

## SUPPLEMENTARY INFORMATION

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## Supplementary Methods

**Ecological-Risk Assessment Measures of Neighborhood Disadvantage.** Ecological risk assessment was conducted by combining information from four independent sources of data: Geodemographic data from local governments, official crime data from the UK police, Google Streetview-based Systematic Social Observation (SSO), and surveys of neighborhood residents.

1. Geodemographic Data from Local Governments. We obtained information about the Index of Multiple Deprivation from the Department for Communities and Local Government. The Index is the official measure of relative deprivation for neighborhoods in England. Every small area in England is ranked from 1 (most deprived area) to 32,844 (least deprived area), these rankings are then converted into deciles. The Index of Multiple Deprivation is created based on 37 separate indicators, that are organized in seven domains of deprivation (Employment Deprivation; Health Deprivation and Disability; Education, Skills and Training Deprivation; Crime; Barriers to Housing and Services; and Living Environment Deprivation), and combined with appropriate weights to calculate the Index of Multiple Deprivation (IMD). Households were assigned a neighborhood IMD based on street address at the time of the age-5, age-7, age-10, and age-12 in-home visits. We analyzed the average IMD value across these four measurements.
2. Official Crime Data. We measured local area crime by mapping a 1-mile radius around each E-Risk Study family's home and tallying the total number of crimes that occurred in the area each month. Street-level crime data, including information on the type of crime, date of occurrence, and approximate location, were accessed online as part of an open data sharing effort about crime and policing in England and Wales (<https://data.police.uk/>) and geocoded to the home address of the study members. An Application Program Interface was used to extract street-level crime data for each of the geospatial coordinates marking the family's home. For a full description see: <https://data.police.uk/about/#location-anonymisation>.
3. Google Street View Virtual Systematic Social Observation (SSO). The Google Streetview-SSO consisted of trained raters taking a "virtual walk" through the neighborhoods of the E-Risk families. Raters then coded neighborhoods based on what they saw on that virtual walk. Street View is a freely available tool that generates panoramic street-level views using high definition images taken from camera-equipped cars. Signals from global positioning devices are used to accurately position images in the online maps. To avoid gaps in the imagery, adjacent cameras on the car take overlapping pictures and the images are then stitched together to create a continuous 360-degree image of the street. Images are then smoothed and re-projected onto a sphere to create the image displayed in Street View (see **Figure 2**). To protect the privacy of individuals, face- and license-blurring technology is applied to ensure that people on the street and cars in the photographs cannot be identified. Google Street View came online in the United Kingdom in March 2009 and by March 2010, 94% of the E-risk children's neighborhoods were available for viewing. The Google Street View Systematic Social Observation (SSO) was completed by adapting SSO instruments for the virtual context and training raters to reliably code neighborhood features while taking a virtual walk down the street. We have reported full details of the Google Street View SSO

method, inter-rater reliability and predictive validity of the measures elsewhere<sup>19</sup>. We analyzed Google Street View SSO measures of environmental decay and disorder and perceived dangerousness.

4. **Resident Surveys.** A survey of residents living alongside E-Risk families was conducted when the children were 13-14 years of age to capture neighborhood-level social processes that cannot easily be captured via official records or direct observation. The sampling frame for the Neighborhood Survey was drawn using UK-Info Pro V13 <http://www.192.com/products/>. The survey responses were anonymous; no identifying information was collected. In Britain, a postcode area typically contains 15 households, with at most 100 households (e.g., a large apartment block). Therefore, survey respondents were typically living on the same street or within the same apartment block as the children in our study. Surveys were mailed to every household in the postcode registered to the electoral role, with the exception of the E-Risk family, resulting in 20,529 surveys being mailed to households to capture information on E-Risk families. On average, we received 5 (SD=3) completed surveys per neighborhood (range= 0-18 respondents). We achieved at least 3 responses for 80% of target neighborhood and at least 2 responses for 95% (resulting in a total of 5601 completed questionnaires). Survey responses were received for N=1,077 of the 1,116 families in the study. We analyzed survey measures of the following neighborhood-level social processes: fear of crime, direct victimization, neighborhood problems, and social disconnectedness.

