Data supplement for Rask-Andersen et al., Modification of Heritability for Educational Attainment and Fluid Intelligence by Socioeconomic Deprivation in the UK Biobank. Am J Psychiatry (doi: 10.1176/appi.ajp.2020.20040462)

TABLE S1. Previous studies on the interaction between heritability and socioeconomic status

Study	Year	Sample	N	Setting	Age category (mean age)	Phenotype	Moderator(s)	Effect of moderator(s) on heritability	SES interaction**
Fischbein S.	1980	12-year-old twins born in 1952	213 twin pairs	Sweden	12-year-olds	Verbal and inductive ability	Father's occupational status classified into three categories: "´social groups"	Higher concordance in MZ twins from high SES homes reported	No formal testing for differences (+)
Rowe *et al.*	1999	Non-Hispanic whites and African American sibling pairs from the National Longitudinal study of Adolescent health (NLSAH).	1,909	U.S.	Adolescents (~16 years)	Peabody picture vocabulary IQ test (verbal IQ)	Parental education	Heritability correlated with parental education	+
Turkheimer *et al.*	2003	Seven-year-old twins from the National Perinatal Collaborative Project	319 twin pairs	U.S.	7-year-olds	Wechsler Intelligence Scale for Children verbal-, performance- and full-scale IQ	SES determined by parental education, occupational status, and income	Higher heritability in children from high-SES	+
Asbury *et al.*	2005	Four-year-old, same sex twins	4,446	England and Wales	4-year-olds	Verbal ability (MCDI) and nonverbal ability (PARCA)	SES and nine environmental correlates	Results suggest greater heritability for verbal ability in high-risk environments (diathesis-stress model) but were not significant for SES. Interactions observed with 'Family chaos', 'Instructive parent-child communication', 'Informal parent-child communication'.	no

Kremen et al.	2005	347 middle aged male twins from the Vietnam era twin registry	347 pairs	U.S.	Middle-age (~48 ± 3 years)	Word recognition ability (WRAT-3)	Parental education	Parental education was not found to moderate the magnitude of genetic effects.	no
Harden et al.	2007	839 twin pairs born in 1945	839 pairs	U.S.	Adolescents (~17 years)	Cognitive aptitude measured with the National Merit Scholar-ship Qualifying Test (NMSQT)	Parental education and income	Greater heritability for cognitive aptitude in children from higher education parents	+
van der Sluis et al.	2008	Young adult twins (mean age 26 years) & older adult twins (mean age 49 years)	755	Netherlands	Younger (26 years, N=385), older (49 years, N=370)	Full scale IQ (FSIQ) measured with WAIS-III	Parental and partner educational levels, urbanization, mean real estate price of the participant's residential area	No interaction could be observed	no
Bartels et al.	2009	12-year-old twins from the Netherlands Twin Register	6,569	Netherlands	Adolescents (12 or 14+ years)	Dutch CITO-elementary test	Maternal educational level	84% of the variance in cognitive abilities is accounted for by genetic effects in the offspring of low educated mothers, 78% in offspring of middle educated mother. The difference was reported to be significant.	-
Grant et al.	2010	Male twins (age 19.6 ± 1.5 years) from the Vietnam Era Twin Registry	3,203 male twin pairs	U.S.	Early adulthood (19.6 ± 1.5 years)	General cognitive ability assessed with AFQT	Parental education	No interaction could be observed	no

Tucker-Drob *et al.*	2011	750 pairs of twins drawn from the Early Childhood Longitudinal Study, Birth Cohort (ECLS-B)'	750 twin pairs	U.S.	Infants assessed at ten months, and then again at two years of age	Infant mental ability measured w. BSF-R	Five-component SES (paternal & maternal education, occupation and family income)	SES was observed to moderate the genetic influence on cognitive development between ten months and two years of age	+
Hanscombe *et al.*	2012	Twins Early Development Study (TEDS). Twins ages 2, 3, 4, 7, 9, 10, 12 and 14 years	8,716	United Kingdom	Longitudinal followup from two-, to 14 years of age	Composite general cognitive ability (g) from: age 2-4 - PARCA or BSID-II and CDI-III; Age 7 - 14: WISC-III-UK, CAT3, WISC-III-PI AND Raven's progressive matrices.	SES	No interaction could be observed	no
Bates *et al.*	2013	Adult twins aged 24-84	1,702	U.S.	Adults (~54 ± 12 years)	Composite score from five cognitive-ability tests in MIDUS-II*	Childhood SES	Childhood SES amplifies genetic effects	+
Bates *et al.*	2016	Brisbane Adolescent 2307 adolescents from the Brisbane Adolescent Twin Study	1176 twin pairs	Australia	Adolescents (~16 ± 0.5 years)	Five IQ subtests of the Multidimensional Aptitude Battery (MAB)	Childhood SES	No interaction could be observed	no

Abbreviations: MZ = monozygotic, DZ = dizygotic, SES = Socioeconomic status, WISC = The Wechsler Intelligence scale for children, MCDI = MacArthur Communicative Development Inventory, PARCA = Parent Report of Children's Abilities, WRAT3 = Wide range achievement test, WAIS-III = Wechsler Adult Intelligence Scale v3, AFQT = the Armed Forces Qualification Test, BSF-R = the Bayley Short Form-Research Edition, BSID-II = Bayley Scales of Infant Development 2nd edition, CDI-III = MacArthur–Bates Communicative Development Inventories for children 30—37 months of age, WISC-III-UK = Wechsler Intelligence Scale for Children Third UK Edition, WISC-III-PI = Wechsler Intelligence Scale for Children Third Edition as a process instrument, CAT3 = Cognitive Abilities Test 3, CITO = Cito Eindtoets Basisonderwijs (Cito final test primary education), MIDUS-II = Midlife in the United States survey. * The five tests in MIDUS-II were: word-list recall, backward digit span measure of working memory, category-fluency measure of verbal fluency, inductive reasoning measure of fluid intelligence and a backward-counting-task. ** Plus and minus signs in the SES interaction column indicates if the heritability is higher (+) or lower (-) with high SES. No denotes no observed interaction. It should be highlighted that a positive value for SES (measured in most previous studies) corresponds to a negative value for TDI (as measured in our study)

TABLE S2. Questions used to assess fluid intelligence score in UK Biobank participants

