More than Nature and Nurture, indirect genetic effects on children's academic achievement are consequences of dynastic social processes

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Abstract (147 words)

Families transmit genes and environments across generations. When parents' genetics affect their children's environments, these two modes of inheritance can produce an "indirect genetic effect." Such indirect genetic effects may account for up to half of the estimated genetic variance in educational attainment. We tested if indirect genetic effects reflect within-nuclear-family transmission ("genetic nurture") or instead a multi-generational process of social stratification ("dynastic effects"). We analyzed indirect genetic effects on children's academic achievement in their 5^{th}-9^{th} years of schooling in N=37,117 parent-offspring trios in the Norwegian Mother, Father, and Child Cohort Study (MoBa). We used pairs of genetically-related families (parents were siblings, children were cousins; N=10,913) to distinguish within-nuclear-family genetic-nurture effects from dynastic effects shared by cousins in different nuclear families. We found that indirect genetic effects on children's academic achievement cannot be explained by processes that operate exclusively within the nuclear family.

Introduction

Genetically-informed research designs offer strong evidence that education is transmitted across generations via the inheritance of environmental advantage. Adoption[1], twin[2], molecular genetic[3], and genome wide association studies (GWAS)[4–6] all offer evidence that the intergenerational transmission of educational attainment occurs via both genetic and environmental (i.e. social) mechanisms (Table 1). Studies of adoptees show that children resemble their adoptive (social) parents in education, despite not being genetically related to them[7]. Studies of twins reveal educational similarities within monozygotic and dizygotic pairs that are in line with a role for both the genome and the environment[8]. Molecular genetics studies have also established evidence for environmental mechanisms of intergenerational transmission of educational attainment (EA)[9,10]. Molecular-genetic studies of parent-offspring trios, of adopted parent-child dyads, and of biological siblings all show that people's EA is associated with the genetic variants they did *not* inherit—an association that can only operate via the environment/social context[11–14].

A new wave of molecular genetic studies measures genetic correlations with EA using polygenic indices (PGIs). The PGI method uses results from GWAS to summarize information about hundreds of thousands of genetic variants associated with a target trait or behavior into a single number for each research participant. Taken at face value, PGIs based on GWAS of EA can predict as much as 12-16% of variation in EA in independent, population-based samples[15], a level of explanatory power similar to parental education. In these studies, PGIs are measured from DNA collected from the same individuals whose education is being measured. However, PGI associations with EA reflect more than direct genetic influences on the development of characteristics that promote success in school. Studies of gene-environment correlations reveal that children's EA PGIs are correlated with environments they inherit from their parents, including the social and economic circumstances of their families and neighborhoods[14,16,17]. EA PGIs therefore measure not just a child's genetic background, but their environment as well.

EA PGIs are associated with not just educational outcomes, but a range of social and economic behaviors, including where and how far people move from home, who they have children with, and how they parent[16–19]. A parent generation's EA PGIs therefore become their children's environment. In family-based PGI studies, researchers can separate out the effects of genetics that are passed on from parents to children (transmitted genotypes) from those that parents' possess, but which their children do not inherit (non-transmitted genotypes). These studies find

that children's EA is influenced by PGIs based on both the transmitted and non-transmitted genotypes[11,12]. The effects of the non-transmitted genotypes reflect a process of inheritance that is mediated by the environment. These "indirect" genetic effects will be detected in GWAS and subsequently affect downstream PGI analyses of EA[20]. Indirect genetic effects are also viewed as a means to study how parental traits affect childhood outcomes, while accounting for the direct genetic effects on offspring outcomes[21].

Evidence for indirect genetic effects on EA come from PGI studies of siblings and adoptees. In sibling studies, GWAS of educational differences between siblings estimate lower heritability as compared to GWAS of unrelated individuals[4]. PGI studies based on these GWAS find that effect-sizes for PGIs based on sibling-difference GWAS are smaller than effect-sizes for PGIs based on between-family GWAS[6,22]. In adoption studies, two findings stand out. First, adoptive parents' PGIs are associated with their adopted children's outcomes[23], an association that could not be mediated by direct genetic transmission. Second, PGI effect-sizes are larger for children living with their biological parents than for adoptees who live with social parents to whom they are not genetically related[24]. A key difference between these two groups of children is that the adoptee's PGIs are uncoupled from environments correlated with their parents' genotypes.

While there is consistent evidence for the presence of indirect genetic effects on EA, the mechanisms that produce these effects remain unclear. Among the most evocative descriptions of indirect genetic effects on EA are "Genetic nurture" and "dynastic effects"[11,25]. "Genetic nurture" invokes the transmission of skills and values from parents to children within nuclear families via "nurturing" parenting behaviors. Evidence for genetic nurture-type mechanisms comes from studies that find parenting behaviors mediate indirect-genetic-effect associations of parental genotypes with their children's educational outcomes[26]. The term "dynastic effects" invokes the transmission of wealth and social status within family lineages across generations. Evidence for dynastic-type mechanisms comes from studies that show multi-generational socioeconomic stratification correlated to the parental genotype[22], assortative mating[27–29], and subtle population stratification[30,31].

Indirect genetic effects are defined as the association of one individual's genotype with another individual's phenotype, above and beyond that individual's own genotype. Within the regression framework, indirect genetic effects on EA are estimated by including the child's genotype in a model testing the association between their parents' genotype and the child's EA. The control

for the child's genotype isolates the environmentally-mediated portion of the effect of the parent's genotype. We define nurture effects as the consequence of mechanisms, operating within the nuclear family, flowing from parental actions or status that introduce a correlation between parental genotypes and child outcomes above and beyond the effect of the genotypes transmitted to the child. We negatively define "dynastic effects" as any social or historical process that introduces a correlation between parental genotype and offspring outcomes that is not nurture, as such it includes processes like assortative mating and population stratification. Assortative mating may contribute to indirect effects by capturing the genetic component of the phenotype with which non-transmitted alleles of the parents are correlated.[32] Population stratification occurs when differences in genotype frequency spuriously correlate with environmental differences, and this induces confounding between genotype and outcome. We choose these specific definitions of nurture and dynastic effects as in our design we can sharply distinguish nurture from other causes of indirect genetic effects, but we cannot directly differentiate between other mechanisms behind the indirect effects.

An extended-pedigree design that includes multiple families in which some of the parents are siblings makes possible a further decomposition of the effect of the parent's genotype. In the extended-pedigree design, the indirect genetic effect isolated by the control for the child's genotype can be further divided into two components: (1) the between-family indirect genetic effect, identified as the effect of the average genotype among the siblings in the parental generation, and (2) the within-family indirect genetic effect, identified as the effect of the deviation of the parent's genotype from their sibship average. Within the regression framework, this is accomplished by including the parental-sibship-average genotype as a covariate in the model. This covariate effectively captures the effects of the grandparental genotype as well as effects of any environments that are shared within the extended-family pedigree (the parent and their siblings) and correlated to genotype. This design further includes a control for subtle population stratification, as the parent and their sibling have identical ancestry. An alternate specification is to regress the child's educational attainment on their own genotype, their parents genotype and their uncle or aunts' genotype. If the parental genotype correlates with the child's outcome because of nurture in the nuclear family, the genotype of the child's aunt/uncle should be independent from the child's outcome conditional on the parents genotype.

Within the extended-pedigree genetic-nurture model, the within-family indirect genetic effect represents "nurture", i.e., environmentally-mediated effects operating within the nuclear family

environment. This could include effects mediated by parenting behaviors or direct investments by parents in their children. In parallel, the estimate of the between-family indirect genetic effect captures both indirect effects that operate via "dynastic transmission" and those that act via nurture. This could include effects mediated by multigenerational stratification in environments. Between family indirect genetic effects could also be a function of a bias introduced in the estimated relations between genotype and phenotype introduced by people systematically selecting mates that are similar in terms of education or related traits ("assortative mating") across multiple generations. This bias does not persist within families. Therefore assortment among spouses would introduce a between family indirect genetic effect but not a within family indirect genetic effect.

We conducted extended-pedigree analysis of indirect genetic effects on academic achievement in the Norwegian Mother, Father, and Child Cohort Study (MoBa), in which both children and their parents are genotyped, and which includes over 10,000 sibling pairs in the parental generation. MoBa recorded children's grade-5, -8, and -9 standardized test scores on three subjects (reading comprehension in Norwegian [for almost all children their first language], math, English). We computed four PGIs from the most recent GWASs of EA and related phenotypes; a PGI for EA (GWAS N > 3 million)[15], PGIs for cognitive- (GWAS N = 257,700) and non-cognitive-skill (GWAS N = 510,795) contributions to EA[33], and a PGI based on a GWAS of EA performed within sibling pairs (GWAS N = 128,777)[4].

We structure our analysis around four models (outlined in detail in the methods section). We first establish that the children's own PGI's are related to their academic achievement in this sample (model 1). Next, we establish the presence of indirect genetic effects following the standard approach of regressing children's achievement on parental PGIs while conditioning on children's own PGIs (model 2). Then, in order to test whether the indirect effects reflect genetic nurture or dynastic effects, we specify a model that includes the mean of one parent and sibling PGIs, the parent-sibling's deviation from that mean, and the PGI of the parent that does not have a sibling in the data (model 3). The presence of a within family indirect effect is consistent with nurture-like processes, while its absence in the presence of a between family indirect effect is consistent with dynastic-like processes. Finally, we consider an alternative specification where the child's achievement is regressed on their own PGI, their parents' PGI's and the PGI of a sibling of one of the parents (i.e. the child's aunt's or uncle's PGI). In this final model, the logic is

that the PGI of the aunt or uncle would not relate to the child's achievement through nurture within the nuclear family (model 4).

Results

Figure 1 shows results from all four models estimated on the parent-sibling sample, with numerical results available in Supplementary Tables 2-4.

Associations of children's PGIs with academic achievement

In the MoBa child cohort included in our analysis, the effect-size (standardized beta) for the association of the EA4 PGI with academic achievement was 0.24 ($t(10287) = 30.3$; SE = 0.008; $p<0.001$). For the PGIs of cognitive (Cog) and non-cognitive (NonCog) contributions to education, which were analyzed as concurrent predictors, effect-sizes were 0.26 ($t(10318) = 32.9$; SE=0.008; $p<0.001$) for Cog and 0.14 ($t(10281) = 17.1$; SE=0.008; $p<0.001$) for Non-Cog. For the PGI from the within-family GWAS of EA (WFEA), the effect-size was 0.17 ($t(10315) = 22.1$; SE=0.008; $p<0.001$).

Indirect genetic effect estimates from parent-offspring data

In all models that include an indirect genetic effect, the direct genetic effects remained significant, but were attenuated, with standardized betas that were reduced by 15% - 35% compared to models that did not include indirect genetic effects (see Figure 1 and Supplementary Tables S2-S4 for numerical results). The parent-offspring model (model 2) includes PGIs for parents and their child as concurrent predictors of the child's academic achievement. In these models, the effect-estimate for the parental PGIs can be interpreted as an indirect genetic effect (because directly inherited genetic influences are captured by the child's PGI). Effect-sizes for indirect genetic effects were modest, but in the expected direction and statistically different from zero at the alpha=0.05 level. For the EA4 PGI, effect-sizes for fathers and mothers were 0.05 (mothers: $t(10271) = 5.22$; SE=0.01; $p<0.001$; fathers: $t(10293) = 4.72$; SE=0.01; $p<0.001$); for the within-family GWAS PGI, the effect-size for fathers was 0.04

(t(10283) = 4.2; SE=0.02; p<0.001) and for mothers was 0.05 (t(10341) = 4.7; SE=0.01; p<0.001). For the Cog and Non-Cog PGIs, which were tested in the same model, Cog effect-sizes were 0.03 (t(10277) = 3.3, SE=0.01, p<0.001) for fathers and 0.04 (t(10295) = 4.0, SE=0.01, p<0.001) for mothers and Non-Cog effect-sizes were 0.05 (t(10285) = 4.8, SE=0.01, p<0.001) for fathers and 0.04 (t(10267) = 4.1, SE = 0.01, p<0.001) for mothers. The model confirms an indirect genetic effect.

Indirect genetic effects estimates from extended pedigrees

Models 3 and 4 are extended-family models. Model 3 includes PGIs for parents and their child as well as the mean PGI for parental siblings as concurrent predictors of the child's academic achievement. In model 3, the estimate for the parental PGIs can be interpreted as a within-family indirect genetic effect because directly inherited genetic influences are captured by the child's PGI and between-family indirect genetic effects are captured by the parental-sibship-mean PGIs.