Calculations to Evaluate How Much of the Neighborhood Gradient in Risk for Poor Educational Attainment and NEET Status Might Be Explained by Gene-Neighborhood Correlation Between the Education Polygenic Score and ACORN and Ecological-Risk Score Measures of Neighborhood Risk. We evaluated the extent to which gene-neighborhood correlations between GWAS discoveries for educational attainment and measures of neighborhood risk might account for the neighborhood gradient in risk for poor educational outcomes and NEET status.

First, we computed the average polygenic risk for E-Risk participants living in very low- and very high-risk neighborhoods (ACORN scores of 1 and 4; Ecological Risk Scores of 150 and 275) based on the regressions reported in **Supplementary Table S4** (see also **Figure 3** of the main text). For the very low- and very high-risk neighborhoods, the predicted values of the education polygenic score were -0.30 and 0.23 for ACORN and -0.21 and 0.31 for the Ecological-Risk Score, differences of about 0.5 standard deviations. (The education polygenic score is reversed in our analysis relative to the original GWAS, so high values correspond to a genetic prediction of low educational attainment.)

Next, we computed predicted values of the phenotypes for participants with those polygenic scores based on the regression reported in **Supplementary Table S1, Panel A** (see also **Figure 1** of the main text). The predicted proportions of individuals with poor educational qualifications corresponding to the low and high polygenic risk values were 19% and 24% based on the ACORN predictions and 20% and 24% based on the Ecological Risk Score predictions, differences of 4-5%. The predicted proportions of individuals who were NEET corresponding to the low and high polygenic risk values were 11% and 12% based on the ACORN predictions and 11% and 13% based on the Ecological Risk Score predictions, differences of 1-2%.

Finally, we computed predicted values of the phenotypes for participants who grew up in very low- and very high-risk neighborhoods based on the regressions reported in **Supplementary Table S3** (see also **Figure 3** of the main text). The predicted proportions of individuals with poor educational qualifications corresponding to the very low- and very high-risk neighborhoods were 8% and 38% based on the ACORN predictions and 14% and 46% based on the Ecological Risk Score predictions, differences of 30-32%. The predicted proportions of individuals who were NEET corresponding to the very low- and very high-risk neighborhoods were 7% and 20% based on the ACORN predictions and 6% and 27% based on the Ecological Risk Score predictions, differences of 13-21%.

To summarize, we observed a difference in polygenic risk for low educational attainment between very low-risk and very high-risk neighborhoods of roughly one half of one standard deviation. Based on our analysis, this difference in genetic risk could account for a difference in the prevalence of poor educational qualifications between very low-risk and very high-risk neighborhoods of 4-5%. The observed difference in the prevalence of poor educational qualifications between very low-risk and very high-risk neighborhoods was 30-32%, 6-7 times larger. The pattern of results was similar for NEET status. Based on our analysis, genetic risk could account for a neighborhood difference of 1-2% in prevalence. The observed difference in prevalence was 13-21%, an order of magnitude larger.

## Supplementary Tables

Supplementary Table 1. Polygenic score and family history associations with E-Risk children's health and social problems.

**Panel A** shows effect-sizes for polygenic risk associations with children's health and social problems. Effect-sizes are relative risks (RR) estimated from Poisson regression models for a 1 SD increase in polygenic risk. Models included all E-Risk Study members with available genotype and phenotype data (N=1,837 for obesity; N=1,863 for mental health problems; N=1,825 for teen pregnancy; N=1,860 for poor educational qualifications; N=1,863 for NEET status). All models were adjusted for sex. Nesting of twins within families was accounted for by clustering standard errors at the family level.

Phenotype	Polygenic Score	RR	95% CI	p-value
Obesity	Body-mass Index	1.26	[1.14-1.38]	1.99E-06
Mental Health Problems	Schizophrenia	1.13	[1.02-1.26]	0.022
Teen Pregnancy	Age-at-first-birth (reversed)	1.40	[1.19-1.63]	3.24E-05
Poor Educational Qualification	Educational	1.46	[1.34-1.59]	8.96E-18
NEET	Attainment (reversed)	1.32	[1.15-1.51]	7.42E-05

Associations of polygenic scores with continuous measurements of selected phenotypes. Analysis of age-at-first-birth and NEET status are omitted because these phenotypes do not have continuous operationalizations.