Part	Category	Question	Answer options
1	Numeric addition test	"Add the following numbers together: 1 2 3 4 5 - is the answer?"	Asked to choose from 13, 14, 15, 16 or 17.
2	Identify largest number	"Which number is the largest?"	Asked to choose from 642, 308, 987, 714 and 253.
3	Word interpolation	"Bud is to Flower as Child is to?".	Offered choice from grow, develop, improve, adult and old.
4	Positional arithmetic	"11 12 13 14 15 16 17 18 Divide the sixth number to the right of twelve by three. Is the answer?"	Offered choice from 5, 6, 7, or 8.
5	Family relationship calculation	"If Truda's mother's brother is Tim's sister's father, what relation is Truda to Tim?"	Offered choice from aunt, sister, niece, cousin, no-relation.
6	Conditional arithmetic	"If sixty is more than half of seventy-five, multiply twenty-three by three. If not subtract 15 from eighty-five. Is the answer?".	Offered choice from 68, 69, 70, 71, 72.
7	Synonym	"Stop means the same as?"	Offered choice from pause, close, cease, break or rest.
8	Chained arithmetic	"If David is twenty-one and Owen is nineteen and Daniel is nine years younger than David, what is half their combined age?"	Offered choice from 25, 26, 27, 28 or 29.
9	Concept interpolation	"Age is to Years as Height is to?".	Offered choice from long, deep, top, metres or tall.
10	Arithmetic sequence recognition	"150 ... 137 ... 125 ... 114 ... 104 ... What comes next?"	Offered choice from 92, 93, 94, 95 or 96.
11	Antonym	"Relaxed means the opposite of?".	Offered choice from calm, anxious, cool, worried, tense.
12	Square sequence recognition	"100 ... 99 ... 95 ... 86 ... 70 ... What comes next?"	Offered choice from 45, 46, 47, 48, 49, 50.
13	Subset inclusion logic	"If some flinks are plinks and some plinks are stinks then some flinks are definitely stinks?"	Offered choice from true, false, neither-true-nor-false.

TABLE S3. Performance of polygenic scores for fluid intelligence in the testing set

Model	$\rho = 1.0$	$\rho = 0.3$	$\rho = 0.1$	$\rho = 0.03$	$\rho = 0.01$	$\rho = 0.003$	$\rho = 0.001$
ΔR^2	4.12%	4.14%	4.17%	4.22%	3.94%	2.90%	0.22%

Squared semi partial correlation coefficients (ΔR^2) for LDpred polygenic scores with different assumptions of the fraction of causal SNPs (ρ) were generated for linear models for fluid intelligence scores. Models included sex, age, Townsend deprivation index, a batch variable for two genotyping arrays, as well as 15 principal components as covariates.

TABLE S4. Performance of polygenic scores for educational attainment in the testing set

	NULL	$\rho = 1.0$	$\rho = 0.3$	$\rho = 0.1$	$\rho = 0.03$	$\rho = 0.01$	$\rho = 0.003$	$\rho = 0.001$
AUC	0.6024 (0.6000-0.6048)	0.6654 (0.6631-0.6677)	0.6658 (0.6635-0.6681)	0.6666 (0.6643-0.6689)	0.6671 (0.6648-0.6694)	0.6624 (0.6601-0.6647)	0.6140 (0.6116-0.6164)	0.6381 (0.6358-0.6405)

Area under the receiver operating characteristic curve (AUROC or AUC) for logistic models for educational attainment were estimated with the pROC package(1) in R. Models included sex, age, Townsend deprivation index, a batch variable for two genotyping arrays, 15 principal components as covariates, as well LDpred polygenic scores with different assumptions of the fraction of causal SNPs (ρ). The *NULL*-field shows the performance of a logistic model for educational attainment that does not include any polygenic score.

TABLE S5. Performance of polygenic scores for years of education in the testing set

Model	$\rho = 1.0$	$\rho = 0.3$	$\rho = 0.1$	$\rho = 0.03$	$\rho = 0.01$	$\rho = 0.003$	$\rho = 0.001$
ΔR^2	4.44%	4.48%	4.56%	4.61%	4.21%	3.27%	1.61%

Squared semi partial correlation coefficients (ΔR^2) for LDpred polygenic scores with different assumptions of the fraction of causal SNPs (p) were generated for linear models for years of education. Models included sex, age, Townsend deprivation index, a batch variable for two genotyping arrays, as well as 15 principal components as covariates.

TABLE S6. Mean polygenic scores per Townsend deprivation-quintile

Polygenic score	1st	2nd	3rd	4th	5th
Fluid intelligence (mean ± SD)	-0.0071 ± 0.2121	-0.0116 ± 0.2147	-0.0146 ± 0.2147	-0.0132 ± 0.2146	-0.0210 ± 0.2156
Educational attainment (mean ± SD)	1.387 ± 0.224	1.377 ± 0.226	1.372 ± 0.227	1.372 ± 0.230	1.353 ± 0.233
Years of education (mean ± SD)	1.712 ± 0.230	1.702 ± 0.232	1.698 ± 0.235	1.697 ± 0.237	1.676 ± 0.241

Quintiles are ordered from lowest to highest Townsend deprivation index. Polygenic scores were generated with LDpred.

TABLE S7. Descriptives of resampled Townsends deprivation index-tertiles with fixed polygenic scores

Fluid intelligence		N	Polygenic score (mean ± SD)	TDI range	Age (years ± SD)	sex (females/males)	Fluid intelligence score (mean ± SD)
	1st	27,769	-0.013 ± 0.210	-6.26 - -3.15	57.7 ± 7.7	14665/13104	6.37 ± 2.04
	2nd	27,769	-0.013 ± 0.210	-3.15 - -0.88	57.3 ± 7.8	14880/12889	6.25 ± 2.08
	3rd	27,769	-0.012 ± 0.210	-0.88 - 9.89	56.4 ± 8.2	14824/12945	6.06 ± 2.16
Educational attainment							**Attended university or college (no/yes)**
	1st	76,721	1.375 ± 0.224	-6.26 - -3.28	57.4 ± 7.8	41228/35493	49638/26180 (34.5%)
	2nd	76,721	1.375 ± 0.224	-3.28 - -0.97	57.2 ± 7.9	41838/34883	52204/23666 (31.2%)
	3rd	76,721	1.375 ± 0.224	-0.97 - 10.88	56.2 ± 8.2	41006/35715	53458/22133 (29.3%)
Years of education							**Years of education (mean ± SD)**
	1st	76,315	1.703 ± 0.230	-6.26 - -3.28	57.4 ± 7.8	40814/35501	14.3 ± 5.0
	2nd	76,315	1.699 ± 0.233	-3.28 - -0.98	57.1 ± 7.9	41500/34815	13.9 ± 5.1
	3rd	76,315	1.694 ± 0.237	-0.98 - 10.82	56.2 ± 8.2	40745/35570	13.4 ± 5.3

