

Genetics & the Geography of Health, Behavior, & Attainment

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SUMMARY

Sociogenomic analyses testing the concentration of polygenic risks for health, behavior, and social problems in children growing up in disadvantaged neighborhoods yielded three findings: We found little consistent evidence for the concentration of polygenic risk for obesity or polygenic risk for mental health problems in children growing up in disadvantaged neighborhoods. In contrast, we found consistent evidence for the concentration of polygenic risks for teen pregnancy and low achievement. Concentration of polygenic risks was mostly explained by children's inheritance of both neighborhood and polygenic risks from their parents. Selective mobility may contribute to concentrations of risks. In neighborhood mobility analysis that followed young people living with their parents during adolescence to where they lived as adults nearly two decades later, participants with higher polygenic risk for teen pregnancy and low achievement exhibited downward neighborhood mobility, moving to more disadvantaged neighborhoods across follow-up.

ABSTRACT

People's life chances can be predicted by their neighborhoods. This observation is driving efforts to improve lives by changing neighborhoods. Some neighborhood effects may be causal, supporting neighborhood-level interventions. Other neighborhood effects may reflect selection of families with different characteristics into different neighborhoods, supporting interventions that target families/individuals directly. To test how selection affects different neighborhood-linked problems, we linked neighborhood data with genetic, health, and social-outcome data for >7,000 European-descent UK and US young people in the E-Risk and Add Health Studies. We tested selection/concentration of genetic risks for obesity, schizophrenia, teen-pregnancy, and poor educational outcomes in high-risk neighborhoods, including genetic analysis of neighborhood mobility. Findings argue against genetic selection/concentration as an explanation for neighborhood gradients in obesity and mental-health problems, suggesting neighborhoods may be causal. In contrast, modest genetic selection/concentration was evident for teen-pregnancy and poor educational outcomes, suggesting neighborhood effects for these outcomes should be interpreted with care.

INTRODUCTION

Young people's life chances can be predicted by characteristics of their neighborhood¹. Children growing up in disadvantaged neighborhoods exhibit worse physical and mental health and suffer poorer educational and economic outcomes compared to children growing up in advantaged neighborhoods. Increasing recognition that aspects of social inequalities tend, in fact, to be geographic inequalities²⁻⁵ is stimulating research and focusing policy interest on neighborhood effects and the role of place in shaping health, behavior, and social outcomes.

A challenge in interpreting neighborhood-effects research is distinguishing causal effects of neighborhood features from processes of selection in which individuals with different characteristics come to live in different neighborhoods^{6,7}. There is growing evidence that at least some neighborhood effects are causal; in a natural experiment arising from immigration policy in Sweden and in a randomized trial of a housing voucher program in the United States, people assigned to better-off neighborhoods tended to have some better health outcomes^{8,9}. Economic benefits of neighborhood interventions are less clear, but may be present for children whose neighborhoods are changed relatively early in life^{10,11}. But selection effects are also apparent. For example, in one study of hurricane survivors, those in poorer health prior to the disaster tended to relocate to higher-poverty communities in its aftermath¹². Selection and causation in neighborhood effects are not mutually exclusive; both can occur¹³. Better understanding of how selection may contribute to apparent neighborhood effects is needed to guide intervention design and policy. Where selection can be ruled out as an explanation of neighborhood effects, neighborhood-level interventions could be prioritized. In instances where apparent neighborhood effects reflect selection processes, interventions delivered to individuals or families directly might prove more effective.

To evaluate the size and scope of selection effects in neighborhood research, methods are needed that quantify selection factors and that are not influenced by neighborhood conditions. The ideal approach is to compare fixed characteristics between children growing up in high-risk neighborhoods and peers growing up in better-off neighborhoods. Because neighborhoods may affect individuals as early as the very beginnings of their lives^{3,14}, traditional social-science measurements are problematic. Recent discoveries from genome-wide association studies (GWAS) provide a new opportunity to quantify selection effects at the level of the individual: polygenic scores. DNA sequence is fixed at conception and never altered by neighborhood environments. Because children inherit their DNA sequence from their parents, measures of genetic risk form a conceptual link between familial characteristics, such as parental education, that may influence selection into neighborhoods, and children's health and social outcomes. In this article, we report proof-of-concept polygenic score analysis to quantify genetic selection into neighborhoods.