Phenotype	Polygenic Score	r	95% CI	p-value
Body-mass Index	Body-mass Index	0.26	[0.21-0.31]	1.04E-21
Mental Health Problems	Schizophrenia	0.06	[0.01-0.11]	0.023
Educational Attainment	Educational Attainment (reversed)	0.28	[0.23-0.33]	1.04E-25

**Panel B** shows correlations between measures of polygenic and family history risk. Maternal body-mass-index (BMI) was measured from mother’s self-reported height and weight when E-Risk participants were aged 12 years (N=900 mothers of 1,780 participants; M=26, SD=6); family history of psychiatric hospitalization was measured based on family histories collected during interviews with children’s mothers as the proportion of relatives with a hospitalization (N=970 mothers of 1,920 participants; M=0.07, SD=0.13); mother’s age at first birth was collected as part of screening for enrollment in the study (N=1,011 mothers of 1,999 participants; M=24 years, SD=6); the highest education of either parent was collected during interviews when participants were aged 5 years (N=1,011 families of 1,999 participants; 12% held no educational credentials, 12% held GCSE Level-1 credentials; 35% held GCSE Level-2 credentials; 41% held GCSE Level-3 or higher credentials).

<b>Polygenic Risk Measure</b>	<b>Family History Measure</b>	<b>Pearson r</b>
BMI Polygenic Score	Maternal BMI	0.14
Schizophrenia Polygenic Score	Family History of Psychiatric Hospitalization	0.01
Age-at-first-birth Polygenic Score	Mother's age at first birth	0.16
Educational Attainment Polygenic Score	Parents' Education	0.23

**Panel C** shows effect-sizes for polygenic risk and family-history associations with children’s health and social problems. Samples are restricted to children with available phenotype, genotype, and family-history information (N=1,666 for obesity; N=1,812 for mental health problems; N=1,825 for teen pregnancy; N=1,860 for poor educational qualifications; and N=1,863 for NEET status). The first column (M1) reports the effect-size for polygenic risk. The second column (M2) reports the effect-size for family-history risk. The third column (M3) reports the multivariate-adjusted effect-sizes for polygenic risk and family-history risk from a model that includes both risk factors. All models were adjusted for sex. Nesting of twins within families was accounted for by clustering standard errors at the family level.

	<b>M1</b>	<b>M2</b> <u>RR [95% CI]</u>	<b>M3</b>
<b>Obesity</b>			
BMI Polygenic Score	1.19 [1.08-1.32]		1.16 [1.04-1.29]
Family History (maternal BMI)		1.23 [1.14-1.34]	1.22 [1.12-1.32]
<b>Mental Health Problems</b>			
Schizophrenia Polygenic Score	1.13 [1.01-1.26]		1.13 [1.01-1.26]
Family History (maternal family history of psychiatric hospitalization)		1.19 [1.08-1.30]	1.19 [1.08-1.30]
<b>Teenaged Pregnancy</b>			
Age-at-first-birth Polygenic Score (reversed)	1.40 [1.19-1.63]		1.25 [1.07-1.47]
Family History (mother's age at first birth)		2.35 [1.81-3.05]	2.24 [1.71-2.92]
<b>Poor Educational Qualifications</b>			
Educational Attainment Polygenic Score (reversed)	1.46 [1.34-1.59]		1.30 [1.19-1.41]
Family History (parents' education)		1.69 [1.57-1.82]	1.61 [1.48-1.74]
<b>NEET</b>			
Educational Attainment Polygenic Score (reversed)	1.32 [1.15-1.51]		1.16 [1.01-1.32]
Family History (parents' education)		1.72 [1.53-1.94]	1.67 [1.48-1.90]

Supplementary Table 2. Means and standard deviations of neighborhood measures and their correlations with one another.

