Parental influences on offspring education: indirect genetic effects of non-cognitive skills

Perline A. Demange[1,2,3], Jouke Jan Hottenga[1], Abdel Abdellaoui[4], Margherita Malanchini[5,6], Benjamin W. Domingue[7,8], Eveline L. de Zeeuw[1,3], Kaili Rimfeld[6], Thalia Eley[6,9], Dorret I. Boomsma[1], Elsje van Bergen[1,3], Gerome Breen[6,9], Michel G. Nivard[1], Rosa Cheesman[10,6]

[1]Department of Biological Psychology, Vrije Universiteit Amsterdam, The Netherlands

[2]Amsterdam Public Health Research Institute, Amsterdam University Medical Centers, Amsterdam, The Netherlands

[3]Research Institute LEARN!, Vrije Universiteit Amsterdam, The Netherlands

[4]Department of Psychiatry, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

[5]Department of Biological and Experimental Psychology, School of Biological and Chemical Sciences, Queen Mary University of London, UK

[6]Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK

[7]Graduate School of Education, Stanford University, USA

[8]Center for Population Health Sciences, Stanford University, USA

[9]NIHR Maudsley Biomedical Research Centre, South London and Maudsley NHS Trust, UK

[10]PROMENTA Research Center, Department of Psychology, University of Oslo, Norway

Abstract

Understanding how parents shape their children's educational trajectories is a socially important research goal. Evidence on the effects of parents' cognitive and non-cognitive skills on offspring education is weakened by poor assessments of non-cognitive skills and inadequate accounting for genetic inheritance. In this preregistered study, we use genetics to assess non-cognitive skills and to index environmental effects of parents, controlling for direct effects of inherited genetic variation. We define the non-cognitive and cognitive heritable contributions to educational attainment using GWAS-by-subtraction, and construct non-cognitive and cognitive skills polygenic scores in three UK and Dutch cohorts. We estimate environmentally mediated effects of polygenic scores (parental indirect genetic effects) on educational achievement and attainment with three designs that include siblings (N=47,459), adoptees (N=6,407), and parent-offspring trios (N=2,534). Heritable non-cognitive and cognitive skills are both involved in parental construction of environments influencing offspring education: indirect genetic effects explain ~37% of total polygenic score effects. This result holds across countries, outcomes, ages and methods, with two exceptions: indirect genetic effects are null for childhood achievement in the Dutch cohort, and lower when estimated with the adoption method. Overall, our findings stress the importance of both non-cognitive and cognitive aspects of the home environment.

Introduction

Parents and children tend to have similar educational outcomes. Given the ties between education, social mobility and health (Deary et al. 2005; Oreopoulos and Salvanes 2011), understanding the mechanisms underlying the intergenerational transmission of education could inform efforts to alleviate inequalities. Relatively few studies have considered the effects of parents' non-cognitive skills (also known as ‘soft skills’ or ‘socio-emotional competencies’) as well as cognitive skills. Both domains show substantial associations with offspring education (Grönqvist et al. 2017), and appear to partially explain the link between parent income and offspring education (Doren and Grodsky 2016).

Two key limitations weaken the base of evidence on effects of parent skills on offspring education: poor phenotypic assessments of parents’ skills, and genetic confounding. First, whereas cognitive skills can be directly measured by tests of domain-specific or general cognitive performance, measurement of non-cognitive skills is more challenging and often incomplete, inconsistent and unreliable (Morris et al. 2018; Gutman and Schoon 2013). Moreover, there is little agreement on what non-cognitive skills to measure in the first place, and studies could have neglected important characteristics. Salient adult non-cognitive contributors to child education could span well beyond the ‘Big Five’ personality traits, into myriad domains of physical and mental health. Nevertheless, consensus is growing and non-cognitive skills have been defined as all skills beyond cognitive skills and knowledge that increase positive life outcomes such as educational attainment (Heckman and Rubinstein 2001).

Genetic methods offer a new approach to defining and estimating the importance of domains of parental skills for offspring education. Both non-cognitive and cognitive skills are substantially genetically influenced, with twin study heritability estimates of 40-70% (Tucker-Drob et al. 2016; Kovas et al. 2015). Demange et al. developed a new method called ‘GWAS-by-subtraction’, using Genomic Structural Equation Modelling (Grotzinger et al. 2019) to ‘subtract’ cognitive ability-related genetic variation from educational attainment genetic variance and assess the remaining latent genetic non-cognitive construct (Demange et al. 2020). These non-cognitive aspects of educational attainment are independent of cognitive skills, and associated

with higher socioeconomic attainment, more open and conscientious personality, and some psychiatric disorders (e.g. higher risk for schizophrenia, lower risk for attention deficit/hyperactivity disorder). However, to our knowledge no research has leveraged GWAS-by-subtraction to understand the effects of *parents'* non-cognitive skills on offspring education.

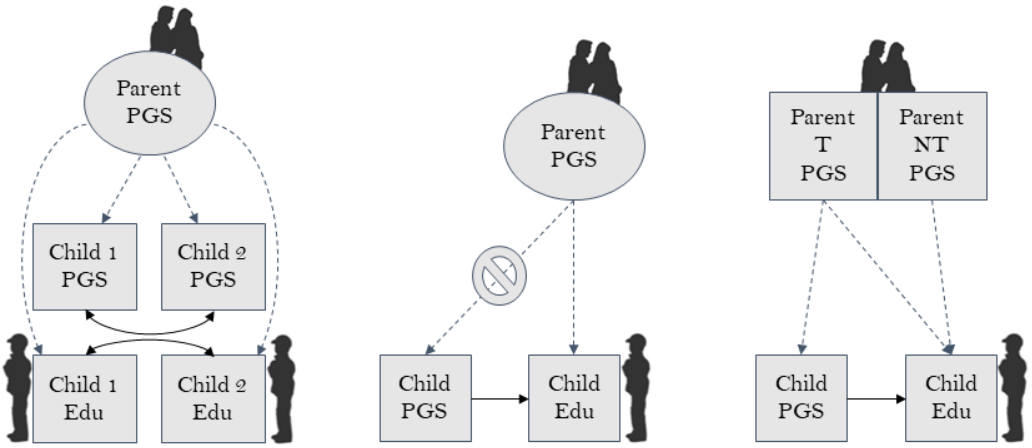
Second, it has been generally assumed that effects of parents' skills on offspring education are primarily due to social causation, whereby parents' skills enable them to provide important resources, or to shape children's education through learning and modelling. Ignoring any shared genetic influences on parents' skills and child educational outcomes confounds estimation of the effects of parental phenotypes on offspring outcome (Hart et al. 2019). For instance, environmental effects of parental education on offspring education have been found to attenuate when genetic transmission is accounted for using adoption or extended twin designs (Holmlund et al. 2011). Thus, naive estimates of intergenerational associations may be poor estimates of the effect parental phenotypes have on offspring' outcomes. In order to establish if parents' (non-)cognitive skills influence child educational outcomes socially, it is vital to account for inherited genetic effects that may confound this association.

Genetic study designs correct for this by separating genetic and environmental effects of parents' skills on offspring education. These designs allow for estimation of a genetic effect of the child's genotype on the child phenotype (direct genetic effect), and an effect of the parental genotype on the child's phenotype, conditional on the child's genotype (parental indirect genetic effect). For example, polygenic scores (individual-level indices of trait-specific genetic endowment; PGS) based on prior GWAS of educational attainment and parents' genotypes that were not transmitted to offspring, are still associated with offspring attainment (Bates et al. 2018; Kong et al. 2018; de Zeeuw et al. 2020). Non-transmitted variants affect offspring attainment indirectly via the environment shaped by parents that influences the development of their children. They denote the effects of numerous heritable parent characteristics, without the need for measures of specific parent phenotypes. Complementary evidence of indirect effects of parents' education-linked genetics on offspring education has also accumulated from sibling and adoption designs, depicted in Figure 1 (Kong et al. 2018; Bates et al. 2018; Selzam et al. 2019; Cheesman et al. 2020). Although no research has systematically compared estimates of indirect genetic effects

across cohorts, they generally are 30-50% the magnitude of direct genetic effects in these studies. It is not known whether parental indirect genetic effects on offspring education occur through cognitive or non-cognitive pathways (or both).