Considering the PGI based on the EA4 GWAS we find a large effect of the child's PGI (beta = 0.184, t(10273) = 16.2, SE = 0.011, p<0.001) on their test score, a modest but significant (p<0.05) effect for the PGI of the parent for whom no sibling is in the data (beta = 0.051, t(10294) = 5.3, SE= 0.011), a similar effect of the mean sibling PGI for the parent and their sibling (who is an aunt/uncle to the child) (beta = 0.053, t(10261) = 5.0, SE= 0.011, p<0.001), while the deviance of their parent relative to their sibling is not significant (beta = 0.014, t(10324) = 0.82, SE = 0.017, p=0.412).

Using the PGI based on the WFEA GWAS we also find a large effect of the child's PGI (beta = 0.126, t(10305) = 10.8, SE = 0.011, p<0.001) on their test score, a modest but significant effect for the PGI of the parent for whom no sibling is in the data (beta = 0.036, t(10329) = 3.6, SE = 0.010, p<0.001), a similar effect of the mean sibling PGI for the parent and their sibling (beta = 0.058, t(10294) = 5.7, SE= 0.010, p<0.001), while the deviance of their parent relative to their sibling is not significant (beta = 0.020, t(10292) = 1.14, SE= 0.017, p=0.252).

We consider the Cog and NonCog PGI jointly, and observe a substantial effect of the child's Cog PGI (beta = 0.222, t(10276) = 19.3, SE= 0.011, p<0.001) and a modest effect of the child's

NonCog PGI (beta = 0.089, t(10271) = 7.71, se = 0.011, p<0.001). The between parental-sibling-pair PGIs were significant for both the Cog PGI (beta = 0.042, t(10280) = 3.87, SE = 0.011, p<0.001) and the NonCog PGI (beta = 0.053, t(10277) = 4.94, SE = 0.011, p<0.001). Crucially, neither the effect of the within parental-sibling-pair Cog (beta = -0.002, t(10270) = -0.14, SE=0.017, p=0.882) nor NonCog (beta = 0.027, t(10339) = 1.59, SE=0.016, p=0.112) PGI was significantly different from zero.

[FIGURE 1 ABOUT HERE]

We performed one-tailed tests of the hypothesis that the difference between the between parental-sibling-pair coefficient(s) and the within parental-sibling-pair coefficient(s) is equal to or smaller than zero (cf. Supplementary Table 5). Tests reject the hypothesis for results obtained with all three PGIs: EA4 (t = 2.16, p = *0.0155,* $\beta_{difference}$ = *0.0394),* Cog/NonCog (t = 2.38, p = 0.0087*,* $\beta_{difference}$ = 0.0696*)*, and WFEA (t = 2.09, p = 0.0183*,* $\beta_{difference}$ = 0.038*)*.

The alternate specification, model 4, includes the PGIs of the child, the parent for whom no sibling is in the data, the parent who has a sibling in the data, and that parent's sibling. The results are as expected (see Table 2 for expectations). Considering the PGI based on the EA4 GWAS, we find a large direct effect of the child's PGI (beta = 0.184, t(10273) = 16.2, SE = 0.011, p<0.001), a modest but significant effect for the PGI of the parent for whom no sibling is in the data (beta = 0.051, t(10294) = 5.3, SE= 0.011, p<0.001), a smaller, and significant effect for the parent for whom a sibling is available (beta = 0.034, t(10298) = 3.09, SE= 0.011, p<0.001), and a significant effect of the PGI of the aunt/uncle on the child (beta = 0.019, t(10315) = 2.08, SE= 0.009, p = 0.038).

We find a large effect of the child's WFEA PGI (beta = 0.126, t(10305) = 10.7, SE = 0.012, p<0.001), a modest but significant effect for the PGI of the parent for whom no sibling is in the data (beta = 0.036, t(10330) = 3.63, SE = 0.010, p < 0.001), a smaller, and significant effect for the parent for whom a sibling is available (beta = 0.038, t(10296) = 3.5, SE= 0.011, p < 0.001), and a significant effect of the PGI of the aunt/uncle on the child (beta = 0.019, t(10286) = 2.11, SE= 0.009, p = 0.035).

Finally, the effect of the child's Cog PGI is quite pronounced (beta = 0.222, t(10276) = 19.4, SE = 0.011, p < 0.001), the effect of the NonCog PGI is modest (beta = 0.088, t(10271) = 7.71, SE = 0.011, p < 0.001), the effect of the PGI of the parent for whom no sibling is in the data is significant and modest (Cog: beta = 0.040, t(10298) = 4.12, SE= 0.01, p<0.001; Non-Cog: beta = 0.040, t(10268) = 4.12, SE = 0.01, p<0.001), the effects of the PGIs for an aunt/uncle are significant for Cog but not NonCog (Cog: beta = 0.021, t(10282) = 2.27, SE = 0.009, p=0.023; Non-Cog: beta = 0.014, t(10333) = 1.48, SE= 0.009, p=0.139), while the Cog and NonCog effects of the parent for whom a sibling is in the data is modest (and insignificant for Cog: beta = 0.020, t(10265) = 1.84, SE= 0.011, p=0.066; Non-Cog: beta = 0.039, t(10307) = 3.57, SE= 0.011, p<0.001).

Results from models 1 and 2 estimated on the largest possible sample, and stratified by school grade and test subject, are shown in Supplementary Figure 1. Results from models 1-4 estimated on the sample of all parent-sibling families, and stratified by school grade and test subject are reported in Supplementary Figure 2-9.

Discussion

The discovery of specific genetic variants associated with EA has given researchers a new tool for investigating the intergenerational transmission of education. In particular, the observation of indirect genetic effects, whereby the parental genotype is associated with offspring outcomes beyond the child's genotype, illustrates the role of the environment in the intergenerational transmission. Our indirect genetic effect estimates are consistent with previous analysis of MoBa[34], and of Dutch[35] and UK[22] cohorts, but somewhat smaller than the average effect from a recent meta-analysis[13]. The meta-analytic average may be stronger because it included studies of educational outcomes obtained from later stages of the life course, such as adult educational attainment.

We used an unique extended pedigree dataset with genotyped relatives from multiple generations to study the environmental processes driving the indirect genetic effect. In contrast to the processes implied by the phrase "genetic nurture," we did not find evidence that a large portion of the indirect genetic effects repeatedly established in previous work, predominantly runs through environmental mechanisms within the nuclear family, such as for example parental

behaviors or investments. Instead, our findings suggest that the majority of the indirect genetic effect in academic achievement, though not necessarily all of it, does not arise within the nuclear family, but instead reflects processes shared across families with common grandparents. Specifically, after accounting for genetics shared at the extended-family-level (between a child's parent and their aunt or uncle), and the child's own genetics, the "genetic nurture" association of a parent's PGI with their child's educational achievement was not statistically different from zero. Another important source of indirect genetic effects that is consistent with our findings is a major role for assortative mating, where repeated spousal selection on characteristics that are related to educational success would introduce indirect genetic effects that in our extended-family design were fully controlled with parental sibling pairs, as those are matched on their history of genetic assortment.

In contrast, the extended-family-level PGI did show a statistically significant association with the child's educational achievement that was comparable in size to the original indirect-genetic-effect estimate. This result does not rule out the presence of within-nuclear-family indirect genetic effects on EA. But it does suggest that genetic nurture processes unique to the nuclear family are likely to be a minor contributor to the indirect genetic effects observed in studies of trios or parent-child dyads.

We acknowledge limitations of the study. There are known biases to models that use PGIs to separate direct from indirect genetic effects. The GWAS from which we derived the per-SNP effect estimates for the Cog, NonCog and EA PGIs are influenced by unmodeled indirect genetic effects. Thus, for each SNP, we rely on an effect estimate that is a mix of direct and indirect effects. This mixture can result in bias to within-family analysis of PGIs derived from these GWAS[36,37]. However, our findings persist in analysis using a PGI derived from within-family GWAS, in which the bias in SNP effects that go into the PGI, induced by gene-environment correlation, are sharply attenuated, though not entirely absent[38].

Our analysis may be under-powered to detect very small within-nuclear-family indirect genetic effects. Our analysis utilizes the largest sample for extended-pedigree indirect-genetic-effect analysis currently available. Our results are consistent across analysis of 3 PGIs and 2 different specifications. Nevertheless, there could be a non-zero within-family indirect genetic effect undetected in our analysis. Power calculations reveal that our analysis was powered to detect effects of half the size (0.04) of the indirect genetic effect on educational outcomes estimated in

a recent meta-analysis[13]. Finally selection bias could affect results. MoBa has relatively high participation rates. Our use of national register data to determine educational achievement limits loss to follow-up as a source of bias. However, the MoBa sample is healthier and wealthier than the Norwegian population. Replications with other samples with the appropriate data structure (for example, the HUNT study[39]) should be a primary concern. Replication should be closely followed by generalization to other educational outcomes, such as high school completion or college enrollment. These outcomes are believed to be more strongly influenced by the nuclear family environment than are children's scores on standardized tests.[35] A recent meta-analysis of indirect genetic effects on a variety of educational outcomes including adult attainment reported an effect size (marked by dashed line in Figure 1) stronger than those obtained in our analysis. The specific educational tests we use have limited consequences for educational careers and therefore could be considered low stakes tests while parents may be more invested (and seek more influence) for educational outcomes that are closer linked to the child's future social position. It would further be desirable to triangulate our result across alternate designs, for example, adoption in the parental generation or directly observed grandparental genotypes. Finally, there is a need to generalize beyond contemporary Norway, which has relatively low income inequality, a high quality tuition-free public education system, and a generous welfare state.

Our results are consistent with the interpretation of indirect genetic effects on academic achievement as in part or largely due to "dynastic effects". Such effects could reflect subtle socioeconomic and genetic-ancestry stratification co-occurring within homogeneous populations[30,31,4].According to this interpretation, the extended-family-level PGI is correlated with a set of inherited social circumstances which affect children's academic achievement. An alternative interpretation is that dynastic effects reflect extended-family-level behaviors and investments that contribute to children's academic achievement. Our results are further consistent with a bias in the population GWAS and PGI estimates introduced by assortative mating. Our analysis cannot isolate the precise mechanisms of indirect genetic effects on EA. However, we can conclude that, for childhood academic achievement in the context of contemporary Norway, the mechanisms that give rise to indirect genetic effects, as indexed by current PGIs, operate mostly beyond the boundaries of nuclear families.

Children from higher SES families perform better on standardized tests of academic achievement. As with PGI associations, correlations between children's test scores and SES

might reflect “nurture” processes occurring within the nuclear family (e.g., parents actively using their resources to support their children’s educational careers with higher incomes pay for private tutoring) as well as dynastic processes that persist across generations (e.g., accumulation of wealth and access to social capital). Our results suggest that, to the extent that currently available PGIs come to be correlated with child academic achievement because they are systematically associated with SES-related environmental variation, they are capturing multigenerational effects of socioeconomic privilege, rather than the more local advantages conferred by individual parents on their own offspring.

Our results do not imply that parenting behaviors or a nurturing family environment do not affect school performance. Instead, they shed light on the mechanisms behind the widely observed indirect genetic effect of parental education-related PGI on offspring education outcomes[11,13,22–24]. Any effects of parenting that are not correlated to the parental educational PGIs are not detected in studies of the indirect genetic effect. By focusing on parental PGI for education-related traits, we omit potentially important parental influences. The education PGI used here would for example not index all parental life events or circumstances that may relate to worse educational outcomes for children. While our analysis can speak to the widely studied effect of parental educational PGI on childhood academic achievement, and is well-designed to avoid genetic confounding, it does not represent a comprehensive evaluation of parental influences on their children’s educational outcomes.

There are strategies to leverage genetic data to study parenting without relying on education-related PGI. One follow-up would be to repeat the current analysis as a GWAS, regressing child outcomes on each SNP in the child, the same SNP in the parent and include the mean SNP of the parent and their sibling as a third covariate. A GWAS of parental effects on childhood outcomes, while using the parental sibling structure to control for confounding (i.e., a within-sibling GWAS), would yield SNP level summary statistics that would allow analytical techniques like LD score regression to test genetic correlations between the indirect effects and hundreds of heritable parental traits like personality, psychopathology, wellbeing and physical health. The primary constraint on this type of analysis is sample size. However, with the continued development of national genetic databases, such extended-family GWAS of genetic nurture may soon be possible. Ultimately, a better understanding of the environmental/social intergenerational transmission of education will benefit from a tighter integration between social scientific data and genetic data.