Participants with polygenic scores and measured traits were sampled into three tertiles based on Townsend deprivation indices. Quantiles were sampled so that the polygenic score of each quantile was similar between quantiles. TDI - Townsend deprivation index.
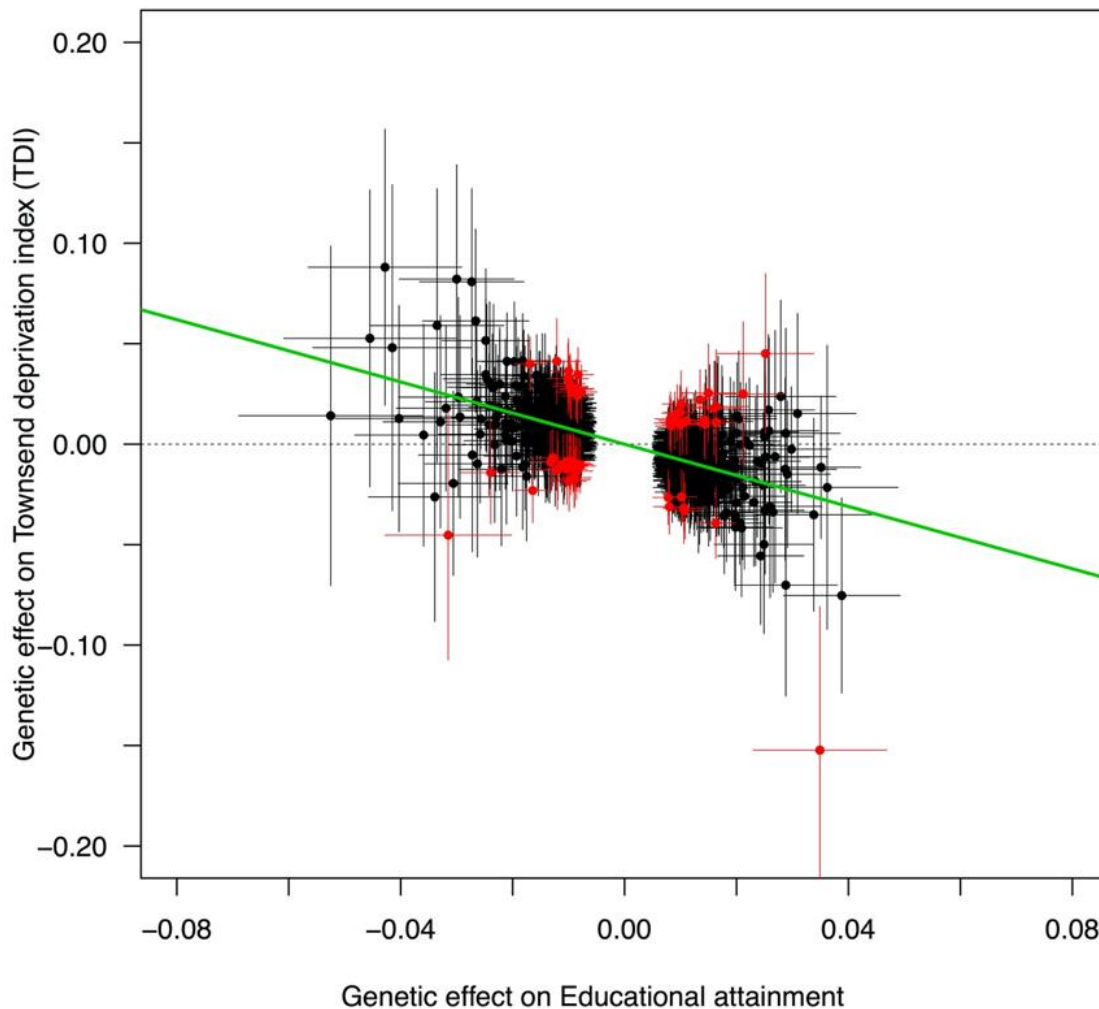
FIGURE S1. Effects of 1207 SNPs from the previous GWAS on educational attainment in 1.1 million participants (3) on educational attainment against their effects on Townsend deprivation index in UK biobank. Red symbols denote 61 horizontally pleiotropic outlier instruments as identified by the HEIDI-outlier procedure incorporated in the R package gsmr (4). These SNPs may potentially affect Townsend deprivation index via pathways that are independent of educational attainment. Black symbols are identified as valid instruments, whose effect on Townsend deprivation index are believed to be exerted only via educational attainment. These remaining 1146 SNPs constitute the basis for the non-pleiotropic polygenic score, for which collider bias should be minimized. The green solid line is the casual effect of educational attainment on Townsend deprivation index, as estimated by gsmr. Error bars denote the 95% confidence intervals of each effect estimate.

TABLE S8. SNP heritabilities for fluid intelligence score, educational attainment and years of education per Townsend deprivation index quintile in UK Biobank

Quintile	Number of respondents (N)	h2 (95%CI)	Deviation from h2 estimates for the combined cohort*	λGC	mean χ2	intercept (95% CI)	Ratio (95%CI)
Fluid intelligence combined	131,688	0.243 (0.223 - 0.263)***	-	1.54	1.70	1.06 (1.03 - 1.08)	0.08 (0.05 - 0.11)
1st	26,263	0.216 (0.162 - 0.269)	3.49E-01	1.09	1.10	1.005 (0.990 - 1.020)	0.047 (-0.102 - 0.195)
2nd	26,262	0.226 (0.178 - 0.273)	5.14E-01	1.11	1.14	1.013 (0.997 - 1.029)	0.099 (-0.020 - 0.217)
3rd	26,298	0.252 (0.206 - 0.298)	7.28E-01	1.14	1.15	1.012 (0.995 - 1.028)	0.078 (-0.031 - 0.186)
4th	26,302	0.264 (0.220 - 0.308)	3.96E-01	1.15	1.16	1.011 (0.996 - 1.026)	0.067 (-0.024 - 0.158)
5th	26,297	0.310 (0.256 - 0.364)	2.26E-02	1.15	1.17	1.009 (0.992 - 1.025)	0.052 (-0.045 - 0.150)
Educational Attainment combined	359,094	0.164 (0.155 - 0.173)***	-	1.98	2.33	1.140 (1.116 - 1.163)	0.105 (0.087 - 0.123)
1st	71,546	0.134 (0.118 - 0.149)**	1.08E-03	1.17	1.20	1.011 (0.997 - 1.025)	0.054 (-0.017 - 0.125)
2nd	71,748	0.150 (0.130 - 0.171)	2.20E-01	1.21	1.23	1.013 (0.998 - 1.028)	0.055 (-0.009 - 0.120)
3rd	71,711	0.142 (0.123 - 0.161)	3.61E-02	1.20	1.23	1.031 (1.016 - 1.046)	0.135 (0.070 - 0.201)
4th	71,715	0.189 (0.168 - 0.211)	3.45E-02	1.27	1.30	1.031 (1.016 - 1.046)	0.101 (0.051 - 0.151)
5th	71,729	0.264 (0.241 - 0.287)**	1.75E-15	1.36	1.41	1.040 (1.024 - 1.055)	0.096 (0.058 - 0.134)
Years of education combined	359,094	0.168 (0.158 - 0.178)***	-	2.01	2.37	1.160 (1.131 - 1.189)	0.117 (0.095 - 0.139)
1st	71,546	0.138 (0.119 - 0.158)**	8.12E-03	1.18	1.21	1.014 (0.997 - 1.031)	0.066 (-0.015 - 0.146)
2nd	71,748	0.146 (0.124 - 0.167)	6.81E-02	1.21	1.23	1.023 (1.006 - 1.041)	0.100 (0.025 - 0.174)
3rd	71,711	0.137 (0.118 - 0.156)	5.07E-03	1.20	1.23	1.039 (1.023 - 1.054)	0.166 (0.100 - 0.233)
4th	71,715	0.182 (0.159 - 0.205)	2.61E-01	1.26	1.30	1.037 (1.021 - 1.052)	0.125 (0.072 - 0.178)
5th	71,729	0.243 (0.218 - 0.267)**	3.29E-08	1.32	1.39	1.048 (1.030 - 1.065)	0.124 (0.078 - 0.169)