Additionally, no prior research has directly compared estimates of parental indirect genetic effects obtained from different designs. Estimation of associations with genome-wide genetic data may involve numerous biases (Morris et al. 2020). Sibling, adoption and non-transmitted allele designs have different assumptions and subtle differences in potential biases affecting the estimated indirect genetic effect. Specifically, indirect genetic effect estimates from the sibling and non-transmitted allele designs, but not the adoption design, are biased by population stratification and assortative mating. Estimates obtained from the adoption design also do not capture intrauterine environmental effects on child education. All designs may estimate parental indirect genetic effects with bias from sibling genetic effects. Triangulation across designs, and comprehensive sensitivity analyses of possible population stratification, assortative mating and sibling effects, can help strengthen our conclusion on the extent of parental indirect genetic effects, quantify the roles of other environmental effects and detect possible biases.

In the current study (pre-registered: https://osf.io/mk938/), we use a novel approach to investigate the parental skills of social importance for offspring education. We deploy GWAS-by-subtraction to estimate individuals' endowments (PGS) for non-cognitive and cognitive skills, and test how much these operate environmentally via parental influences on offspring educational outcomes. We provide the first multi-cohort comparison of parental indirect genetic effects by using three cohorts of genotyped families in two countries with different educational systems (UK Biobank, the UK Twins Early Development Study, Netherlands Twin Register) with multiple outcome measures of achievement (i.e. standardised test results and teacher-reported grades in childhood and adolescence) and attainment (i.e. years of completed education reported in adulthood). For the first time, we triangulate across three different and complementary study designs for estimating parental indirect genetic effects.



	Sibling design	**Adoption design**	**Non-transmitted PGS design**
Total genetic effect	$\beta_{\text{Between-siblings}}$	$\beta_{\text{Non-adopted}}$	$\beta_{\text{Transmitted}}$
Direct genetic effect	$\beta_{\text{Within-siblings}}$	β_{Adopted}	$\beta_{\text{Transmitted}} - \beta_{\text{Non-transmitted}}$
Indirect genetic effect	$\beta_{\text{Between-siblings}} - \beta_{\text{Within-siblings}}$	$\beta_{\text{Non-adopted}} - \beta_{\text{Adopted}}$	$\beta_{\text{Non-transmitted}}$

Figure 1. Analytical designs to estimate direct and parental indirect genetic effects. Note: β = estimated effect of polygenic score (PGS) on outcome; square = observed, circle = unobserved; the total effect of a PGS (equivalent to that typically estimated in standard population analyses of unrelated individuals) captures both direct and indirect genetic effects; direct genetic effects (controlling for indirect genetic effects) are represented with solid arrows. **The sibling design** estimates indirect genetic effects by comparing between-family and within-family (i.e. between-sibling or between-DZ twin) polygenic score associations. The within-family direct genetic effect estimate leverages random genetic differences between siblings, and the indirect genetic effect is estimated by subtracting this from the between-family PGS effect estimate. **The adoption design** capitalises on the fact that adoptees are unrelated to their parents, so their PGS do not capture indirect genetic effects. Associations between adoptee PGS and educational outcomes therefore estimate the direct genetic effect. The indirect genetic effect is estimated by subtracting this direct effect from the total PGS effect estimated in the control group of non-adopted individuals. **The non-transmitted PGS design** estimates the indirect genetic effect as the effect of the parental PGS based on genetic variants that were not transmitted to children and therefore act via the environment.

Results

GWAS-by-subtraction results

We identified the genetic components of cognitive and non-cognitive skills using Genomic SEM, following the approach of Demange et al. 2020, in samples that excluded participants used for polygenic score analyses. Educational attainment and cognitive performance meta-analysed summary statistics (see Methods) were regressed on two independent latent variables, *Cog* and *NonCog* (see **Supplementary Figure 1**). These two latent factors were then regressed on each SNP; we obtained associations for 1,071,804 HapMap3 SNPs. The LD score regression-based SNP heritabilities of *NonCog* and *Cog* were 0.05 (SE=0.00) and 0.18 (SE=0.01), respectively. More information on the GWAS is presented in **Supplementary Table 1**.

Descriptive statistics

We used SNP associations with the *NonCog* and *Cog* latent variables to create individual-level polygenic scores in 3 cohorts with family data and educational achievement and/or attainment outcomes. Sample sizes for individuals with polygenic score and educational outcome data were: 39,500 UK Biobank siblings, 6,409 UK Biobank adoptees, up to 4,796 DZ twins in the Twin early Development Study (TEDS), up to 3,163 twins and siblings in the Netherlands Twin Register (NTR), and up to 2,534 NTR individuals with both parents genotyped. Full phenotypic descriptive statistics are available in **Supplementary Table 2**.

Parents' heritable non-cognitive and cognitive skills both influence offspring education indirectly via the environment.

NonCog and *Cog* PGS were similarly associated with educational outcomes (indicated by the total height of the bars in **Figure 2A**). *Cog* PGS showed slightly greater penetrance in the overall meta-analysis across cohorts, designs and outcomes (total β_{NonCog}=0.23, SE=0.02; total β_{Cog}=0.26, SE=0.02). We investigated environmental effects of parents' non-cognitive and cognitive skills on offspring education by estimating the contribution of parental indirect genetic

effects to the total effects of *NonCog* and *Cog* PGS. **Figure 2A** shows that, for *both NonCog* and *Cog* PGS, indirect genetic effects of parents on offspring education were present (meta-analytic indirect β_{NonCog}=0.09, SE=0.04; indirect β_{Cog}=0.10, SE=0.02), in addition to direct genetic effects (direct β_{NonCog}=0.13, SE=0.02; direct β_{Cog}=0.16, SE=0.01). Averaged across all designs, outcomes and cohorts, indirect environmentally-mediated effects explained 36% of the total effect of the *NonCog* PGS, and 38% of the total effect of the *Cog* PGS. However, results varied depending on the methods used and outcomes investigated. Results per cohort, outcome and design**,** as well as total genetic effects and the ratio of indirect to total effects are reported in **Supplementary Table 3** and **Supplementary Figure 2, 3 & 4**. Meta-analytic results are reported in **Supplementary Table 4**. Z-tests results comparing direct and indirect effects are reported **Supplementary Table 5**.

A.

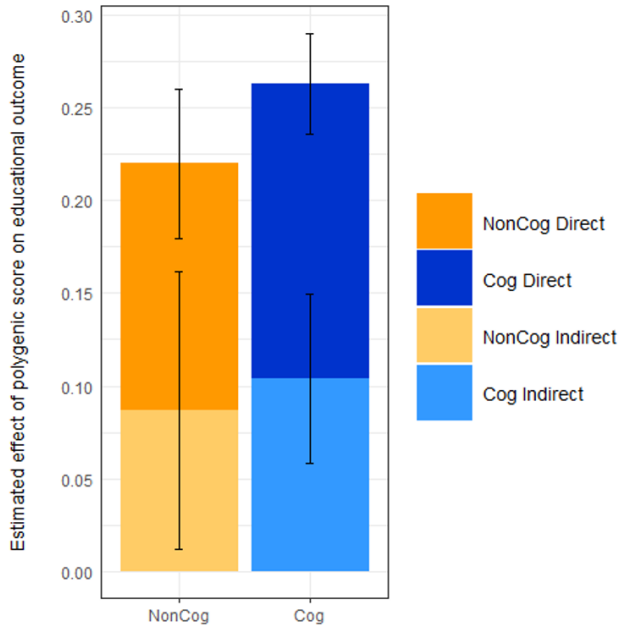


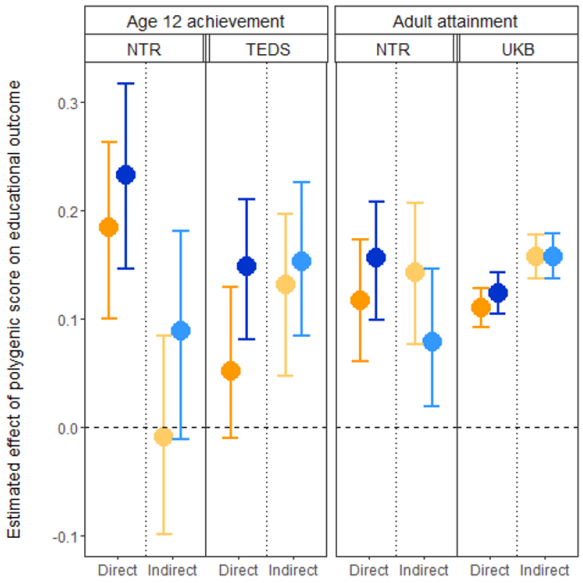
Figure 2.