Methods

Participants

The Norwegian Mother, Father and Child Cohort Study (MoBa) is a population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health[40]. Participants were recruited from all over Norway from 1999-2008. Women consented to participation in 41% of the pregnancies. The cohort now includes 114,500 children, 95,200 mothers and 75,200 fathers. Not all participants have yet been genotyped, and legal restrictions related to consent reduce our effective sample size relative to some other versions of the data. The current study is based on version 12 of the quality-assured survey data files released for research in January 2019 and MoBaPsychGen v.1. The establishment of MoBa and initial data collection was based on a license from the Norwegian Data Protection Agency and approval from The Regional Committees for Medical and Health Research Ethics. The MoBa cohort is now based on regulations related to the Norwegian Health Registry Act. The current study was considered by The Regional Committees for Medical and Health Research Ethics.

In our version of the data, 39,230 nuclear families have genotype information on complete trios (mother, father, and child) where both parents were born in Norway. The Norwegian system of personal ID numbers facilitates linking of data from MoBa to register-based information for educational outcomes, basic demography and links between parents and their siblings. The data structure is illustrated in Supplementary Figure 10. For 37,117 complete trio families, children have one or more educational outcomes available. In our analytic sample, there are 10.913 nuclear families where the child and both parents are genotyped, the child has taken at least one standardized test, and one parent has a sibling that is a genotyped parent in another MoBa family in the data set.

Measures

Academic achievement is measured by children's results on national standardized tests ("Nasjonale prøver") in reading (i.e., reading comprehension in Norwegian, for almost all children their first language), math, and English. Reading and math were administered in 5th, 8th and 9th grades and English in 5th and 8th grades. Nearly all MoBa children have data on 5th grade tests, while the youngest cohorts do not yet have data on 8th and 9th grade tests. The test scores were obtained from Norwegian administrative registries. The scores were standardized within the test and year to control for test version and changes over time.

PGIs were computed for all individuals using the LDpred2 software. GWAS summary statistics were obtained from a GWAS-by-subtraction, for cognitive (Cog) and non-cognitive (Non-Cog) SNP effects on EA[33], and from the within-family GWAS of EA [15,41]. For the EA PGIs, we relied on the top 10,000 publicly reported SNPs.[15]

Statistical analysis

Regression models

We fit four models. All eight test scores are included, with test fixed-effects and a child-specific random intercept included in all models. The first two models establish the presence of an indirect genetic effect in the sample of all genotyped parent-offspring trios. Model 1 estimates the total genetic effect measured by the PGI.

$$Edu_{ij} = \beta_{PGI} PGI_{child\ i} + \ldots + u_i + e_{ij} \quad \text{(model 1)}$$

Model 2 adds additional parameters for parents' PGIs and decomposes the total genetic effect into a direct component, measured by β_{dir} (for the child's PGI) and indirect components, measured by β_{fath} and β_{moth} (for the parents' PGIs).

$$Edu_{ij} = \beta_{dir} PGI_{child\ i} + \beta_{fath} PGI_{father\ i} + \beta_{moth} PGI_{mother\ i} + \ldots u_i + e_{ij} \quad \text{(model 2)}$$

We then decompose the indirect genetic effect into within- and between-family components. First, we select parents with one or more siblings in the MoBa sample. We next compute the following predictors:

$$PGI_{\mu} = \frac{\sum_{1}^{m} PGI_m}{m}$$

where PGI_{μ} is the mean PGI for a sibship of size m;

$$PGI_{\Delta} = PGI_{m} - PGI_{\mu}$$

where $PGI_{\Delta}$is the deviation of each parent's PGI from their sibship-mean PGI (PGI_{μ}), and PGI_{other}, which is the PGI of parents who do not have a sibling in the data. Finally, we combine these parameters in the equation for model 3:

$$Edu_{ij} = \beta_{dir} PGI_{child\ i} + \beta_{within} PGI_{\Delta} + \beta_{between} PGI_{\mu} + \beta_{other} PGI_{other\ parent} \ldots + u_{i} + e_{ij}$$

(model 3)

Children for whom neither parent has a sibling in the data are omitted (N=28,317). The model specification, which follows previous work[22] results in identical between-family and within-family effects in the absence of population stratification and/or the absence of a multigenerational effect on childhood academic achievement[42]. In the presence of either, we expect the between parental-sibling-pair effect to be larger than the within parental-sibling-pair effect.

As an alternative specification to Model 3, we fit a parallel model that parametrizes within- and between-family indirect genetic effects using a different approach. In this alternative specification, model 4, we include the PGIs of the parents and their siblings (i.e., the uncle or aunt of the child) in the regression.

$$Edu_{ij} = \beta_{dir} PGI_{child\ i} + \beta_{focal} PGI_{focal\ parent} + \beta_{uncle/aunt} PGI_{u/a} + \beta_{other} PGI_{other\ parent} \ldots + u_{i} + e_{ij}$$

(model 4)

Here, an indirect genetic effect consisting of purely within-family ("genetic nurture") mechanisms would result in a parameter estimate of zero for $\beta_{uncle/aunt}$. In contrast, an indirect effect consisting of only between-family ("dynastic effect") mechanisms would result in a parameter estimate of zero for β_{focal}.

All regression models include a set of child covariates indicated by the ellipsis (...): sex, birth year, test subject and grade fixed effects (to account for systematic differences in achievement

between tests), the first 10 genetic principal components (to account for population stratification), and genotyping-batch fixed effects (to account for batch-to-batch variation in genotype processing and measurement). We performed a power analysis and established we had > 80% power to detect a β_{within} sibling-pair effect half that of previous meta-analytic indirect genetic effects[13]. All tests are two-tailed unless otherwise specified.

Relation between parameter and conceptual processes

In the regression models above we define 3 parameters that relate in the following way to underlying mechanisms that generate associations between parental PGIs and child's outcome conditional on the child's own PGI. In model 2 we define: β_{moth} and β_{fath} which are the sum of influences of genetic nurture, dynastic effects and assortative mating. In model 3 and 4 we define β_{within} which is a consequence of genetic nurture but not dynastic effects or assortment. $\beta_{between}$ and β_{other} are again the sum of the effects of influences of genetic nurture, dynastic effects and assortative mating.

If β_{within} is not different from zero we find no evidence for "genetic nurture", while if β_{within} is not different from to $\beta_{between}$ and not different from the average of β_{moth} and β_{fath} (which are estimated in a larger sample, and hence with more power) this would be consistent with the absence of the influence of a "dynastic effect" or "assortative mating". For convenience summarize the relations between the mechanisms that can generate PGI-phenotype associations and the regression parameters we estimate in Table 2. The relationships are confirmed through simulations available on the GitHub repository that accompanies this paper.

Data availability statement

The data analyzed in the study are administrative data maintained by Statistics Norway and genotype data from MoBa Genetics. The data are not publicly available, but available to researchers upon application to the respective data owners. Such applications require approval by the appropriate ethics / research data access authorities. Access to administrative data from Statistics Norway can be applied for at Statistics Norway (http://www.ssb.no/mikrodata/) and access to MoBa Genetics can be applied for at the Norwegian Public Health Institute (http://www.fhi.no/studier/moba/). In Norway, the appropriate ethics and research data boards are the Regional Committee on Medical Research Ethics (REK) or SIKT. The consent given by the MoBa participants does not open for storage of data on an individual level in repositories or journals.

Code availability statement

No custom computer code was used in the study. The software used in the data preparation and analysis were R 4.0, LDPred 2, and plink 1.9. R scripts for data preparation and analysis are available at http://github.com/torkildl/nurturenature

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Author contributions

MGN, DWB, KPH and THL designed the study. THL prepared data. MGN and THL analyzed data. MGN, DWB, KPH, TB, OAA, EY, EvB, and THL interpreted results. MGN, DWB, KPH, and THL wrote the paper. All authors provided critical comments and feedback on the manuscript.

Competing interest statement

The authors declare no competing interests.

Tables

Table 1. Evidence from Genetically Informed Studies for Environmental Transmission of Educational Outcomes

Design	Key Comparison
Twins	Are dizygotic twins more similar in their EA than can be accounted for by their genetic relatedness?
Twins + offspring	Are children of (e.g., female) monozygotic twins more similar in their EA to their mother than to their aunt?
Adoptees	Do adopted offspring resemble their adoptive parents more than their biological parents in their EA?
Adoptees + siblings	Do offspring adopted into more environmentally advantaged homes have higher EA than their siblings who were not adopted away?
Adoptees + PGIs	Do adoptive parents' PGIs predict adopted children's EA? Is the association between one's own PGI and one's own EA stronger if raised by biological parents than by adoptive parents?
Parent-offspring trios + PGIs	Is the portion of the parental genotype that is not inherited by the offspring (untransmitted PGI) associated with offspring's EA?
Siblings + PGIs	Is the PGI-EA association attenuated after controlling for a family-specific effect or family's socioeconomic status (SES)?

Table 2. Expectations for indirect genetic effect parameter estimates for two model specifications under three conditions.

Condition	*Model specification*	
	Model 3: Mean of parent and sibling PGIs and parent's deviation PGI	*Model 4: Uncle and aunt PGI*
Only genetic nurture	$\beta_{within} = \beta_{between} = \beta_{other} = \beta_{moth}$ and β_{fath}	$\beta_{focal} = \beta_{other}$ & $\beta_{u/a} = 0$
Only assortative mating	$\beta_{within} = 0$	$\beta_{focal} = \beta_{u/a} = 0.5\beta_{other}$
Only dynastic effects	$\beta_{within} = 0$	$\beta_{focal} = \beta_{u/a} = 0.5\beta_{other}$

Figures legends & captions

Figure 1. Results from four models of academic achievement using three definitions of polygenic scores.

From left to right results for the models 1 and 2 (N=37,117 families) and 3 and 4 (N=10,913 families) where achievement is regressed on a set of PGIs and covariates (age, year, test, genomic principal components), with a child-specific random effect. Figure only presents the effect of the PGIs of interest. Upper panel shows coefficients the educational attainment (EA4) PGI; middle panel, show coefficients for cognitive skills (blue) and noncognitive skills (orange) PGIs and lower panel coefficients for within-family PGI for educational attainment. Symbols represent point estimates and vertical error bars represent 95% confidence intervals. Dashed line is a reference value for the indirect genetic effect as established in previous meta-analysis (that did not include MoBa) of educational outcomes.

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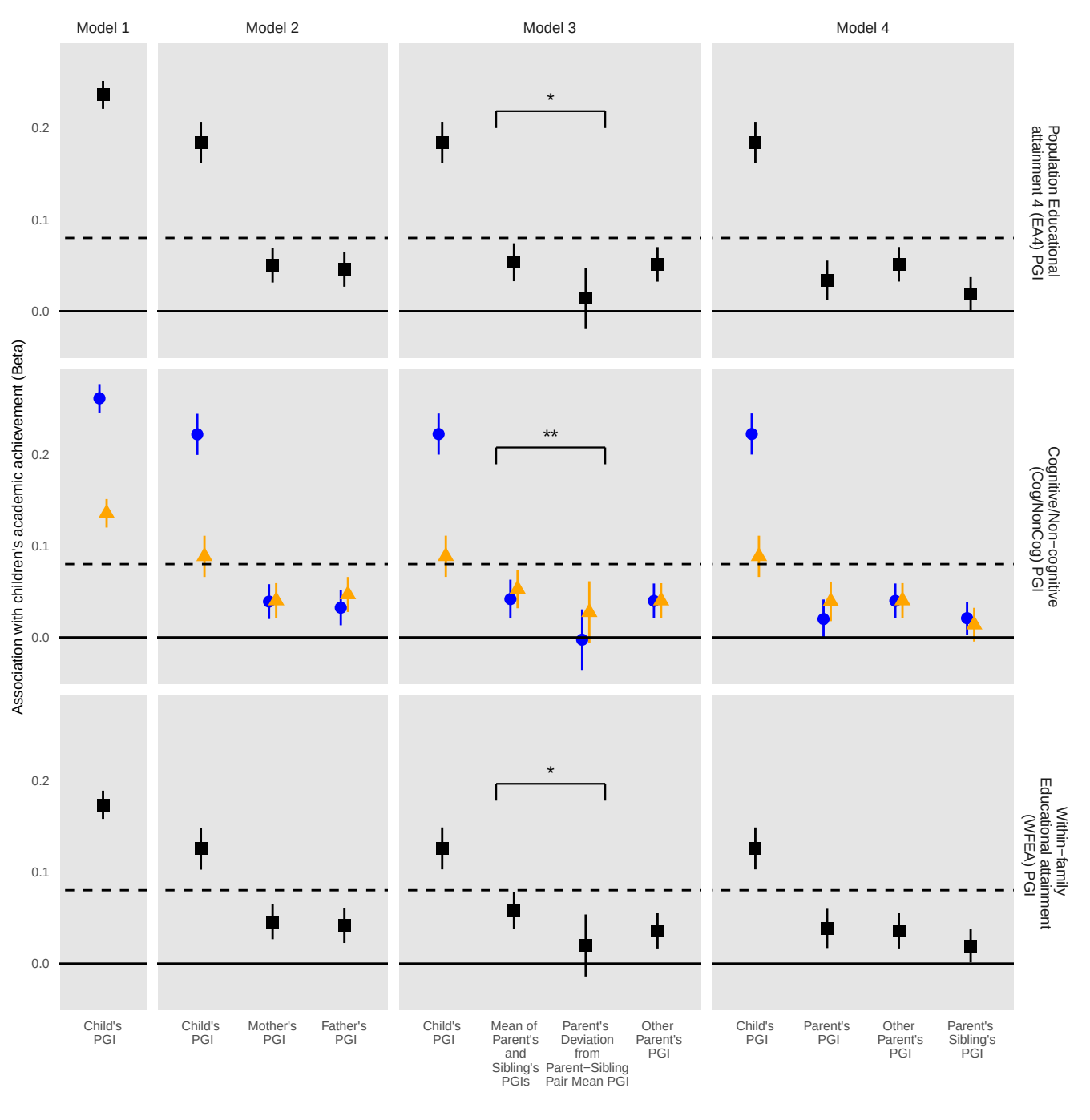
Model 1
Model 2
Model 3
Model 4
Population Educational attainment 4 (EA4) PGI
Cognitive/Non−cognitive (Cog/NonCog) PGI
Within−family Educational attainment (WFEA) PGI
Association with children's academic achievement (Beta)
0.0
0.1
0.2
*
**
*
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's and Sibling's PGIs
Parent's Deviation from Parent−Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Other Parent's PGI
Parent's Sibling's PGI