	M	SD	<b>Pearson Correlation</b>					
			(1)	(2)	(3)	(4)	(5)	(6)
(1) ACORN	2.49	1.10						
(2) Composite Ecological-Risk Index	198.46	32.77	0.65					
(3) Deprived	49.54	9.85	0.53	0.76				
(4) Dilapidated	49.73	9.79	0.52	0.85	0.50			
(5) Disconnected	49.72	9.94	0.50	0.81	0.44	0.58		
(6) Dangerous	49.39	9.88	0.61	0.89	0.58	0.72	0.64	



Supplementary Table 3. Associations between neighborhood disadvantage measures and children’s health and social problems. Table shows relative risks (RR) estimated from Poisson regression models. Nesting of twins within families was accounted for by clustering standard errors at the family level. Panel A shows results for ACORN (N=1,857) and the composite Ecological-Risk Index (N=1,822). Effect-sizes for ACORN classification are reported for a 1-category increase in social disadvantage. Effect-sizes for composite Ecological-Risk Index are reported for a 1-SD increase in ecological risk. Panel B shows results for individual ecological-risk measures. Effect-sizes are reported for a 1-SD increase in ecological risk.

**Panel A**

	RR	95% CI	p-value
ACORN Classification			
Obesity	1.20	[1.10-1.31]	5.52E-05
Mental Health Problems	1.19	[1.08-1.31]	6.35E-04
Teen Pregnancy	1.56	[1.34-1.83]	1.69E-08
Poor Educational Qualification	1.53	[1.40-1.67]	1.26E-20
NEET	1.52	[1.33-1.74]	1.22E-09
Composite Ecological-Risk Index			
Obesity	1.15	[1.03-1.29]	0.011
Mental Health Problems	1.30	[1.14-1.47]	5.58E-05
Teen Pregnancy	1.55	[1.30-1.85]	1.06E-06
Poor Educational Qualification	1.47	[1.33-1.62]	9.61E-14
NEET	1.59	[1.36-1.85]	5.38E-09

**Panel B**

	RR	95% CI	p-value
Economic Deprivation			
Obesity	1.13	[1.03-1.24]	0.010
Mental Health Problems	1.11	[1.01-1.23]	0.037
Teen Pregnancy	1.26	[1.11-1.43]	4.60E-04
Poor Educational Qualification	1.20	[1.10-1.31]	3.54E-05
NEET	1.34	[1.19-1.51]	1.18E-06
Physical Dilapidation			
Obesity	1.09	[1.00-1.19]	0.053
Mental Health Problems	1.25	[1.12-1.40]	5.05E-05
Teen Pregnancy	1.40	[1.22-1.61]	2.47E-06
Poor Educational Qualification	1.34	[1.24-1.46]	5.02E-12
NEET	1.46	[1.30-1.64]	5.21E-10
Social Disconnection			
Obesity	1.11	[1.01-1.22]	0.037
Mental Health Problems	1.18	[1.06-1.31]	0.003
Teen Pregnancy	1.35	[1.15-1.59]	2.52E-04
Poor Educational Qualification	1.31	[1.20-1.43]	2.75E-09
NEET	1.28	[1.12-1.47]	4.47E-04
Danger			
Obesity	1.08	[0.98-1.19]	0.110
Mental Health Problems	1.26	[1.11-1.42]	2.88E-04
Teen Pregnancy	1.42	[1.18-1.72]	2.40E-04
Poor Educational Qualification	1.43	[1.30-1.58]	1.02E-12
NEET	1.49	[1.27-1.75]	1.34E-06

Supplementary Table 4. Associations between neighborhood disadvantage and children’s polygenic risk for obesity, schizophrenia, young age at first birth, and low educational attainment. Table shows unstandardized coefficients from linear regression models. Nesting of twins within families was accounted for by clustering standard errors at the family level. Only one monozygotic twin from each pair was included in analysis because monozygotic twins share identical neighborhood disadvantage and polygenic score values. Panel A shows results for ACORN (N=1,441) and the composite Ecological-Risk Index (N=1,414). Coefficients can be interpreted as expected SD increase in polygenic risk per unit increase in ACORN disadvantage classification and SD increase in polygenic score per SD increase in composite Ecological-Risk Index. Panel B shows results for individual ecological-risk measures. Coefficients can be interpreted as expected SD increase in polygenic risk per SD increase in ecological-risk.