A. Total effects of *NonCog* and *Cog* PGS on educational outcomes include both direct and indirect genetic mechanisms. Indirect genetic effects work through the environment that parents provide for their children. Notes: beta coefficients were obtained from meta-analysis of effects across cohorts, designs and outcome phenotypes; bars=95% CIs.

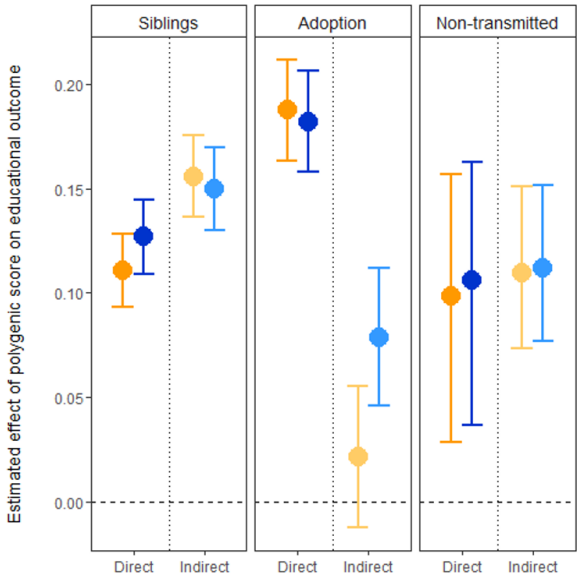
B. Estimates of direct and indirect effects of *NonCog* and *Cog* PGS by **cohort** (for age 12 and adult outcomes). Only results for the sibling method; NTR = Dutch cohort (N=1631 and N=3163 respectively), TEDS (N=2862) and UKB (N=16,624) are UK cohorts.

C. Estimates of direct and indirect effects of *NonCog* and *Cog* PGS by analytical **design**. Sample sizes: N=42,663 siblings (results meta-analysed across UKB and NTR cohorts and outcome); N=6407 adoptees and 6500 non-adopted individuals (UKB); N=2534 trios in NTR (results meta-analysed across outcomes).

B.



C.



Estimates of parental indirect genetic effects vary slightly by age, outcome and cohort.

Figure 2B shows estimates of direct and indirect genetic effects of *NonCog* and *Cog* PGS for different cohorts and educational outcomes, holding the design constant (i.e. the sibling design, which was available for all cohorts and outcomes). Estimates were highly consistent across cohorts except for age 12 achievement in Dutch versus UK cohorts: there was no indirect effect of *NonCog* or *Cog* in NTR (indirect β_{NonCog}=-0.01, SE=0.05; indirect β_{Cog}=0.09, SE=0.05; standardized test outcome) while the indirect effect represented most of the total effect in TEDS (indirect β_{NonCog}=0.13, SE=0.04; indirect β_{Cog}=0.15, SE=0.04; teacher reported outcome). In TEDS, the standardized test taken at 16 years-old in the UK (GCSE) was also associated with indirect genetic effects (indirect β_{NonCog}=0.19, SE=0.03; indirect β_{Cog}=0.14, SE=0.03), suggesting that formalized examinations do not eliminate parental environmental effects in general. For adult educational attainment, estimates of direct and indirect effects were similar in the Dutch (NTR: indirect β_{NonCog}=0.14, SE=0.03; indirect β_{Cog}=0.08, SE=0.03) and UK (UKB: indirect β_{NonCog}=0.16, SE=0.01; indirect β_{Cog}=0.16, SE=0.01) cohorts.

Estimates of indirect genetic effect depend on the analytical design: adoption-based estimates are lower.

Figure 2C shows estimates of direct and indirect genetic effects of *NonCog* and *Cog* PGS for different designs, holding the phenotype constant (i.e. educational attainment, which was available for all three methods). While estimates obtained with sibling and non-transmitted PGS methods indicate similar direct and indirect effect sizes (indirect βs ranged between 0.11 and 0.16; see Supplementary Tables 3 and 4), the adoption design yielded low to null indirect genetic effects for both *NonCog* and *Cog* PGS (indirect β_{NonCog}=0.02, SE=0.02; indirect β_{Cog}=0.08, SE=0.02).

Figure 3 summarises potential contributors to estimates of parental indirect genetic effects in the three designs, thus highlighting explanations for the lower adoption-based estimates. The adoption design estimates indirect genetic effects with less bias from population stratification

and assortative mating than the sibling and non-transmitted allele designs: assuming that the magnitudes of these biases is consistent between adopted and non-adopted groups, estimating the indirect genetic effect by comparing the groups ($\beta_{adopted}$ - $\beta_{non\text{-}adopted}$) will cancel them out. Also, unlike the sibling and non-transmitted allele designs, the adoption design does not capture indirect genetic effects occurring in the prenatal period. Any excess indirect genetic effect estimated in the sibling/non-transmitted allele designs compared to the adoption design therefore indicates the overall impact of population stratification, assortative mating, and prenatal indirect genetic effects. However, these comparisons cannot shed light on sibling indirect effects, since these likely contribute to parental indirect genetic effect estimates in all of the designs.

We found a larger discrepancy between adoption versus sibling- and trio-based estimates of indirect genetic effects for the *NonCog* PGS than for *Cog*. Using the adoption design, the indirect genetic effect of the *NonCog* PGS is 88% lower than with the sibling design, while it is 47% lower for *Cog*. This suggests that estimates for *NonCog* are affected more strongly than *Cog* by population stratification, assortative mating and/or prenatal indirect genetic effects.

	Sibling design	Adoption design	Non-transmitted alleles design
Parental indirect effect	X	X	X
Prenatal indirect effect	X		X
Sibling indirect effect	X	X	X
Population stratification	X		X
Assortative mating	X		X

Figure 3. Potential components and biases of estimated parental indirect genetic effects depending on the analytical design. Note: X= a component (parental prenatal and postnatal indirect genetic effects) or bias (sibling indirect genetic effects, population stratification, and assortative mating) is present**.** The sibling and non-transmitted allele designs have the same patterns of biases and are likely to give an upper bound measure of the indirect genetic effect. The adoption design can be viewed as a lower bound estimate of indirect genetic effects.

Population stratification and assortative mating, but not sibling indirect effects, might inflate estimates of indirect genetic effects from sibling and non-transmitted alleles designs.

Although triangulating designs suggested that population stratification, assortative mating, and prenatal indirect genetic effects contribute to the higher estimated parental indirect genetic effects from trio/sibling designs relative to the adoption design, this approach cannot disentangle the relative importance of these individual biases. Comparing results from these designs also does not allow us to detect sibling indirect genetic effects. To this end, we conducted additional sensitivity analyses to assess the magnitudes of these biases (not pre-registered).

First, we analysed the GWAS summary data on which the polygenic scores were based, using LD score regression in order to detect an influence of population stratification. The LD score regression ratio statistics of uncorrected educational attainment and cognitive performance GWAS was estimated at 0.11 (SE=0.01) and 0.06 (SE=0.01), respectively (**Supplementary Table 1**). These non-null estimates indicated that a small but significant portion of the GWAS signal was potentially attributable to residual population stratification. As CP seems less prone to population stratification than EA, it is possible our estimates of direct and indirect genetic effects of *NonCog* were more biased by population stratification than *Cog*.