Supplementary information

Supplementary information, tables and figures for Nivard et al. (2023), “More than Nature and Nurture, indirect genetic effects on children’s academic performance are consequences of dynastic social processes”

Contents

Supplementary Information 1: Power analysis

An insightful reviewer requested we perform power analyses for detecting a nurture effect using the association between educational outcomes and PGIs. We did this before analyzing the new, larger sample. We define the nurture effect as an effect of PGI deviance between parent and their sibling on the child's outcome, conditional on the child's PGI, the mean of the parent-sibling PGIs , and the other parent's PGI.

From the literature (Wang et al. 2021) we obtain a precise meta-analytic estimate of the total indirect genetic effect expressed as a standardized regression coefficient (where both outcome and predictors are scaled to unit variance) of 0.08 (95% CI = 0.07-0.09). As this estimate does have unknown heterogeneity arising from sample, study, and statistical design, we also consider an effect size consistent with half the explained variance (±0.056) and half the effect size (0.04) as reported in Wang et al. (2021).

Power simulation

```
# Clear memory:
rm(list=ls())
gc()
```

```
          used (Mb) gc trigger (Mb) limit (Mb) max used (Mb)
Ncells  566943 30.3    1285188 68.7         NA   669297 35.8
Vcells 1035174  7.9    8388608 64.0      24576  1839975 14.1
```

```
# requirements and seed:
require(gt)
```

```
Loading required package: gt
```

```
set.seed(123)
```

```
n <- 5200 # parental sibs
s <- 2 # sibship size

rep <- 1000
out <- matrix(NA,rep,3)
```

We simulate 1000 datasets with PGIs for 2 siblings, their spouses, and their kids. We then simulate a direct PGI effect of 0.17 (standardized beta) and an indirect effect that is pure nurture and an effect size of 0.08 (standardized beta) based on previous literature. These effects are from the meta-analysis (n > 38.000) that did not contain MoBa results. We then simulate scenario's half the squared effect size (half of r2) and with half the effect size.
We evaluate power as the proportion of simulations given each scenario in which the effect of the parents' PGI deviation from the parent and their sibling mean is significantly related to the outcome at alpha 0.05, 0.01 or 0.005, conditional on the child's PGI, the other parent's PGI and the parent and sibling mean PGI. The simulated sample size is 5200 extended families. Each extended family consists of two "nuclear families". In each of the nuclear families, one parent is a sibling of a parent in the other nuclear family. Thus, the sample

consists of a sibling pair (of which both are parents), their spouses (the other parent) and children (N = 10.200, i.e. one child for each sibling). The sample size is similar to our empirical data.

```
# loop power sim:
for(i in 1:rep){
bp_pgi_f <- rnorm(n)
wf_g1a <- rnorm(n) # within family V(g) 50%
wf_g1b <- rnorm(n) # within family V(g) 50%

fp_pgi <-  sqrt(.5) *  bp_pgi_f + sqrt(.5)*wf_g1a
fp2_pgi <-  sqrt(.5) *  bp_pgi_f  + sqrt(.5)*wf_g1b

# betwene family parental PGI
bp_pgi <- rep((fp_pgi+fp2_pgi)/2,2)

# within family parental PGI:
wp_pgi <- c(fp_pgi,fp2_pgi) - bp_pgi

# parental PGI:
fp_pgi_c <- c(fp_pgi,fp2_pgi)
# Other parent PGI:
op_pgi <- rnorm(n*s)

# within fam V(a) kids;
wf_g2 <- rnorm(n*s) # within family V(g) 50%

# child PGI:
fc_pgi <- sqrt(.25)*fp_pgi_c + sqrt(.25)*op_pgi + sqrt(.5)*wf_g2
var(fc_pgi) # should be 1
cor(fc_pgi,fp_pgi_c) # cor with your parent should be .5
cor(fc_pgi[1:n],fp_pgi_c[(n+1):(s*n)]) # cor with uncle/aunt should
be .25


# family identifier for later use:
fam_id <- rep(1:n,s)


environment <- rnorm(s*n)
cor_env_g <- rnorm(n)
environment <- scale(environment + c(cor_env_g,cor_env_g)) #
environments ( & unmeasured genetic fx) are correlated between sibs!


# true within family nurture, effect size size same as meta-analysis
by Wang et al.
#(Wang, B., Baldwin, J. R., Schoeler, T., Cheesman, R., Barkhuizen,
W., Dudbridge, F., ... & Pingault, J. B. (2021).
#Robust genetic nurture effects on education:
#A systematic review and meta-analysis based on 38,654 families
across 8 cohorts.
```

```
#The American Journal of Human Genetics, 108(9), 1780-1791.):

nurture <- 0.08
direct <- 0.17
phenotype <-  direct*fc_pgi  + nurture *fp_pgi_c + nurture *op_pgi +
sqrt(.9-nurture-direct)*environment

ak <- lmerTest::lmer(phenotype ~ fc_pgi + wp_pgi + bp_pgi + op_pgi
+(1|fam_id))
out[i,1] <- summary(ak)$coef[3,1]/summary(ak)$coef[3,2]



# true within family nurture, effect size size HALF r2 Wang et al.
#(Wang, B., Baldwin, J. R., Schoeler, T., Cheesman, R., Barkhuizen,
W., Dudbridge, F., ... & Pingault, J. B. (2021).
#Robust genetic nurture effects on education:
#A systematic review and meta-analysis based on 38,654 families
across 8 cohorts.
#The American Journal of Human Genetics, 108(9), 1780-1791.):

nurture <- sqrt(.5*(.08^2))
direct <- 0.17
phenotype <-  direct*fc_pgi  + nurture *fp_pgi_c + nurture *op_pgi +
sqrt(.9-nurture-direct)*environment

ak <- lmerTest::lmer(phenotype ~ fc_pgi + wp_pgi + bp_pgi + op_pgi
+(1|fam_id))
out[i,2] <-  summary(ak)$coef[3,1]/summary(ak)$coef[3,2]



# true within family nurture, effect size size HALF r Wang et al.
#(Wang, B., Baldwin, J. R., Schoeler, T., Cheesman, R., Barkhuizen,
W., Dudbridge, F., ... & Pingault, J. B. (2021).
#Robust genetic nurture effects on education:
#A systematic review and meta-analysis based on 38,654 families
across 8 cohorts.
#The American Journal of Human Genetics, 108(9), 1780-1791.):

nurture <- 0.04
direct <- 0.17
phenotype <-  direct*fc_pgi  + nurture *fp_pgi_c + nurture *op_pgi +
sqrt(.9-nurture-direct)*environment

ak <- lmerTest::lmer(phenotype ~ fc_pgi + wp_pgi + bp_pgi + op_pgi
+(1|fam_id))
out[i,3] <- summary(ak)$coef[3,1]/summary(ak)$coef[3,2]
}
```

Our analysis reveals that we have ample power in most scenarios to detect non-zero nurture effects that are at least half the effect of half the squared effect size:

```r
# Power at alpha = 5% two sided:
p1_05 <- (sum(out[,1] > sqrt(qchisq(0.95,1))) / rep) * 100
p2_05 <- (sum(out[,2] > sqrt(qchisq(0.95,1))) / rep) * 100
p3_05 <- (sum(out[,3] > sqrt(qchisq(0.95,1))) / rep) * 100

# Power at alpha = 1% two sided:
p1_01 <- (sum(out[,1] > sqrt(qchisq(0.99,1))) / rep) * 100
p2_01 <- (sum(out[,2] > sqrt(qchisq(0.99,1))) / rep) * 100
p3_01 <- (sum(out[,3] > sqrt(qchisq(0.99,1))) / rep) * 100

# Power at alpha = 0.5% two sided:
p1_005 <- (sum(out[,1] > sqrt(qchisq(0.995,1))) / rep) * 100
p2_005 <- (sum(out[,2] > sqrt(qchisq(0.995,1))) / rep) * 100
p3_005 <- (sum(out[,3] > sqrt(qchisq(0.995,1))) / rep) * 100

Power <- c(p1_05,p2_05,p3_05,p1_01,p2_01,p3_01,p1_005,p2_005,p3_005)

Effect_Source <- rep(c("Wang et al.", "50% of the squared beta
implied Wang et al.","50% of the beta implied in Wang et al."),3)
Effect <- round(c(0.08,sqrt(.5*(0.08)^2),0.04),4)
Alpha <- rep(c("0.05","0.01","0.005"),3)


tab <- gt(cbind.data.frame(Effect_Source,Effect ,Alpha,Power))

tab
```

Effect_Source	Effect	Alpha	Power
Wang et al.	0.0800	0.05	100.0
50% of the squared beta implied Wang et al.	0.0566	0.01	99.4
50% of the beta implied in Wang et al.	0.0400	0.005	89.5
Wang et al.	0.0800	0.05	100.0
50% of the squared beta implied Wang et al.	0.0566	0.01	98.3
50% of the beta implied in Wang et al.	0.0400	0.005	71.9
Wang et al.	0.0800	0.05	100.0
50% of the squared beta implied Wang et al.	0.0566	0.01	96.5
50% of the beta implied in Wang et al.	0.0400	0.005	63.9

Power exceeds 60% in all cases and exceeds 80% unless we consider effects that are half the power observed in the previous meta-analysis at an alpha of 0.01 or 0.005. Inevitably, there are various modeled potential processes that could mean our power analysis is too optimistic or pessimistic. For example, in the empirical analysis we consider repeated assessments of educational achievement which could yield us additional power, the meta-analysis includes multiple statistical designs and data from countries with more deeply stratified educational systems, which could result in bigger indirect genetic effects, which would cost us power. We feel that, by considering various reasonable effect sizes, and

alpha's, we cover the magnitude of genetic effects that is currently referred to as "genetic nurture" and could conceivably be viewed as product of within-family nurturing processes.

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Wang, Biyao, Jessie R. Baldwin, Tabea Schoeler, Rosa Cheesman, Wikus Barkhuizen, Frank Dudbridge, David Bann, Tim T. Morris, and Jean-Baptiste Pingault. 2021. "Robust Genetic Nurture Effects on Education: A Systematic Review and Meta-Analysis Based on 38,654 Families Across 8 Cohorts." The American Journal of Human Genetics 108 (9): 1780–91. https://doi.org/10.1016/j.ajhg.2021.07.010.

Frequently Asked Questions

Contents

What did this study do?

This study examined how genes and environments were related to educational outcomes in Norwegian children, who completed standardized academic tests (“Nasjonale prøver”) of reading comprehension, mathematics and English (as a second language) at ages 10,15 and 16. For every children we calculated something known as a **polygenic index**, which is a measure of genes thought to be correlated with going further in formal education. In addition, we also calculated the polygenic index of the children’s parents and of any of their parents’ siblings. In our work, the correlations between genes and outcome, education in this case, aren't thought of as immutable or fixed, but rather a function of society, environment and population. If a society shifts its emphasis on what is thought of as important to attain education, then that will subtly shift which genes correlate to educational outcomes.

Our study tested three things. First, does a child’s own genes predict their own academic test performance? Second, does a child’s parents’ genes predict their test performance, above and beyond the child’s own genes? Such an association (termed **indirect genetic effects**) cannot be due to genetic inheritance and is evidence for an environmental process.