**Panel A**

	<b>B</b>	<b>95% CI</b>	<b>p-value</b>
<u>Polygenic Score</u>	ACORN Classification		
Body-mass Index	-0.01	[-0.07 , 0.04]	0.686
Schizophrenia	0.04	[-0.01 , 0.10]	0.094
Age at first birth (reversed)	0.12	[0.06 , 0.17]	2.63E-05
Educational Attainment (reversed)	0.18	[0.12 , 0.23]	3.46E-10
	Composite Ecological-Risk Index		
Body-mass Index	-0.01	[-0.08 , 0.07]	0.863
Schizophrenia	0.08	[0.01 , 0.15]	0.033
Age at first birth (reversed)	0.12	[0.04 , 0.19]	0.003
Educational Attainment (reversed)	0.17	[0.09 , 0.25]	3.48E-05

**Panel B**

	<b>B</b>	<b>95% CI</b>	<b>p-value</b>
<u>Polygenic Score</u>	Economic Deprivation		
Body-mass Index	0.03	[-0.03 , 0.10]	0.278
Schizophrenia	0.10	[0.04 , 0.16]	0.001
Age at first birth (reversed)	0.09	[0.03 , 0.16]	0.004
Educational Attainment (reversed)	0.11	[0.04 , 0.17]	0.002
	Physical Dilapidation		
Body-mass Index	-0.02	[-0.09 , 0.05]	0.582
Schizophrenia	0.06	[0.00 , 0.12]	0.054
Age at first birth (reversed)	0.07	[0.01 , 0.13]	0.025
Educational Attainment (reversed)	0.10	[0.03 , 0.16]	0.002
	Social Disconnection		
Body-mass Index	-0.02	[-0.08 , 0.04]	0.539
Schizophrenia	0.02	[-0.04 , 0.07]	0.585
Age at first birth (reversed)	0.04	[-0.02 , 0.10]	0.159
Educational Attainment (reversed)	0.10	[0.04 , 0.17]	0.002
	Danger		
Body-mass Index	-0.02	[-0.09 , 0.05]	0.564
Schizophrenia	0.04	[-0.02 , 0.10]	0.197
Age at first birth (reversed)	0.10	[0.04 , 0.17]	0.002
Educational Attainment (reversed)	0.15	[0.08 , 0.21]	1.60E-05

Supplementary Table 5. Association between neighborhood disadvantage and mother’s polygenic risk for obesity, schizophrenia, young age at first birth, and low educational attainment. Table shows unstandardized coefficients from linear regression models. Panel A shows results for ACORN (N=858) and the composite Ecological-Risk Index (N=841). Coefficients can be interpreted as expected SD increase in polygenic risk per unit increase in ACORN disadvantage classification and SD increase in polygenic score per SD increase in composite Ecological-Risk Index. Panel B shows results for individual ecological-risk measures. Coefficients can be interpreted as expected SD increase in polygenic risk per SD increase in ecological-risk.

**Panel A**

	<b>B</b>	<b>95% CI</b>	<b>p-value</b>
<u>Polygenic Score</u>			
	ACORN Classification		
Body-mass Index	0.00	[-0.07 , 0.06]	0.957
Schizophrenia	0.02	[-0.04 , 0.08]	0.508
Age at first birth (reversed)	0.14	[0.08 , 0.20]	8.45E-06
Educational Attainment (reversed)	0.19	[0.13 , 0.26]	3.99E-10
	Composite Ecological-Risk Index		
Body-mass Index	0.04	[-0.05 , 0.12]	0.388
Schizophrenia	0.01	[-0.08 , 0.09]	0.834
Age at first birth (reversed)	0.21	[0.13 , 0.29]	6.89E-07
Educational Attainment (reversed)	0.20	[0.12 , 0.28]	2.86E-06