Second, we detected slight evidence of assortative mating, which appeared stronger in the UK than Dutch cohorts. In NTR, parental PGS correlations are non-significant (*NonCog* r= 0.03, *Cog* r=0.02). Sibling PGS intraclass correlations ranged between 0.49-0.52 in NTR, and between 0.53-0.56 in TEDS and UK Biobank. This supports the presence of assortative mating on *NonCog* and *Cog* PGS potentially biasing our estimates of indirect genetic effects in UK cohorts, but less in our Dutch cohort. See **Supplementary Table 6** for full correlations.

Third, we performed three different sensitivity analyses, none of which supported the presence of indirect effects of siblings' *NonCog* and *Cog* PGS on individuals' educational outcomes. Our first approach leveraged sibling polygenic scores, the rationale being that in the presence of a sibling effect, a sibling's PGS will influence a child's outcome even conditional on the PGS of

the child and parents. Using twins and their parents in NTR, we found no effects of siblings' *NonCog* or *Cog* on achievement or attainment (**Supplementary Table 7**). In a second approach, the difference in PGS effects on EA between monozygotic (MZ) and dizygotic (DZ) individuals was tested. Since MZ twins are more genetically similar than DZ twins, their PGS should capture more of the indirect genetic effect of their twin. In NTR and TEDS, PGS effects were not significantly different between MZ and DZ twins, indicating the absence of sibling indirect effects (**Supplementary Table 8 & Supplementary Figure 5**). Finally, in UKB, we tested the strength of PGS effects on EA given the number of siblings an individual reported having. If having more siblings leads to a stronger overall sibling effect, this will be captured as an increased effect of an individual's own PGS on the outcome in the presence of more genetically related siblings. As a negative control, we conducted the same analysis in adoptees. Adoptees were not genetically related to their adopted siblings, thus we expect no change in predictive accuracy as the number of siblings increases. We observed an increase of β_{Cog} (and more moderately of β_{NonCog}, both with large SEs) with an increased number of siblings. However, this pattern was also present in adoptees (unrelated to their siblings). This indicates that the increased penetrance is not due to sibling indirect effects but rather to other environmental characteristics of families with numerous children (**Supplementary Table 9 & Supplementary Figure 6**).

Discussion

We used genetic methods to study environmental effects of parents' skills on child education. We found evidence that characteristics tagged by *NonCog* and *Cog* polygenic scores (PGS) are both involved in how parents provide environments conducive to offspring education. Indeed, indirect genetic effects explain ~37% of the total effects of both PGS overall (total β_{NonCog}=0.23, total β_{Cog}=0.26). This result was consistent across two countries, generations, outcomes and analytic designs, with two notable exceptions. First, estimated parental indirect genetic effects were null for childhood achievement in our Dutch cohort (NTR), but not for comparable outcomes in our UK cohort (TEDS). Second, parental indirect genetic effects estimated with the adoption design were lower than for the sibling and non-transmitted allele designs, particularly for the *NonCog* PGS. Given that the adoption-based estimates of indirect genetic effects are

more robust to population stratification and assortative mating, we hypothesised that these biases may contribute substantially in the other two designs, especially for the *NonCog* PGS. This hypothesis was supported by results from sensitivity analyses.

This study demonstrates the power of using genetically sensitive approaches to assess elusive phenomena: non-cognitive skills, and genuine environmental influences of parents unconfounded by effects of genetic inheritance. Compared to analysing a set of measured parental non-cognitive skills, our GWAS-by-subtraction approach captures a wider array of traits linked genetically to attainment, and therefore broadly quantifies the overall salience of parents' non-cognitive skills. Our evidence that parents' non-cognitive and cognitive skills are both important for children's education complements the growing literature that has considered effects of specific skills within both of these domains (Grönqvist et al. 2017; Doren and Grodsky 2016). Importantly, the parental indirect genetic effects we have identified may capture proximal forms of 'nurture' (e.g. a parent directly training their child's cognitive skills, or cultivating their child's learning habits through participation and support) and/or more distal environmental effects (e.g. a parent's openness to experience leading them to move to an area with good schools). The environmental effects of parents' non-cognitive and cognitive skills are likely to be even larger than we estimate, because our approach only captures effects of parent skills tagged by current GWAS. Polygenic scores index a subset of the common genetic component of parent skills, which is in turn a fraction of the total genetic component (missing heritability (Manolio et al. 2009; Young 2019)), and cannot account for the non-heritable component of parent skills.

The lower importance of parental indirect genetic effects for child achievement in the Netherlands compared to similar UK outcomes indicates that our UK achievement outcomes more strongly capture variation in family background. This difference could result from the design of these achievement measures: while Dutch achievement test results are adjusted for subgroup differences (including region), UK teacher reports might still be affected by student social background. Differences between the Dutch and UK societies and educational systems could also produce this result. It has previously been suggested that estimates of family shared environmental variance in twin studies can serve as indicators of social inequality, and the same logic holds for indirect genetic effects (Kovas et al. 2013). For adult attainment, results were

more consistent across UK and Dutch cohorts, corresponding with recent twin study meta-analytic evidence for consistent shared environment influence on educational attainment across social models (Silventoinen et al. 2020). This consistency also suggests that the difference in childhood is not due to a cohort or population difference. The higher indirect genetic effects in adult attainment might reflect an increase in environmental variance due to tracking in secondary schools in the Netherlands (de Zeeuw et al. 2020). Socioeconomic disparities in academic performance seem to increase more between ages 10 and 15 in the Netherlands than they do in the UK (OECD 2018). Despite no parental indirect genetic effects on the achievement test at 12, children whose parents have a high education are more likely to enroll in a higher educational track (van Spijker et al. 2017), suggestive of higher parental effects on secondary and later education, which should be tested in further studies.

We found that the choice of the method used to estimate indirect genetic effects matters, with estimates based on the adoption design being systematically lower. Direct comparison of results across designs suggested that 47% (for *Cog*) and 88% (for *NonCog*) of the indirect genetic effects estimated using the sibling design are due to population stratification and assortative mating (as well as prenatal indirect genetic effects; see below). The importance of population stratification for genetic associations with educational attainment was suggested by recent UK Biobank studies (Young et al. 2020; Kong et al. 2020), and was reflected in our sensitivity analyses. Our LD score regression results indicated the presence of residual population stratification in CP GWAS, and more strongly in EA GWAS, suggesting that population stratification is stronger for *NonCog.* There was some evidence of assortative mating, with sibling PGS correlations above their expectation (>0.5) particularly in the UK cohorts. This country difference in assortment was supported by the lower estimated spouse PGS correlations in NTR (0.02 for *Cog*, 0.03 for *NonCog*) compared to that previously estimated for the EA PGS in the UK Biobank (0.06) (Yengo et al. 2018). There was no difference in assortative mating between *Cog* and *NonCog*, suggesting that population stratification explains the particularly large design-based discrepancy between estimates of indirect genetic effects for *NonCog*. Population stratification should be carefully considered in studies using *NonCog* PGS. Methods should be developed to parse the contributions of assortative mating, population stratification, indirect and direct genetic effects to complex traits. This could be achieved using genomic data

on extended pedigrees, inspired by extended twin family designs (Keller et al. 2009). Additionally, indirect genetic effects on education might not only arise from parents but might span across more than a single generation, for example the influence of grandparents. Since cumulative indirect genetic effects are all removed when a child is adopted, their presence would contribute to the observed difference in indirect effect between the adoption and other designs.

We did not find evidence that indirect effects of siblings' *NonCog* and *Cog* PGS affect individual differences in educational outcomes, using three different approaches. This corresponds with null findings regarding indirect effects of siblings' educational attainment genetics in the UK Biobank (Kong et al. 2020; Young et al. 2020). This does not rule out the existence of indirect sibling genetic effects in other populations (or effects such as parental compensation of sibling PGS differences (Fletcher et al. 2020)). Indirect genetic effects of sibling EA PGS were found in an Icelandic cohort (Kong et al. 2018). One extended twin study found that the sibling environment contributed 12% of the total variation in educational attainment in Norway, whereas the environment provided by parents explained only 2.5% of the variance (Lyngstad et al. 2017). It is possible that our PGS analyses were not sufficiently powered to detect indirect genetic effects of siblings, since they were based on lower sample size than our main analyses. However, our results suggest that indirect genetic effects of siblings on education are small. Therefore, our methods provide good proxies for parental indirect genetic effects, with minimal inflation from sibling effects.