METHODS

We analyzed polygenic scores and neighborhood conditions in 1,999 young people from the E-Risk Longitudinal Study, a birth cohort ascertained from a birth registry in England and Wales and followed prospectively through age 18 years. We studied phenotypes that represent substantial public health and economic burdens, have been linked with neighborhood risk in prior studies, are prevalent among 18-year-olds in England and Wales, and have been subject to large-scale genome-wide association study meta-analyses: obesity, mental health problems, teen pregnancy, and poor educational outcomes. We measured children's genetic risk using four polygenic scores computed based on results from published GWAS of obesity, schizophrenia, age at first birth, and educational attainment¹⁵⁻¹⁸. We measured their neighborhoods using administrative, survey, and systematic-social-observation¹⁹ data collected during their childhoods. We tested for the expected associations of polygenic and neighborhood risk with E-Risk children's development of obesity and mental-health problems, teen pregnancy, earning poor educational qualifications, and not being in education, employment, or training (NEET), as measured during home visits at age 18 years. To test for genetic selection effects, we tested for gene-environment correlations in which young people who carried elevated burdens of polygenic risk tended to have grown up in more disadvantaged neighborhoods. To test if genetic selection effects reflected the passive inheritance of genetics and neighborhood conditions from parents, we also analyzed the genetics of the children's mothers. Finally, to test how genetics might become correlated with neighborhood conditions, we tested genetic associations with neighborhood mobility using data from 5,325 participants in the US-based National Longitudinal Study of Adolescent to Adult Health, a nationally representative longitudinal study of American adolescents followed prospectively through their late 20s/early 30s.

Figure 1. Children with higher genetic risk had more social and health problems by age 18 years