Quintiles are ordered from lowest (1st) to highest (5th) Townsend deprivation index. $h2$ - SNP heritability. $λGC$ - genomic inflation. mean $χ2$ - mean chi-squared value for all included SNPs. Intercept - LD score regression intercept (should be close to 1). Ratio - (intercept-1)/(mean $χ2$-1): measures the proportion of inflation in mean $χ2$. *P-values from Z-tests for differences between quintile-specific $h2$ estimates and the $h2$ estimates for the combined cohort. Unadjusted P-values are reported. Bonferroni correction was used to adjust for multiple testing and P-values<0.05/15 were considered statistically significant. **95% CIs did not overlap with h^2 estimates generated from GWAS summary stats from analyses on the full cohort (Table S4). *** h^2 estimates when all quintiles are analyzed as a combined cohort.

TABLE S9. Genetic correlation between Townsend deprivation index-stratified quintiles of the UK Biobank

Fluid intelligence	2nd TDI-quintile	3rd	4th	5th
1st TDI quintile	0.917 (0.761 - 1.073)	1.057 (0.892 - 1.222)	1.087 (0.918 - 1.256)	0.898 (0.749 - 1.048)
2nd		1.004 (0.866 - 1.142)	1.036 (0.891 - 1.180)	0.899 (0.775 - 1.023)
3rd			0.969 (0.860 - 1.078)	0.969 (0.855 - 1.083)
4th				1.037 (0.917 - 1.156)
Educational attainment				
1st TDI quintile	0.921 (0.842- 1.000)	0.986 (0.893- 1.079)	0.951 (0.884- 1.018)	**0.899 (0.833- 0.964)**
2nd		0.955 (0.875- 1.036)	0.941 (0.866- 1.016)	**0.892 (0.821- 0.964)**
3rd			1.055 (0.979- 1.131)	0.998 (0.937- 1.059)
4th				0.988 (0.930- 1.045)
Years of education				
1st TDI quintile	1.018 (0.920 - 1.116)	1.059 (0.965 - 1.154)	1.001 (0.919 - 1.083)	**0.906 (0.827 - 0.985)**
2nd		1.033 (0.939 - 1.126)	0.974 (0.894 - 1.054)	**0.915 (0.838 - 0.992)**
3rd			1.085 (1.003 - 1.167)	1.035 (0.956 - 1.113)
4th				1.014 (0.953 - 1.075)

Genetic correlation was estimated using LDSC. Correlations are presented with 95% CI. Estimates that differ (Student's t-test, $p < 0.05$) are highlighted in bold type.

TABLE S10. Genetic correlation (r_g) between educational traits, fluid intelligence score and Townsend deprivation index. 95% confidence intervals are displayed in parentheses

	Educational attainment	Years of education	Fluid intelligence score
Years of education	1.001 (0.996 – 1.006)		
Fluid intelligence score	0.713 (0.682 – 0.744)	0.714 (0.683 – 0.746)	
Townsend deprivation index	-0.517 (-0.569 – -0.464)	-0.502 (-0.554 – -0.450)	-0.245 (-0.305 – -0.186)

TABLE S11. Results for linear regression analyses for fluid intelligence

	β estimate	$\pm$ 95%CI	t-value	P
Intercept	7.11	3.46E-01	40.24	0.00E+00
PGS_{fluid}	2.86	4.83E-01	11.63	3.20E-31
$batch$	-1.90E-02	3.24E-01	-0.11	0.91
sex	3.22E-01	2.12E-01	2.98	2.89E-03
age	-2.61E-02	5.71E-03	-8.97	2.97E-19
TDI	-1.17E-01	3.72E-02	-6.18	6.30E-10
$PC1$	-7.06E-03	8.77E-03	-1.58	0.12
$PC2$	4.81E-03	9.12E-03	1.03	0.30
$PC3$	9.59E-03	8.83E-03	2.13	3.33E-02
$PC4$	-1.50E-02	6.66E-03	-4.41	1.06E-05
$PC5$	-6.12E-03	2.99E-03	-4.01	6.08E-05
$PC6$	4.48E-05	8.44E-03	0.01	0.99
$PC7$	-1.51E-02	7.59E-03	-3.89	9.96E-05
$PC8$	-4.73E-03	7.67E-03	-1.21	0.23
$PC9$	8.13E-04	3.28E-03	0.49	0.63
$PC10$	-4.29E-03	7.31E-03	-1.15	0.25
$PC11$	-1.22E-02	5.52E-03	-4.34	1.41E-05
$PC12$	7.83E-03	7.31E-03	2.10	3.58E-02
$PC13$	1.54E-03	8.34E-03	0.36	0.72
$PC14$	1.95E-02	4.64E-03	8.26	1.53E-16
$PC15$	4.08E-03	7.22E-03	1.11	0.27
$PGS_{fluid}{:}batch$	-5.37E-02	2.00E-01	-0.53	0.60
$PGS_{fluid}{:}sex$	-1.43E-02	1.23E-01	-0.23	0.82
$PGS_{fluid}{:}age$	-1.39E-02	7.76E-03	-3.50	4.66E-04
$PGS_{fluid}{:}TDI$	4.36E-02	2.21E-02	3.87	1.10E-04
$batch{:}sex$	1.98E-03	8.75E-02	0.04	0.97
$batch{:}age$	1.91E-03	5.62E-03	0.67	0.51
$batch{:}TDI$	2.14E-02	1.50E-02	2.79	5.27E-03
$sex{:}age$	-2.31E-03	3.40E-03	-1.33	0.18
$sex{:}TDI$	-2.68E-02	9.70E-03	-5.41	6.22E-08
$age{:}TDI$	6.25E-04	6.01E-04	2.04	4.17E-02

Interaction terms for all secondary interactions between covariates were included in the models. β-coefficients were estimated by linear regression modeling in R using the 'lm' function. The terms that were included in the model are highlighted in italic. $\pm$ 95%CI are included for the beta coefficients. Coefficients were tested for deviation from zero by t-tests. The interaction term for the polygenic score (PGS) and Townsend deprivation index (TDI), $PGS_{fluid}{:}TDI$, was of interest and $p<0.05$ was considered significant.