Our data suggest that the adoption design provides a useful lower-bound estimate of indirect genetic effects of parents. Given that there appears to be no sibling effects of the *Cog* or *NonCog* PGS, our adoption-based estimates, unbiased by population stratification and assortative mating, are likely a closer measure of parental indirect genetic effects. However, three other factors potentially make the adoption-based estimates of indirect genetic effects (too) conservative. First, adoption based indirect effect estimates exclude prenatal indirect genetic effects (and indirect genetic effects taking place between the birth and moment of adoption), which might influence educational outcomes (Armstrong-Carter et al. 2019; Trejo 2020). While we are unable to test for prenatal indirect effects, these could be investigated in cohorts with pregnancy information, adjusting for postnatal indirect genetic effects. Second, adoptees may have been

exposed to a narrower range of environments (e.g. family socioeconomic status) compared to non-adopted individuals (McGue et al. 2007). This form of selection bias is likely to increase the genetic variance at the expense of the indirect genetic effect. Third, selective placement of children in adoptive families matching characteristics of their biological families could result in correlation between child and parent genotypes, leading to an underestimation of the indirect genetic effect. There is modest evidence for selective placement of adoptees based on education in the US (Ho et al. 1979). We cannot directly test for selection factors in the UK Biobank, since there is no information on the adoptive parents.

We acknowledge several limitations. First, while we suggest that an attribute of our study is the broad and hypothesis-free characterisation of non-cognitive skills, our GWAS-by-subtraction approach is still limited by measures of cognitive performance and educational attainment in the original GWAS. Some cognitive skills might not be reflected in the available Cognitive Performance GWAS, which could lead to contamination of the *NonCog* factor by genetic influences affecting cognition. However, previous analyses have shown that *NonCog* PGS predicts significantly less variation in cognition than the *Cog* PGS (Demange et al. 2020). Additionally, our *NonCog* latent variable reflects the residual variance of adult educational attainment, and therefore is a measure of non-cognitive aspects of *adult* EA. Non-cognitive aspects of childhood achievement might differ somewhat, which might lead to an underestimation of indirect genetic effects of the *NonCog* PGS on these outcomes. Second, the generalisability of our results is limited. Highly educated individuals are over-represented in all cohorts. Participation bias also affects GWAS results (Pirastu et al. 2020). Selection effects may be especially strong in the adoption design as adoptions may depend on (partially heritable) phenotypes of the biological parents, and many adoptive parents are also selected on the basis of their (partially heritable) behavioural phenotypes. Additionally, only participants of European descent were included in the analysis. Third, replication efforts are needed. Special effort should be targeted to include diverse ancestry participants. While our overall estimates are well powered due to the aggregation of cohorts, some analyses rely on a single sample (e.g. non-transmitted allele and adoption designs were only performed in NTR and UK Biobank cohorts, respectively). As such, results from these analyses might reflect specifics of these samples and not design-specific biases, and should be replicated.

Several future research directions are apparent. First, given that we have quantified overall environmental effects of parents on offspring education tagged by *NonCog* and *Cog* PGS, the next step could be to identify specific mediating parent characteristics, whether proximal or distal. Researchers could also examine mediating *child* characteristics on the pathway between their parents' characteristics and their own educational outcomes. We speculate that parents' non-cognitive skills do not affect offspring education by affecting those same non-cognitive skills in offspring. This is because existing twin research shows no influence of shared environmental factors on individual differences in children's measured non-cognitive skills such as grit and self-control (Rimfeld et al. 2016; Malanchini et al. 2018; Willems et al. 2019).
A second future direction is to incorporate gender and socioeconomic status into research on indirect genetic effects on education. Twin data show that shared environmental contributions to educational attainment are larger for women than for men (Silventoinen et al. 2020). It is unknown whether this finding holds for indirect genetic effects, including on childhood educational achievement outcomes. Another gender aspect to consider is differential maternal and paternal indirect genetic effects (Eilertsen et al. 2020). There is some evidence (although not genetically informed) that mother and father skills show unique associations with offspring education (Grönqvist et al. 2017). Indirect effects of parents' genetic endowment for non-cognitive skills on child education might be mediated or moderated by parents' income or cultural capital (including school-related skills and habits). While one qualitative study suggested that middle class parents are more likely than working class parents to 'cultivate' children's cognitive and non-cognitive skills in fostering educational achievement (Lareau 2011), there is recent quantitative evidence that low-income mothers report more frequent activities that facilitate cognitive stimulation (Cooper 2020).

In sum, this study provides evidence for environmental effects of parents' non-cognitive and cognitive skills on offspring educational outcomes, indexed by indirect genetic effects of polygenic scores. Combining cohorts and comparing three methods for estimating indirect genetic effects allowed us to obtain robust findings and assess important biases. These results have significance for human health, as the role parents play in successful cognitive development and (mental) health development go hand in hand.

Methods

The study methods were pre-registered on the Open Science Framework (https://osf.io/mk938/). Additional non-preregistered analyses are indicated as such below and should be considered exploratory. Additional deviations from the pre-registration are detailed in **Supplementary Note**.

Samples

UK Biobank

The UK Biobank is an epidemiological resource including British individuals aged 40 to 70 at recruitment (Allen et al. 2014). Genome-wide genetic data came from the full release of the UK Biobank data, and were collected and processed according to the quality control pipeline (Bycroft et al. 2018).

We defined three subsamples of the UK Biobank to be used for polygenic score analyses: adopted participants, a control group of non-adopted participants, and siblings. Starting with UK Biobank participants with QC genotype data and educational attainment data (N=451,229), we first identified 6407 unrelated adopted individuals who said yes to the question "Were you adopted as a child?" (Data-Field 1767). We restricted the sample to unrelated participants (kinship coefficient <1/(2^9/2)) (Manichaikul et al. 2010). Second, our comparison sample (N=6500) was drawn at random from non-adopted participants who were unrelated to each other and to the adopted participants. Third, we identified 39,500 full-siblings, excluding adopted individuals. We defined full-siblings as participants with a kinship coefficient between 1/(2^(3/2)) and 1/(2^(5/2)) and a probability of zero IBS sharing >0.0012, as suggested by (Bycroft et al. 2018) and (Manichaikul et al. 2010).

After excluding the three sub-samples for polygenic score analyses and individuals related to these participants, we were left with 388,196 UK Biobank individuals with educational attainment (EA) data, and 202,815 individuals with cognitive performance (CP) data. We used

these remaining individuals for the GWAS of EA and CP, and later meta-analysis with external GWASs (Lee et al. 2018) (see 'Statistical Analyses' and **Supplementary Note**).

Twins Early Development Study (TEDS)

The Twins Early Development Study (TEDS) is a multivariate, longitudinal study of >10,000 twin pairs representative of England and Wales, recruited 1994–1996 (Rimfeld et al. 2019). The demographic characteristics of TEDS participants and their families closely match those of families in the UK. Written informed consent was obtained from parents prior to data collection and from TEDS participants themselves past the age of 18. Analyses were conducted on a sub-sample of dizygotic (DZ) twin pairs with genome-wide genotyping and phenotypic data on school achievement at age 12 (1431 DZ pairs) and age 16 (2398 pairs).

Netherlands Twins Register (NTR)

The Netherlands Twin Register (NTR) (Ligthart et al. 2019) is established by the Department of Biological Psychology at the Vrije Universiteit Amsterdam and recruits children and adults twins for longitudinal research. Data on health, personality, lifestyle and others, as well as genotyping data have been collected on participants and their families. We included in our analyses european-ancestry participants with available genotypic data.