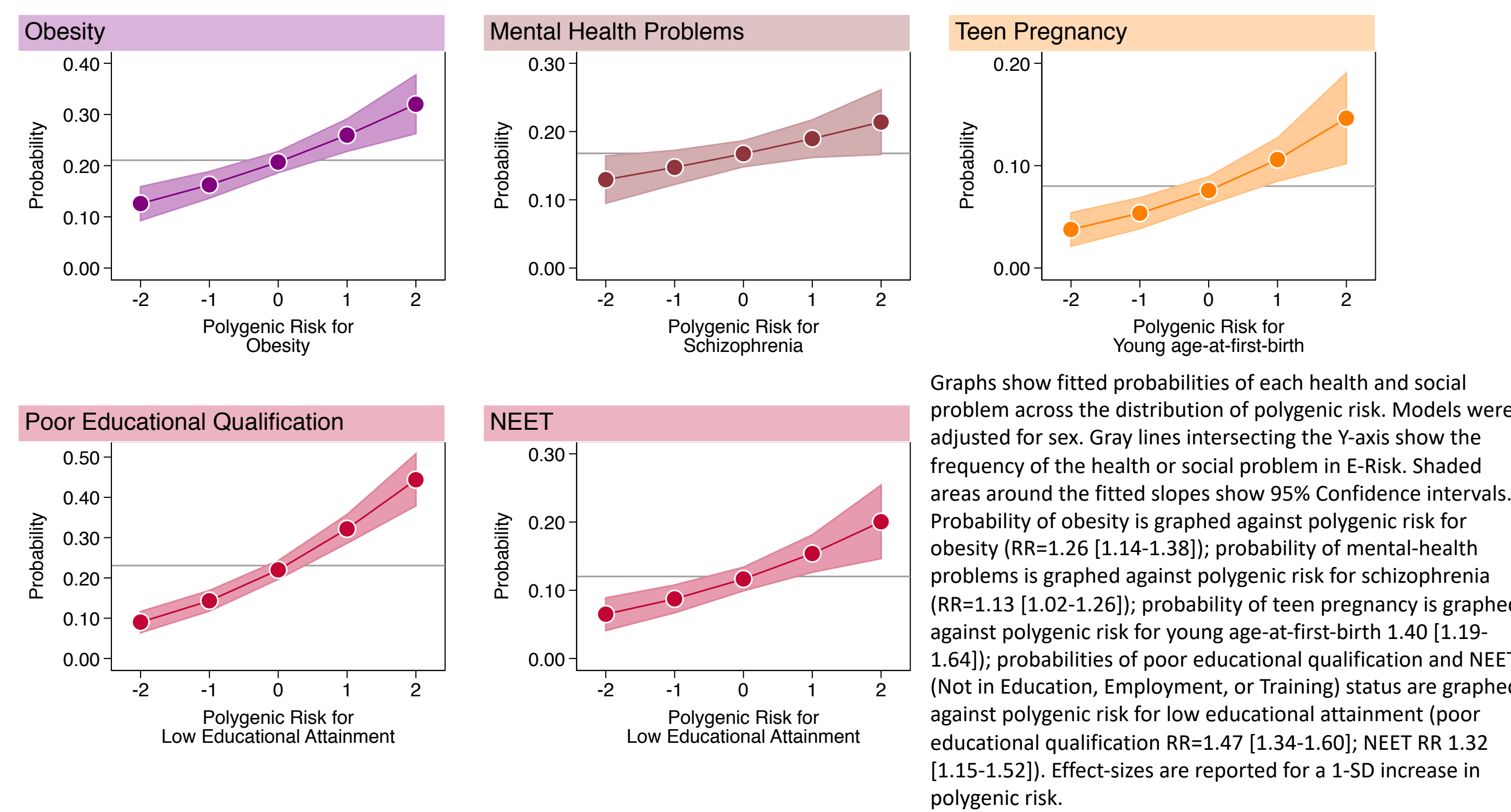


Figure 2. Quantification of E-Risk families' neighborhood disadvantage using ACORN and a composite Ecological-Risk Index.

