associations between environmental exposures and developmental outcomes were explained by trait-associated polygenic variation for education, BMI, and schizophrenia (*SI Appendix, Fig. S3*). We examined associations between environmental exposures and three developmental outcomes: educational achievement, inattention-hyperactivity symptoms, and conduct problems. Of the three polygenic scores, only the education polygenic score captured covariation between environmental exposures and the three developmental outcomes (*SI Appendix, Table S3*).

On average education-associated polygenic variation explained 15% of the associations between the environmental measures and children's developmental outcomes. For example, the education polygenic score explained 23% ( $P = 1.2\text{e-}18$ ) of the  $\beta = 0.19$  covariance between child educational achievement and breastfeeding. Education-associated polygenic variation also captured 6% ( $P = 1.9\text{e-}05$ ) and 7% ( $P = 4.4\text{e-}06$ ) of the associations between parental slapping/smacking and conduct problems and hyperactivity/inattention problems ( $\beta = 0.20$  for both).

## Discussion

We report evidence for covariation between trait-associated polygenic variation and early environmental exposures independently



**Fig. 1.** (Left) Single-polygenic score models: associations between polygenic scores and environmental exposures and single-predictor effects of polygenic scores for years of education, BMI, and schizophrenia on the environmental exposures. (Right) Multipolygenic score models: joint estimation of effects of polygenic scores on environmental exposures and effects of polygenic scores for years of education, BMI, and schizophrenia on the environmental exposures while adjusting for other predictors, respectively. Color gradients represent effect sizes as standardized coefficients—that is, SDs change in the environmental exposure, per SD increase in the polygenic predictor (see *SI Appendix, Tables S1–S3* for full statistics). \*Uncorrected  $P < 0.05$ , \*\*multiple testing corrected  $P < 0.05$  (see *Materials and Methods*).

of population stratification. We show that a wide range of parental, neighborhood, and parent–child perinatal characteristics, representing key early life “environmental” influences, present at birth or early in life, correlate with offspring genetic propensity—specifically, with the allele frequency at loci associated with education, BMI, and schizophrenia. We also demonstrate that covariance between environments and important developmental outcomes are partially captured by education-associated polygenic variation.

The present study combines family and molecular data. In addition to replicating the general finding that individuals’ environmental exposures vary as a function of their genotype, the current findings suggest that trait GWASs are detecting genetic variants associated with parental characteristics and their correlation with child outcomes.

Importantly, the association between exposures and outcomes was by no means entirely captured by offspring trait-associated polygenic variation. There are three likely, nonmutually exclusive, explanations for this. First, a substantial proportion of the exposure–outcome associations is likely due to nongenetic factors. Second, polygenic scores intrinsically underestimate the total genetic effects on the exposure–outcome associations because they are limited to the additive effects of common variants on a particular trait that the discovery GWAS was powered to detect. Third, we only measure offspring polygenic variation, but offspring phenotype can be influenced not only by transmitted but also by nontransmitted parental alleles via parental phenotype (i.e., child exposure).

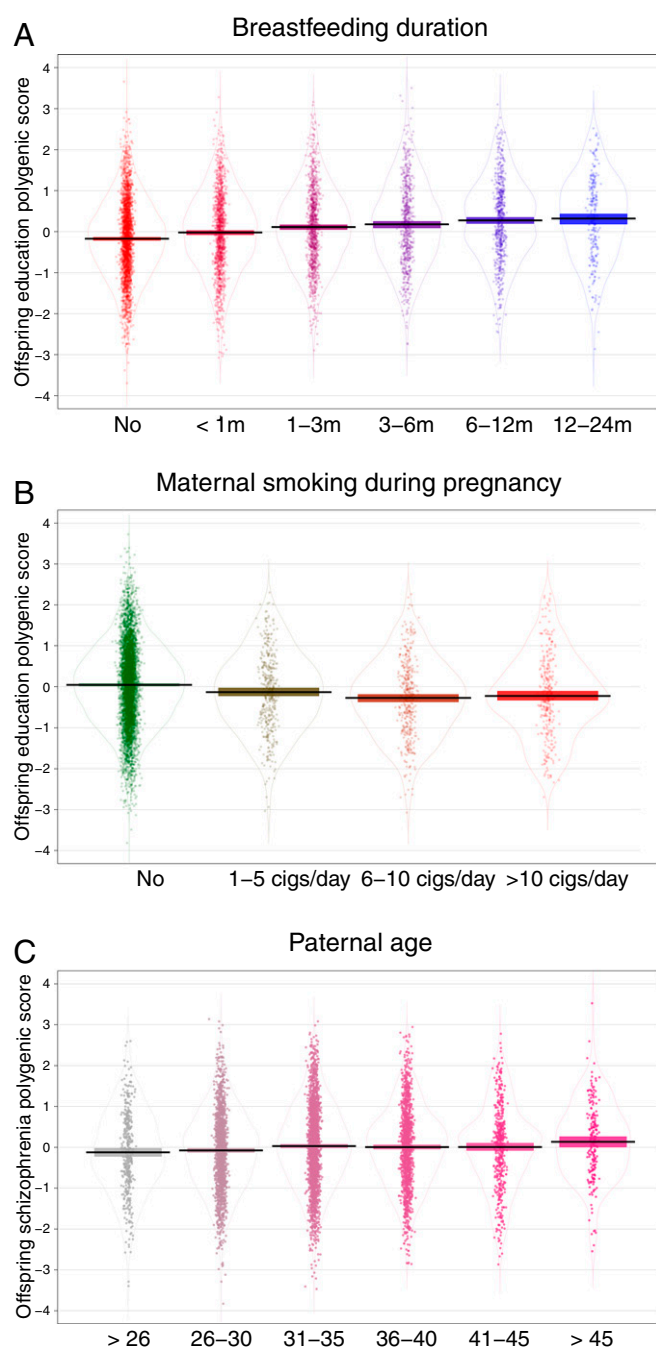
The education-associated polygenic variation showed the strongest and most consistent correlations with environmental exposures. This is consistent with research showing associations between educational attainment and many parental behaviors and characteristics (e.g., refs. 12, 31, 62, and 63). Moreover, the multipolygenic score models showed that the association between BMI-associated polygenic variation and environmental exposures such as television watching and parental education is explained by education-associated genetic variations. This suggests the potential for

multipolygenic models for isolating polygenic effects, provided the underlying discovery GWASs are similarly powered. The finding of an association between paternal age and offspring genetic risk for schizophrenia is consistent with previous evidence for older fathers’ elevated risk for conceiving a child who will go on to develop schizophrenia (18, 19, 63). Although the current findings provide evidence for the relevance of gene–environment correlation for polygenic trait prediction methods, they are not informative about the mechanisms involved.

The observed associations could arise from passive or active gene–environment correlation or via environmentally mediated genetic effects, all of which are nonmutually exclusive. Fig. 3 illustrates these possibilities schematically. Many of the observed associations between offspring genotype and environment-providing parental characteristics are outside of the offspring’s influence (e.g., parental age and education level at child birth) and are therefore likely to result from passive gene–environment correlation. That is, parental genetic propensities that were passed down to offspring are also associated with environment-providing parental behavior (through both path a and b, Fig. 3). However, some of the investigated parental behaviors could partially be evoked by offspring genetic propensities (through paths c and d in Fig. 3; e.g., breastfeeding, watching television). Finally, genetic correlations could arise as a result of environmentally mediated genetic effects (e.g., if education-associated genetic variation influenced mothers’ predisposition to smoke during pregnancy and prenatal exposure to nicotine had an environmental effect on offspring attention problems, this could result in offspring education-associated polygenic variation being associated with maternal smoking pregnancy as well as capturing part of its correlation with offspring attention problems).

The design of the current study is unable to distinguish environmentally mediated genetic effects, passive, and evocative gene–environment correlations. One way to investigate the contributions of these different mechanisms would be to use samples incorporating parental genotype data. In analyses of such samples,





**Fig. 2.** (A) Offspring adjusted education polygenic score (standardized) by level of breastfeeding. Education polygenic score was adjusted for schizophrenia and BMI polygenic scores. Positive association ( $R^2 = 0.021$ ,  $\beta = 0.144$ ;  $P = 7\text{e-}30$ ). Children who were breastfed had, on average, an education polygenic score approximately one third SD higher (Hedges'  $g = 0.30$ ) than children who were not breastfed ( $t = -11.55$ ,  $df = 5,664.2$ ;  $P = 1.6\text{e-}30$ ). (B) Offspring adjusted education polygenic score (standardized) by level of maternal smoking during pregnancy. Education polygenic score was adjusted for schizophrenia and BMI polygenic scores. Negative association ( $R^2 = 0.008$ ,  $\beta = -0.090$ ;  $P = 5\text{e-}13$ ). Children exposed to maternal smoking prenatally had, on average, an education polygenic score approximately one quarter SD lower (Hedges'  $g = 0.26$ ) than children whose mothers did not smoke ( $t = 7.93$ ,  $df = 1,556.3$ ;  $P = 4\text{e-}15$ ). (C) Offspring adjusted schizophrenia polygenic score (standardized) by paternal age at birth of offspring. Genetic risk for schizophrenia was adjusted for education and BMI polygenic scores. Positive association ( $R^2 = 0.002$ ,  $\beta = 0.049$ ;  $P = 1\text{e-}04$ ). Children whose father was aged over 45 at their birth had, on average, a genetic risk score for schizophrenia over one quarter SD (Hedges'  $g = 0.26$ ) higher than

confounding of offspring genotype by parental genotypes could be accounted for. Provided that paternal, maternal, and offspring genotype and phenotype data were available in a single sample, cross-generational effects of genetics and environment could be further disentangled (see Fig. 3 for schematic illustration).

Nurture has a genetic component; trait-associated alleles in the offspring explain variation in environment-providing parental behaviors and their covariation with offspring developmental outcomes. This provides evidence that the observed effects from GWASs are not only reflecting direct trait effects. This evidence resonates with the hypothesis that trait GWASs capture variation in risk factors as well as direct genetic effects on the trait (64). Here we showed that polygenic scores derived from trait GWASs predict variation in variables beyond the target trait, including variables often presumed to be environmental in origin such as parenting. This suggests incorporating genetic variants associated with environmental risk or predictive factors into polygenic prediction models might improve trait prediction.

In summary, we show that genetic variation identified by trait GWASs partially captures environmental risk or protective factors, indicating that some of the same genetic variation underlies both traits and environments. In contrast to the conceptual dichotomy often imposed between traits and environments, this finding implies that the pleiotropy widely found in phenotype–genome associations also crosses over to the realm of environments and manifests across generations. Findings illustrate the relevance of gene–environment correlation for polygenic prediction models and that combining family and molecular data might help reveal mechanisms by which genetic variation is translated into phenotypic variation.

## Materials and Methods

We used genome-wide SNP and environment-wide phenotype data from 6,710 unrelated individuals drawn from the UK-representative TEDS (57, 58). TEDS data can be accessed in accordance with the Data Access Policy, which can be viewed at [www.teds.ac.uk/research/collaborators-and-data/teds-data-access-policy](http://www.teds.ac.uk/research/collaborators-and-data/teds-data-access-policy). We processed the 6,710 genotypes using stringent quality control procedures followed by imputation of SNPs to the Haplotype Reference Consortium reference panel (65) (SI Appendix, Methods S1). This included removing one individual from any pair of individuals with an estimate SNP marker relatedness  $> 0.05$ . After quality control, 7,581,516 genotyped or well-imputed (info  $> 0.70$ ) variants remained.

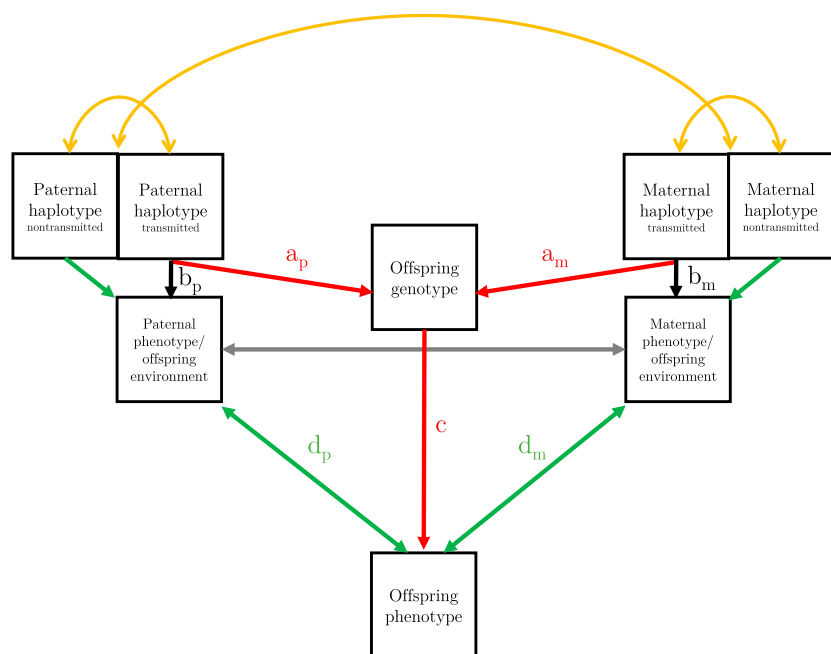
**Polygenic Scores.** For each individual in the sample, we created polygenic scores for years of education, schizophrenia, and BMI. After coordinating overlapping markers between each of the three GWA summary statistics and the target data by excluding markers due to nucleotide inconsistencies or low minor allele frequency ( $< 1\%$ ), we retained 5,690,632 for the years of education (45), 5,781,731 for schizophrenia (47), and 1,810,667 for BMI (46). We constructed polygenic scores as the effect-size weighted sums of individuals' trait-associated alleles across all SNPs. We used LDpred (60), which places a prior on the markers' effect sizes and adjusts summary statistics for LD between markers. For each trait, we created the score using three different priors on the fraction of causal markers—0.01, 0.1, and 1.0—from which the one yielding the largest  $R^2$  in the single-polygenic score models was then entered into the multipolygenic score model. For details on the polygenic score construction, see SI Appendix, Methods S2.