**Panel B**

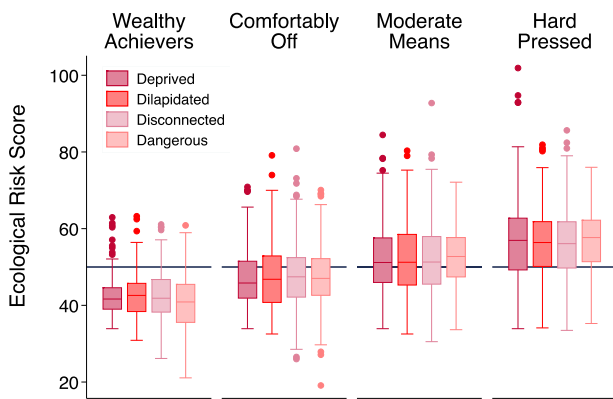
	<b>B</b>	<b>95% CI</b>	<b>p-value</b>
<u>Polygenic Score</u>			
	Economic Deprivation		
Body-mass Index	0.04	[-0.03 , 0.10]	0.262
Schizophrenia	0.03	[-0.05 , 0.10]	0.484
Age at first birth (reversed)	0.13	[0.06 , 0.19]	1.55E-04
Educational Attainment (reversed)	0.15	[0.08 , 0.21]	9.82E-06
	Physical Dilapidation		
Body-mass Index	0.02	[-0.05 , 0.09]	0.562
Schizophrenia	0.00	[-0.07 , 0.08]	0.899
Age at first birth (reversed)	0.15	[0.09 , 0.22]	4.76E-06
Educational Attainment (reversed)	0.10	[0.03 , 0.17]	0.005
	Social Disconnection		
Body-mass Index	0.02	[-0.04 , 0.09]	0.507
Schizophrenia	-0.03	[-0.09 , 0.04]	0.463
Age at first birth (reversed)	0.12	[0.05 , 0.19]	0.001
Educational Attainment (reversed)	0.14	[0.07 , 0.21]	1.21E-04
	Danger		
Body-mass Index	0.03	[-0.05 , 0.10]	0.488
Schizophrenia	0.01	[-0.06 , 0.08]	0.721
Age at first birth (reversed)	0.16	[0.09 , 0.23]	1.04E-05
Educational Attainment (reversed)	0.15	[0.08 , 0.22]	3.04E-05

Supplementary Table 6. Effect-sizes for associations between children’s neighborhood and polygenic risks before and after covariate adjustment for their mothers’ polygenic risk. Table shows unstandardized coefficients from linear regression model of associations between neighborhood disadvantage and polygenic risk (rGE). Unadjusted associations are parallel to results reported in Supplementary Table 4 with a sample restricted to the subset of E-Risk participants for whom maternal polygenic score values were available (N=1,235 participants in 858 families for ACORN analysis and N=1,213 participants in 841 families for Ecological-Risk Index analysis). Standard errors were clustered at the family level to account for non-independence of data. Only one monozygotic twin from each pair was included in analysis because monozygotic twins share identical neighborhood disadvantage and polygenic score values.

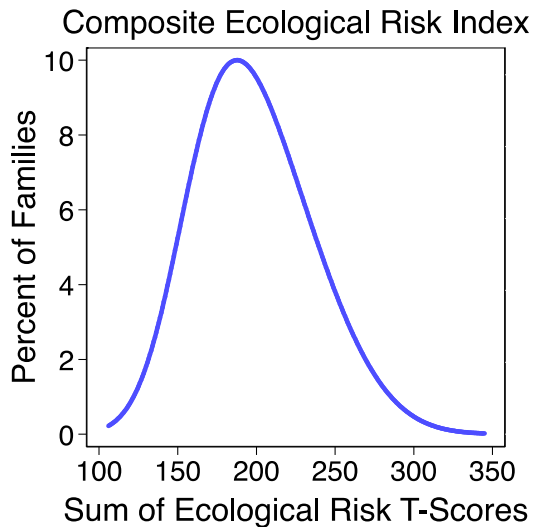
	ACORN		Ecological-Risk Index	
	B	[95% CI]	B	[95% CI]
<b>BMI Polygenic Score</b>				
Unadjusted rGE	-0.01	[-0.07-0.05]	0.00	[-0.09-0.08]
Maternal PGS-adjusted	-0.01	[-0.06-0.04]	-0.02	[-0.09-0.05]
<b>Schizophrenia Polygenic Score</b>				
Unadjusted rGE	0.04	[-0.02-0.09]	0.05	[-0.03-0.12]
Maternal PGS-adjusted	0.04	[-0.01-0.09]	0.05	[-0.01-0.12]
<b>Age-at-first-birth Polygenic Score (reversed)</b>				
Unadjusted rGE	0.11	[0.05-0.17]	0.13	[0.04-0.21]
Maternal PGS-adjusted	0.04	[-0.01-0.09]	0.02	[-0.05-0.08]
<b>Educational Attainment Polygenic Score (reversed)</b>				
Unadjusted rGE	0.17	[0.11-0.23]	0.16	[0.08-0.25]
Maternal PGS-adjusted	0.06	[0.01-0.11]	0.05	[-0.02-0.12]