We created a subsample of full-siblings. NTR contains information on numerous monozygotic multiples (twins or triplets). Because MZ multiples share the same genes, we randomly excluded all individuals but one per MZ multiple. Only siblings with complete genetic and outcome data were subsequently included in the analyses: 1631 siblings with CITO (achievement test taken during the last year of primary school) data (from 757 families) and 3163 siblings with EA data available (from 1309 families).

We created a subsample with complete offspring, maternal and paternal genotypic data (i.e. trios). Among individuals with available parental genotypes, respectively 1526 (from 765 families) and 2534 (from 1337 families) had reported CITO and EA information.

The siblings and trios subsets are not independent: for CITO, 823 participants are present in both subsets, 1374 for EA.

Phenotypic Measures

UK Biobank

Educational attainment and *cognitive performance* phenotypes were defined following Lee et al. 2018. From data-field 6238, educational attainment was defined according to ISCED categories and coded as the number of Years of Education. The response categories are: none of the above (no qualifications) = 7 years of education; Certificate of Secondary Education (CSEs) or equivalent = 10 years; O levels/GCSEs or equivalent = 10 years; A levels/AS levels or equivalent = 13 years; other professional qualification = 15 years; National Vocational Qualification (NVQ) or Higher National Diploma (HNC) or equivalent = 19 years; college or university degree = 20 years of education. For cognitive performance, we used the (standardized) mean of the standardized scores of the fluid intelligence measure (data-field 20016 for in-person and 20191 for an online assessment).

TEDS

Educational achievement at age 12 was assessed by teacher reports, aggregated across the three core subjects (Maths, English, and Science).

Educational achievement at age 16 was assessed by self-reported results for standardized tests taken at the end of compulsory education in the United Kingdom -- General Certificate of Secondary Education; GCSE). GCSE grades were coded from 4 (G; the minimum pass grade) to 11 (A∗; the highest possible grade). As with the age 12 measure, we analysed a variable representing mean score for the compulsory core subjects.

NTR

Educational attainment was measured by self-report of the highest obtained degree (Abdellaoui et al. 2015). This measure was re-coded as the number of years in education, following what was done in Okbay et al. 2016.

Academic achievement is assessed in the Netherlands by a nation-wide standardized educational performance test (CITO) around the age of 12 during the last year of primary education. CITO is used to determine tracking placement in secondary school in the Netherlands, in combination with teacher advice. The total score ranges from 500 to 550, reflecting the child's position relative to the other children taking the test this particular year.

Genotype quality control

UK Biobank

SNPs from HapMap3 CEU (1,345,801 SNPs) were filtered out of the imputed UK Biobank dataset. We then did a pre-PCA QC on unrelated individuals, and filtered out SNPs with MAF < .01 and missingness > .05, leaving 1,252,123 SNPs. After removing individuals with non-European ancestry, we repeated the SNP QC on unrelated Europeans (N = 312,927), excluding SNPs with MAF < .01, missingness >.05 and HWE $p < 10^{-10}$, leaving 1,246,531 SNPs. The HWE p-value threshold of 10^{-10} was based on: http://www.nealelab.is/blog/2019/9/17/genotyped-snps-in-uk-biobank-failing-hardy-weinberg-equilibrium-test. We then created a dataset of 1,246,531 QC-ed SNPs for 456,064 UKB subjects of European ancestry. Principal components were derived from a subset of 131,426 genotyped SNPs, pruned for LD ($r^2 > 0.2$) and long-range LD regions removed (Abdellaoui et al. 2013). PCA was conducted on unrelated individuals using flashPCA v2 (Abraham et al. 2017).

TEDS

Two different genotyping platforms were used because genotyping was undertaken in two separate waves. AffymetrixGeneChip 6.0 SNP arrays were used to genotype 3,665 individuals.

Additionally, 8,122 individuals (including 3,607 DZ co-twin samples) were genotyped on Illumina HumanOmniExpressExome-8v1.2 arrays. After quality control, 635,269 SNPs remained for AffymetrixGeneChip 6.0 genotypes, and 559,772 SNPs for HumanOmniExpressExome genotypes.

Genotypes from the two platforms were separately phased and imputed into the Haplotype Reference Consortium (release 1.1) through the Sanger Imputation Service before merging. Genotypes from a total of 10,346 samples (including 3,320 DZ twin pairs and 7,026 unrelated individuals) passed quality control, including 3,057 individuals genotyped on Affymetrix and 7,289 individuals genotyped on Illumina. The identity-by-descent (IBD) between individuals was < 0.05 for 99.5% in the merged sample excluding the DZ co-twins (range = 0.00 – 0.12) and ranged between 0.36 and 0.62 for the DZ twin pairs (mean = 0.49). There were 7,363,646 genotyped or well-imputed SNPs (for full genotype processing and quality control details, see (Selzam et al. 2018)).

To ease high computational demands for the current study, we excluded SNPs with MAF <1% and info < 1. Following this, 619216 SNPs were included in polygenic score construction.

Principal components were derived from a subset of 39,353 common (MAF > 5%), perfectly imputed (info = 1) autosomal SNPs, 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.

NTR

Genotyping was done on multiple platforms, following manufacturers protocols: Perlegen-Affymetrix, Affymetrix 6.0, Affymetrix Axiom, Illumina Human Quad Bead 660, Illumina Omni 1M and Illumina GSA. For each genotype platform, samples were removed if DNA sex did not match the expected phenotype, if the PLINK heterozygosity F statistic was < -0.10 or > 0.10, or if the genotyping call rate was < 0.90. SNPs were excluded if the MAF < 1×10-6, if the Hardy-Weinberg equilibrium p-value was < 1×10-6, and/or if the call rate was < 0.95. The genotype data was then aligned with the 1000 Genomes reference panel using the HRC and 1000 Genomes

checking tool, testing and filtering for SNPs with allele frequency differences larger than 0.20 as compared to the CEU population, palindromic SNPs and DNA strand issues. The data of the different platforms was then merged into a single dataset, and one platform was chosen for each individual. Based on the ~10.8k SNPs that all platforms have in common, DNA identity-by-descent state was estimated for all individual pairs using the Plink and King programs. Samples were excluded if these estimates did not correspond to expected familial relationships. CEU population outliers, based on per platform 1000 Genomes PC projection with the Smartpca software, were removed from the data. Then, per platform, the data was phased using Eagle and then imputed to 1000 Genomes and Topmed using Minimac following the Michigan imputation server protocols. Post-imputation, the resulting separate platform VCF files were merged with Bcftools into a single file per chromosome for each reference, for SNPs present on all platforms. For the polygenic scoring and parental re-phasing, the imputed data were converted to best guess data and were filtered to include only ACGT SNPs, SNPs with MAF > 0.01, HWE p > 10 -5 and a genotype call rate > 0.98, and to exclude SNPs with more than 2 alleles. All mendelian errors were set to missing. The remaining SNPs represent the transmitted alleles dataset. 20 PCs were calculated with Smartpca using LD-pruned 1000 Genomes–imputed SNPs genotyped on at least one platform, having MAF > 0.05 and not present in the long-range LD regions. Using the --tucc option of the Plink 1.07 software pseudo-controls for each offspring were created, given the genotype data of their parents. This resulted in the non-transmitted alleles dataset, as these pseudo-controls correspond to the child's non-transmitted alleles. To determine the parental origin of each allele, the transmitted and non-transmitted datasets were phased using the duoHMM option of the ShapeIT software. The phased datasets were then split based on parental origin, resulting in a paternal and maternal haploid dataset for the transmitted and non-transmitted alleles.

Statistical analyses

NonCog GWAS-by-subtraction

In order to generate *NonCog* summary statistics, we implemented a GWAS-by-subtraction using Genomic SEM following Demange et al. 2020 using summary statistics of EA and cognitive performance obtained in samples independent from our polygenic score samples.

We ran a GWAS of Educational Attainment and Cognitive Performance in UK Biobank (polygenic score sample left-out). We meta-analysed them with the EA GWAS by Lee et al. excluding 23andMe, UK Biobank and NTR cohorts, and with the CP GWAS by Trampush et al. respectively (EA total N=707,112 and CP N=238,113). More information on these methods and intermediate GWAS are found in **Supplementary Note** and **Supplementary Table 1**.