To account for population stratification, we adjusted the polygenic predictors by the first 30 principal components (PCs) generated from genotype data before the analysis. We used the top 30 PCs as well as genotyping array and plate to create a  $N \times P$  matrix  $Z$  of eigenvectors across the  $P$  selected PCs. We then regressed the genetic polygenic predictor onto the eigenvectors as  $S = \mu + Z\beta + e$ , where  $\mu$  is the mean and  $\beta$  is a  $P \times 1$  vector of the regression coefficients and  $e$  is the residual error.

**Single-Score and Multiscore Genomic-Relatedness Matrix Restricted Maximum-Likelihood Models.** When estimating genetic effects on environmental exposures, the possibility of population stratification is especially salient. This is because genetic and common environment effects, even if uncorrelated, may

children whose father was under the age of 26 at their birth ( $t = -3.01$ ,  $df = 411.91$ ;  $P = 3\text{e-}03$ ). Horizontal lines and bars represent means and 95% confidence intervals. Violin shapes represent probability densities.

## Schematic illustration of genotype and phenotype effects within family triad



**Fig. 3.** Schematic illustration of cross-generational effects within family triad. Because of the lack of parental genotype data, the present study was unable to distinguish passive and evocative gene–environment correlation. Passive gene–environment correlation:  $a_{m,p} \times b_{m,p}$ . Evocative gene–environment correlation:  $c \times b_{m,p}$ . Offspring phenotype can be influenced by both the transmitted paternal and maternal alleles (red arrows) and by nontransmitted alleles via parental phenotype (green arrows). Provided that paternal, maternal, and offspring genotype and phenotype data were available in a single sample, the effect of parental trait-associated alleles on offspring phenotype independently of genetic sharing between parents and offspring (green arrows) could be estimated (70–72). A testable assumption for investigating these mechanisms is there is no correlation between parental genotypes and between each parent's haplotypes (i.e., assortative mating) (yellow arrows).

be confounded as close relatives share both genes and their environment to a greater extent than other individuals. We control this type of confounding because, under only population stratification, we would not expect an association between polygenic predictors and environmental measures within the mixed effect model of Eqs. 1 and 2. This is because they account for population stratification by both regressing PCs from the polygenic predictors (see above) and fitting a relationship matrix estimated from all SNP markers (see below).

To estimate the degree to which trait-associated polygenic variation captures variation in environmental measures, we estimated the relationship between the polygenic scores and the environmental measures, while controlling for net genetic relatedness by fitting the effects of all of the SNPs as random effects by a mixed linear model:

$$\text{Single-score model: } \text{var}(y) = \mu + S_i\beta + A\sigma_g^2 + I\sigma_e^2 \quad [1]$$

$$\text{Multiscore model: } \text{var}(y) = \mu + S_{BMI}\beta + S_{SCZ}\beta + S_{EDU}\beta + A\sigma_g^2 + I\sigma_e^2, \quad [2]$$

$y$  is an  $n \times 1$  vector containing the level of environmental exposure, with  $n$  being the sample size.  $\beta$  is a vector of fixed effects estimating the effects of the polygenic predictor, independently of overall genetic relatedness  $g$ .

In the single-score model (Eq. 1),  $S_i$  is a vector containing individuals' polygenic score for one of  $i \in [\text{years of education (EDU) (45), BMI (46), schizophrenia (SCZ) (47)}]$ , adjusted for 30 PCs, genotyping array, and plate (see section above).  $g$  is an  $n \times 1$  vector of the total genetic effects of the individuals, independently of  $\beta$ , with  $g \sim N(0, A\sigma_g^2)$ , and  $A$  is interpreted as the genetic relationship matrix (GRM) between individuals ( $\text{MAF} > 0.01$ ; relatedness  $< 0.05$  as described above). The genomic relationship of each pair of subjects  $j$  and  $k$  is calculated as  $A_{jk} = 1/N \sum_i x_{ij}x_{ik} = 1/(x_{ij} - 2p_i)(x_{ik} - 2p_i)/2p_i(1 - p_i)$  with  $x_{ij}$  being the number of copies of the reference allele for the  $i$ th SNP of the  $j$ th individual and  $p_i$  being the frequency of the reference allele (66).

In the multiscore model (Eq. 2), the effects of the three polygenic predictors are being estimated jointly, thereby allowing the effect of each polygenic predictor independently of each other and of overall genetic relatedness  $g$ .

The genetic relatedness matrix accounts for population stratification in the environmental exposure, because it is equivalent to fitting all of the PCs within the model. Eqs. 1 and 2 were estimated using the restricted maximum likelihood (REML) approach implemented in the *reml* function in GCTA v1.26.0 (67).

**Decomposition of Covariance Between Environmental Exposures and Developmental Outcomes.** We fit structural equation models to decompose the covariance between environmental exposures and developmental outcomes into effects of the three polygenic scores and residual covariance (SI Appendix, Fig. 3). The

total covariance estimated as  $\text{Cov}_{\text{total}} = (a * d) + (b * e) + (c * f) + g$  was decomposed into the effect of the education score  $\text{Cov}_{\text{EDU}} = (a * d)$ , that of the BMI score  $\text{Cov}_{\text{BMI}} = (b * e)$ , that of the schizophrenia score  $\text{Cov}_{\text{SCZ}} = (c * f)$ , and residual covariance  $g$ . We used maximum likelihood estimation with robust (Huber–White) SEs. The analyses were conducted using the *lavaan* package in R (68).

**Multiple Testing Correction.**  $P$  values obtained for each statistic were corrected for multiple testing using the Sidák correction (69). The Sidák adjusted alpha level is equal to  $1 - (1 - \alpha)^{(1/k)}$ , where  $k$  is the number of tests. The total number of tests was: 357, with 153 (3 scores  $\times$  3 priors  $\times$  17 exposures) tests for the single-polygenic score models, 51 (3 scores  $\times$  17 exposures) tests for the multipolygenic score model, and 153 (3 scores  $\times$  17 exposures  $\times$  3 outcomes) test for the decomposition of covariance models. The multiple comparison adjustments were applied to  $\alpha = 0.05$ . Hence, the corrected “experimentwise”  $\alpha$  level was  $1 - (1 - 0.05)^{(1/357)} = 1.44e-04$ .

**Environmental Exposures and Child Outcome Measures.** For a detailed description of all measures, see SI Appendix, Methods S3.

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## **Supporting information**

### **The nature of nurture: Widespread covariation of early environmental exposures and trait-associated polygenic variation**

#### **Supplementary Figures**

Supplementary Figure S1: Correlations between environmental exposures

Supplementary Figure S2: Correlations between polygenic scores

Supplementary Figure S3: Path model: Decomposition of covariance between environmental exposures and developmental outcomes

#### **Supplementary Tables**

Supplementary Table S1: Effect estimates single-score models

Supplementary Table S2: Effect estimates multi-score models

Supplementary Table S3: Path estimates and fit statistics for decomposition of covariance between environmental exposures and developmental outcomes

#### **Supplementary Notes**

Supplementary Methods S1: Genotyping protocol and quality control

Supplementary Methods S2: Polygenic score creation

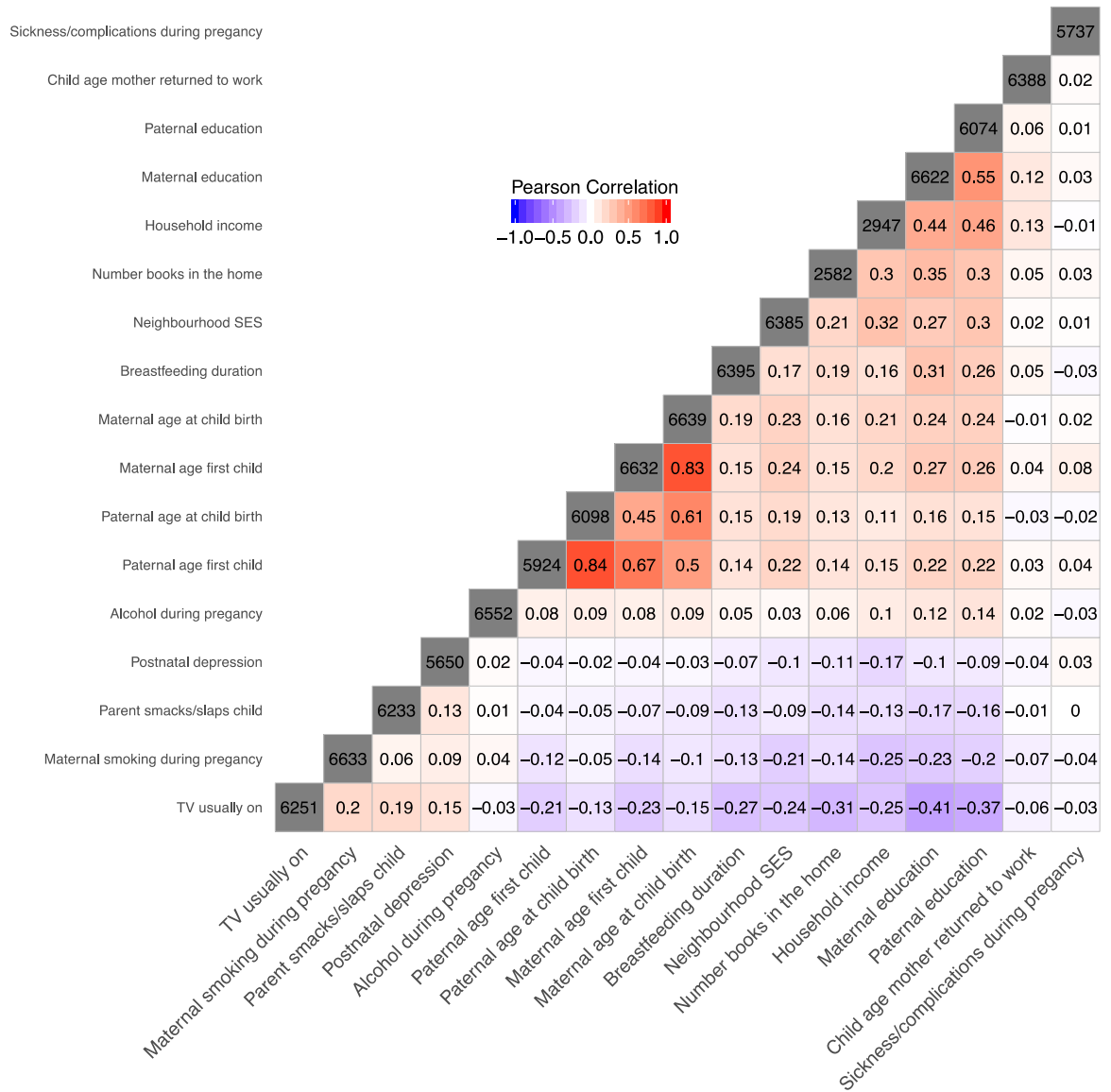
Supplementary Methods S3: Description of environmental behavioral measures

Supplementary Methods S4: Robustness analyses for prediction of parental education

Supplementary References



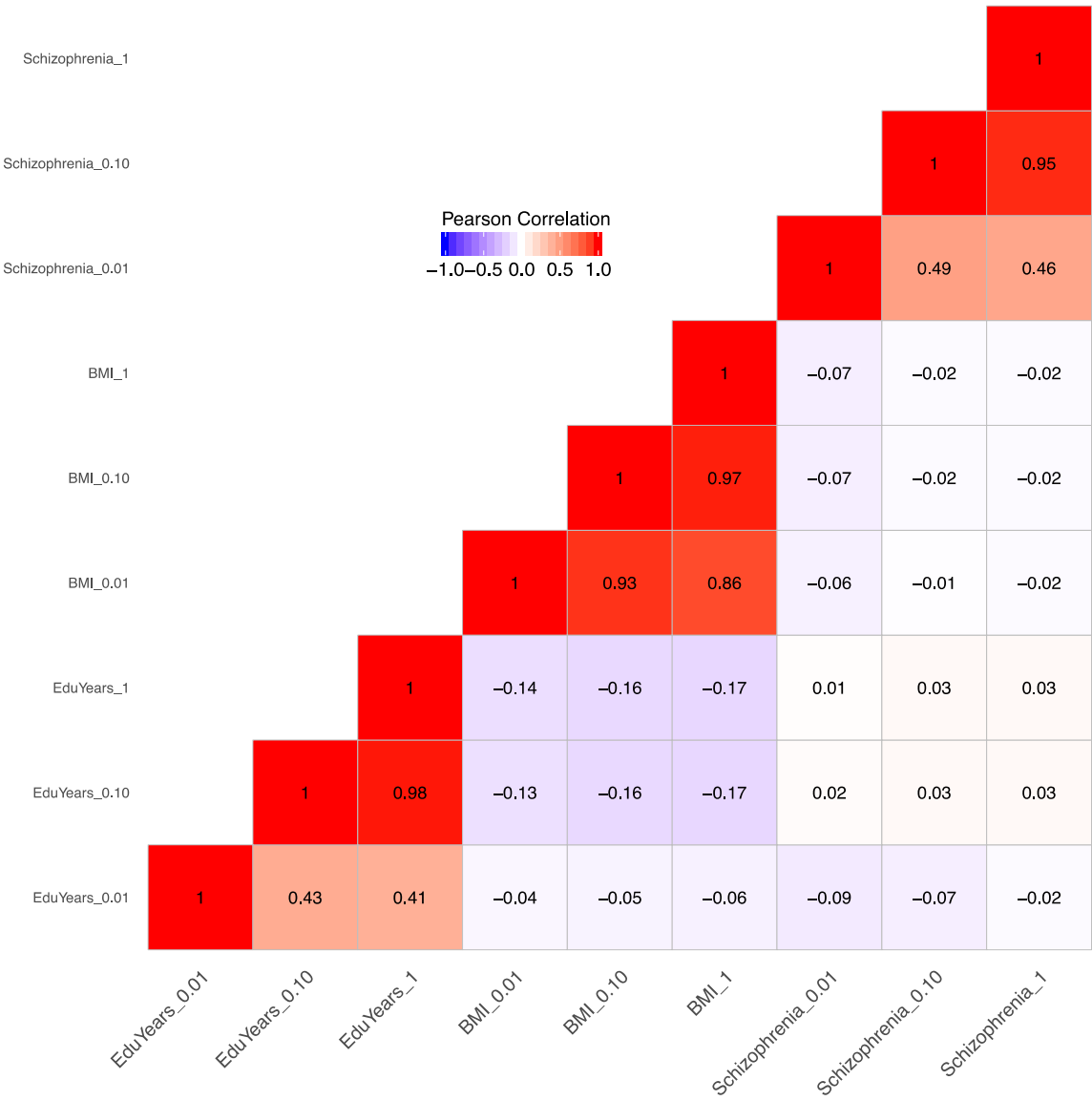
**Supplementary Figure S1: Correlations between environmental exposures**



For a description of all measures see Supplementary Methods S2. Numbers at diagonal represent sample sizes.