TABLE S12. Results for logistic regression analyses for educational attainment

	Estimate	± 95% CI	t	P
Intercept	-2.05E-01	9.36E-02	-4.28	1.83E-05
PGS$_{EA}$	6.59E-01	6.12E-02	21.10	9.64E-99
batch	1.37E-02	5.40E-02	0.50	6.19E-01
sex	-1.96E-01	3.48E-02	-11.04	2.36E-28
age	-1.53E-03	1.52E-03	-1.97	4.91E-02
TDI	-2.53E-02	5.86E-03	-8.47	2.41E-17
PC1	-1.77E-03	1.17E-03	-2.97	2.95E-03
PC2	1.33E-04	1.22E-03	0.21	8.30E-01
PC3	1.30E-03	1.18E-03	2.16	3.10E-02
PC4	-4.22E-03	8.95E-04	-9.24	2.60E-20
PC5	4.65E-04	3.89E-04	2.34	1.92E-02
PC6	1.12E-05	1.13E-03	0.02	9.85E-01
PC7	-2.13E-03	1.02E-03	-4.11	3.95E-05
PC8	9.81E-04	1.02E-03	1.89	5.94E-02
PC9	-2.47E-03	4.11E-04	-11.77	5.49E-32
PC10	-1.00E-03	9.75E-04	-2.02	4.39E-02
PC11	-2.86E-03	7.25E-04	-7.73	1.05E-14
PC12	9.50E-04	9.71E-04	1.92	5.52E-02
PC13	-3.61E-04	1.11E-03	-0.63	5.26E-01
PC14	5.54E-03	5.79E-04	18.76	1.66E-78
PC15	5.37E-04	9.59E-04	1.10	2.72E-01
PGS$_{EA}$:batch	6.04E-02	2.54E-02	4.66	3.15E-06
PGS$_{EA}$:sex	3.04E-02	1.58E-02	3.78	1.57E-04
PGS$_{EA}$:age	-4.79E-03	9.85E-04	-9.54	1.48E-21
PGS$_{EA}$:TDI	8.76E-03	2.66E-03	6.46	1.08E-10
batch:sex	1.41E-02	1.16E-02	2.38	1.74E-02
batch:age	-9.74E-04	7.38E-04	-2.59	9.71E-03
batch:TDI	5.45E-03	1.87E-03	5.71	1.12E-08
sex:age	2.92E-03	4.50E-04	12.72	4.62E-37
sex:TDI	-7.05E-03	1.23E-03	-11.25	2.39E-29
age:TDI	3.50E-05	7.57E-05	0.91	3.65E-01

Interaction terms for all secondary interactions between covariates were included in the models. *β*-coefficients were estimated by logistic regression modeling in R using the 'glm' function. The terms that were included in the model are highlighted in italic. ± 95%CI are included for the beta coefficients. Coefficients were tested for deviation from zero by *t*-tests. The interaction term for polygenic risk scores (PGS) and Townsend Deprivation index (TDI), *PGS$_{EA}$:TDI,* was of interest and p<0.05 was considered significant.

TABLE S13. Results for linear regression analyses for years of education

	β estimate	± 95% CI	t-value	P
Intercept	10.9	9.11E-01	23.44	2.4E-121
$PGS_{eduyears}$	6.84	5.85E-01	22.91	5.0E-116
batch	-4.28E-02	5.42E-01	-0.15	0.88
sex	-2.48	3.54E-01	-13.76	4.7E-43
age	-0.124	1.49E-02	-16.30	1.0E-59
TDI	-5.27E-02	5.95E-02	-1.74	8.3E-02
PC1	-1.36E-02	1.23E-02	-2.16	3.1E-02
PC2	4.38E-03	1.27E-02	0.67	0.50
PC3	1.61E-02	1.24E-02	2.55	1.1E-02
PC4	-4.19E-02	9.38E-03	-8.76	1.9E-18
PC5	3.91E-03	4.07E-03	1.88	6.0E-02
PC6	-5.86E-03	1.18E-02	-0.97	0.33
PC7	-2.11E-02	1.07E-02	-3.89	1.0E-04
PC8	5.29E-03	1.07E-02	0.97	0.33
PC9	-2.34E-02	4.30E-03	-10.68	1.2E-26
PC10	-7.57E-03	1.02E-02	-1.45	0.15
PC11	-3.00E-02	7.62E-03	-7.72	1.2E-14
PC12	1.30E-02	1.02E-02	2.50	1.2E-02
PC13	-9.08E-03	1.17E-02	-1.52	0.13
PC14	6.23E-02	6.08E-03	20.11	7.4E-90
PC15	-2.30E-03	1.01E-02	-0.45	0.65
$PGS_{eduyears}$:*batch*	0.51	2.44E-01	4.11	4.0E-05
$PGS_{eduyears}$:*sex*	-5.17E-02	1.51E-01	-0.67	0.50
$PGS_{eduyears}$:*age*	-4.88E-03	9.43E-03	-1.01	0.31
$PGS_{eduyears}$:*TDI*	9.16E-02	2.55E-02	7.04	1.9E-12
batch:sex	7.22E-02	1.21E-01	1.17	0.24
batch:age	-4.59E-03	7.70E-03	-1.17	0.24
batch:TDI	3.59E-02	1.97E-02	3.57	3.5E-04
sex:age	5.40E-02	4.73E-03	22.41	4.5E-111
sex:TDI	-0.11	1.29E-02	-17.16	5.4E-66
age:TDI	-3.69E-03	7.98E-04	-9.07	1.2E-19

Interaction terms for all secondary interactions between covariates were included in the models. *β*-coefficients were estimated by linear regression modeling in R using the 'lm' function. The terms that were included in the model are highlighted in italic. ± 95%CI are included for the beta coefficients. Coefficients were tested for deviation from zero by *t*-tests. The interaction term for polygenic risk scores (PGS) and Townsend Deprivation index (TDI), PGS_{EA}:*TDI,* was of interest and p<0.05 was considered significant.