## Supplementary Figures

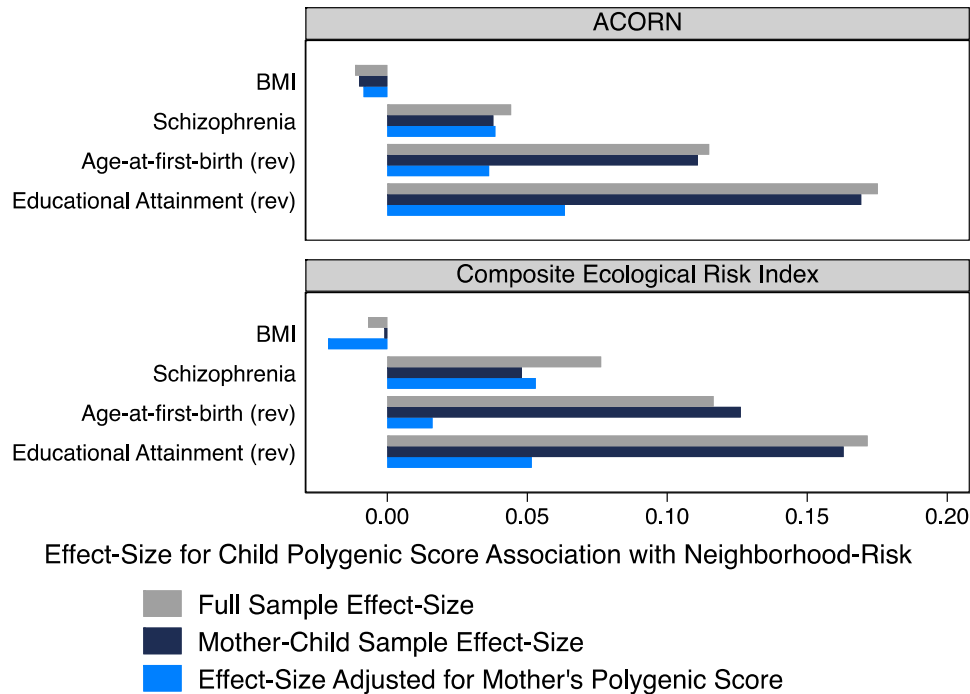
### Panel A.