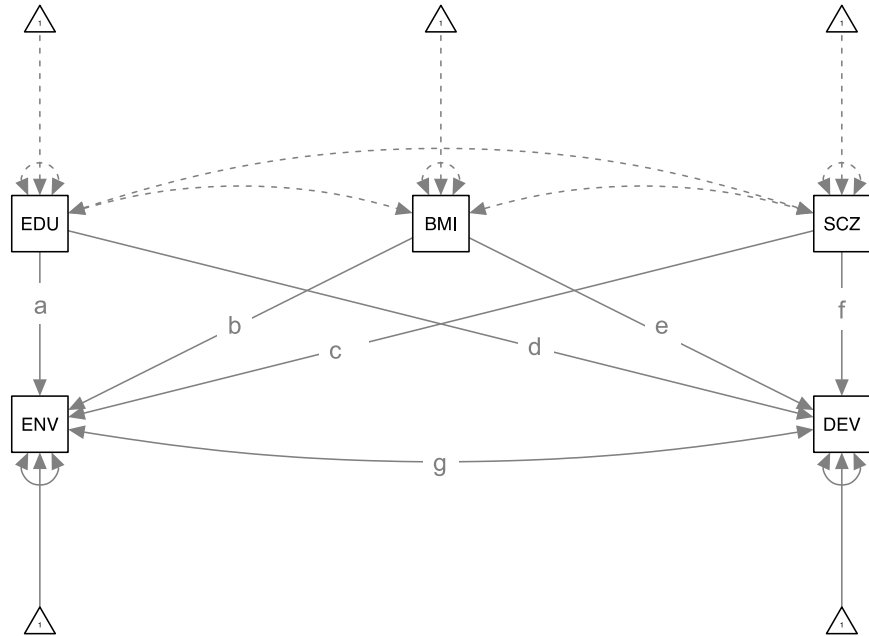


**Supplementary Figure S2: Correlations between polygenic scores**



For a description of the polygenic score construction see the Materials & Methods in the main manuscript text.

**Supplementary Figure S3: Path model: Decomposition of covariance between environmental exposures and developmental outcomes**



EDU, BMI, and SCZ represent polygenic scores for years of education, Body-mass Index, and schizophrenia, adjusted for 30 principal components and genotyping array and plate

ENV represents the environmental exposure

DEV represents the developmental outcome (educational achievement, conduct problems, inattention/hyperactivity)

Solid lines represent estimated parameters

Double-headed arrows represent correlations

Single-headed arrows represent coefficients

The total covariance estimated as  $Cov_{total} = (a * d) + (b * e) + (c * f) + g$  is

decomposed into the effect of the education score:  $Cov_{EDU} = (a * d)$ , that of the

BMI score:  $Cov_{BMI} = (b * e)$ , that of the schizophrenia score  $Cov_{SCZ} = (c * f)$ , and

residual covariance  $g$ .

**Supplementary Table S1: Effect estimates single-score models**

Environmental measure	Predictor	Gaussian prior	Std coeff	SE	$\chi^2$	P
TV usually on	EduYears	0.010	-0.088	0.014	-38.63	5e-10
TV usually on	EduYears	0.100	-0.186	0.013	-216.55	5e-49
TV usually on	EduYears	1.000	-0.188	0.013	-224.32	1e-50
Maternal smoking during pregnancy	EduYears	0.010	-0.020	0.012	-2.55	1e-01
Maternal smoking during pregnancy	EduYears	0.100	-0.091	0.012	-54.86	1e-13
Maternal smoking during pregnancy	EduYears	1.000	-0.093	0.012	-58.32	2e-14
Parent smacks/slaps child	EduYears	0.010	-0.045	0.013	-12.25	5e-04
Parent smacks/slaps child	EduYears	0.100	-0.099	0.013	-61.33	5e-15
Parent smacks/slaps child	EduYears	1.000	-0.102	0.013	-66.07	4e-16
Postnatal depression	EduYears	0.010	-0.033	0.014	-6.11	1e-02
Postnatal depression	EduYears	0.100	-0.048	0.013	-13.09	3e-04
Postnatal depression	EduYears	1.000	-0.050	0.013	-14.13	2e-04
Alcohol during pregnancy	EduYears	0.010	0.037	0.014	7.26	7e-03
Alcohol during pregnancy	EduYears	0.100	0.052	0.013	17.00	4e-05
Alcohol during pregnancy	EduYears	1.000	0.053	0.013	17.58	3e-05
Paternal age first child	EduYears	0.010	0.053	0.014	14.46	1e-04
Paternal age first child	EduYears	0.100	0.103	0.013	62.99	2e-15
Paternal age first child	EduYears	1.000	0.107	0.013	68.26	1e-16
Paternal age at child birth	EduYears	0.010	0.045	0.013	11.14	8e-04
Paternal age at child birth	EduYears	0.100	0.095	0.013	55.58	9e-14
Paternal age at child birth	EduYears	1.000	0.100	0.013	60.70	7e-15
Maternal age first child	EduYears	0.010	0.080	0.013	37.68	8e-10
Maternal age first child	EduYears	0.100	0.145	0.012	140.14	2e-32
Maternal age first child	EduYears	1.000	0.148	0.012	147.19	7e-34
Maternal age at child birth	EduYears	0.010	0.079	0.013	37.80	8e-10
Maternal age at child birth	EduYears	0.100	0.141	0.012	134.24	5e-31
Maternal age at child birth	EduYears	1.000	0.145	0.012	142.27	9e-33
Breastfeeding duration	EduYears	0.010	0.082	0.013	37.02	1e-09
Breastfeeding duration	EduYears	0.100	0.152	0.013	146.83	9e-34
Breastfeeding duration	EduYears	1.000	0.149	0.013	142.46	8e-33
Neighbourhood SES	EduYears	0.010	0.059	0.014	18.17	2e-05
Neighbourhood SES	EduYears	0.100	0.140	0.013	122.74	2e-28
Neighbourhood SES	EduYears	1.000	0.141	0.013	125.29	4e-29
Number books in the home	EduYears	0.010	0.089	0.021	17.27	3e-05
Number books in the home	EduYears	0.100	0.159	0.020	66.72	3e-16
Number books in the home	EduYears	1.000	0.159	0.019	67.09	3e-16
Household income	EduYears	0.010	0.089	0.020	19.34	1e-05
Household income	EduYears	0.100	0.178	0.018	96.29	1e-22
Household income	EduYears	1.000	0.181	0.018	100.00	2e-23
Maternal education	EduYears	0.010	0.134	0.014	90.38	2e-21
Maternal education	EduYears	0.100	0.259	0.012	459.91	5e-102
Maternal education	EduYears	1.000	0.260	0.012	466.10	2e-103
Paternal education	EduYears	0.010	0.124	0.014	75.79	3e-18
Paternal education	EduYears	0.100	0.257	0.012	426.52	9e-95
Paternal education	EduYears	1.000	0.261	0.012	442.29	3e-98
Child age mother returned to work	EduYears	0.010	0.023	0.013	3.11	8e-02
Child age mother returned to work	EduYears	0.100	0.055	0.013	19.04	1e-05
Child age mother returned to work	EduYears	1.000	0.052	0.013	17.46	3e-05
Sickness/complications during pregnancy	EduYears	0.010	-0.001	0.013	-0.00	1e+00
Sickness/complications during pregnancy	EduYears	0.100	0.008	0.013	0.39	5e-01
Sickness/complications during pregnancy	EduYears	1.000	0.006	0.013	0.21	6e-01

Environmental measure	Predictor	Gaussian prior	Std coeff	SE	$\chi^2$	P
TV usually on	Schizophrenia	0.010	-0.014	0.014	-1.01	3e-01
TV usually on	Schizophrenia	0.100	-0.014	0.013	-1.19	3e-01
TV usually on	Schizophrenia	1.000	-0.013	0.013	-1.08	3e-01
Maternal smoking during pregnancy	Schizophrenia	0.010	0.002	0.012	0.02	9e-01
Maternal smoking during pregnancy	Schizophrenia	0.100	0.010	0.012	0.67	4e-01
Maternal smoking during pregnancy	Schizophrenia	1.000	0.015	0.012	1.48	2e-01
Parent smacks/slaps child	Schizophrenia	0.010	-0.008	0.013	-0.35	6e-01
Parent smacks/slaps child	Schizophrenia	0.100	0.001	0.013	0.01	9e-01
Parent smacks/slaps child	Schizophrenia	1.000	0.010	0.013	0.55	5e-01
Postnatal depression	Schizophrenia	0.010	0.030	0.013	4.85	3e-02
Postnatal depression	Schizophrenia	0.100	0.009	0.013	0.41	5e-01
Postnatal depression	Schizophrenia	1.000	0.011	0.013	0.71	4e-01
Alcohol during pregnancy	Schizophrenia	0.010	0.004	0.014	0.08	8e-01
Alcohol during pregnancy	Schizophrenia	0.100	0.007	0.013	0.27	6e-01
Alcohol during pregnancy	Schizophrenia	1.000	-0.002	0.013	-0.03	9e-01
Paternal age first child	Schizophrenia	0.010	0.003	0.014	0.03	9e-01
Paternal age first child	Schizophrenia	0.100	0.032	0.013	5.99	1e-02
Paternal age first child	Schizophrenia	1.000	0.024	0.013	3.32	7e-02
Paternal age at child birth	Schizophrenia	0.010	0.019	0.014	2.00	2e-01
Paternal age at child birth	Schizophrenia	0.100	0.052	0.013	16.07	6e-05
Paternal age at child birth	Schizophrenia	1.000	0.044	0.013	11.75	6e-04
Maternal age first child	Schizophrenia	0.010	0.015	0.013	1.24	3e-01
Maternal age first child	Schizophrenia	0.100	0.030	0.013	5.87	2e-02
Maternal age first child	Schizophrenia	1.000	0.023	0.012	3.27	7e-02
Maternal age at child birth	Schizophrenia	0.010	0.032	0.013	6.04	1e-02
Maternal age at child birth	Schizophrenia	0.100	0.038	0.012	9.29	2e-03
Maternal age at child birth	Schizophrenia	1.000	0.029	0.012	5.63	2e-02
Breastfeeding duration	Schizophrenia	0.010	0.021	0.014	2.29	1e-01
Breastfeeding duration	Schizophrenia	0.100	0.022	0.013	3.10	8e-02
Breastfeeding duration	Schizophrenia	1.000	0.015	0.013	1.42	2e-01
Neighbourhood SES	Schizophrenia	0.010	0.020	0.014	2.02	2e-01
Neighbourhood SES	Schizophrenia	0.100	0.008	0.013	0.36	5e-01
Neighbourhood SES	Schizophrenia	1.000	0.003	0.013	0.07	8e-01
Number books in the home	Schizophrenia	0.010	-0.006	0.021	-0.09	8e-01
Number books in the home	Schizophrenia	0.100	0.001	0.020	0.00	9e-01
Number books in the home	Schizophrenia	1.000	0.002	0.020	0.01	9e-01
Household income	Schizophrenia	0.010	0.006	0.020	0.08	8e-01
Household income	Schizophrenia	0.100	-0.005	0.019	-0.08	8e-01
Household income	Schizophrenia	1.000	-0.008	0.019	-0.19	7e-01
Maternal education	Schizophrenia	0.010	0.014	0.014	0.93	3e-01
Maternal education	Schizophrenia	0.100	0.015	0.013	1.34	2e-01
Maternal education	Schizophrenia	1.000	0.009	0.013	0.49	5e-01
Paternal education	Schizophrenia	0.010	0.004	0.014	0.09	8e-01
Paternal education	Schizophrenia	0.100	0.003	0.013	0.05	8e-01
Paternal education	Schizophrenia	1.000	0.000	0.013	0.00	1e+00
Child age mother returned to work	Schizophrenia	0.010	-0.012	0.013	-0.89	3e-01
Child age mother returned to work	Schizophrenia	0.100	-0.015	0.013	-1.38	2e-01
Child age mother returned to work	Schizophrenia	1.000	-0.019	0.013	-2.19	1e-01
Sickness/complications during pregnancy	Schizophrenia	0.010	0.006	0.013	0.19	7e-01
Sickness/complications during pregnancy	Schizophrenia	0.100	0.015	0.013	1.36	2e-01
Sickness/complications during pregnancy	Schizophrenia	1.000	0.012	0.013	0.84	4e-01