TABLE S14. Results for analyses of interaction between educational attainment-associated SNPs and TDI

SNP	Chr	Position (bp)	A1	Number of participants (N)	β-estimate	P
rs2071206	3	50,160,109	A	358,084	2.60E-03	8.97E-04
rs7921305	10	133,775,196	A	357,281	3.03E-03	9.33E-04
rs71415374	2	104,155,414	T	354,755	4.32E-03	1.03E-03
rs12531825	7	8,005,174	A	353,773	-3.93E-03	1.61E-03
rs112682854	5	63,013,782	G	349,900	-2.48E-03	2.07E-03
rs146831114	2	23,903,557	T	356,882	-6.65E-03	2.84E-03
rs35084376	16	51,163,120	C	353,665	-4.72E-03	4.37E-03
rs10071763	5	60,569,133	G	349,889	2.17E-03	5.47E-03
rs10191477	2	44,858,687	T	354,231	2.17E-03	5.69E-03
rs75654367	3	48,710,739	T	352,584	-4.10E-03	7.14E-03
rs61881642	10	111,871,630	T	357,200	3.03E-03	7.91E-03
rs7444298	5	87,730,027	G	357,572	2.17E-03	1.17E-02
rs113011189	3	49,250,007	T	354,714	-3.58E-03	1.21E-02
rs12986089	19	36,150,764	G	346,161	2.17E-03	1.36E-02
rs3897821	1	243,420,388	G	358,152	-2.05E-03	1.61E-02
rs6744428	2	100,310,060	C	352,535	2.17E-03	1.69E-02
rs6565192	16	30,585,535	C	343,820	-1.92E-03	1.79E-02
rs1572198	13	58,330,048	T	352,642	-2.09E-03	2.18E-02
rs3759586	14	104,091,434	A	356,359	-1.96E-03	2.25E-02
rs375572610	13	97,031,192	A	358,030	8.56E-02	2.59E-02
rs12375949	9	124,617,900	T	358,152	-1.74E-03	3.16E-02
rs66495454	1	72,748,567	GTCCT	350,268	1.73E-03	3.78E-02
rs111517923	4	2,946,138	AT	353,774	1.73E-03	3.96E-02
rs889925	2	161,971,597	C	353,222	-1.70E-03	4.27E-02
3:49638084_AAAATT_A	3	49,638,084	A	350,600	1.73E-03	4.85E-02

β-estimates for the interaction term: SNP:TDI, are presented above. P-values represent the results from student's t-tests for whether β-estimates deviate from zero. Results are presented for 25 SNPs that were observed to interact with TDI at the nominal level of significance ($P < 0.05$). 188 SNPs were tested in total. No interactions between SNPs and TDI could be observed after adjusting for multiple testing ($P < 2.7*10-4$). abbreviations: Chr - chromosome, A1 - effect allele.
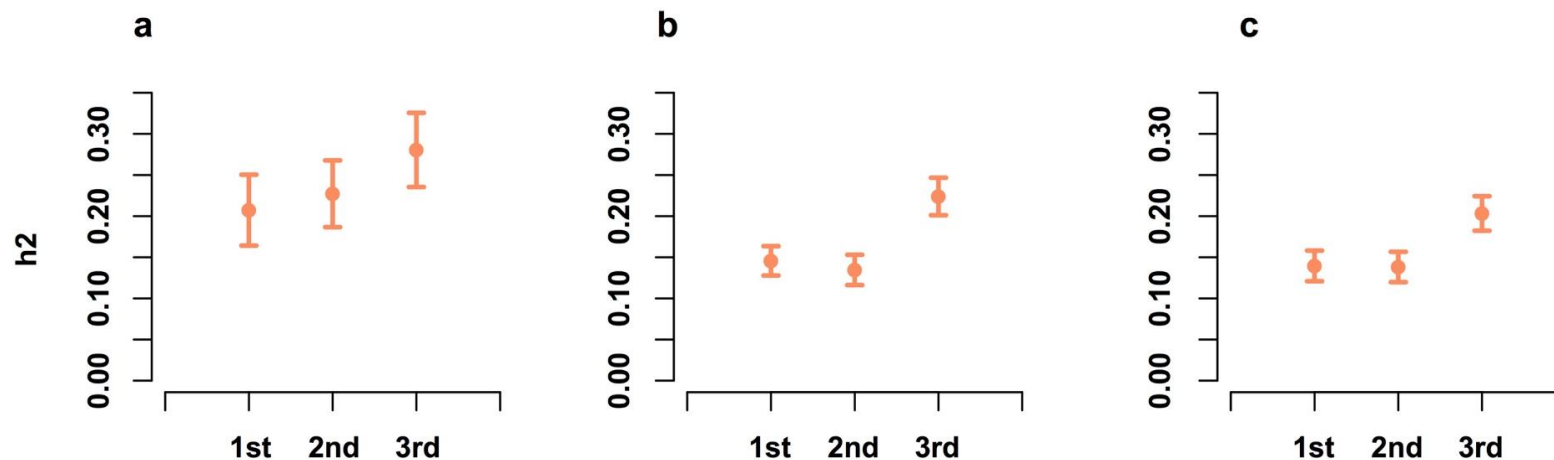
FIGURE S2. SNP-heritabilities on fixed polygenic score resampled Townsend deprivation index (TDI)-stratified subsets. UK Biobank participants were sampled into three TDI-based tertiles with similar polygenic scores for **(a)** fluid intelligence score, **(b)** educational attainment and **(c)** years of education. GWAS was run in each sampled subset and SNP-heritabilities for each quantile and each trait were estimated with LD score regression(2).

TABLE S15. Effect estimates of polygenic scores that include SNPs that were identified from previous GWAS on educational attainment in 1.1 million participants (4)

Polygenic score: all SNPs	β-estimate	95% CI	P
TDI:PGS interaction*	0.094	0.084 - 0.105	2.04E-65
1st quintile (low TDI)	1.642	1.577 - 1.707	$< 10^{-308}$
2nd	1.742	1.676 - 1.808	$< 10^{-308}$
3rd	1.768	1.702 - 1.835	$< 10^{-308}$
4th	2.016	1.949 - 2.083	$< 10^{-308}$
5th	2.373	2.302 - 2.445	$< 10^{-308}$
Polygenic score: non-pleiotropic SNPs	β-estimate	95% CI	P
TDI:PGS interaction*	0.095	0.083 - 0.106	2.69E-62
1st quintile (low TDI)	1.649	1.582 - 1.715	$< 10^{-308}$
2nd	1.752	1.684 - 1.82	$< 10^{-308}$
3rd	1.780	1.712 - 1.849	$< 10^{-308}$
4th	2.034	1.965 - 2.103	$< 10^{-308}$
5th	2.378	2.305 - 2.451	$< 10^{-308}$