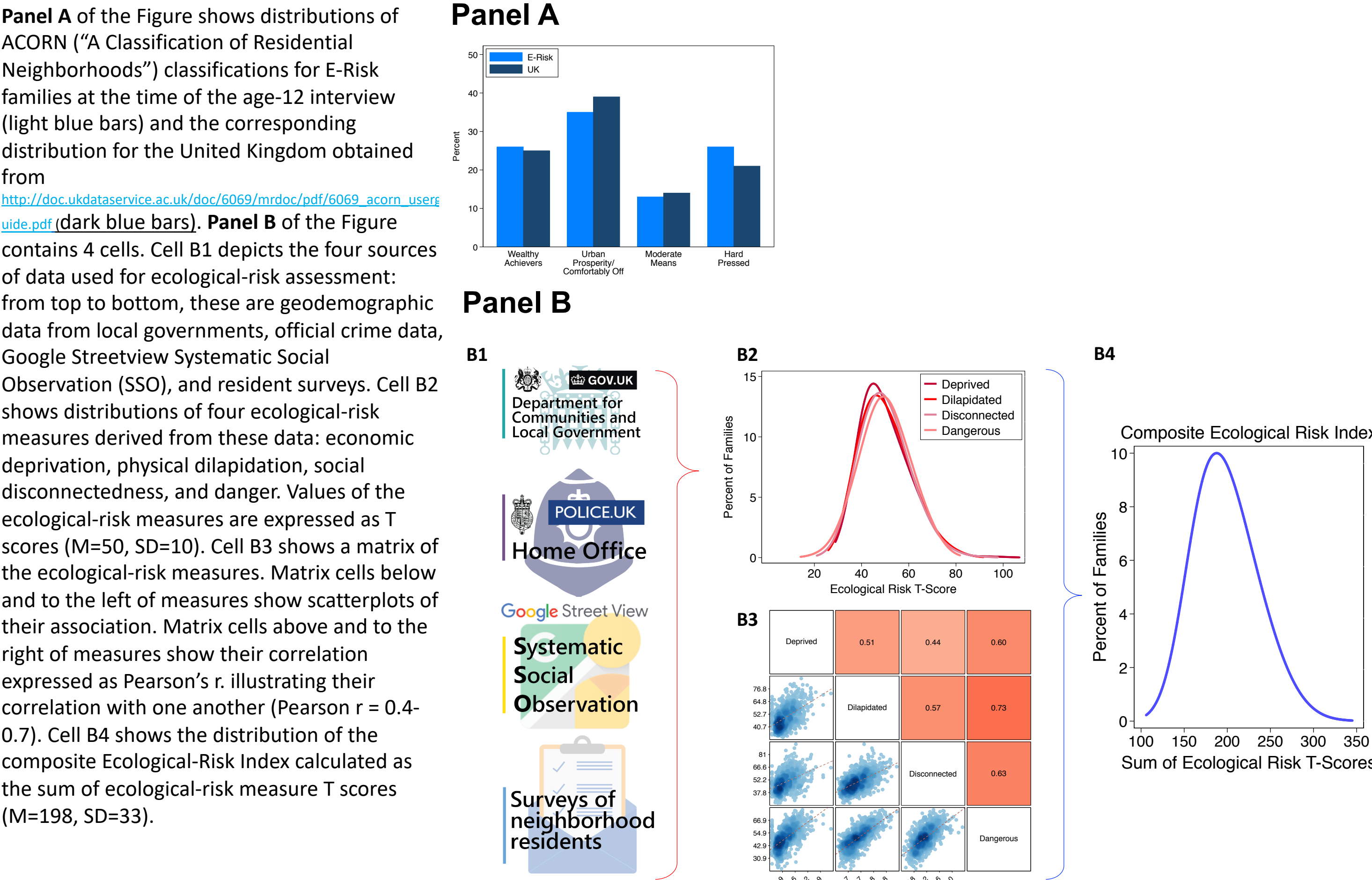


Figure 3. Children growing up in more disadvantaged neighborhoods were at increased risk for social and health problems by age 18 years.