Environmental measure	Predictor	Gaussian prior	Std coeff	SE	$\chi^2$	P
TV usually on	BMI	0.010	0.046	0.013	12.58	4e-04
TV usually on	BMI	0.100	0.052	0.013	16.42	5e-05
TV usually on	BMI	1.000	0.056	0.013	18.99	1e-05
Maternal smoking during pregnancy	BMI	0.010	0.033	0.012	7.15	7e-03
Maternal smoking during pregnancy	BMI	0.100	0.035	0.012	8.20	4e-03
Maternal smoking during pregnancy	BMI	1.000	0.039	0.012	9.89	2e-03
Parent smacks/slaps child	BMI	0.010	0.019	0.013	2.18	1e-01
Parent smacks/slaps child	BMI	0.100	0.025	0.013	3.93	5e-02
Parent smacks/slaps child	BMI	1.000	0.030	0.013	5.57	2e-02
Postnatal depression	BMI	0.010	0.004	0.013	0.07	8e-01
Postnatal depression	BMI	0.100	0.013	0.013	0.96	3e-01
Postnatal depression	BMI	1.000	0.018	0.013	1.91	2e-01
Alcohol during pregnancy	BMI	0.010	-0.005	0.013	-0.16	7e-01
Alcohol during pregnancy	BMI	0.100	-0.012	0.013	-0.96	3e-01
Alcohol during pregnancy	BMI	1.000	-0.014	0.013	-1.20	3e-01
Paternal age first child	BMI	0.010	-0.031	0.013	-5.53	2e-02
Paternal age first child	BMI	0.100	-0.037	0.013	-7.95	5e-03
Paternal age first child	BMI	1.000	-0.038	0.013	-8.17	4e-03
Paternal age at child birth	BMI	0.010	-0.017	0.013	-1.82	2e-01
Paternal age at child birth	BMI	0.100	-0.020	0.013	-2.48	1e-01
Paternal age at child birth	BMI	1.000	-0.020	0.013	-2.52	1e-01
Maternal age first child	BMI	0.010	-0.028	0.012	-5.26	2e-02
Maternal age first child	BMI	0.100	-0.041	0.012	-10.97	9e-04
Maternal age first child	BMI	1.000	-0.043	0.012	-11.76	6e-04
Maternal age at child birth	BMI	0.010	-0.028	0.012	-5.10	2e-02
Maternal age at child birth	BMI	0.100	-0.040	0.012	-10.61	1e-03
Maternal age at child birth	BMI	1.000	-0.042	0.012	-11.60	7e-04
Breastfeeding duration	BMI	0.010	-0.057	0.013	-20.39	6e-06
Breastfeeding duration	BMI	0.100	-0.065	0.013	-25.92	4e-07
Breastfeeding duration	BMI	1.000	-0.066	0.013	-26.98	2e-07
Neighbourhood SES	BMI	0.010	-0.014	0.013	-1.25	3e-01
Neighbourhood SES	BMI	0.100	-0.029	0.013	-5.18	2e-02
Neighbourhood SES	BMI	1.000	-0.033	0.013	-6.72	1e-02
Number books in the home	BMI	0.010	-0.017	0.020	-0.76	4e-01
Number books in the home	BMI	0.100	-0.021	0.020	-1.14	3e-01
Number books in the home	BMI	1.000	-0.025	0.020	-1.66	2e-01
Household income	BMI	0.010	-0.025	0.018	-1.87	2e-01
Household income	BMI	0.100	-0.029	0.018	-2.40	1e-01
Household income	BMI	1.000	-0.034	0.019	-3.40	7e-02
Maternal education	BMI	0.010	-0.056	0.013	-19.49	1e-05
Maternal education	BMI	0.100	-0.069	0.013	-30.04	4e-08
Maternal education	BMI	1.000	-0.072	0.013	-32.70	1e-08
Paternal education	BMI	0.010	-0.060	0.013	-21.60	3e-06
Paternal education	BMI	0.100	-0.063	0.013	-23.59	1e-06
Paternal education	BMI	1.000	-0.068	0.013	-26.97	2e-07
Child age mother returned to work	BMI	0.010	-0.001	0.013	-0.01	9e-01
Child age mother returned to work	BMI	0.100	0.000	0.013	0.00	1e+00
Child age mother returned to work	BMI	1.000	-0.004	0.013	-0.13	7e-01
Sickness/complications during pregnancy	BMI	0.010	-0.003	0.013	-0.06	8e-01
Sickness/complications during pregnancy	BMI	0.100	-0.003	0.013	-0.04	8e-01
Sickness/complications during pregnancy	BMI	1.000	0.000	0.013	0.00	1e+00

**Supplementary Table S2: Effect estimates multi-score models**

Environmental measure	Predictors in model	Standardized coefficient	Standard error	$\chi^2$	P
TV usually on	BMI	0.024	0.013	3.53	6e-02
	EduYears	-0.184	0.013	-207.63	5e-47
	Schizophrenia	-0.009	0.013	-0.52	5e-01
Maternal smoking during pregnancy	BMI	0.024	0.012	3.63	6e-02
	EduYears	-0.090	0.012	-52.38	5e-13
	Schizophrenia	0.018	0.012	2.20	1e-01
Parent smacks/slaps child	BMI	0.013	0.013	0.99	3e-01
	EduYears	-0.100	0.013	-61.71	4e-15
	Schizophrenia	0.013	0.013	0.99	3e-01
Postnatal depression	BMI	0.012	0.014	0.82	4e-01
	EduYears	-0.048	0.013	-12.89	3e-04
	Schizophrenia	0.031	0.013	5.42	2e-02
Alcohol during pregnancy	BMI	-0.005	0.013	-0.15	7e-01
	EduYears	0.052	0.013	16.46	5e-05
	Schizophrenia	0.005	0.013	0.18	7e-01
Paternal age first child	BMI	-0.019	0.013	-2.03	2e-01
	EduYears	0.103	0.013	61.33	5e-15
	Schizophrenia	0.028	0.013	4.75	3e-02
Paternal age at child birth	BMI	-0.002	0.013	-0.02	9e-01
	EduYears	0.098	0.013	57.03	4e-14
	Schizophrenia	0.049	0.013	14.47	1e-04
Maternal age first child	BMI	-0.018	0.012	-2.03	2e-01
	EduYears	0.145	0.012	135.77	2e-31
	Schizophrenia	0.025	0.012	4.30	4e-02
Maternal age at child birth	BMI	-0.017	0.012	-1.90	2e-01
	EduYears	0.142	0.012	131.25	2e-30
	Schizophrenia	0.034	0.012	7.78	5e-03
Breastfeeding duration	BMI	-0.041	0.013	-10.24	1e-03
	EduYears	0.144	0.013	128.86	7e-30
	Schizophrenia	0.017	0.013	1.79	2e-01
Neighbourhood SES	BMI	-0.009	0.013	-0.45	5e-01
	EduYears	0.139	0.013	118.67	1e-27
	Schizophrenia	0.017	0.014	1.51	2e-01
Number books in the home	BMI	0.002	0.020	0.01	9e-01
	EduYears	0.160	0.020	64.98	8e-16
	Schizophrenia	-0.009	0.020	-0.19	7e-01
Household income	BMI	-0.001	0.018	-0.01	9e-01
	EduYears	0.181	0.018	96.35	1e-22
	Schizophrenia	-0.012	0.018	-0.40	5e-01
Maternal education	BMI	-0.028	0.012	-5.21	2e-02
	EduYears	0.255	0.012	435.03	1e-96
	Schizophrenia	0.007	0.012	0.38	5e-01
Paternal education	BMI	-0.023	0.013	-3.39	7e-02
	EduYears	0.257	0.013	416.49	1e-92
	Schizophrenia	-0.006	0.013	-0.18	7e-01
Child age mother returned to work	BMI	0.005	0.013	0.13	7e-01
	EduYears	0.056	0.013	19.42	1e-05
	Schizophrenia	-0.020	0.013	-2.56	1e-01
Sickness/complications during pregnancy	BMI	-0.002	0.013	-0.02	9e-01
	EduYears	0.007	0.013	0.31	6e-01
	Schizophrenia	0.015	0.013	1.30	3e-01

Supplementary Table S3: Path estimates and fit statistics for decomposition of covariance between environmental exposures and developmental outcomes

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Conduct problems	TV usually on	a	0.2	5.2e-33	-26455.666086329
Conduct problems	TV usually on	b	0.01	5.7e-01	
Conduct problems	TV usually on	c	0.01	3.6e-01	
Conduct problems	TV usually on	d	0.1	2.3e-09	
Conduct problems	TV usually on	e	0	9.3e-01	
Conduct problems	TV usually on	f	-0.02	1.2e-01	
Conduct problems	TV usually on	g	0.11	8.5e-13	
Conduct problems	TV usually on	COVtotal	0.13	3.4e-16	
Conduct problems	TV usually on	COVEduYears	0.02	3.1e-07	
Conduct problems	TV usually on	COVBMI	0	9.3e-01	
Conduct problems	TV usually on	COVSchizophrenia	0	4.1e-01	
Conduct problems	TV usually on	COVres	0.11	8.5e-13	
Conduct problems	TV usually on	Log-likelihood			
Conduct problems	Parent smacks/slaps child	a	0.12	1.9e-12	-26417.3187099334
Conduct problems	Parent smacks/slaps child	b	-0.02	3.5e-01	
Conduct problems	Parent smacks/slaps child	c	0.01	6.9e-01	
Conduct problems	Parent smacks/slaps child	d	0.1	1.0e-09	
Conduct problems	Parent smacks/slaps child	e	0	8.6e-01	
Conduct problems	Parent smacks/slaps child	f	-0.02	1.4e-01	
Conduct problems	Parent smacks/slaps child	g	0.19	6.7e-25	
Conduct problems	Parent smacks/slaps child	COVtotal	0.2	2.3e-27	
Conduct problems	Parent smacks/slaps child	COVEduYears	0.01	2.0e-05	
Conduct problems	Parent smacks/slaps child	COVBMI	0	8.6e-01	
Conduct problems	Parent smacks/slaps child	COVSchizophrenia	0	6.9e-01	
Conduct problems	Parent smacks/slaps child	COVres	0.19	6.7e-25	
Conduct problems	Parent smacks/slaps child	Log-likelihood			
Conduct problems	Maternal smoking during pregnancy	a	0.07	2.7e-05	-26925.2716102177
Conduct problems	Maternal smoking during pregnancy	b	-0.01	5.9e-01	
Conduct problems	Maternal smoking during pregnancy	c	-0.02	2.8e-01	
Conduct problems	Maternal smoking during pregnancy	d	0.09	1.0e-08	
Conduct problems	Maternal smoking during pregnancy	e	0	9.8e-01	
Conduct problems	Maternal smoking during pregnancy	f	-0.02	1.7e-01	
Conduct problems	Maternal smoking during pregnancy	g	0.09	3.0e-06	
Conduct problems	Maternal smoking during pregnancy	COVtotal	0.1	8.5e-07	
Conduct problems	Maternal smoking during pregnancy	COVEduYears	0.01	1.4e-03	
Conduct problems	Maternal smoking during pregnancy	COVBMI	0	9.8e-01	
Conduct problems	Maternal smoking during pregnancy	COVSchizophrenia	0	4.2e-01	
Conduct problems	Maternal smoking during pregnancy	COVres	0.09	3.0e-06	
Conduct problems	Maternal smoking during pregnancy	Log-likelihood			
Conduct problems	Breastfeeding duration	a	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	b	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	c	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	d	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	e	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	f	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	g	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	COVtotal	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	COVEduYears	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	COVBMI	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	COVres	not decomposed	not decomposed	not decomposed
Conduct problems	Breastfeeding duration	Log-likelihood	not decomposed		not decomposed
Conduct problems	Household income	a	-0.21	2.1e-18	-13382.8482080027
Conduct problems	Household income	b	-0.02	4.9e-01	
Conduct problems	Household income	c	0.01	5.5e-01	
Conduct problems	Household income	d	0.12	7.4e-07	
Conduct problems	Household income	e	0.01	5.3e-01	
Conduct problems	Household income	f	-0.01	5.2e-01	
Conduct problems	Household income	g	-0.13	2.5e-08	
Conduct problems	Household income	COVtotal	-0.16	7.2e-11	
Conduct problems	Household income	COVEduYears	-0.03	6.4e-05	
Conduct problems	Household income	COVBMI	0	6.6e-01	
Conduct problems	Household income	COVSchizophrenia	0	6.9e-01	
Conduct problems	Household income	COVres	-0.13	2.5e-08	
Conduct problems	Household income	Log-likelihood			

[illegible]



Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Conduct problems	Postnatal depression	a	0.05	5.8e-03	
Conduct problems	Postnatal depression	b	-0.01	4.0e-01	
Conduct problems	Postnatal depression	c	-0.04	2.9e-02	
Conduct problems	Postnatal depression	d	0.11	2.2e-10	
Conduct problems	Postnatal depression	e	0.01	6.9e-01	
Conduct problems	Postnatal depression	f	-0.02	1.9e-01	
Conduct problems	Postnatal depression	g	0.18	2.4e-21	
Conduct problems	Postnatal depression	COVtotal	0.18	7.7e-22	
Conduct problems	Postnatal depression	COVEduYears	0.01	1.8e-02	
Conduct problems	Postnatal depression	COVBMI	0	6.9e-01	
Conduct problems	Postnatal depression	COVSchizophrenia	0	2.9e-01	
Conduct problems	Postnatal depression	COVres	0.18	2.4e-21	
Conduct problems	Postnatal depression	Log-likelihood			-24378.3856532579
Conduct problems	Sickness/complications during pregnancy	a	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	b	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	c	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	d	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	e	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	f	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	g	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	COVtotal	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	COVEduYears	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	COVBMI	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	COVres	not decomposed	not decomposed	not decomposed
Conduct problems	Sickness/complications during pregnancy	Log-likelihood	not decomposed		not decomposed
Conduct problems	Neighbourhood SES	a	-0.13	9.2e-16	
Conduct problems	Neighbourhood SES	b	-0.01	5.0e-01	
Conduct problems	Neighbourhood SES	c	-0.02	1.5e-01	
Conduct problems	Neighbourhood SES	d	0.09	6.5e-08	
Conduct problems	Neighbourhood SES	e	-0.01	6.7e-01	
Conduct problems	Neighbourhood SES	f	-0.01	4.9e-01	
Conduct problems	Neighbourhood SES	g	-0.09	2.5e-08	
Conduct problems	Neighbourhood SES	COVtotal	-0.11	5.3e-10	
Conduct problems	Neighbourhood SES	COVEduYears	-0.01	2.0e-05	
Conduct problems	Neighbourhood SES	COVBMI	0	7.1e-01	
Conduct problems	Neighbourhood SES	COVSchizophrenia	0	5.2e-01	
Conduct problems	Neighbourhood SES	COVres	-0.09	2.5e-08	
Conduct problems	Neighbourhood SES	Log-likelihood			-25821.8491896221
Conduct problems	Maternal education	a	-0.26	9.6e-59	
Conduct problems	Maternal education	b	0.02	3.1e-01	
Conduct problems	Maternal education	c	-0.01	6.3e-01	
Conduct problems	Maternal education	d	0.1	5.7e-09	
Conduct problems	Maternal education	e	0	9.0e-01	
Conduct problems	Maternal education	f	-0.02	1.1e-01	
Conduct problems	Maternal education	g	-0.09	3.2e-10	
Conduct problems	Maternal education	COVtotal	-0.12	3.3e-14	
Conduct problems	Maternal education	COVEduYears	-0.03	1.6e-07	
Conduct problems	Maternal education	COVBMI	0	9.0e-01	
Conduct problems	Maternal education	COVSchizophrenia	0	6.3e-01	
Conduct problems	Maternal education	COVres	-0.09	3.2e-10	
Conduct problems	Maternal education	Log-likelihood			-26711.9211955392
Conduct problems	Paternal education	a	-0.27	4.8e-58	
Conduct problems	Paternal education	b	0.01	7.5e-01	
Conduct problems	Paternal education	c	0.01	6.8e-01	
Conduct problems	Paternal education	d	0.09	3.4e-08	
Conduct problems	Paternal education	e	-0.01	6.5e-01	
Conduct problems	Paternal education	f	-0.02	2.8e-01	
Conduct problems	Paternal education	g	-0.1	6.8e-10	
Conduct problems	Paternal education	COVtotal	-0.12	1.4e-13	
Conduct problems	Paternal education	COVEduYears	-0.03	4.9e-07	
Conduct problems	Paternal education	COVBMI	0	8.1e-01	
Conduct problems	Paternal education	COVSchizophrenia	0	7.1e-01	
Conduct problems	Paternal education	COVres	-0.1	6.8e-10	
Conduct problems	Paternal education	Log-likelihood			-25092.1020841378