Third, does a child's parents' genes predict their test performance, even after controlling for the parents' *siblings*' genes? This type of analysis is unusual because most studies don't have data on extended pedigrees of relatives. This analysis is important because it tests whether the environmental processes that are "tagged" by polygenic indices, and are associated with children's educational outcomes, are operating within nuclear families (parents and children) or are operating multi-generationally.

What is a polygenic index and how is it calculated?

As a genetic effect the study considers a polygenic index, which is a weighted sum of your genotypes, weighted by their suspected effect on education, based on previous genetic studies. Since these previous genetic studies are large, a polygenic index of education explains about ±7-13% of variance in educational outcomes, though that includes both contributions from direct and indirect genetic effects.

What are "indirect" genetic effects?

Indirect genetic effects – sometimes called genetic nurture – is a term for the presence of an association between your parents' genotypes, and your outcome, over and above the effect the genotype has through its presence in you, as you have inherited genes from your parents. If ignored in the analysis of genetic effect, or environmental effects for that matter, indirect genetic effects might appear like direct genetic effects and inflate our estimate of those. In particular when it comes to educational outcomes, genetic effects and environmental effects seem steeply correlated, which has inflated the estimates of genetic

effects on educational outcomes, but also raises the question what causes these indirect genetic effects to occur?

There are a few processes researchers think might give rise to indirect genetic effects on educational outcomes. For example genetic variants that every so slightly improve you parents socio-economic position (for example, trough effects on their education), will become correlated to your education if their socio-economic advantage puts you in a better school/neighborhood, or if it means they have more time to be available to help you learn, resulting in better educational outcomes. However, there are also competing explanations where the indirect genetic effects don't really act through your parents in some way shaping your environment. If for example people with similar education levels consistently (for a number of generations) marry and have kids, this could also give rise to indirect genetic effects, without any effect through nurture or socio-economic advantage on part of your parents. We would like to find out whether these indirect genetic effects, of your parents' polygenic index for education on your school outcomes, reflect processes that plays out within the nuclear family, or are consequences of some of these multi-generational mate choice processes.

Who are the people in this study?

The research used data from Norwegian Mother, Father and Child Cohort Study, a large cohort data set collected in Norway. MoBa is a unique study where over 90,000 pregnant women were recruited from 1998 to 2008. More than 70,000 fathers have participated. It provides data on children, mothers and fathers from questionnaires, biobanks and administrative registers. For more information about MoBa, see its homepage.

Norway, the country in which data were collected, is a Scandinavian welfare state with a universal, free education system. The Norwegian state also provides a range of social insurance and benefits to the population. The results of the research must be interpreted in this context. Results might not be similar in other countries that have different economies and educational systems.

What do the findings mean for the effects of parents' nurturing behavior on children?

Our findings related parents' polygenic indices for education to their child's educational achievement. Obviously, your nurturing behavior is more than your propensity for having a long education. Any nurture processes that do not correlate to the education PGI, of which there are probably many, can obviously influence kids' success, and other outcomes in their lives. As so often, our findings are narrow and specific, and don't easily translate to broad lay concepts like "nurture" or "parenting". So our findings are not a test of the importance of nurture, rather they are a test of the particular indirect genetic effect researchers have previously observed.

What do the findings mean for the research on education and educational performance?

Our work, and that of many others, highlights that there are many sociological and historical reasons why your genotype can be correlated with any outcome. In particular, when that outcome is as socially determined as education, this inevitably leads to gene-environment correlation. Our work suggests the source of gene-environment correlation is likely predominantly due to a longer term process. One such process is assortative mating, the phenomenon where partners – and thus parents – are matched on their education level or other traits that are partially shaped by genetics. It is then also important to understand that assortment itself is a very complex sociological and psychological process, profoundly shaped by social and cultural factors. We can't fully rule out a modest effect of your parents' educational polygenic index on your success in school, nor can we rule out other multi-generation processes that would slowly introduce gene-environment correlation.

Supplementary Table S1: Descriptive statistics for analysis variables

	All available trios					Sibling sample				
Variable	N	M	SD	Min	Max	N	M	SD	Min	Max
Math 5th	36532	0.10	0.95	-2.65	2.04	10234	0.15	0.96	-2.45	2.04
Math 8th	18519	-0.13	0.81	-2.38	2.02	5292	-0.09	0.82	-2.38	1.62
Math 9th	12435	0.00	0.85	-2.74	1.53	3552	0.04	0.86	-2.57	1.53
Reading 5th	36139	0.24	0.97	-2.94	2.29	10123	0.28	0.97	-2.94	2.29
Reading 8th	18496	0.09	0.99	-2.96	2.16	5279	0.12	1.00	-2.96	2.16
Reading 9th	12458	0.15	0.96	-3.29	1.73	3563	0.18	0.96	-3.29	1.73
English 5th	36268	0.19	1.05	-2.67	2.57	10165	0.19	1.04	-2.67	2.57
English 8th	18419	0.07	0.99	-2.37	2.19	5253	0.07	1.01	-2.37	2.02
Child Year of Birth	39230	2005.47	1.89	2002.00	2009.00	10913	2005.45	1.88	2002.00	2009.00
Mother Year of Birth	39230	1974.79	4.73	1956.00	1991.00	10913	1974.83	4.38	1960.00	1990.00
Father Year of Birth	39218	1972.40	5.41	1942.00	1989.00	10913	1972.56	4.92	1946.00	1988.00

Supplementary Table S2. Results from four models of academic achievement using EA4 PGIs

	Model 1		Model 2		Model 3		Model 4	
	Beta	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
(Intercept)	0.197	[0.134, 0.260]	0.196	[0.133, 0.259]	0.195	[0.132, 0.258]	0.195	[0.132, 0.258]
Child PGI EA4	0.236	[0.221, 0.251]	0.184	[0.162, 0.207]	0.184	[0.162, 0.207]	0.184	[0.162, 0.207]
Mother PGI EA4			0.050	[0.031, 0.069]				
Father PGI EA4			0.046	[0.027, 0.065]				
Parent-Sibship Deviation EA4					0.014	[-0.019, 0.047]		
Parent-Sibship Mean EA4					0.053	[0.033, 0.074]		
Other parent PGI EA4					0.051	[0.032, 0.070]	0.051	[0.032, 0.070]
Sibling parent PGI EA4							0.034	[0.012, 0.055]
Uncle/aunt PGI EA4							0.019	[0.001, 0.037]
SD(Child intercepts)	0.731		0.729		0.729		0.729	
SD(Tests)	0.593		0.593		0.593		0.593	
N	53461		53461		53461		53461	
logLik	-58872.4		-58860.6		-58861.2		-58862.0	
AIC	117802.8		117783.1		117786.4		117788.1	

Supplementary Table S3. Results from four models of academic achievement using Cog/NonCog PGIs

	Model 1		Model 2		Model 3		Model 4	
	Beta	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
(Intercept)	0.187	[0.125, 0.250]	0.186	[0.124, 0.248]	0.186	[0.123, 0.248]	0.186	[0.123, 0.248]
Child PGI Cog	0.261	[0.245, 0.276]	0.222	[0.199, 0.244]	0.222	[0.199, 0.244]	0.222	[0.199, 0.244]
Child PGI NonCog	0.135	[0.120, 0.151]	0.088	[0.066, 0.111]	0.089	[0.066, 0.111]	0.088	[0.066, 0.111]
Mother PGI Cog			0.039	[0.020, 0.058]				
Mother PGI NonCog			0.040	[0.021, 0.059]				
Father PGI Cog			0.032	[0.013, 0.052]				
Father PGI NonCog			0.047	[0.028, 0.066]				
Parent-Sibship Mean Cog					0.042	[0.021, 0.063]		
Parent-Sibship Deviation Cog					-0.002	[-0.036, 0.031]		
Parent-Sibship Mean NonCog					0.053	[0.032, 0.074]		
Parent-Sibship Deviation NonCog					0.027	[-0.006, 0.061]		
Sibling parent PGI Cog							0.020	[-0.001, 0.041]
Sibling parent PGI NonCog							0.039	[0.018, 0.061]
Other parent PGI Cog					0.040	[0.021, 0.059]	0.040	[0.021, 0.059]
Other parent PGI NonCog					0.040	[0.021, 0.059]	0.040	[0.021, 0.059]
Uncle/aunt PGI Cog							0.021	[0.003, 0.039]
Uncle/aunt PGI NonCog							0.014	[-0.005, 0.032]
SD(Child intercepts)	0.722		0.720		0.720		0.720	
SD(Tests)	0.593		0.593		0.593		0.593	
N	53461		53461		53461		53461	

	Model 1		Model 2		Model 3		Model 4	
	Beta	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
logLik	-58763.8		-58757.6		-58760.4		-58762.0	
AIC	117587.6		117583.3		117592.8		117596.0	

Supplementary Table S4. Results from four models of academic achievement using WFEA PGIs

	Model 1		Model 2		Model 3		Model 4	
	Beta	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
(Intercept)	0.198	[0.134, 0.262]	0.196	[0.132, 0.260]	0.195	[0.131, 0.260]	0.195	[0.131, 0.260]
Child PGI WFEA	0.173	[0.158, 0.189]	0.125	[0.102, 0.148]	0.126	[0.103, 0.149]	0.126	[0.103, 0.149]
Mother PGI WFEA			0.046	[0.027, 0.065]				
Father PGI WFEA			0.041	[0.023, 0.060]				
Parent-Sibship Deviation WFEA					0.020	[-0.014, 0.054]		
Parent-Sibship Mean WFEA					0.058	[0.038, 0.078]		
Other parent PGI WFEA					0.036	[0.016, 0.055]	0.036	[0.016, 0.055]
Sibling parent PGI WFEA							0.038	[0.017, 0.060]
Uncle/aunt PGI WFEA							0.019	[0.001, 0.037]
SD(Child intercepts)	0.747		0.746		0.746		0.746	
SD(Tests)	0.593		0.593		0.593		0.593	
N	53461		53461		53461		53461	
logLik	-59074.4		-59066.4		-59066.7		-59067.3	
AIC	118206.7		118194.9		118197.3		118198.6	

Supplementary Table 5: Tests of mean and deviation coefficients in sibling models (Model 3)

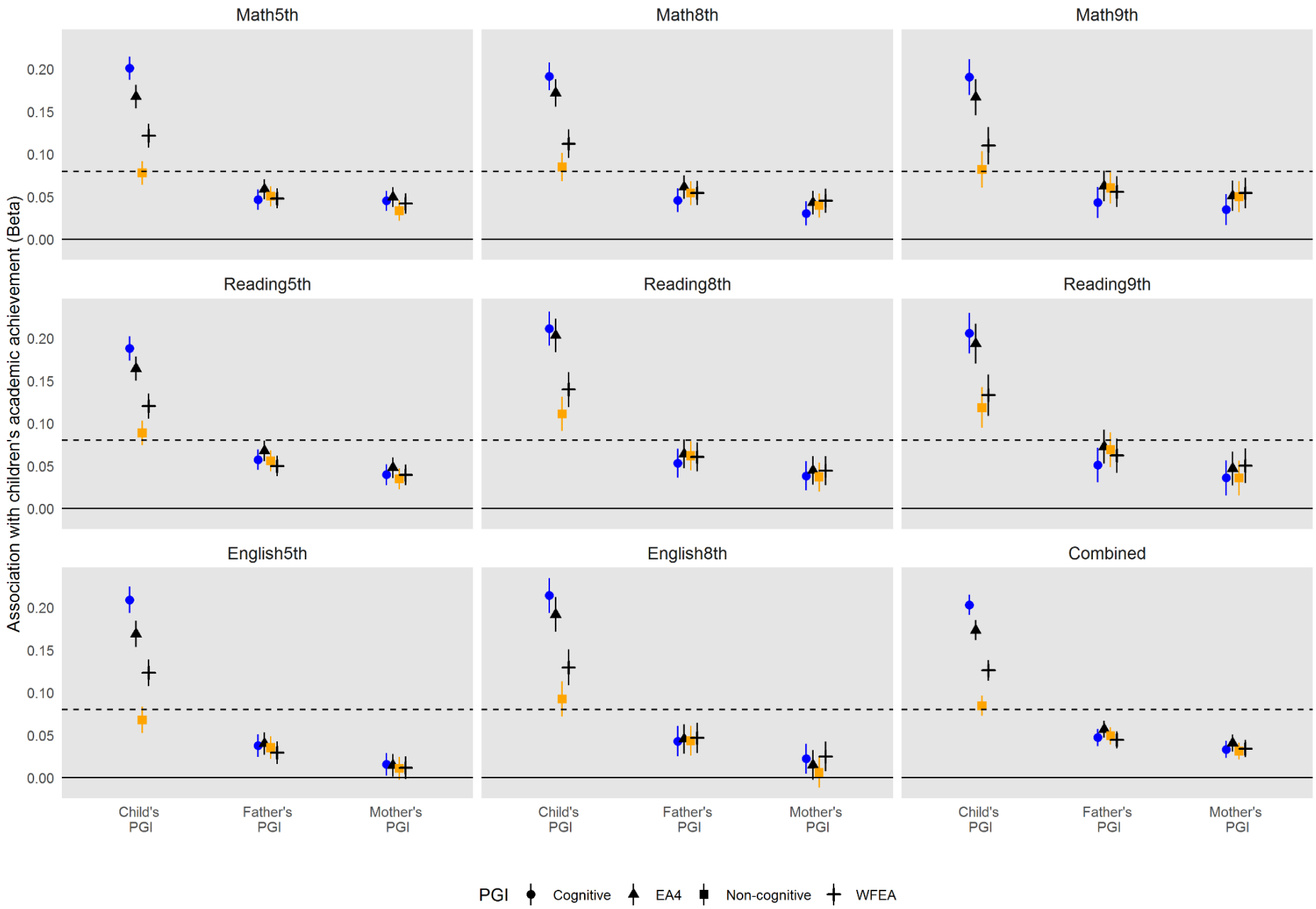
Tests were one-tailed t-tests of the hypothesis that the difference in coefficients for Parent-Sibship Mean and Parent-Sibling Deviation were larger than zero. Tests were not adjusted for multiple comparisons.