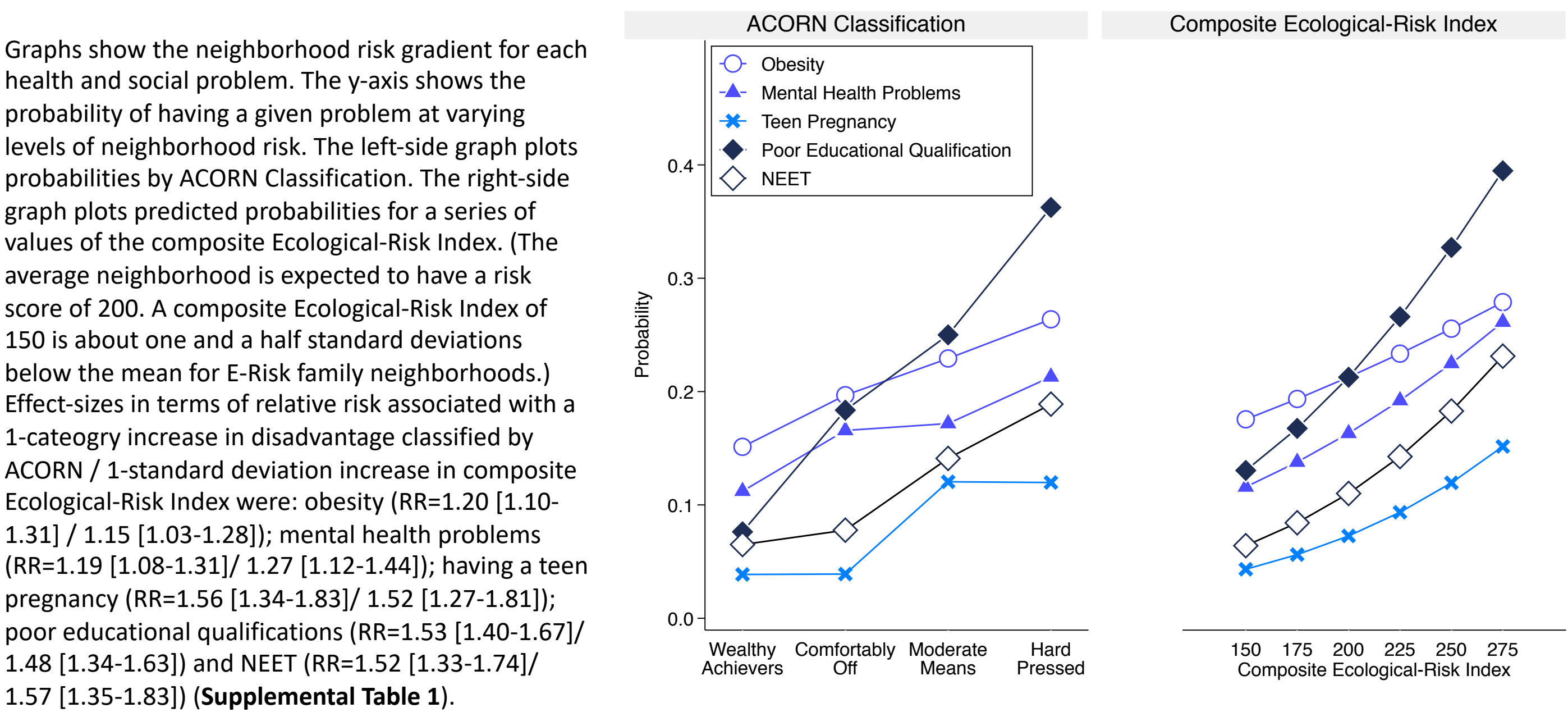
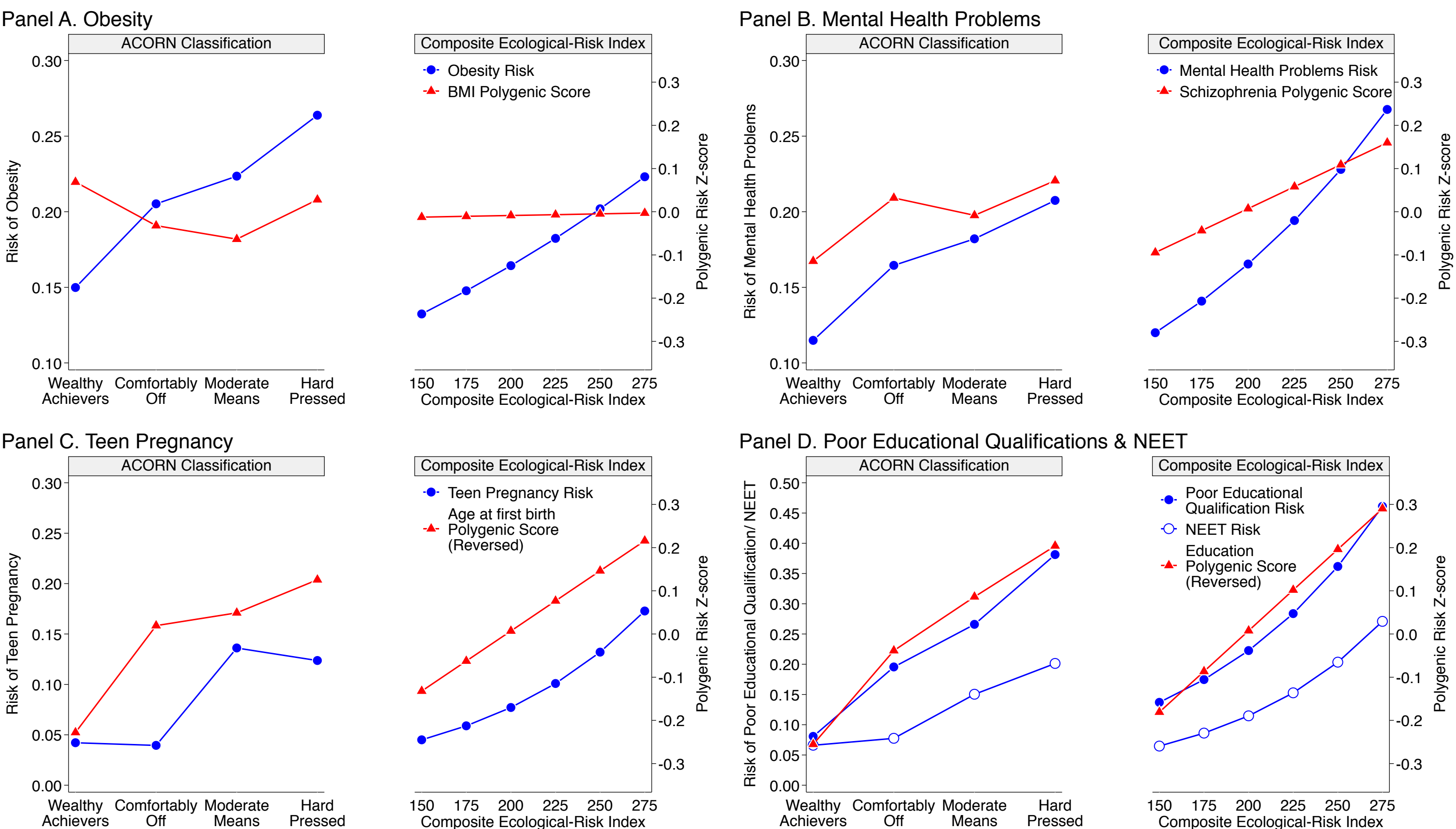