Following Demange et al. 2020, we then regressed the EA and CP meta-analysed summary statistics on a latent variable, *Cog*, representing cognitive performance genetic variance. EA was also regressed on a second latent variable, *NonCog*. As we set *Cog* and *NonCog* to be independent, *NonCog* represents the residual genetic variance of EA when regressing out cognitive performance variance (**Supplementary Figure 1**). These two latent factors were regressed on each SNP: we obtained association for 1,071,804 SNPs (HapMap3 SNPs, as recommended when comparing PGS analyses across cohorts). We calculate the effective sample size of these GWAS to be 458,211 for *NonCog* and 223,819 for *Cog*.

Polygenic Score construction in UK Biobank, TEDS and NTR

Polygenic scores of *NonCog* and *Cog* were computed with Plink software (version 1.9 for NTR, 2 for UKB and TEDS) (Purcell et al. 2007; Chang et al. 2015) based on weighted betas obtained using the LD-pred v1.0.0 software using infinitesimal prior, a LD pruning window of 250kb and 1000Genomes phase 3 CEU population as LD reference. Weighted betas were computed in a shared pipeline. In NTR, scores for non-transmitted and transmitted genotypes were obtained for fathers and mothers separately so we average them to obtain the mid-parent score.

Three designs for estimating direct and indirect polygenic score effects

To estimate direct child-led and indirect parent-led effects of cognitive and non-cognitive polygenic scores on educational outcomes, we used three family-based genomic methods. The three designs are summarised in **Figure 1**. Importantly, a direct genetic effect is only direct in the sense that it does not originate from another individual's genotype. Direct effects are also not necessarily 'purely' genetic, but lead to educational outcomes via intermediate pathways, and are expressed in the context of environments.

1. Sibling design (applied to the UK Biobank, TEDS, and NTR)

Firstly, indirect genetic effects can be estimated by comparing between-family and within-family (i.e. between-sibling or between-DZ twin) polygenic score associations with a mixed-effects regression model (**Equation 1**) (Selzam et al. 2019).

$$\textbf{Equation 1:}\ EA_{ij} = \alpha_0 + \beta_{Within_Cog}(PGS(Cog)_{ij} - \overline{PGS(Cog)}_j) + \beta_{Between_Cog}(\overline{PGS(Cog)}_j) + \beta_{Within_NonCog}(PGS(NonCog)_{ij} - \overline{PGS(NonCog)}_j) + \beta_{Between_NonCog}(\overline{PGS(NonCog)}_j) + sex + age + sex*age + 10PC + genotyping\ platform + \gamma_j$$

EA is the educational outcome, PGS is the polygenic score (for *Cog* PGS(*Cog*) and *NonCog* PGS(*NonCog*)). $\overline{PGS}$ refers to the average polygenic score in the family j. i refers to the individual sibling. α_0 refers to the intercept and γ_j refers to the random effect for the family.

The total effect of a polygenic score is measured by its effect on phenotypic variation among different families (represented by their average family member): the between-family beta; $\beta_{Between}$ in Equation 1. Note that total effects are equivalent to PGS effects estimated in standard population analyses that do not use within-family data.

The direct effect of a polygenic score is estimated by leveraging genetic differences between siblings, which are due to random segregations of parental genetic material, independent of shared family effects (including parental indirect genetic effects). Specifically, the direct effect is estimated using a variable representing individuals' (i) polygenic scores minus the average

polygenic score for their family (j): the within-family beta (β_{Within} in Equation 1). To the extent that sibling polygenic score differences explain differences in their phenotypes, this is due to direct effects of their own genetic variation. By allowing a random intercept per family, we account for additional familial factors that contribute to sibling similarity. However, any sibling genetic effects would still remain in the direct genetic effect, since these are not removed when adjusting for shared family effects.

The parental indirect genetic effect is estimated as the total between-family effect minus the direct within-family effect of the polygenic score. This means that the indirect genetic effect could be inflated by assortment or population stratification, as these effects are captured in the between-family effect but not the within-family effect. In contrast, sibling indirect genetic effects are likely to be included in both the between-family and within-sibling effects. Positive sibling genetic effects would deflate the within-sibling effect, leading to overestimation of the indirect genetic effect (Boardman and Fletcher 2015, Kohler et al. 2011). Negative sibling effects, which decrease the similarity between siblings, might have different effects on results from the sibling design.

2. Adoption design (applied to the UK Biobank)

Secondly, indirect genetic effects can be estimated by comparing polygenic score associations estimated in a sample of adoptees against those estimated for individuals who were reared by their biological parents (Cheesman et al. 2020). Therefore, we estimate the regression model shown in **Equation 2** separately for adoptees and for non-adopted individuals.

$$\textbf{Equation 2:}\ EA_{ij} = \alpha_0 + \beta_{Cog}(PGS(Cog)_{ij}) + \beta_{NonCog}(PGS(NonCog)_{ij}) + \text{sex} + \text{age} + \text{sex*age} + 10PC + \text{genotyping platform}$$

The total effect is estimated as the polygenic score effect on phenotypic variation among non-adopted individuals (i.e. a combination of direct and indirect genetic mechanisms).

The direct genetic effect is the effect of the polygenic score among adoptees. Adoptees do not share genes by descent with their adoptive parents, we expect their polygenic scores to be

uncorrelated with the genotype of their adoptive parents. Therefore the polygenic score effect in adoptees cannot be inflated by environmentally mediated parental indirect genetic effects. Adoptees are also not genetically related to their siblings (adoptees related to each other were excluded), so polygenic scores effects in adoptees are not biased by sibling indirect genetic effects. One exception is (maternal) prenatal indirect genetic effects, as adoptees' prenatal environment is provided by their birth parents.

The indirect genetic effect is the total effect of the polygenic score (β in non-adopted individuals) minus the direct genetic effect (β for adoptees). Assuming that population stratification and assortative mating effects are similar in adoptees and non-adopted individuals, these will cancel out in estimating the indirect genetic effect. The assumption of equal population stratification and assortative mating bias in adopted and non-adopted groups cannot be tested due to the lack of parental data in UKB. However, both adoptees and non-adopted individuals are from British ancestry, and there is scarce and inconsistent evidence regarding differences in assortment between biological parents of adoptees and other parents (Plomin et al. 1977; Ho 1986). In contrast to the other designs, which estimate the overall impact of prenatal and postnatal parental indirect genetic effects, the adoption design only captures the postnatal component. Sibling genetic effects remain in the estimated indirect genetic effects, as they are present in the total but not the direct genetic effect.

Notably, our adoption design differs slightly from another approach for estimating indirect genetic effects which uses genomic data on adoptive parents rather than adopted individuals (Domingue and Fletcher 2019).

3. Non-transmitted alleles design (applied to NTR)

Thirdly, indirect genetic effects can be estimated, and disentangled from direct genetic effects, using information on parental genetic variation that was not transmitted to offspring (Kong et al. 2018; Bates et al. 2018) (see **Equation 3**).

Equation 3: $$EA = \alpha_0 + \beta_{T_Cog}(PGS(Cog)_T) + \beta_{T_NonCog}(PGS(NonCog)_T) + \beta_{NT_Cog}(PGS(Cog)_{NT}) + \beta_{NT_NonCog}(PGS(NonCog)_{NT}) +$$

$$\text{sex} + \text{age} + \text{sex*age} + 10\text{PC} + \text{genotyping platform} + \gamma_j$$

The total genetic effect is measured by the variance explained by a polygenic score based on transmitted variants (β_T). Transmitted genetic variants are present in a child and in at least one of their parents, and so may exert effects on child education via both direct and indirect mechanisms.

The parental indirect genetic effect is estimated as the effect of a polygenic score based on parental variants that were not transmitted to offspring (β_{NT}). Non-transmitted variants can only take effect on offspring education through the environment. Since non-transmitted alleles are not only shared with parents, but also partially with (full) siblings, β_{NT} might capture sibling indirect effects additionally to parental indirect effects.