Model	estimate	std.error	statistic	adj.p.value
EA4	0.0394	0.0183	2.16	0.0155
CogNonCog	0.0696	0.0292	2.38	0.00867
WFEA	0.038	0.0182	2.09	0.0183

Supplementary Figure 1. Results from Models 1 and 2 estimated on full trio sample

Supplementary Figure S1: Results from Models 1 and 2 of eight test scores for academic achievement and a model of all test scores combined (N=37,117). Models were estimated using three different sets of PGIs: Cognitive (blue dots) and Non-cognitive (orange squares) PGIs, EA4 (black triangles), and within-family EA (black crosses). Point estimates (indicated by symbols) are shown with associated 95% confidence intervals.

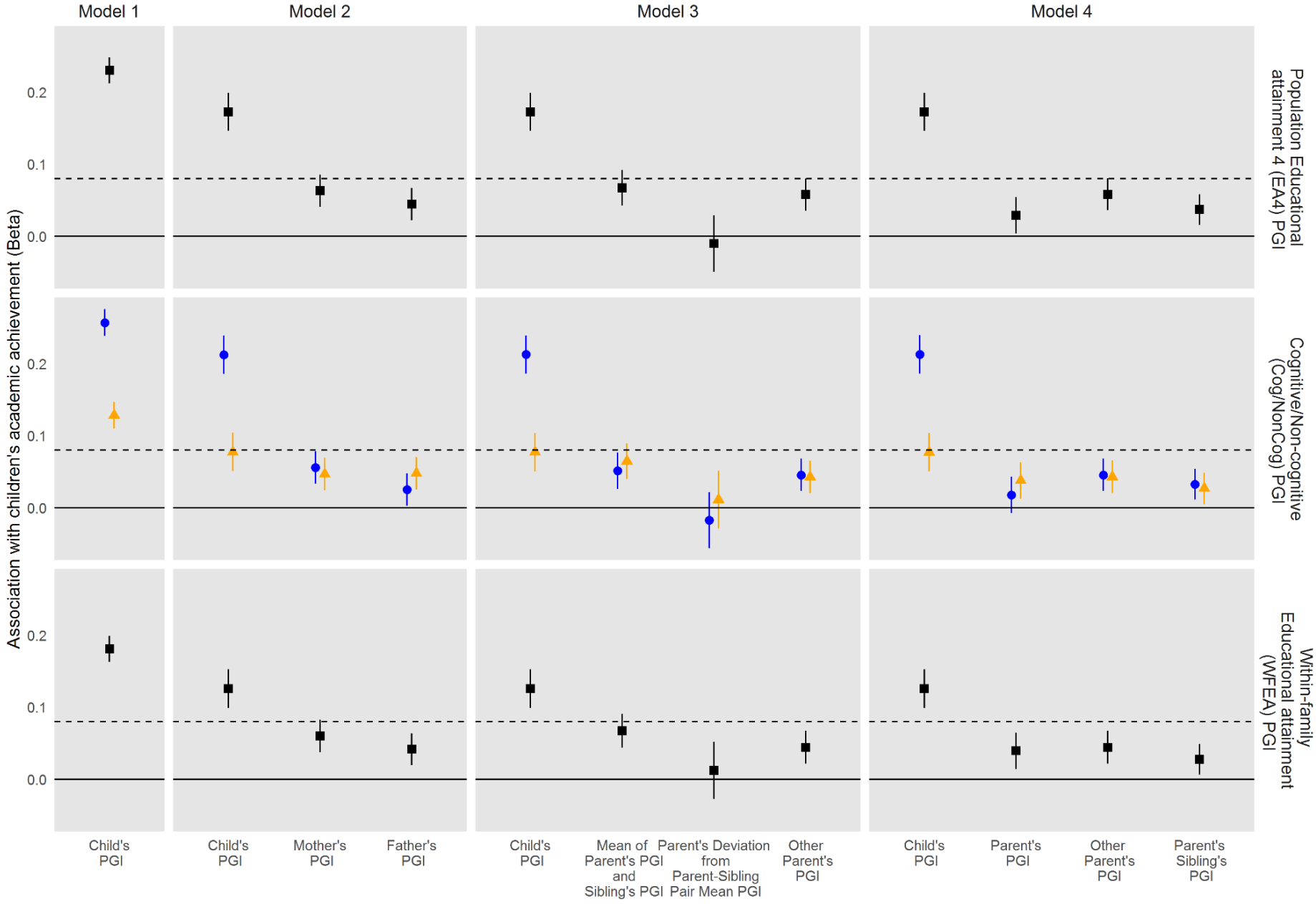
Figure shown on next page

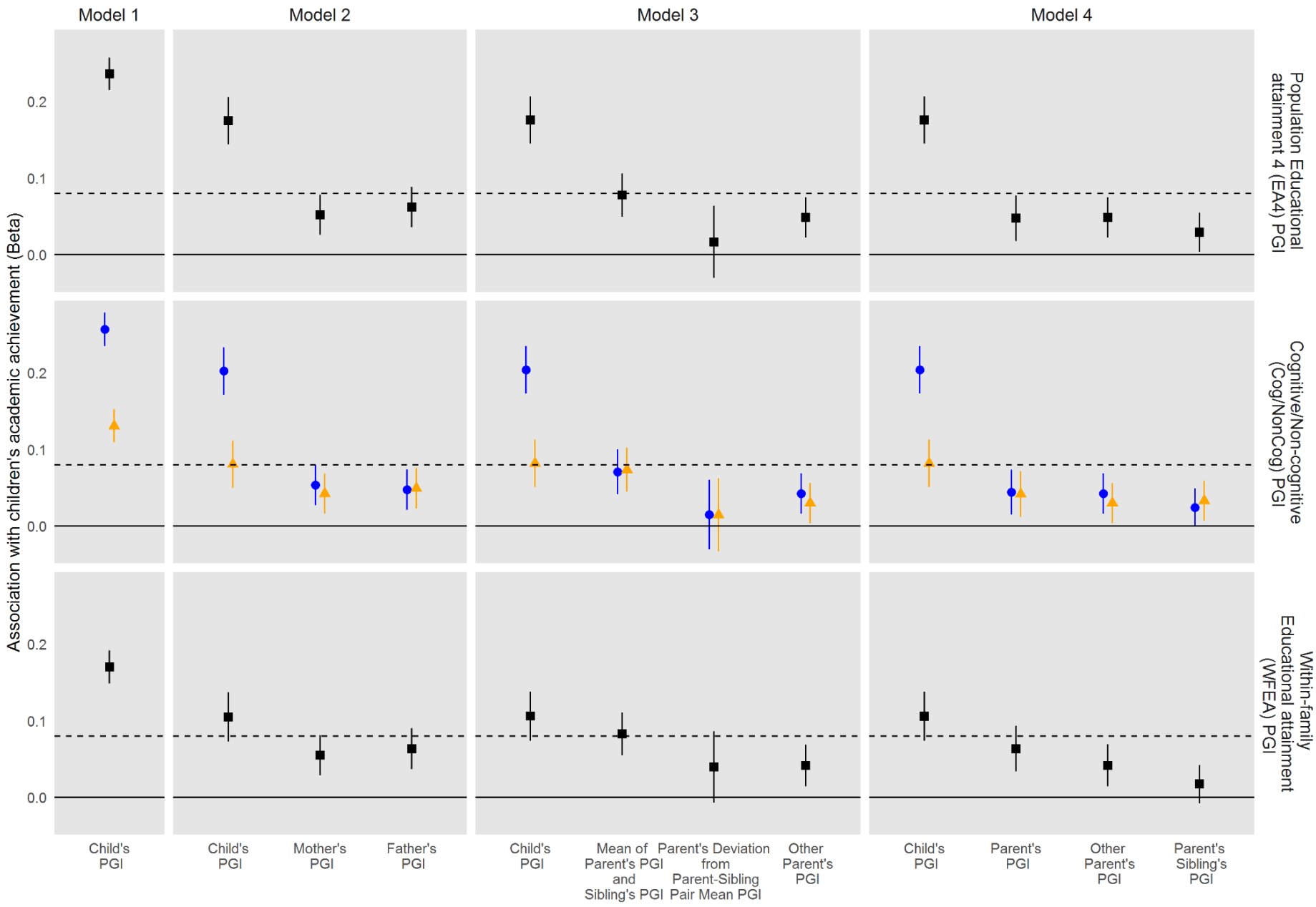

Math5th
Math8th
Math9th
Reading5th
Reading8th
Reading9th
English5th
English8th
Combined
Association with children's academic achievement (Beta)
0.20
0.15
0.10
0.05
0.00
Child's PGI
Father's PGI
Mother's PGI
PGI
Cognitive
EA4
Non-cognitive
WFEA

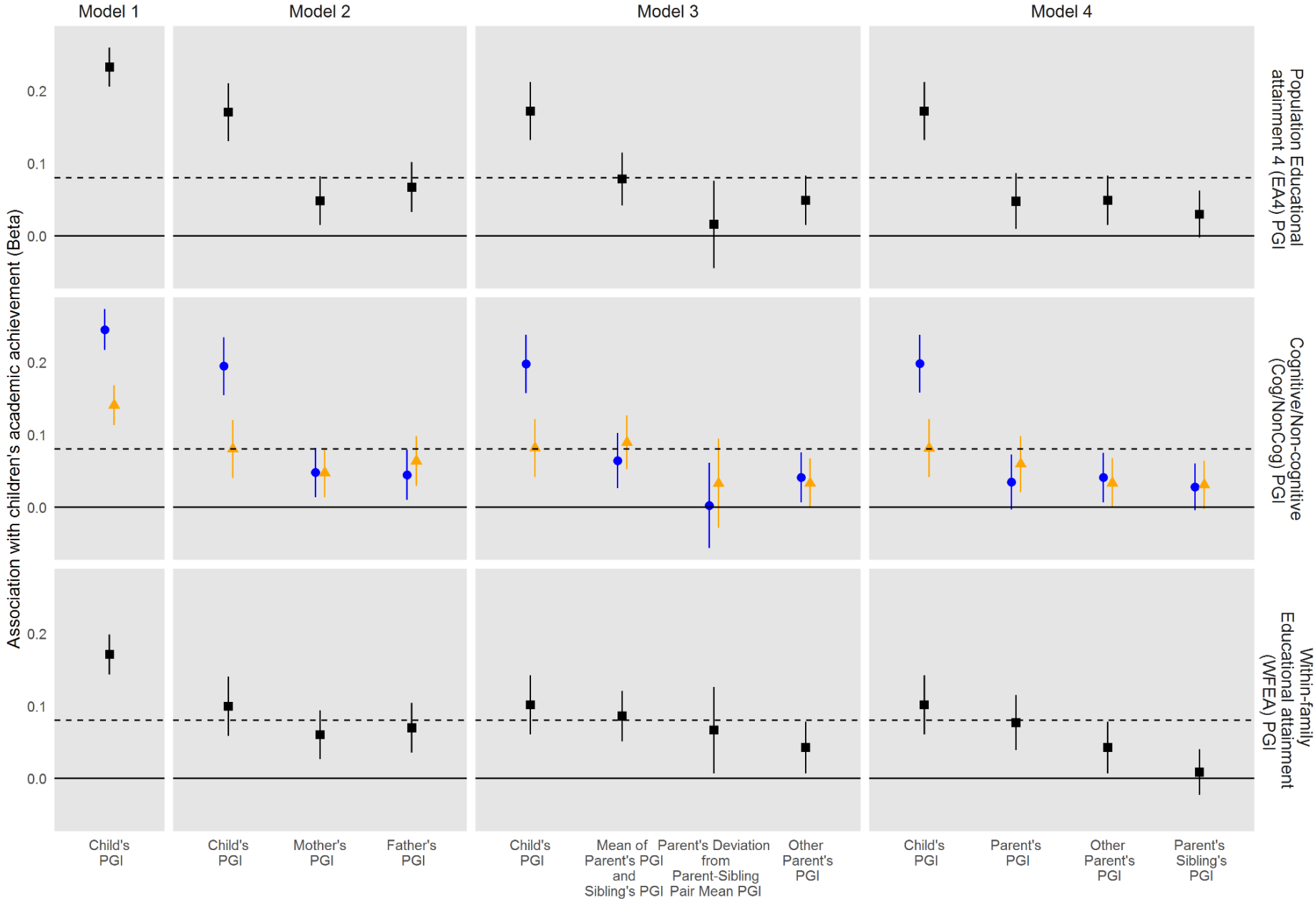
Supplementary Figures 2-9. Results from Models 1 to 4 for eight separate tests by grade and subject