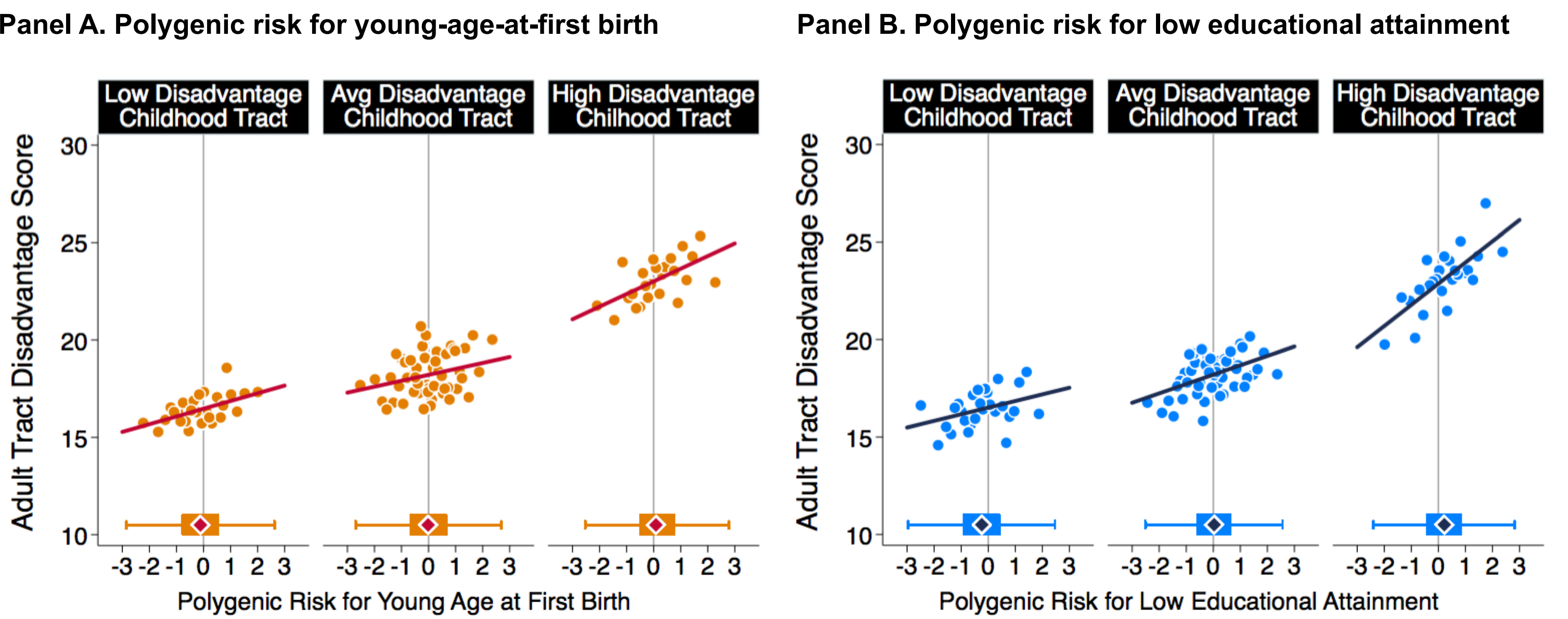