The direct genetic effect is estimated by partialling out the effect of the non-transmitted polygenic score from that of the transmitted polygenic score i.e. removing the indirect effect from the total effect (β_T - β_{NT}).

As the effects of both the transmitted and the non-transmitted allele PGS are influenced by assortment and population stratification, taking their difference (the direct effect estimate) cancels the effects of these biases. However, the indirect genetic effect estimate (i.e. the effect of the non-transmitted allele PGS) is potentially inflated by assortment and population stratification.

Maternal and paternal genotypes were combined in order to create overall parental non-transmitted polygenic scores. Our trio dataset (NTR) includes twins, so we used the R lme function with a random intercept for each family to correct for this family structure.

Covariates and bootstrapping

Each model included cognitive and non-cognitive polygenic scores simultaneously and controlled for: 10 ancestry principal components (PCs), sex and age, interaction between sex and age, and cohort-specific platform covariate (NTR: genotyping platform, UKB: array, TEDS: batch). Polygenic scores and outcome variables were scaled. Age was estimated by year of birth, age at recruitment or age at testing depending on the cohorts, see **Supplementary Table 2**.

Correlations between *NonCog* and *Cog* PGS, as well as between and within-family PGS are reported **Supplementary Table 10**.

Using the boot package in R with 10 000 replications, we obtained bootstrapped standard errors for the total, direct and indirect effects, as well as the ratios of indirect/direct and indirect/total effect. We tested for the difference between the direct and indirect effect in both *Cog* and *NonCog* and the difference between the ratio indirect/total for *Cog* and *NonCog*, using Z-tests.

Additional analyses (not pre-registered)

Meta-analyses

In order to estimate the overall indirect and direct effects of *NonCog* and *Cog* polygenic scores, we meta-analysed estimates across cohorts, designs and phenotypic outcomes.

In order to compare results obtained across the three different designs, we meta-analysed effect sizes obtained from the sibling design across cohorts and outcome measures, and we meta-analysed effect sizes obtained from the non-transmitted allele design across both outcomes available in NTR. The adoption design was only applied to EA in UKB, hence no meta-analysis was necessary.

Meta-analyses were conducted using the command rma.mv() in the R package metafor. Design was specified as a random intercept factor, except when results were meta-analysed within-design.

Investigation of the presence of biases

Population stratification

Population stratification refers to the presence of systematic difference in allele frequencies across subpopulations, arising from ancestry difference due to non-random mating and genetic drift. This leads to confounding in genetic association studies. In a PGS analysis, bias due to population stratification can arise from both the GWAS used to create the scores and the target

sample. We corrected for population stratification in the target sample by adjusting analyses for PCs (although this may not remove fine-scale stratification). For the GWAS summary statistics, the ratio statistics LDSC output is a standard measure of population stratification (Bulik-Sullivan et al. 2015). As a rule of thumb a LDSC intercept higher than 1 (inflated) indicates presence of population stratification. Because we corrected the standard errors of the EA GWAS for inflation and GenomicSEM corrects for inflation as well, the ratio statistics of the *Cog* and *NonCog* GWAS are not a valid indication of population stratification (ratio <0 following GC correction). We therefore use the ratio statistics of uncorrected EA and CP GWAS as proxies. Ratio and LDscore intercept was assessed with the ldsc software (Bulik-Sullivan et al. 2015).

Assortative mating

Assortative mating refers to the non-random mate choice, with a preference for spouses with similar phenotypes. If these prefered phenotypes have a genetic component, assortative mating leads to an increased genetic correlation between spouses, as well as between relatives (Yengo et al. 2018). Assortative mating can therefore be inferred from elevated correlations between polygenic scores in siblings (correlations would be 0.5 without assortative mating) and between parents (correlations would be 0 without assortative mating). We estimated sibling intraclass correlations of *Cog* and *NonCog* PGS in UKB, TEDS and NTR, and Pearson's correlations of paternal and maternal *Cog* and *NonCog* PGS in NTR. Notably, these observed correlations cannot distinguish assortative mating from population stratification.

Sibling effects

We performed three additional analyses to investigate indirect genetic effects of siblings on educational outcomes.

First, we ran a linear mixed model extending our main non-transmitted alleles design to include polygenic scores of siblings (**Equation 4**). To this end, we used data from NTR on DZ pairs and both of their parents. Sample sizes of genotyped 'quads' with offspring CITO or EA phenotypes were 657 and 788, respectively.

$$\textbf{Equation 4:}\ EA = \alpha_0 + \beta_{T_Cog}(PGS(Cog)_T) + \beta_{T_NonCog}(PGS(NonCog)_T) + \beta_{NT_Cog}(PGS(Cog)_{NT}) + \beta_{NT_NonCog}(PGS(NonCog)_{NT}) + \beta_{Sibling_Cog}(PGS(Cog)_{Sibling}) + \beta_{Sibling_NonCog}(PGS(NonCog)_{Sibling}) + sex + age + sex*age + 10PC + genotyping\ platform + \gamma_j$$

Second, we can also assess the presence of sibling genetic effects using monozygotic and dizygotic twins. Because monozygotic twins have the same genotypes, the genetically-mediated environment provided by the cotwin is more correlated to the twin genotype in MZ twins than in DZ twins. The sibling genetic effect is more strongly reflected in the polygenic score prediction of the educational outcome for MZ twins than for DZ twins. If the sibling genetic effect is negative, the polygenic score effect (betas) on the outcome in people that have an MZ twin will be lower than in people that have a DZ twin, it will be higher in those with an MZ twin then those with an DZ twin if the sibling genetic effect is positive. We therefore compare Betas from **Equation 2** in a subset of MZ twins and in a subset of DZ twins (one individual per pair) in both NTR (N_{MZ}=818 & N_{DZ}=865 for CITO and N_{MZ}=1600 & N_{DZ}=1369 for EA) and TEDS (N_{MZ}=546 & N_{DZ}=2709)

Third, the presence of sibling genetic effects can be assessed using data on the number of siblings participants have. If an individual has more siblings we expect their polygenic scores to be more correlated to sibling effects. As the number of siblings increases (if we assume linear increase) so does the degree to which a PRS captures sibling effects. If the sibling genetic effect is positive, the effect of the *Cog* and *NonCog* PRS on the educational outcome should increase with the number of siblings. However, family characteristics and environment might differ across families depending on the number of children. Therefore, changes in the effect of the PGS on our outcome with the number of siblings could be due to factors other than sibling genetic effects (for example, there is a known negative genetic association between number of children and EA (Barban et al. 2016) which could result in confounding). By also looking at changes in the effect of the *Cog* and *NonCog* PRS on the educational outcome in adopted (unrelated) sibships, we break the correlation between PRS and any sibling effects. So if there is a change in PRS effect on the educational outcome in adopted children dependent on the number of (non-biological) siblings, we can assume this effect to be caused by mechanisms other than a sibling

effect. We finally contrast the change in PRS depending on family size in biological and adopted siblings to get an idea of the sibling effect minus any other confounding effects of family size. We use the total number of reported siblings (full siblings for non-adopted and adopted siblings for adopted individuals, data-fields: 1873, 1883, 3972 & 3982).

Data availability

Summary Statistics of *Cog* and *NonCog* used in this paper are available upon request. Summary Statistics of cognitive performance from the COGENT cohort, of EA excluding NTR and UKBiobank cohorts are available upon request to the communicating author of these papers.

For UK Biobank dataset access, see: https://www.ukbiobank.ac.uk/using-the-resource/.

Netherlands Twin Register data may be accessed, upon approval of the data access committee, email: ntr.datamanagement.fgb@vu.nl

Researchers can apply for access to TEDS data: https://www.teds.ac.uk/researchers/teds-data-access-policy

Code availability

All scripts used to run the analyses are available at:
https://github.com/PerlineDemange/GeneticNurtureNonCog

All additional software used to perform these analyses are available online.

Preregistration of the study and additional presentations are available on OSF:
https://osf.io/mk938/

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