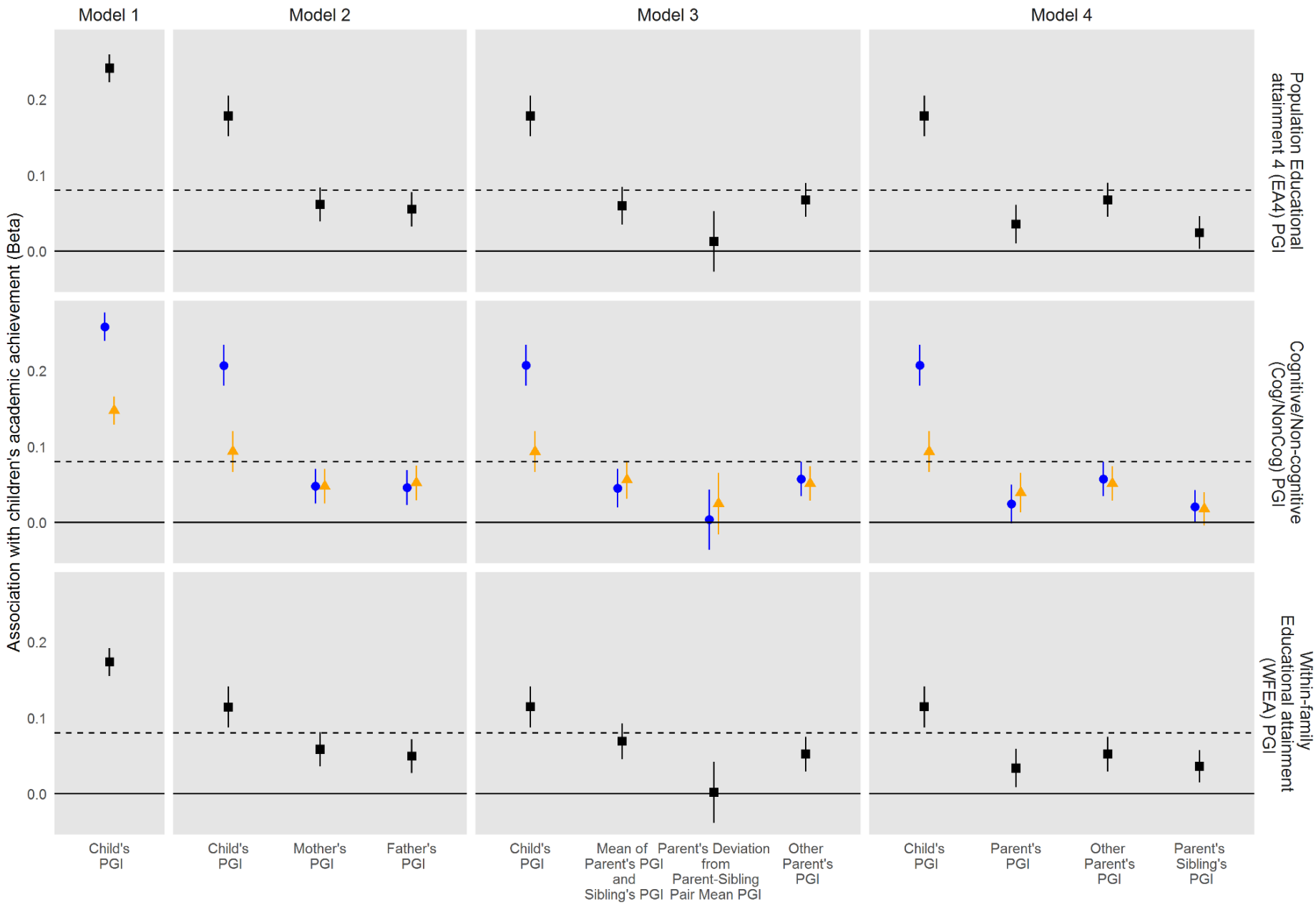
Figures S2-S9: Results for eight regression models (models 1 and 2: N_{max}=37,117 families; models 3 and 3: N_{max} = 10,913 families) of test scores including PGIs for child, non-sibling parent, sibling parent deviation from sibship mean, sibling parent sibship mean. Each panel includes estimates for Cognitive (blue dots) and Non-cognitive (orange squares) PGIs, EA4 (black triangles), and within-family EA (black crosses). Point estimates indicated by symbols and associated 95% confidence intervals indicated by vertical lines.

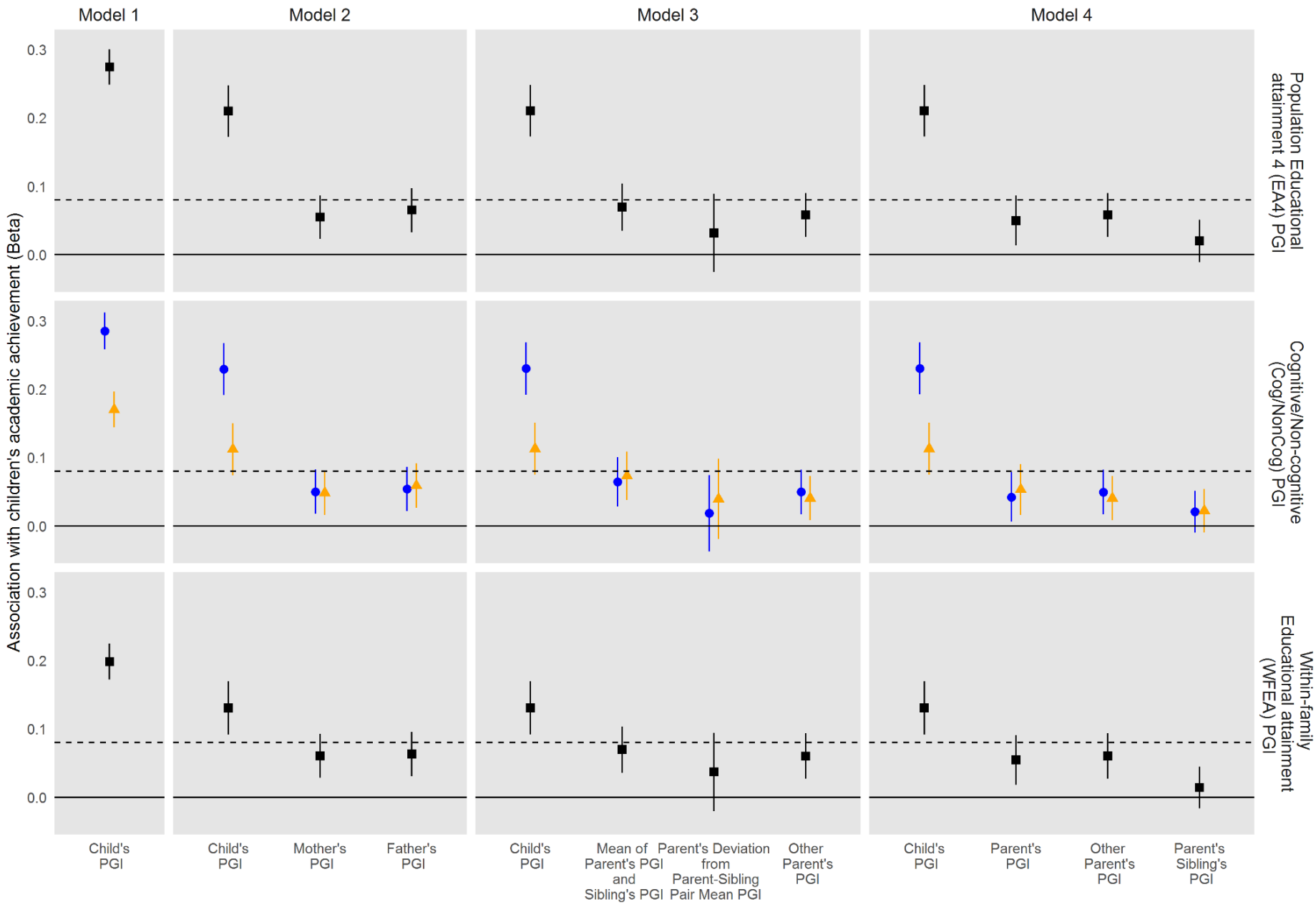
Figures in the following order: Math 5th, Math 8th, Math 9th, Reading 5th, Reading 8th, Reading 9th, English 5th, English 8th.