Figure 4. Neighborhood gradients in phenotypic and genetic risk for obesity, mental health problems, teen pregnancy, poor educational qualifications, and NEET status.



Figures graph E-Risk young adults' phenotypic risk (blue slopes, left-side y-axes showing risk expressed as a predicted probability) and genetic risk (red slopes, right-side y-axes showing polygenic risk expressed on Z scale) across the distribution of neighborhood disadvantage (x-axes). The left figure panes graph results for ACORN classification of neighborhood disadvantage. The right figure panes graph results for ecological-risk score quantification of neighborhood disadvantage. **Panel A** graphs risk of obesity (blue) and body-mass-index (BMI) polygenic score (red). The panel shows that E-Risk participants growing up in more disadvantaged neighborhoods more often became obese, but did not differ from peers in their polygenic risk for obesity. **Panel B** graphs risk of mental health problems (blue) and schizophrenia polygenic score (red). The panel shows that E-Risk participants growing up in more disadvantaged neighborhoods more often developed mental health problems and were at higher polygenic risk for schizophrenia, although the genetic association was statistically significant only for the ecological-risk score measure of neighborhood disadvantage. **Panel C** graphs risk of teen pregnancy (blue) and age-at-first-birth polygenic score (red). Age-at-first-birth polygenic score values are reversed for the graph so that higher values correspond to genetic prediction of younger age at first birth. The panel shows that E-Risk participants growing up in more disadvantaged neighborhoods more often had teen pregnancies and had higher polygenic risk for early first birth. **Panel D** graphs risk of poor educational qualifications (blue dots) and NEET status (blue circles), and educational attainment polygenic score (red). Education polygenic score values are reversed for the graph so that higher values correspond to genetic prediction of lower educational attainment. The panel shows that E-Risk participants growing up in more disadvantaged neighborhoods more often struggled with education and employment and tended to have higher polygenic risk for low educational attainment.

Figure 6*. Education polygenic score association with neighborhood mobility in the Add Health Study.



The figure plots polygenic risk associations with adult neighborhood disadvantage at the Census tract level for Add Health Participants who grew up in low-, middle-, and high-disadvantage Census tracts. For the figure, low-, middle-, and high-disadvantage Census tracts were defined as the bottom quartile, middle 50%, and top quartiles of the childhood tract disadvantage score distribution. The individual graphs show binned scatterplots in which each plotted point reflects average X- and Y- coordinates for a "bin" of 50 Add Health participants. The regression lines are plotted from the raw data. The box-and-whisker plots at the bottom of the graphs show the distribution of polygenic risk for each childhood-neighborhood-disadvantage category. The blue diamond in the middle of the box shows the median; the box shows the interquartile range; and the whiskers show upper and lower bounds defined by the 25th percentile minus 1.5x the interquartile range and the 75th percentile plus 1.5x the interquartile range, respectively. The vertical line intersecting the X-axis shows the cohort average polygenic risk. The figure illustrates three findings. First, adult participants tended to live in Census tracts with similar levels of disadvantage to the ones where they grew up. Second, children's polygenic risks and their neighborhood disadvantage were correlated; the box plots show polygenic risk tended to be lower for participants who grew up in low-disadvantage tracts and higher for participants who grew up in high disadvantage tracts. Third, across strata of childhood neighborhood disadvantage, children at higher polygenic risk tended to move to more disadvantaged Census tracts no matter where they grew up.

* Figure 5 not shown. See online MS