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Conduct problems	Number books in the home	a	-0.19	3.2e-13	-11799.747626528
Conduct problems	Number books in the home	b	0	8.6e-01	
Conduct problems	Number books in the home	c	0.01	7.9e-01	
Conduct problems	Number books in the home	d	0.12	1.7e-05	
Conduct problems	Number books in the home	e	0.02	4.1e-01	
Conduct problems	Number books in the home	f	-0.01	6.6e-01	
Conduct problems	Number books in the home	g	-0.09	6.0e-04	
Conduct problems	Number books in the home	COVtotal	-0.12	4.1e-05	
Conduct problems	Number books in the home	COVEduYears	-0.02	4.8e-04	
Conduct problems	Number books in the home	COVBMI	0	8.7e-01	
Conduct problems	Number books in the home	COVSchizophrenia	0	8.3e-01	
Conduct problems	Number books in the home	COVres	-0.09	6.0e-04	
Conduct problems	Number books in the home	Log-likelihood			
Conduct problems	Alcohol during pregnancy	a	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	b	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	c	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	d	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	e	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	f	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	g	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	COVtotal	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	COVEduYears	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	COVBMI	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	COVres	not decomposed	not decomposed	not decomposed
Conduct problems	Alcohol during pregnancy	Log-likelihood	not decomposed		not decomposed
Educational achievement	TV usually on	a	0.18	1.0e-36	-34367.6565535098
Educational achievement	TV usually on	b	-0.02	2.6e-01	
Educational achievement	TV usually on	c	0.01	3.0e-01	
Educational achievement	TV usually on	d	-0.32	4.7e-108	
Educational achievement	TV usually on	e	-0.01	4.1e-01	
Educational achievement	TV usually on	f	-0.01	6.2e-01	
Educational achievement	TV usually on	g	-0.3	3.7e-117	
Educational achievement	TV usually on	COVtotal	-0.36	1.9e-144	
Educational achievement	TV usually on	COVEduYears	-0.06	1.7e-21	
Educational achievement	TV usually on	COVBMI	0	4.2e-01	
Educational achievement	TV usually on	COVSchizophrenia	0	6.9e-01	
Educational achievement	TV usually on	COVres	-0.3	3.7e-117	
Educational achievement	TV usually on	Log-likelihood			
Educational achievement	Parent smacks/slaps child	a	0.1	1.6e-12	-34546.0449968867
Educational achievement	Parent smacks/slaps child	b	-0.02	2.5e-01	
Educational achievement	Parent smacks/slaps child	c	-0.01	7.2e-01	
Educational achievement	Parent smacks/slaps child	d	-0.32	2.5e-108	
Educational achievement	Parent smacks/slaps child	e	-0.01	4.1e-01	
Educational achievement	Parent smacks/slaps child	f	0	9.6e-01	
Educational achievement	Parent smacks/slaps child	g	-0.16	6.8e-31	
Educational achievement	Parent smacks/slaps child	COVtotal	-0.19	1.4e-39	
Educational achievement	Parent smacks/slaps child	COVEduYears	-0.03	2.0e-10	
Educational achievement	Parent smacks/slaps child	COVBMI	0	4.6e-01	
Educational achievement	Parent smacks/slaps child	COVSchizophrenia	0	9.5e-01	
Educational achievement	Parent smacks/slaps child	COVres	-0.16	6.8e-31	
Educational achievement	Parent smacks/slaps child	Log-likelihood			
Educational achievement	Maternal smoking during pregnancy	a	0.08	5.3e-09	-36170.8415992377
Educational achievement	Maternal smoking during pregnancy	b	-0.01	4.2e-01	
Educational achievement	Maternal smoking during pregnancy	c	-0.01	4.1e-01	
Educational achievement	Maternal smoking during pregnancy	d	-0.31	7.2e-111	
Educational achievement	Maternal smoking during pregnancy	e	-0.01	4.7e-01	
Educational achievement	Maternal smoking during pregnancy	f	0	9.2e-01	
Educational achievement	Maternal smoking during pregnancy	g	-0.16	5.9e-22	
Educational achievement	Maternal smoking during pregnancy	COVtotal	-0.19	1.4e-26	
Educational achievement	Maternal smoking during pregnancy	COVEduYears	-0.03	6.7e-08	
Educational achievement	Maternal smoking during pregnancy	COVBMI	0	5.5e-01	
Educational achievement	Maternal smoking during pregnancy	COVSchizophrenia	0	9.1e-01	
Educational achievement	Maternal smoking during pregnancy	COVres	-0.16	5.9e-22	
Educational achievement	Maternal smoking during pregnancy	Log-likelihood			

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Educational achievement	Breastfeeding duration	a	-0.14	1.9e-22	-34706.0794422
Educational achievement	Breastfeeding duration	b	0.04	1.0e-02	
Educational achievement	Breastfeeding duration	c	-0.01	3.5e-01	
Educational achievement	Breastfeeding duration	d	-0.31	2.1e-102	
Educational achievement	Breastfeeding duration	e	-0.01	4.5e-01	
Educational achievement	Breastfeeding duration	f	-0.01	5.9e-01	
Educational achievement	Breastfeeding duration	g	0.15	1.8e-29	
Educational achievement	Breastfeeding duration	COVtotal	0.19	2.7e-42	
Educational achievement	Breastfeeding duration	COVEduYears	0.04	2.1e-16	
Educational achievement	Breastfeeding duration	COVBMI	0	4.4e-01	
Educational achievement	Breastfeeding duration	COVSchizophrenia	0	6.7e-01	
Educational achievement	Breastfeeding duration	COVres	0.15	1.8e-29	
Educational achievement	Breastfeeding duration	Log-likelihood			
Educational achievement	Household income	a	-0.18	1.8e-18	-17314.4165276373
Educational achievement	Household income	b	-0.01	6.7e-01	
Educational achievement	Household income	c	0	8.2e-01	
Educational achievement	Household income	d	-0.31	1.4e-53	
Educational achievement	Household income	e	-0.02	4.2e-01	
Educational achievement	Household income	f	0	9.5e-01	
Educational achievement	Household income	g	0.34	2.6e-66	
Educational achievement	Household income	COVtotal	0.4	3.8e-81	
Educational achievement	Household income	COVEduYears	0.06	7.5e-11	
Educational achievement	Household income	COVBMI	0	7.4e-01	
Educational achievement	Household income	COVSchizophrenia	0	9.4e-01	
Educational achievement	Household income	COVres	0.34	2.6e-66	
Educational achievement	Household income	Log-likelihood			
Educational achievement	Maternal age first child	a	-0.14	7.4e-22	-36092.9425666268
Educational achievement	Maternal age first child	b	0.02	2.6e-01	
Educational achievement	Maternal age first child	c	-0.03	3.9e-02	
Educational achievement	Maternal age first child	d	-0.31	1.4e-110	
Educational achievement	Maternal age first child	e	-0.01	5.3e-01	
Educational achievement	Maternal age first child	f	-0.01	6.6e-01	
Educational achievement	Maternal age first child	g	0.19	2.6e-42	
Educational achievement	Maternal age first child	COVtotal	0.23	1.6e-56	
Educational achievement	Maternal age first child	COVEduYears	0.04	3.8e-16	
Educational achievement	Maternal age first child	COVBMI	0	5.4e-01	
Educational achievement	Maternal age first child	COVSchizophrenia	0	6.8e-01	
Educational achievement	Maternal age first child	COVres	0.19	2.6e-42	
Educational achievement	Maternal age first child	Log-likelihood			
Educational achievement	Paternal age first child	a	-0.09	1.4e-09	-32773.54394358
Educational achievement	Paternal age first child	b	0.02	2.6e-01	
Educational achievement	Paternal age first child	c	-0.02	1.1e-01	
Educational achievement	Paternal age first child	d	-0.31	2.7e-98	
Educational achievement	Paternal age first child	e	0	7.7e-01	
Educational achievement	Paternal age first child	f	0	7.4e-01	
Educational achievement	Paternal age first child	g	0.16	1.8e-28	
Educational achievement	Paternal age first child	COVtotal	0.19	1.6e-34	
Educational achievement	Paternal age first child	COVEduYears	0.03	3.0e-08	
Educational achievement	Paternal age first child	COVBMI	0	7.7e-01	
Educational achievement	Paternal age first child	COVSchizophrenia	0	7.5e-01	
Educational achievement	Paternal age first child	COVres	0.16	1.8e-28	
Educational achievement	Paternal age first child	Log-likelihood			

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Educational achievement	Maternal age at child birth	a	-0.13	1.2e-21	-36173.9929046913
Educational achievement	Maternal age at child birth	b	0.01	5.5e-01	
Educational achievement	Maternal age at child birth	c	-0.04	2.1e-03	
Educational achievement	Maternal age at child birth	d	-0.31	4.4e-110	
Educational achievement	Maternal age at child birth	e	-0.01	5.3e-01	
Educational achievement	Maternal age at child birth	f	-0.01	6.3e-01	
Educational achievement	Maternal age at child birth	g	0.14	7.2e-23	
Educational achievement	Maternal age at child birth	COVtotal	0.18	1.3e-34	
Educational achievement	Maternal age at child birth	COVEduYears	0.04	2.1e-16	
Educational achievement	Maternal age at child birth	COVBMI	0	6.4e-01	
Educational achievement	Maternal age at child birth	COVSchizophrenia	0	6.5e-01	
Educational achievement	Maternal age at child birth	COVres	0.14	7.2e-23	
Educational achievement	Maternal age at child birth	Log-likelihood			
Educational achievement	Paternal age at child birth	a	-0.09	3.0e-10	-33742.4712270681
Educational achievement	Paternal age at child birth	b	0	8.4e-01	
Educational achievement	Paternal age at child birth	c	-0.05	2.9e-04	
Educational achievement	Paternal age at child birth	d	-0.31	6.0e-101	
Educational achievement	Paternal age at child birth	e	0	7.7e-01	
Educational achievement	Paternal age at child birth	f	0	7.6e-01	
Educational achievement	Paternal age at child birth	g	0.09	5.4e-11	
Educational achievement	Paternal age at child birth	COVtotal	0.12	8.4e-16	
Educational achievement	Paternal age at child birth	COVEduYears	0.03	5.9e-09	
Educational achievement	Paternal age at child birth	COVBMI	0	8.7e-01	
Educational achievement	Paternal age at child birth	COVSchizophrenia	0	7.6e-01	
Educational achievement	Paternal age at child birth	COVres	0.09	5.4e-11	
Educational achievement	Paternal age at child birth	Log-likelihood			
Educational achievement	Child age mother returned to work	a	-0.05	7.4e-04	-34770.3181068965
Educational achievement	Child age mother returned to work	b	0	8.6e-01	
Educational achievement	Child age mother returned to work	c	0.02	1.6e-01	
Educational achievement	Child age mother returned to work	d	-0.31	2.7e-102	
Educational achievement	Child age mother returned to work	e	0	7.3e-01	
Educational achievement	Child age mother returned to work	f	-0.01	7.1e-01	
Educational achievement	Child age mother returned to work	g	0.04	1.0e-02	
Educational achievement	Child age mother returned to work	COVtotal	0.05	6.3e-04	
Educational achievement	Child age mother returned to work	COVEduYears	0.01	9.6e-04	
Educational achievement	Child age mother returned to work	COVBMI	0	8.8e-01	
Educational achievement	Child age mother returned to work	COVSchizophrenia	0	7.2e-01	
Educational achievement	Child age mother returned to work	COVres	0.04	1.0e-02	
Educational achievement	Child age mother returned to work	Log-likelihood			
Educational achievement	Postnatal depression	a	0.03	5.3e-02	-31271.980303066
Educational achievement	Postnatal depression	b	-0.01	4.0e-01	
Educational achievement	Postnatal depression	c	-0.03	2.6e-02	
Educational achievement	Postnatal depression	d	-0.31	9.1e-96	
Educational achievement	Postnatal depression	e	-0.01	5.4e-01	
Educational achievement	Postnatal depression	f	0.02	2.5e-01	
Educational achievement	Postnatal depression	g	-0.09	1.6e-09	
Educational achievement	Postnatal depression	COVtotal	-0.1	2.7e-10	
Educational achievement	Postnatal depression	COVEduYears	-0.01	5.6e-02	
Educational achievement	Postnatal depression	COVBMI	0	6.1e-01	
Educational achievement	Postnatal depression	COVSchizophrenia	0	3.4e-01	
Educational achievement	Postnatal depression	COVres	-0.09	1.6e-09	
Educational achievement	Postnatal depression	Log-likelihood			
Educational achievement	Sickness/complications during pregnancy	a	-0.01	7.2e-01	-31825.3674177091
Educational achievement	Sickness/complications during pregnancy	b	0.01	6.6e-01	
Educational achievement	Sickness/complications during pregnancy	c	-0.01	3.6e-01	
Educational achievement	Sickness/complications during pregnancy	d	-0.31	1.6e-98	
Educational achievement	Sickness/complications during pregnancy	e	0	7.5e-01	
Educational achievement	Sickness/complications during pregnancy	f	-0.01	3.3e-01	
Educational achievement	Sickness/complications during pregnancy	g	0.05	4.3e-04	
Educational achievement	Sickness/complications during pregnancy	COVtotal	0.05	5.4e-04	
Educational achievement	Sickness/complications during pregnancy	COVEduYears	0	7.2e-01	
Educational achievement	Sickness/complications during pregnancy	COVBMI	0	7.9e-01	
Educational achievement	Sickness/complications during pregnancy	COVSchizophrenia	0	5.2e-01	
Educational achievement	Sickness/complications during pregnancy	COVres	0.05	4.3e-04	
Educational achievement	Sickness/complications during pregnancy	Log-likelihood			



Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Educational achievement	Neighbourhood SES	a	-0.13	4.1e-20	-34783.9843148349
Educational achievement	Neighbourhood SES	b	0	7.5e-01	
Educational achievement	Neighbourhood SES	c	-0.01	3.8e-01	
Educational achievement	Neighbourhood SES	d	-0.32	1.0e-107	
Educational achievement	Neighbourhood SES	e	-0.01	7.1e-01	
Educational achievement	Neighbourhood SES	f	0.02	1.2e-01	
Educational achievement	Neighbourhood SES	g	0.21	7.1e-53	
Educational achievement	Neighbourhood SES	COVtotal	0.25	1.3e-68	
Educational achievement	Neighbourhood SES	COVEduYears	0.04	4.7e-15	
Educational achievement	Neighbourhood SES	COVBMI	0	7.8e-01	
Educational achievement	Neighbourhood SES	COVSchizophrenia	0	3.9e-01	
Educational achievement	Neighbourhood SES	COVres	0.21	7.1e-53	
Educational achievement	Neighbourhood SES	Log-likelihood			
Educational achievement	Maternal education	a	-0.25	1.7e-69	-35729.5772720826
Educational achievement	Maternal education	b	0.02	9.6e-02	
Educational achievement	Maternal education	c	-0.02	7.9e-02	
Educational achievement	Maternal education	d	-0.32	1.3e-111	
Educational achievement	Maternal education	e	-0.01	5.3e-01	
Educational achievement	Maternal education	f	-0.01	5.9e-01	
Educational achievement	Maternal education	g	0.33	1.1e-138	
Educational achievement	Maternal education	COVtotal	0.4	6.2e-188	
Educational achievement	Maternal education	COVEduYears	0.08	6.6e-31	
Educational achievement	Maternal education	COVBMI	0	4.9e-01	
Educational achievement	Maternal education	COVSchizophrenia	0	6.4e-01	
Educational achievement	Maternal education	COVres	0.33	1.1e-138	
Educational achievement	Maternal education	Log-likelihood			
Educational achievement	Paternal education	a	-0.25	6.4e-65	-33228.7698415538
Educational achievement	Paternal education	b	0.01	5.5e-01	
Educational achievement	Paternal education	c	0.01	5.9e-01	
Educational achievement	Paternal education	d	-0.32	3.0e-105	
Educational achievement	Paternal education	e	-0.01	7.0e-01	
Educational achievement	Paternal education	f	0.03	2.5e-02	
Educational achievement	Paternal education	g	0.33	1.3e-139	
Educational achievement	Paternal education	COVtotal	0.41	8.2e-191	
Educational achievement	Paternal education	COVEduYears	0.08	3.6e-29	
Educational achievement	Paternal education	COVBMI	0	6.8e-01	
Educational achievement	Paternal education	COVSchizophrenia	0	6.3e-01	
Educational achievement	Paternal education	COVres	0.33	1.3e-139	
Educational achievement	Paternal education	Log-likelihood			
Educational achievement	Number books in the home	a	-0.16	2.7e-13	-15131.9340278462
Educational achievement	Number books in the home	b	-0.02	4.5e-01	
Educational achievement	Number books in the home	c	0	9.7e-01	
Educational achievement	Number books in the home	d	-0.29	4.8e-44	
Educational achievement	Number books in the home	e	-0.01	6.9e-01	
Educational achievement	Number books in the home	f	0.04	9.8e-02	
Educational achievement	Number books in the home	g	0.24	4.0e-27	
Educational achievement	Number books in the home	COVtotal	0.29	1.2e-34	
Educational achievement	Number books in the home	COVEduYears	0.05	7.4e-09	
Educational achievement	Number books in the home	COVBMI	0	7.5e-01	
Educational achievement	Number books in the home	COVSchizophrenia	0	9.7e-01	
Educational achievement	Number books in the home	COVres	0.24	4.0e-27	
Educational achievement	Number books in the home	Log-likelihood			

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Educational achievement	Alcohol during pregnancy	a	-0.06	1.7e-04	-35727.9943674258
Educational achievement	Alcohol during pregnancy	b	0	8.5e-01	
Educational achievement	Alcohol during pregnancy	c	-0.01	5.8e-01	
Educational achievement	Alcohol during pregnancy	d	-0.31	9.9e-109	
Educational achievement	Alcohol during pregnancy	e	-0.01	3.7e-01	
Educational achievement	Alcohol during pregnancy	f	-0.01	6.0e-01	
Educational achievement	Alcohol during pregnancy	g	0.05	1.7e-05	
Educational achievement	Alcohol during pregnancy	COVtotal	0.07	1.8e-07	
Educational achievement	Alcohol during pregnancy	COVEduYears	0.02	2.6e-04	
Educational achievement	Alcohol during pregnancy	COVBMI	0	8.5e-01	
Educational achievement	Alcohol during pregnancy	COVSchizophrenia	0	7.2e-01	
Educational achievement	Alcohol during pregnancy	COVres	0.05	1.7e-05	
Educational achievement	Alcohol during pregnancy	Log-likelihood			
Hyperactivity/Inattention	TV usually on	a	0.19	6.8e-33	-26406.9154652039
Hyperactivity/Inattention	TV usually on	b	0.01	5.8e-01	
Hyperactivity/Inattention	TV usually on	c	0.01	3.6e-01	
Hyperactivity/Inattention	TV usually on	d	0.12	3.6e-13	
Hyperactivity/Inattention	TV usually on	e	0.01	4.6e-01	
Hyperactivity/Inattention	TV usually on	f	0	9.3e-01	
Hyperactivity/Inattention	TV usually on	g	0.15	1.0e-19	
Hyperactivity/Inattention	TV usually on	COVtotal	0.18	1.2e-24	
Hyperactivity/Inattention	TV usually on	COVEduYears	0.02	8.9e-09	
Hyperactivity/Inattention	TV usually on	COVBMI	0	6.8e-01	
Hyperactivity/Inattention	TV usually on	COVSchizophrenia	0	9.3e-01	
Hyperactivity/Inattention	TV usually on	COVres	0.15	1.0e-19	
Hyperactivity/Inattention	TV usually on	Log-likelihood			
Hyperactivity/Inattention	Parent smacks/slaps child	a	0.12	2.2e-12	-26396.2835536902
Hyperactivity/Inattention	Parent smacks/slaps child	b	-0.02	3.5e-01	
Hyperactivity/Inattention	Parent smacks/slaps child	c	0.01	6.9e-01	
Hyperactivity/Inattention	Parent smacks/slaps child	d	0.12	1.7e-13	
Hyperactivity/Inattention	Parent smacks/slaps child	e	0.01	4.3e-01	
Hyperactivity/Inattention	Parent smacks/slaps child	f	0	7.8e-01	
Hyperactivity/Inattention	Parent smacks/slaps child	g	0.18	2.2e-24	
Hyperactivity/Inattention	Parent smacks/slaps child	COVtotal	0.2	2.0e-27	
Hyperactivity/Inattention	Parent smacks/slaps child	COVEduYears	0.01	3.9e-06	
Hyperactivity/Inattention	Parent smacks/slaps child	COVBMI	0	5.1e-01	
Hyperactivity/Inattention	Parent smacks/slaps child	COVSchizophrenia	0	8.0e-01	
Hyperactivity/Inattention	Parent smacks/slaps child	COVres	0.18	2.2e-24	
Hyperactivity/Inattention	Parent smacks/slaps child	Log-likelihood			
Hyperactivity/Inattention	Maternal smoking during pregnancy	a	0.07	2.6e-05	-26888.0284422625
Hyperactivity/Inattention	Maternal smoking during pregnancy	b	-0.01	5.9e-01	
Hyperactivity/Inattention	Maternal smoking during pregnancy	c	-0.02	2.8e-01	
Hyperactivity/Inattention	Maternal smoking during pregnancy	d	0.11	2.8e-12	
Hyperactivity/Inattention	Maternal smoking during pregnancy	e	0.01	5.7e-01	
Hyperactivity/Inattention	Maternal smoking during pregnancy	f	-0.01	7.5e-01	
Hyperactivity/Inattention	Maternal smoking during pregnancy	g	0.12	1.3e-08	
Hyperactivity/Inattention	Maternal smoking during pregnancy	COVtotal	0.12	2.8e-09	
Hyperactivity/Inattention	Maternal smoking during pregnancy	COVEduYears	0.01	7.4e-04	
Hyperactivity/Inattention	Maternal smoking during pregnancy	COVBMI	0	6.8e-01	
Hyperactivity/Inattention	Maternal smoking during pregnancy	COVSchizophrenia	0	7.6e-01	
Hyperactivity/Inattention	Maternal smoking during pregnancy	COVres	0.12	1.3e-08	
Hyperactivity/Inattention	Maternal smoking during pregnancy	Log-likelihood			
Hyperactivity/Inattention	Breastfeeding duration	a	-0.17	6.9e-24	-25832.2917211945
Hyperactivity/Inattention	Breastfeeding duration	b	0.03	4.2e-02	
Hyperactivity/Inattention	Breastfeeding duration	c	-0.02	2.0e-01	
Hyperactivity/Inattention	Breastfeeding duration	d	0.12	3.1e-13	
Hyperactivity/Inattention	Breastfeeding duration	e	0.01	7.6e-01	
Hyperactivity/Inattention	Breastfeeding duration	f	0	9.5e-01	
Hyperactivity/Inattention	Breastfeeding duration	g	-0.08	1.4e-06	
Hyperactivity/Inattention	Breastfeeding duration	COVtotal	-0.1	2.7e-09	
Hyperactivity/Inattention	Breastfeeding duration	COVEduYears	-0.02	1.7e-08	
Hyperactivity/Inattention	Breastfeeding duration	COVBMI	0	7.6e-01	
Hyperactivity/Inattention	Breastfeeding duration	COVSchizophrenia	0	9.5e-01	
Hyperactivity/Inattention	Breastfeeding duration	COVres	-0.08	1.4e-06	
Hyperactivity/Inattention	Breastfeeding duration	Log-likelihood			

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Hyperactivity/Inattention	Household income	a	-0.2	4.1e-18	-13354.4515262494
Hyperactivity/Inattention	Household income	b	-0.02	4.8e-01	
Hyperactivity/Inattention	Household income	c	0.01	5.7e-01	
Hyperactivity/Inattention	Household income	d	0.13	2.2e-08	
Hyperactivity/Inattention	Household income	e	0.04	7.5e-02	
Hyperactivity/Inattention	Household income	f	0	9.3e-01	
Hyperactivity/Inattention	Household income	g	-0.15	7.0e-12	
Hyperactivity/Inattention	Household income	COVtotal	-0.18	5.4e-15	
Hyperactivity/Inattention	Household income	COVEduYears	-0.03	2.2e-05	
Hyperactivity/Inattention	Household income	COVBMI	0	5.3e-01	
Hyperactivity/Inattention	Household income	COVSchizophrenia	0	9.3e-01	
Hyperactivity/Inattention	Household income	COVres	-0.15	7.0e-12	
Hyperactivity/Inattention	Household income	Log-likelihood			
Hyperactivity/Inattention	Maternal age first child	a	-0.13	2.1e-15	-26854.2187574908
Hyperactivity/Inattention	Maternal age first child	b	0.01	5.0e-01	
Hyperactivity/Inattention	Maternal age first child	c	-0.03	7.8e-02	
Hyperactivity/Inattention	Maternal age first child	d	0.12	4.1e-13	
Hyperactivity/Inattention	Maternal age first child	e	0.01	6.4e-01	
Hyperactivity/Inattention	Maternal age first child	f	0	9.8e-01	
Hyperactivity/Inattention	Maternal age first child	g	-0.05	9.4e-03	
Hyperactivity/Inattention	Maternal age first child	COVtotal	-0.06	5.7e-04	
Hyperactivity/Inattention	Maternal age first child	COVEduYears	-0.02	2.5e-07	
Hyperactivity/Inattention	Maternal age first child	COVBMI	0	7.0e-01	
Hyperactivity/Inattention	Maternal age first child	COVSchizophrenia	0	9.8e-01	
Hyperactivity/Inattention	Maternal age first child	COVres	-0.05	9.4e-03	
Hyperactivity/Inattention	Maternal age first child	Log-likelihood			
Hyperactivity/Inattention	Paternal age first child	a	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	b	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	c	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	d	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	e	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	f	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	g	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	COVtotal	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	COVEduYears	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	COVBMI	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	COVres	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age first child	Log-likelihood	not decomposed		not decomposed
Hyperactivity/Inattention	Maternal age at child birth	a	-0.13	6.6e-16	-26887.476768777
Hyperactivity/Inattention	Maternal age at child birth	b	0	7.6e-01	
Hyperactivity/Inattention	Maternal age at child birth	c	-0.04	2.3e-02	
Hyperactivity/Inattention	Maternal age at child birth	d	0.12	3.5e-13	
Hyperactivity/Inattention	Maternal age at child birth	e	0.01	6.6e-01	
Hyperactivity/Inattention	Maternal age at child birth	f	0	9.8e-01	
Hyperactivity/Inattention	Maternal age at child birth	g	-0.05	3.6e-03	
Hyperactivity/Inattention	Maternal age at child birth	COVtotal	-0.07	1.5e-04	
Hyperactivity/Inattention	Maternal age at child birth	COVEduYears	-0.02	2.0e-07	
Hyperactivity/Inattention	Maternal age at child birth	COVBMI	0	8.0e-01	
Hyperactivity/Inattention	Maternal age at child birth	COVSchizophrenia	0	9.8e-01	
Hyperactivity/Inattention	Maternal age at child birth	COVres	-0.05	3.6e-03	
Hyperactivity/Inattention	Maternal age at child birth	Log-likelihood			
Hyperactivity/Inattention	Paternal age at child birth	a	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	b	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	c	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	d	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	e	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	f	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	g	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	COVtotal	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	COVEduYears	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	COVBMI	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	COVres	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Paternal age at child birth	Log-likelihood	not decomposed		not decomposed