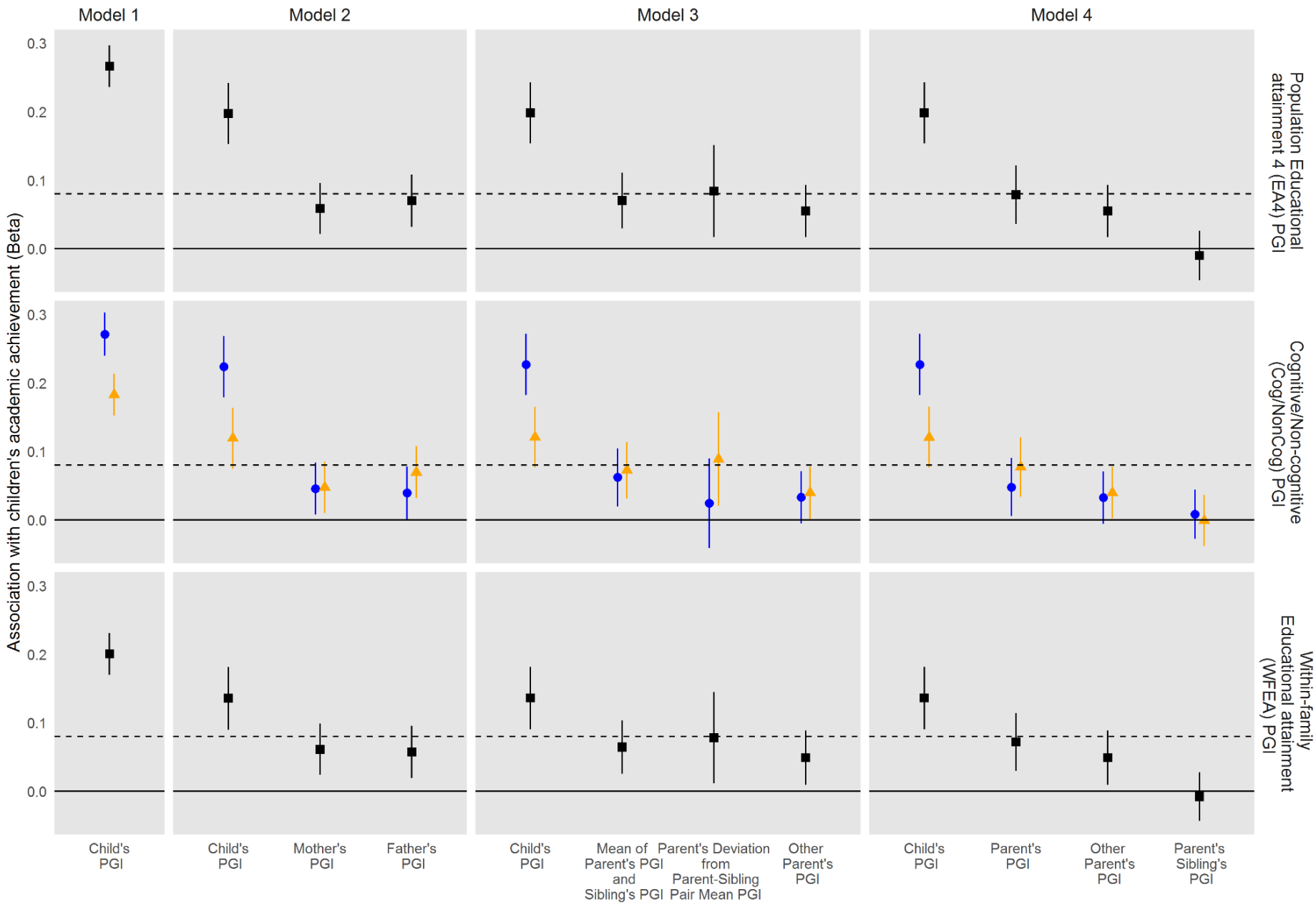

Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI

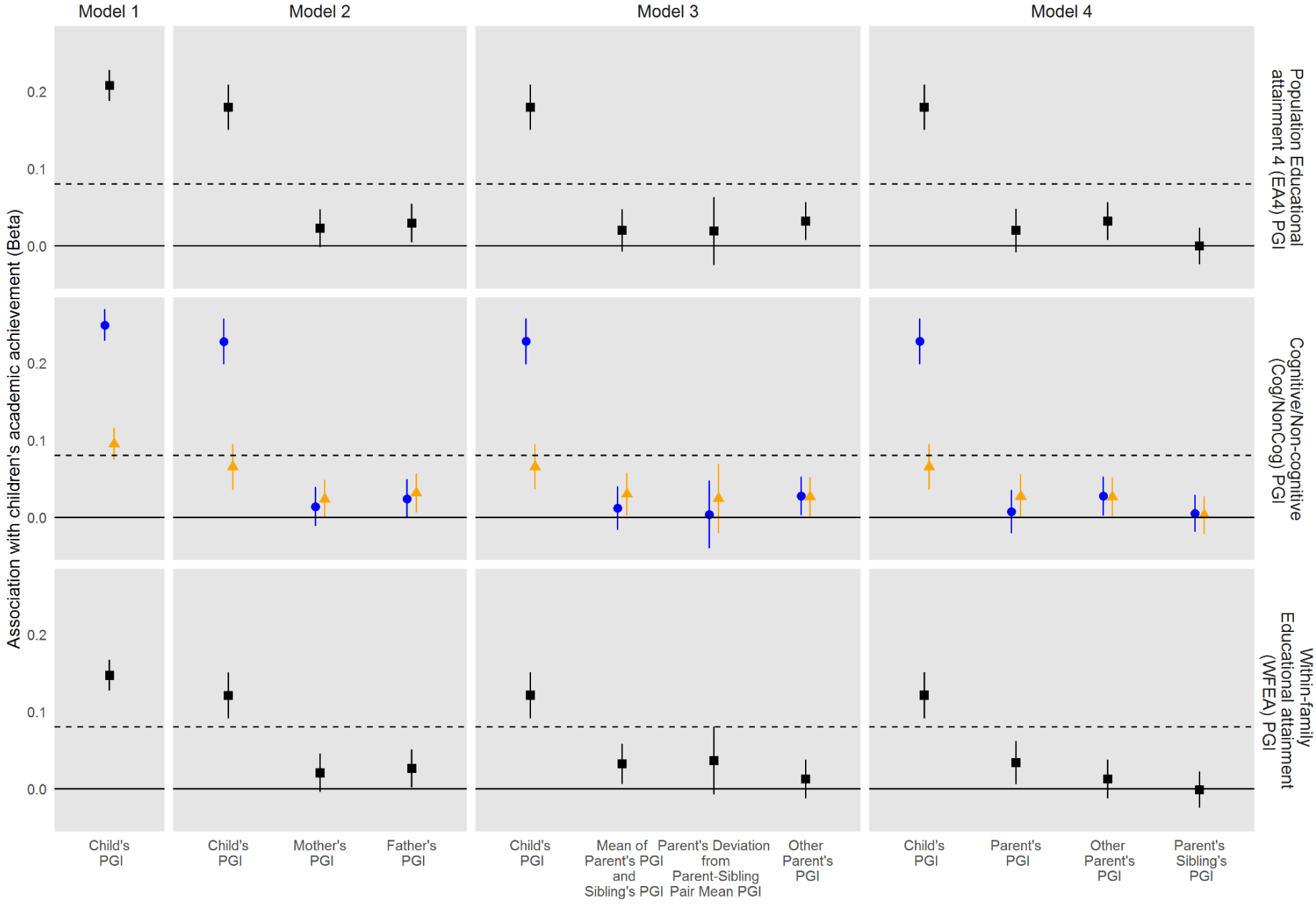

Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI


Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI


Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI


Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.3
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI


Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.3
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI


Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
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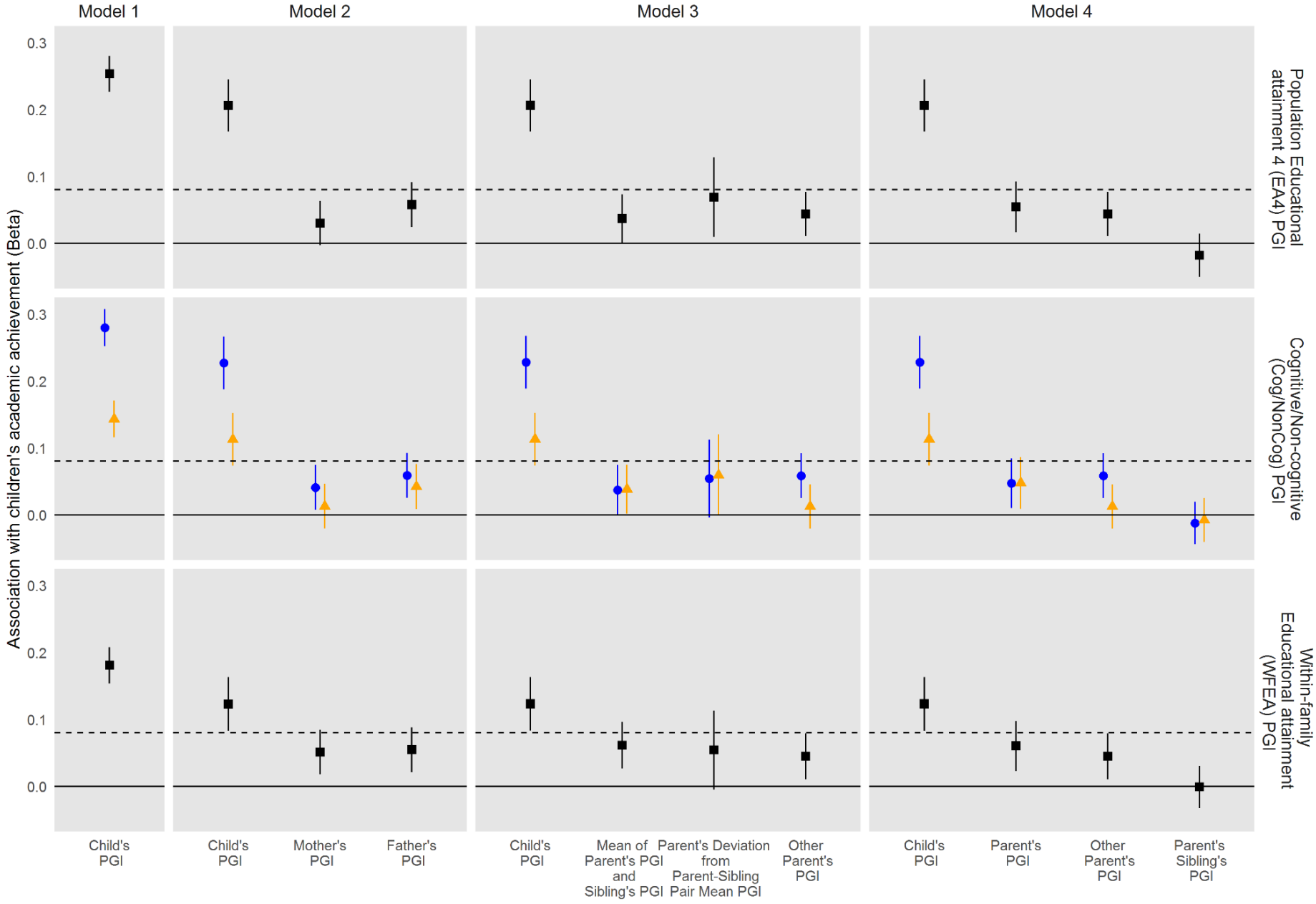
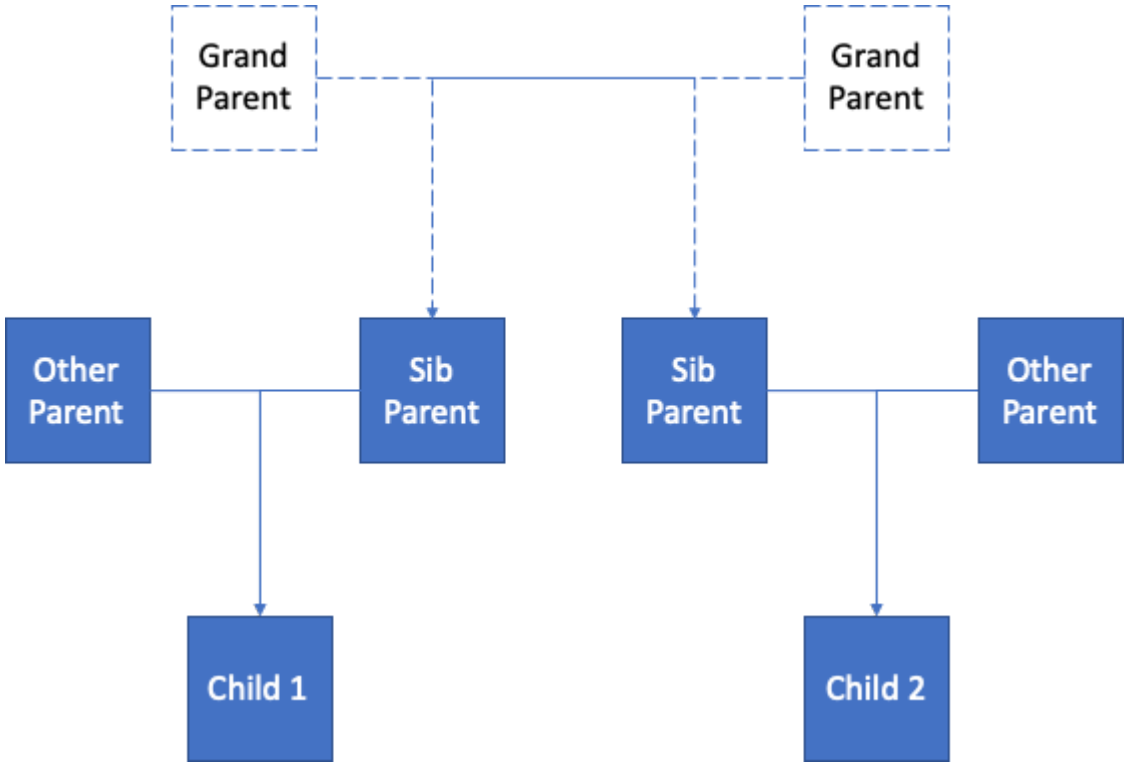
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI


Model 1
Model 2
Model 3
Model 4
Association with children's academic achievement (Beta)
0.3
0.2
0.1
0.0
Population Educational attainment 4 (EA4) PGI
Cognitive/Non-cognitive (Cog/NonCog) PGI
Within-family Educational attainment (WFEA) PGI
Child's PGI
Mother's PGI
Father's PGI
Mean of Parent's PGI and Sibling's PGI
Parent's Deviation from Parent-Sibling Pair Mean PGI
Other Parent's PGI
Parent's PGI
Parent's Sibling's PGI

Supplementary Figure 10. Illustration of data structure



Blue squares indicate MoBa participants. White squares (grandparents) are identified through register links.

Supplementary Figure 11. Results from sensitivity analysis for relatedness

Supplementary Figure S11: Results for the full sample and for a sample restricted by excluding close relatives (except those involved in identification of parameters in models 3 and 4; for models 1 and 2: N_{full}=37,117 and $N_{restricted}$=31,326 ; for models 3 and 4: N_{full}=10,913 and $N_{restricted}$=8,485 families) of test scores including EA4 PGIs for child, non-sibling parent, sibling parent deviation from sibship mean, sibling parent sibship mean. Estimates and their associated 95% confidence intervals for the full sample indicated by squares and whole lines. Estimates and associated 95% confidence intervals for the restricted sample are indicated by triangles and dashed lines.