Estimates of the interaction term between Townsend deprivation index (TDI) and the polygenic score are included, as well as effect estimates in each TDI quintile. Beta-estimates for the interaction terms and in quintiles between the two polygenic scores were compared with student's t-tests and no significant differences could be observed (p > 0.05). Thus, effect estimates and the increases in effect with TDI were consistent between the polygenic score that was based on all independent SNPs (1207 variants) and the polygenic score that was based only on non-pleiotropic SNPs (1146 variants). *Interaction between the polygenic score and TDI was assessed by multiple linear regression models that included interaction terms for all included covariates. The estimate +- 95% and P-value are presented for the beta-estimates for the TDI:polygenic score interaction terms.
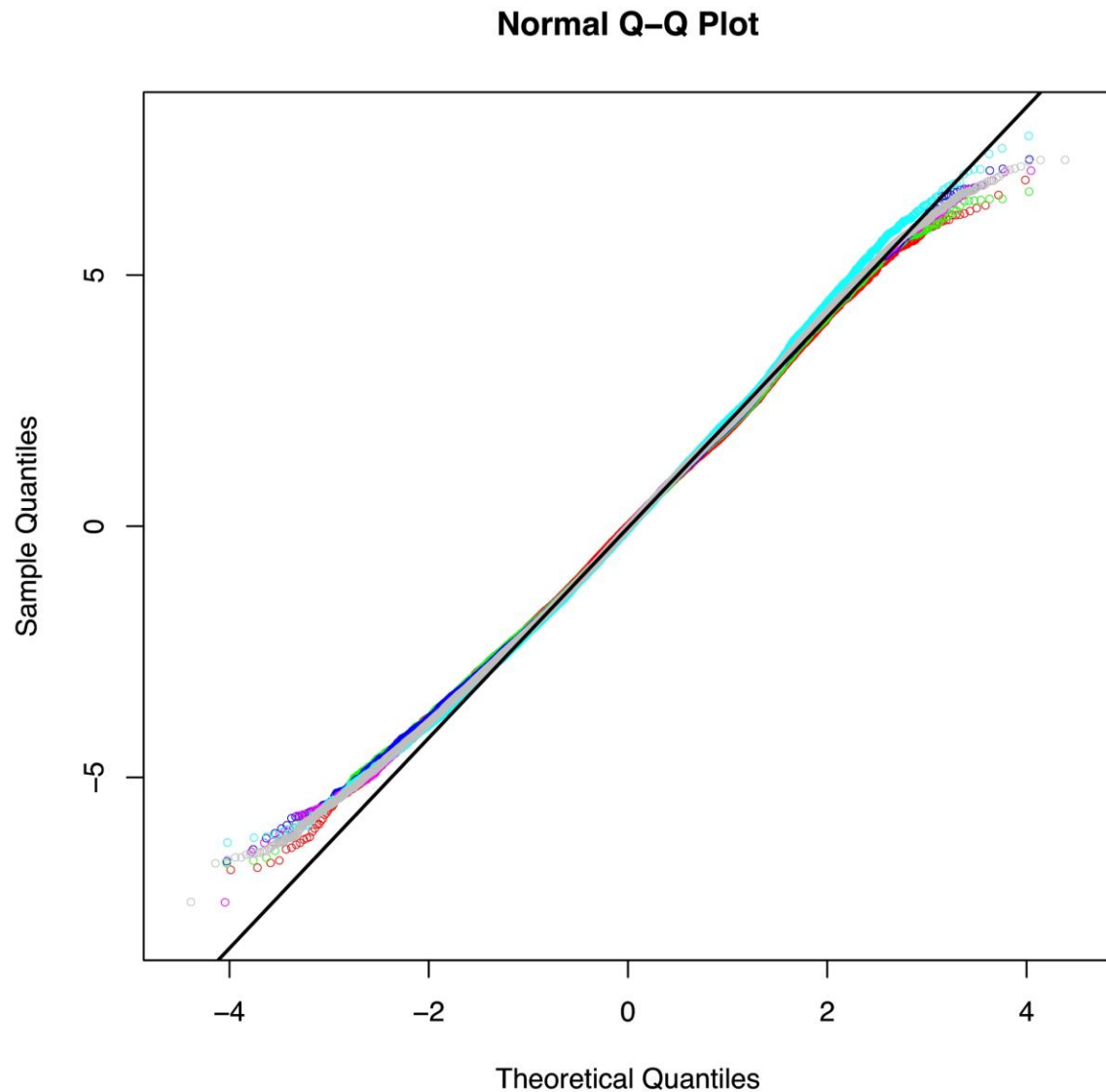
Normal Q–Q Plot

FIGURE S3. Model residuals for fluid intelligence
Model residuals for each Townsend deprivation index (TDI)-quintile are shown in colored symbols, from quintile 1-5: red, green, blue, magenta, and cyan. The residuals for the unstratified model, excluding TDI as covariate, are shown in grey. The black, normal line is forced to pass through the first and third quartile of the unstratified residuals. None of the residuals in the TDI-quintiles show strong deviations from the unstratified residuals, suggesting that the error distributions are similar and sample truncation bias is of limited concern.
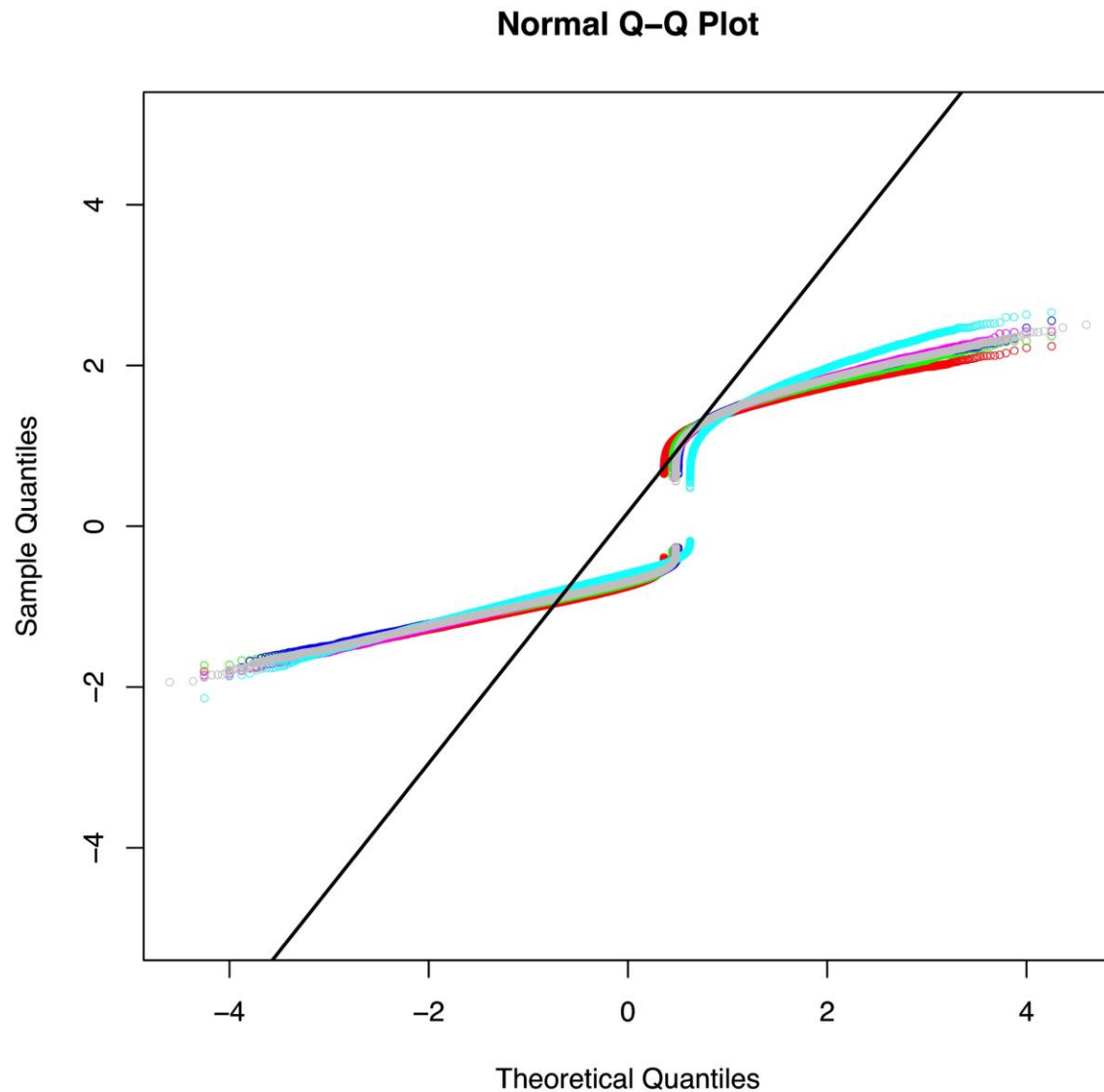
Normal Q–Q Plot