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Hyperactivity/Inattention	Child age mother returned to work	a	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	b	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	c	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	d	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	e	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	f	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	g	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	COVtotal	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	COVEduYears	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	COVBMI	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	COVres	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Child age mother returned to work	Log-likelihood	not decomposed		not decomposed
Hyperactivity/Inattention	Postnatal depression	a	0.05	6.1e-03	
Hyperactivity/Inattention	Postnatal depression	b	-0.01	4.0e-01	
Hyperactivity/Inattention	Postnatal depression	c	-0.04	2.8e-02	
Hyperactivity/Inattention	Postnatal depression	d	0.12	2.7e-12	
Hyperactivity/Inattention	Postnatal depression	e	0.01	5.4e-01	
Hyperactivity/Inattention	Postnatal depression	f	-0.01	3.9e-01	
Hyperactivity/Inattention	Postnatal depression	g	0.15	8.1e-18	
Hyperactivity/Inattention	Postnatal depression	COVtotal	0.16	1.7e-18	
Hyperactivity/Inattention	Postnatal depression	COVEduYears	0.01	1.5e-02	
Hyperactivity/Inattention	Postnatal depression	COVBMI	0	5.9e-01	
Hyperactivity/Inattention	Postnatal depression	COVSchizophrenia	0	4.4e-01	
Hyperactivity/Inattention	Postnatal depression	COVres	0.15	8.1e-18	
Hyperactivity/Inattention	Postnatal depression	Log-likelihood			-24369.5352712768
Hyperactivity/Inattention	Sickness/complications during pregnancy	a	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	b	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	c	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	d	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	e	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	f	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	g	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	COVtotal	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	COVEduYears	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	COVBMI	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	COVres	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Sickness/complications during pregnancy	Log-likelihood	not decomposed		not decomposed
Hyperactivity/Inattention	Neighbourhood SES	a	-0.13	8.7e-16	
Hyperactivity/Inattention	Neighbourhood SES	b	-0.01	5.0e-01	
Hyperactivity/Inattention	Neighbourhood SES	c	-0.02	1.5e-01	
Hyperactivity/Inattention	Neighbourhood SES	d	0.12	1.9e-12	
Hyperactivity/Inattention	Neighbourhood SES	e	0	9.3e-01	
Hyperactivity/Inattention	Neighbourhood SES	f	0	9.4e-01	
Hyperactivity/Inattention	Neighbourhood SES	g	-0.09	3.6e-08	
Hyperactivity/Inattention	Neighbourhood SES	COVtotal	-0.11	1.7e-10	
Hyperactivity/Inattention	Neighbourhood SES	COVEduYears	-0.02	5.9e-07	
Hyperactivity/Inattention	Neighbourhood SES	COVBMI	0	9.4e-01	
Hyperactivity/Inattention	Neighbourhood SES	COVSchizophrenia	0	9.4e-01	
Hyperactivity/Inattention	Neighbourhood SES	COVres	-0.09	3.6e-08	
Hyperactivity/Inattention	Neighbourhood SES	Log-likelihood			-25798.8872643513
Hyperactivity/Inattention	Maternal education	a	-0.26	2.0e-58	
Hyperactivity/Inattention	Maternal education	b	0.02	3.1e-01	
Hyperactivity/Inattention	Maternal education	c	-0.01	6.2e-01	
Hyperactivity/Inattention	Maternal education	d	0.12	6.7e-13	
Hyperactivity/Inattention	Maternal education	e	0.01	7.3e-01	
Hyperactivity/Inattention	Maternal education	f	0	8.9e-01	
Hyperactivity/Inattention	Maternal education	g	-0.13	4.4e-16	
Hyperactivity/Inattention	Maternal education	COVtotal	-0.16	5.3e-22	
Hyperactivity/Inattention	Maternal education	COVEduYears	-0.03	7.7e-10	
Hyperactivity/Inattention	Maternal education	COVBMI	0	7.3e-01	
Hyperactivity/Inattention	Maternal education	COVSchizophrenia	0	8.9e-01	
Hyperactivity/Inattention	Maternal education	COVres	-0.13	4.4e-16	
Hyperactivity/Inattention	Maternal education	Log-likelihood			-26670.2281631161

Child outcome	Environmental measure	Parameter	Standardized estimate	P	Model fit
Hyperactivity/Inattention	Paternal education	a	-0.27	6.3e-58	-25054.4629887296
Hyperactivity/Inattention	Paternal education	b	0.01	7.5e-01	
Hyperactivity/Inattention	Paternal education	c	0.01	7.0e-01	
Hyperactivity/Inattention	Paternal education	d	0.12	7.3e-13	
Hyperactivity/Inattention	Paternal education	e	0.01	7.5e-01	
Hyperactivity/Inattention	Paternal education	f	-0.01	6.0e-01	
Hyperactivity/Inattention	Paternal education	g	-0.12	3.1e-13	
Hyperactivity/Inattention	Paternal education	COVtotal	-0.15	9.2e-20	
Hyperactivity/Inattention	Paternal education	COVEduYears	-0.03	7.3e-10	
Hyperactivity/Inattention	Paternal education	COVBMI	0	8.0e-01	
Hyperactivity/Inattention	Paternal education	COVSchizophrenia	0	7.7e-01	
Hyperactivity/Inattention	Paternal education	COVres	-0.12	3.1e-13	
Hyperactivity/Inattention	Paternal education	Log-likelihood			
Hyperactivity/Inattention	Number books in the home	a	-0.19	3.1e-13	-11768.5601962136
Hyperactivity/Inattention	Number books in the home	b	0	8.5e-01	
Hyperactivity/Inattention	Number books in the home	c	0.01	7.2e-01	
Hyperactivity/Inattention	Number books in the home	d	0.13	4.2e-07	
Hyperactivity/Inattention	Number books in the home	e	0.05	6.9e-02	
Hyperactivity/Inattention	Number books in the home	f	0.01	6.7e-01	
Hyperactivity/Inattention	Number books in the home	g	-0.13	8.1e-07	
Hyperactivity/Inattention	Number books in the home	COVtotal	-0.16	2.6e-08	
Hyperactivity/Inattention	Number books in the home	COVEduYears	-0.02	1.7e-04	
Hyperactivity/Inattention	Number books in the home	COVBMI	0	8.5e-01	
Hyperactivity/Inattention	Number books in the home	COVSchizophrenia	0	7.7e-01	
Hyperactivity/Inattention	Number books in the home	COVres	-0.13	8.1e-07	
Hyperactivity/Inattention	Number books in the home	Log-likelihood			
Hyperactivity/Inattention	Alcohol during pregnancy	a	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	b	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	c	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	d	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	e	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	f	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	g	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	COVtotal	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	COVEduYears	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	COVBMI	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	COVSchizophrenia	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	COVres	not decomposed	not decomposed	not decomposed
Hyperactivity/Inattention	Alcohol during pregnancy	Log-likelihood	not decomposed		not decomposed

**Supplementary Table S3: Path estimates and fit statistics for decomposition of covariance between environmental exposures and developmental outcomes**

Covariation between environmental exposures and developmental outcomes captured by trait-associated polygenic variation.

EDU, BMI, and SCZ represent polygenic scores for years of education, Body-mass Index, and schizophrenia, adjusted for 30 principal components and genotyping array and plate

ENV represents the environmental exposure

DEV represents the developmental outcome (educational achievement, conduct problems, inattention/hyperactivity)

The total covariance estimated as  $Cov_{total} = (a * d) + (b * e) + (c * f) + g$  is decomposed into the effect of the education score:  $Cov_{EDU} = (a * d)$ , that of the BMI score:  $Cov_{BMI} = (b * e)$ , that of the schizophrenia score  $Cov_{SCZ} = (c * f)$ , and residual covariance  $g$ .

We only decomposed covariance where the standardized coefficient of the total covariance was  $>.05$  or  $< -.05$ .

**[see the following pages]**



### **Supplementary Methods S1: Genotyping protocol and quality control**

DNA for 4,649 individuals was extracted from saliva and buccal cheek swab samples and hybridized to HumanOmniExpressExome-8v1.2 genotyping arrays at the Institute of Psychiatry, Psychology and Neuroscience Genomics & Biomarker Core Facility. The raw image data from the array were normalized, pre-processed, and filtered in GenomeStudio according to Illumina Exome Chip SOP v1.4. (<http://confluence.brc.iop.kcl.ac.uk:8090/display/PUB/Production+Version%3A+Illumina+Exome+Chip+SOP+v1.4>). 869 multi-mapping SNPs were removed. The ZCALL (4) was used to augment the genotype calling for samples and SNPs that passed the initial QC.

DNA from 3,665 samples was extracted from buccal cheek swabs and genotyped at Affymetrix, Santa Clara, California, USA. Samples were successfully hybridized to AffymetrixGeneChip 6.0 SNP genotyping arrays ([http://www.affymetrix.com/support/technical/datasheets/genomewide\\_snp6\\_datasheet.pdf](http://www.affymetrix.com/support/technical/datasheets/genomewide_snp6_datasheet.pdf)) using experimental protocols recommended by the manufacturer (Affymetrix Inc., Santa Clara, CA). The raw image data from the arrays were normalized and pre-processed at the Wellcome Trust Sanger Institute, Hinxton, UK for genotyping as part of the Wellcome Trust Case Control Consortium 2 (<https://www.wtccc.org.uk/cc2/>) according to the manufacturer's guidelines ([http://www.affymetrix.com/support/downloads/manuals/genomewidesnp6\\_manual.pdf](http://www.affymetrix.com/support/downloads/manuals/genomewidesnp6_manual.pdf)). Genotypes for the Affymetrix arrays were called using CHIAMO ([https://mathgen.stats.ox.ac.uk/genetics\\_software/chiamo/chiamo.html](https://mathgen.stats.ox.ac.uk/genetics_software/chiamo/chiamo.html)).

After initial quality control and genotype calling, the same quality control was performed on the samples genotyped on the Illumina and Affymetrix platforms separately using PLINK(5,6), R (7), and vcftools (8).

Samples were removed from subsequent analyses based on call rate (<0.99), suspected non-European ancestry, heterozygosity, array signal intensity, and relatedness. SNPs were excluded if the minor allele frequency was <0.5%, if more than 1% of genotype data were missing, or if the Hardy Weinberg  $p$ -value was lower than  $10^{-5}$ . Non-autosomal markers and indels were removed. Association between the SNP and the platform, batch, or plate on which samples were genotyped was calculated; SNPs with an effect  $p$ -value less than  $10^{-3}$  were excluded. A total sample of 6,710 samples, with 3,617 individuals and 600,034 SNPs genotyped on Illumina and 3,093 individuals and 525,859 SNPs genotyped on Affymetrix remained after quality control.

Genotypes from the two platforms were separately imputed using the Haplotype Reference Consortium (9) and Minimac3 1.0.13 (10,11) available on the *Michigan Imputation Server* as reference data. A series of quality checks was performed before merging data from the two platforms' imputation (e.g. platform effects, allele frequencies by imputation quality). For the present analyses, we limited our analyses to variants genotyped or imputed at info >.70 on both platforms, allele frequency difference between platforms smaller than 5%, and Hardy Weinberg  $p$ -value was greater than  $10^{-5}$ . Using these criteria, 7,581,516 genotyped and well-imputed SNPs were retained for the analyses.

We performed principal component analysis on a subset of 42,859 common (MAF>5%) autosomal HapMap3 SNPs (12), after stringent pruning to remove markers in linkage disequilibrium ( $r^2 > 0.1$ ) and excluding high linkage disequilibrium genomic regions to ensure that only genome-wide effects were detected.

### **Supplementary Methods S2: Polygenic score creation**

Using these summary statistics, we constructed polygenic scores as the weighted sums of the individual's genotype across all SNPs. The scores are calculated as

the weighted sums of individual  $i$ 's SNPs:  $GPS_{ki} = \sum_{j=1}^m \hat{\beta}_{kj} g_{kji}$

$GPS_{ik}$  represents the individual  $i$ 's polygenic score based on summary statistics

from GWAS<sub>k</sub>.  $\hat{\beta}_{kj}$  is an estimate of marker  $j$ 's effect size for discovery trait  $k$ , that is, the effect of having one more copy of the reference allele at SNP<sub>kj</sub>.  $g_{kji}$  is individual  $i$ 's genotype at marker  $j$  for discovery trait  $k$ , coded as having 0, 1, or 2 copies of the reference allele at marker  $kj$ .

Conventionally, the  $\hat{\beta}_{kj}$  for SNP<sub>j</sub> is simply the GWAS  $k$  estimate for SNP<sub>jk</sub>. However, due to local linkage disequilibrium (LD) (i.e. correlation) between SNPs,  $\hat{\beta}_{kj}$  captures any effects of the SNP<sub>kj</sub> and its correlates. Therefore, to correct for the multiple counting problem of effectively counting the effects of markers that are in LD with other markers multiple times, conventionally, markers are thinned down via the process of 'clumping' to a set of uncorrelated markers prior to polygenic score creation. In this study, to avoid a reduction in predictive accuracy and loss of information caused by the conventional approach of LD-based marker pruning and applying a P-value threshold to association statistics, we used *LDpred* (13) (version 0.9.09; <https://github.com/bvilhjal/ldpred>). *LDpred* is a Bayesian approach that infers the posterior mean effect size of each marker by adjusting the effect size from the discovery GWAS using a prior on effect size and information on the LD between the SNPs from a reference panel to obtain a posterior estimate of the causal effect for SNP<sub>jk</sub> independent of the effects of other SNPs. Hence, the *LDpred* GPS for individual  $i$  for GWAS  $k$  is the sum of  $i$ 's genotypes across all SNPs used in the analyses, weighted by the *LDpred* estimates of the genotype effects. The score represents an unbiased estimate of the true genetic burden for individual  $i$  for trait  $k$  (13), albeit with low precision.