### Panel B.

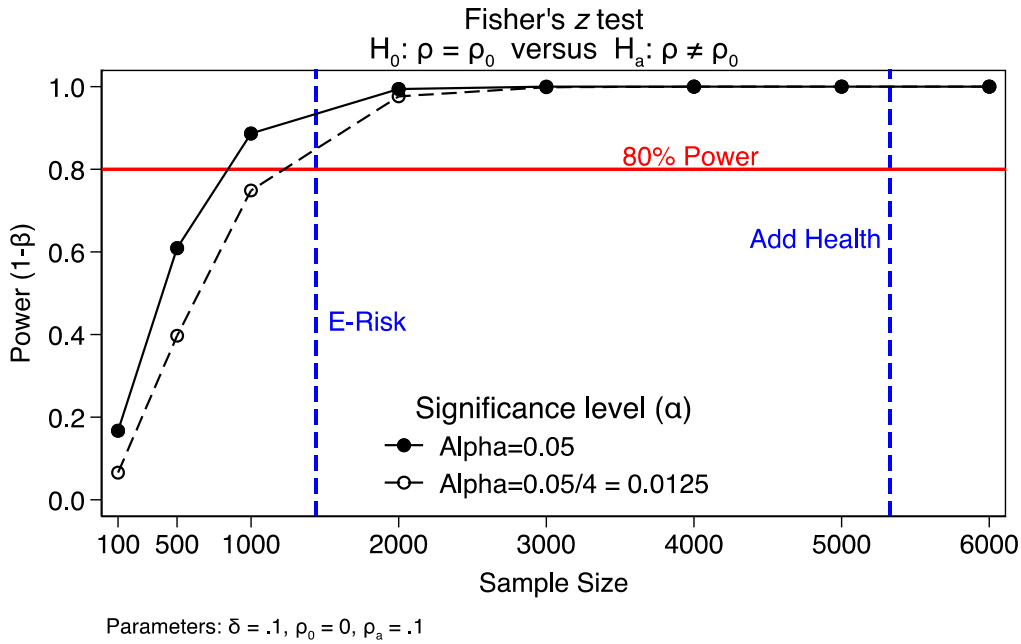


Supplementary Figure 1. Distributions of ecological-risk assessments within ACORN neighborhood classifications. We used two different methods to measure neighborhood disadvantage: A geodemographic index (ACORN) and an Ecological Risk Index based on surveys of neighborhood residents, electronic record data, and Systematic Social Observation using Google Streetview. Neighborhoods with more socially disadvantaged ACORN classification were also more disadvantaged as measured by ecological-risk assessment. **Panel A** graphs distributions of each ecological-risk measure within each ACORN classification for N=985 families for which both ACORN and ecological-risk assessment measurements were available. For each ecological-risk measure, average risk trended upwards from the least disadvantaged ACORN classification (Wealthy Achievers) to the most disadvantaged ACORN classification (Hard Pressed). **Panel B** graphs the distribution of the composite Ecological Risk Index.



Supplementary Figure 2. Effect-sizes for associations between children’s neighborhood and polygenic risks before and after covariate adjustment for their mothers’ polygenic risk. The figure shows effect-sizes for associations between children’s polygenic and neighborhood risks in the full E-Risk sample (gray bars, N=1,441 for ACORN, 1,414 for Ecological-Risk Index, see also Supplementary Table 4), in the mother-child sub-sample which included families with genetic data on mothers and children (dark blue bars, N=1,235 for ACORN, 1,213 for the Ecological-Risk Index), and in the mother-child sub-sample after covariate adjustment for mother’s polygenic score (light blue bars). Nesting of twins within families was accounted for by clustering standard errors at the family level. The top panel shows results for ACORN neighborhood disadvantage classification. Coefficients can be interpreted as expected SD increase in polygenic risk per unit increase in ACORN disadvantage classification. The bottom panel shows results for the composite Ecological-Risk Index. Coefficients can be interpreted as expected SD increase in polygenic risk per SD increase in ecological-risk. Only one monozygotic twin from each pair was included in analysis because monozygotic twins share identical neighborhood disadvantage and polygenic score values.

Power for testing polygenic score association with neighborhood risk at effect-size  $r=0.1$



Supplementary Figure 3. Power for testing genetic associations with neighborhood risk. The figure plots statistical power on the y-axis against sample-size on the x-axis for testing effect-sizes of  $r=0.1$  against a null hypothesis of  $r=0$ . Power is plotted for the conventional alpha threshold of 0.05 as well as an alpha threshold corrected for testing 4 polygenic scores ( $0.05/4=0.0125$ ). The sample-sizes for E-Risk and Add Health tests of genetic association with neighborhood risk are denoted by vertical blue lines. The threshold of 80% power is denoted with a horizontal red line. The graph shows that both samples have  $>80\%$  power to test associations with effect-size of  $r=0.1$ .