FIGURE S4. Model residuals for educational attainment
Model deviance residuals for each Townsend deprivation index (TDI)-quintile are shown
in colored symbols, from quintile 1-5: red, green, blue, magenta, and cyan. The deviance
residuals for the unstratified model, excluding TDI as covariate, are shown in grey. The
black, normal line is forced to pass through the first and third quartile of the unstratified
residuals. Visual inspection reveals that none of the residuals in the TDI-quintiles show
strong deviations from the unstratified residuals. Note that deviance residuals from
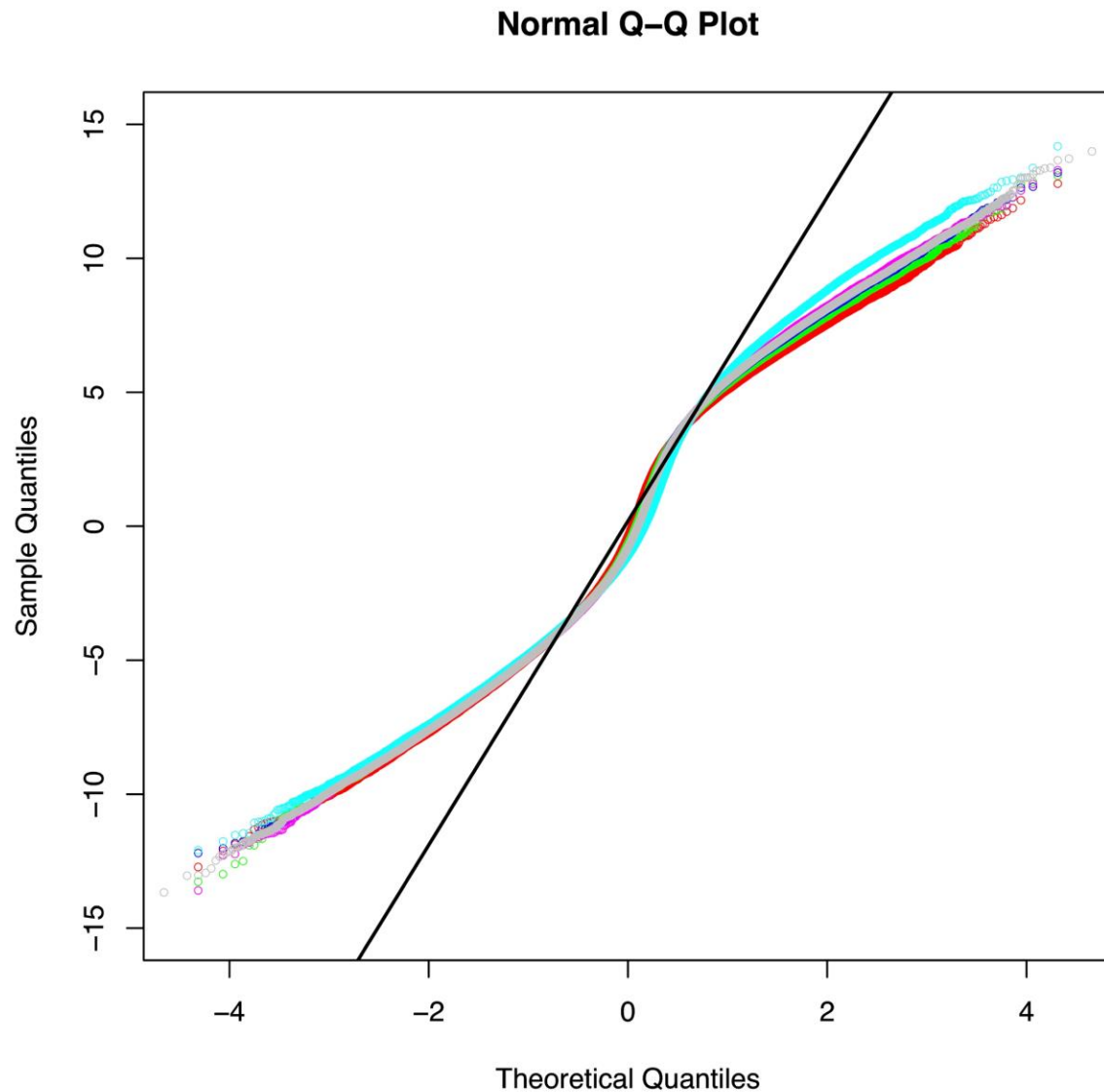logistic models are only approximately normal.

Normal Q–Q Plot

FIGURE S5. Model residuals for years of education
Model residuals for each Townsend deprivation index (TDI)-quintile are shown in colored symbols, from quintile 1-5: red, green, blue, magenta, and cyan. The residuals for the unstratified model, excluding TDI as covariate, are shown in grey. The black, normal line is forced to pass through the first and third quartile of the unstratified residuals. Visual inspection reveals that none of the residuals in the TDI-quintiles show strong deviations from the unstratified residuals.

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