As recommended by the *LDpred* developers (13), we used the target sample genotype data as the LD reference panel. *LDpred* models a prior probability for the fraction of markers assumed to be causal using a Gaussian mixture weight. We created *LDpred* scores for the following prior probabilities of fraction of causal markers: 0.01, 0.1, 1. This limited number of priors was chosen so as to test different priors of polygenicity while avoiding excessive multiple testing and within-sample parameters optimization.

### **Supplementary Methods S3: Description of environmental behavioral measures**

#### **Maternal & paternal occupation**

Parental occupation was assessed by the Standard Occupational Classification (1,2). At first contact when the children were on average 18 months old, parents were asked to report their level of education, which was then coded as: 1=manager, 2=professional, 3=technical, 4=clerical, 5=craft, 6=personal, 7=sales, 8=plant, 9=unskilled.

#### **Maternal & paternal education**

At first contact when the children were on average 18 months old, parents were asked to report their level of education, which was then coded as: 1=none, 2=O/GCSE grade D-G or CSE grade 2-5, 3=O/GCSE grade A-C or CSE grade 1, 4=A/S level, 5=HNC, 6=HND, 7=undergraduate degree, 8=postgrad.

***Duration of breastfeeding***

At first contact when the children were on average 18 months old, mothers were asked a whether they had breastfed (yes/no) and how long they had breastfed (in days).

***Maternal smoking during pregnancy***

At first contact when the children were on average 18 months old, mothers were asked a whether they smoked during pregnancy (yes/no) and "How many cigarettes did you smoke each day, on average?".

***Paternal alcohol consumption during pregnancy***

At first contact when the children were on average 18 months old, mothers were asked whether they drank alcohol during pregnancy (yes/no) and "How many units of alcohol did you drink, per week, on average? (1 unit = 1 glass of wine, OR, 1 measure of spirits, OR, ½ a pint of beer)". The answer was provided as a free numeric.

***Maternal age at birth of first child***

At first contact, when the children were on average 18 months old, parents were asked for their children's and their own date of birth. The date of birth of biological mother and the date of birth of oldest biological sibling (i.e. having the same parents as study participant) were used to calculate age of biological mother at birth of oldest sibling.

***Maternal age at birth of child***

At first contact, when the children were on average 18 months old, parents were asked for their children's and their own date of birth. The date of birth of biological mother and the date of birth of the study participant were used to calculate age of biological mother at birth of study participant.

***Paternal age at birth of first child***

At first contact, when the children were on average 18 months old, parents were asked for their children's and their own date of birth. The date of birth of biological father and the date of birth of oldest biological sibling (i.e. having the same parents as study participant) were used to calculate age of biological father at birth of oldest sibling.

***Paternal age at birth of child***

At first contact, when the children were on average 18 months old, parents were asked for their children's and their own date of birth. The date of birth of biological father and the date of birth of the study participant were used to calculate age of biological father at birth of study participant.

***Mother's return to work after child birth***

Assessed as age of study participant in days when mother returned to work after birth. At first contact, when the children were on average 18 months old, mothers were asked "Have you started working or studying since the birth of your twins?" [yes/no]; "If YES, how old were the twins when you began working or studying?"

***Maternal depression***

The mean (using mean imputation where missing) of the following standardized scales:

Maternal depression was assessed by maternal self-report, at two time points; when study participants were on average 3 years old and when they were on average 3 years old. Maternal depression was assessed using the Edinburgh Postnatal Depression Scale (EPDS), a brief measure of depressed affect, originally used in a large-scale epidemiological study of women's psychological health following childbirth (16). The scale is derived as a mean of 10 items (e.g., "I have

felt sad and miserable”) assessed using a Likert scale ranging from 0 (not at all) to 3 (yes, most of the time). The scale has been validated against diagnostic criteria in the postpartum period (17).

### ***Sickness or complications during pregnancy***

Sum of endorsed items. At first contact, when the children were on average 18 months old, mothers were asked: “During your pregnancy did you experience any of the following: Amniocentesis; High blood pressure; Diabetes; Toxaemia/pre-eclampsia; Vaginal bleeding; Rubella/German Measles; Slow growth of baby/ies; Waters breaking more than 11 hours before labor”.

### ***Parental income***

The mean (using mean imputation where missing) of the following standardized items:

- Child age 9; parent-reported. “On average, what is your household’s income (per year, before tax)”. Scale: 1=under £4500, 2=£4500-9499, 3=£9500-15499, 4=£15500-17499, 5=£17500-24999, 6=£25000-29999, 7=£30000-39999, 8=£40000-49999, 9=£50000-74999, 10=£75000-99999, 11=£100,000 or more
- Child age 12; parent-reported. “What is your household’s income (per year, before tax)? This should include the income for all adults in your household”. Scale: 1=Under £5,000, 2=£5,000 to £9,999, 3=£10,000 to £14,999, 4=£15,000 to £19,999, 5=£20,000 to £24,999, 6=£25,000 to £29,999, 7=£30,000 to £39,999, 8=£40,000 to £49,999, 9=£50,000 to £74,999, 10=£75,000 to £100,000, 11=Over £100,000

### ***Neighborhood-level socioeconomic***

*Neighborhood-level socioeconomic status* at birth was assessed using geodemographic classifications developed by ACORN [A Classification Of Residential Neighborhoods], developed by CACI Inc. for commercial use in the United Kingdom). ACORN coding scheme was created using over 400 variables from the 2001 census and an extensive consumer research database (e.g., age, educational qualifications, unemployment, single-parent status, housing tenure and dwelling type, and car availability) to give a comprehensive picture of socioeconomic differences between areas. The ACORN classifications are provided at the Enumeration District (ED) level (~150 households). Using hierarchical cluster analysis ACORN grouped EDs into 56 neighborhood types and five distinct and homogeneous ordinal groups ranging from ‘Wealthy Achievers’ with high incomes, large single-family houses and access to many amenities to ‘Hard Pressed’ neighborhoods characterized by government-subsidized housing estates, low incomes, high unemployment and single parents. The ACORN codes (released in 1991) were mapped to the postcodes of study participant’s families at first contact shortly after participants were born. In the current analyses we used the a reversely coded variable of “neighborhood type” (1-54), with higher values representing a wealthier demographic.

### ***Television watching***

The mean (using mean imputation where missing) of the following standardized items:

- Child age 3; parent-reported: “There is usually a television turned on somewhere in our home”. Scale: 1=untrue, 2, 3, 4, 5=true
- Child age 4; parent-reported: “There is usually a television turned on somewhere in our home”. Scale: 1=untrue, 2, 3, 4, 5=true
- Child age 9; parent-reported: “There is usually a television turned on somewhere in our home”. Scale: 0=not true, 1=somewhat true, 2=certainly true.
- Child age 9; child-reported: “usually a TV turned on”. Scale: 0=not true, 1=quite true, 2=very true.

- Child age 12; parent-reported. When prompted with the following: "Think about how things have been in the last 3 months." "There is usually a television turned on somewhere in our home". Scale: 0=not true, 1=somewhat true, 2=certainly true
- Child age 12; child-reported. When prompted: "Think about how things have been in the last 3 months." "There is usually a television turned on somewhere in our home". Scale: 0=not true, 1=quite true, 2=very true
- Child age 14; parent-reported. When prompted: "Think about how things have been in the last 3 months". "There is usually a television turned on somewhere in our home". Scale: 0=not true, 1=somewhat true, 2=certainly true
- Child age 14; child-reported. When prompted: "Think about how things have been in the last 3 months." "There is usually a television turned on somewhere in our home". Scale: 0=not true, 1=quite true, 2=very true
- Child age 16; child-reported. When prompted: "Think about how things have been in the last 3 months." "There is usually a television turned on somewhere in our home". Scale: 0=not true, 1=quite true, 2=very true

### ***Smacking or slapping***

The mean (using mean imputation where missing) of the following standardized items:

- Child age 3; parent-reported. When prompted with the following: "Parents have many ways of disciplining their children, and different children need different sorts of discipline. Below, there are some discipline methods that parents often use". "Give a smack or slap". Scale: 1=never, 2, 3=sometimes, 4, 5=usually
- Child age 4; parent-reported. When prompted with the following: "Parents have many ways of disciplining their children, and different children need different sorts of discipline. Below, there are some discipline methods that parents often use. Please show us how often you use each method, for each of your twins". "Give a smack or slap". Scale: 1=never, 2, 3=sometimes, 4, 5=usually
- Child age 9; parent-reported. When prompted with the following: "When my child misbehaves I use the following methods". "Give a smack". Scale: 0=rarely or never, 1=sometimes, 2=often
- Child age 9; child-reported "When I misbehave: I am smacked or slapped". Scale: 0=not true, 1=quite true, 2=very true
- Child age 12; parent-reported. When prompted with the following: "Parents have many ways of helping their children behave well and different children need different sorts of discipline. Here are some methods which parents commonly use. When my child misbehaves I use the following methods: Give a smack ". Scale: 0=rarely or never, 1=sometimes, 2=often
- Child age 12; child-reported. When prompted with the following: "When you are answering these questions it would help us if you could think about the parent you spend the most time with." "When I misbehave I am smacked or slapped". Scale: 0=not true, 1=quite true, 2=very true
- Child age 14; parent-reported. When prompted with the following: "Parents have many ways of helping their children behave well and different children need different sorts of discipline. Here are some methods which parents commonly use. When my child misbehaves I use the following methods: Give a smack". Scale: 0=rarely or never, 1=sometimes, 2=often
- Child age 14; child-reported. When prompted with the following: "When you are answering these questions it would help us if you could think about the parent you spend the most time with: When I misbehave I am smacked or slapped. Scale: 0=not true, 1=quite true, 2=very true
- Child age 16; child-reported. When prompted with the following: "Please think about the parent or guardian you spend the most time with when you answer these questions: When I misbehave I am told off or shouted at". Scale: 0=not true, 1=quite true, 2=very true

**Number of books in the home**

When study participants were on average 9 years old, parents were asked: "How many books (child AND adult) do you have in your home?", Scale: 0=0, 1=1-10, 2=11-25, 3=26-50, 4=51-99, 5=100 or more

**Educational achievement**

Educational achievement was operationalized as performance on the standardized United Kingdom General Certificate of Secondary Education (GCSE), taken by almost all (>99%) pupils at the end of compulsory education at typically at the age of 16 years. English, mathematics and science are compulsory subjects. Five or more GCSEs with grades A\*–C are required for further education, including GCSE English and GCSE mathematics. The joint performance on these three compulsory subjects determines admission to further education and influences employability.

GCSE grades were obtained from the UK National Pupil Database (NPD) (18). Subjects were graded from 4 (G; the minimum pass grade) to 11 (A\*; the best possible grade). 'Ungraded/failed' exams were coded as 0.

For 1,068 individuals in the sample for whom no NPD data were available, we used self- or parent-reported grades. These data were collected by questionnaires sent by mail and by telephone interview of parents and twins themselves (19). After completed forms were received from the families, the grades were coded from 11 (the highest grade: A\*) to 4 (the lowest pass grade: G). No information about the occurrence and number of failed results was available for the self- or parent-reported data. For 9,255 individuals (and 3,584 within the present genotyped sample), self- or parent-reported GCSE results were verified using the data obtained from the UK National Pupil Database (18), yielding correlations of 0.99 for mathematics, 0.98 for English and 0.97 for science.

The GCSE measure for the present analyses was the mean grade of the three compulsory core subjects, mathematics, English (maximum grade of 'English Language' and 'English Literature'), and science (maximum of any science subjects taken). Scores on the three compulsory core subjects were highly correlated ( $r = 0.71$ – $0.79$ ). There was no significant effect of sex on GCSE ( $R^2 < 0.001$ ;  $P = 0.051$ ).

**Conduct problems and hyperactivity/inattention**

Conduct problems and hyperactivity/inattention problems were measured by the Strength and Difficulties (SDQ) (20–22) questionnaire, completed by parents when individuals were aged 16 (mean=16.33; SD=0.68). The SDQ Hyperactivity-Inattention scale is a dimensional and developmental measure of child mental health. Five items, tapping three key symptom domains of attention-deficit/hyperactivity disorder (ADHD): inattention (2 items), hyperactivity (2 items), and impulsiveness (1 item). 3-point Likert scale (Not true; Quite true; Very true). Example: My child is restless, overactive, and cannot stay still for long. The SDQ Conduct scale is a dimensional and developmental measure of child mental health. Five items measuring externalizing behavior problems on 3-point Likert scale (Not true; Quite true; Very true). For example: "Often fights with other children or bullies them"; "Often has temper tantrums or hot tempers". Scale composites were created as the mean of the five items, respectively. The scale composites were regressed on sex and age at assessment before subsequent analyses.



#### ***Supplementary Methods S4: Robustness analyses for prediction of parental qualification level***

To test the robustness of the estimated variance explained in maternal education by the polygenic score for years of schooling (6.8% in the single-score model, 6.5% in the multi-score model), we conducted some additional tests:

The polygenic score for 'years of schooling' used here explains 9.8% of the variation in children's educational achievement (mean exam grades at the end of compulsory education, ~age 16). Note that the parental 'education phenotype' (i.e. qualification level) used here is closer to that of the discovery GWAS (i.e. years of schooling) than the child phenotype, which could explain why the variance in the latter is not quite twice that of the first.

The same polygenic score for 'years of schooling' explained 4.5% of the variance in children's 'university yes/no' in our sample, which could be conceptualized as a cruder phenotype than 'mean exam grade'. Therefore, another possible explanation for the higher  $R^2$  for 'mean exam grade' at the end of compulsory education in the current sample compared to the Okbay (2016)(23) prediction could be the 'crudeness' of the measure.

A polygenic score for 'years of schooling' based on the conventional pruning + thresholding approach using all SNPs explains 6.4% of variance in children's mean exam grades, 4.5% in maternal education, and 4.1% in paternal education. Next, we tested for potential inflation due to possible relatedness between the study samples and samples in the UB Biobank. We re-created a polygenic score for education based on the 'years of education' GWAS excluding the UK Biobank samples, which make up ~1/3 of the overall sample. Consistent with the reduced sample size of the discovery GWAS, the estimates dropped by 1/3 (or less, but not more): 4.2% of variance in children's mean exam grades, 3.8% in maternal education, and 2.9% in paternal education.

Children's polygenic score for BMI explains 5.3% of the variance in their BMI (~age 16), and 2.8% in their father's and 2.6% in the mother's BMI.

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