Childhood Social Disadvantage, Cardiometabolic Risk, and Chronic Disease in Adulthood


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Adverse social environments in early life are hypothesized to become biologically embedded during the first few years of life, with potentially far-reaching implications for health across the life course. Using prospective data from a subset of a US birth cohort, the Collaborative Perinatal Project, started in 1959–1966 (n = 566), we examined associations of social disadvantage assessed in childhood with cardiometabolic function and chronic disease status more than 40 years later (in 2005–2007). Social disadvantage was measured with an index that combined information on adverse socioeconomic and family stability factors experienced between birth and age 7 years. Cardiometabolic risk (CMR) was assessed by combining information from 8 CMR biomarkers; an index of chronic disease status was derived by assessing 8 chronic diseases. Poisson models were used to investigate associations between social disadvantage and CMR or chronic disease scores while adjusting for childhood covariates and potential pathway variables. A high level of social disadvantage was significantly associated with both higher CMR (incident rate ratio = 1.69, 95% confidence interval: 1.19, 2.39) and with a higher number of chronic diseases (incident rate ratio = 1.39, 95% confidence interval: 1.00, 1.92) in minimally adjusted models. Associations with CMR persisted even after accounting for childhood and adult covariates.

biological markers; cardiometabolic risk; cohort studies; psychosocial factors; social disadvantage; social environment; socioeconomic status

Abbreviations: CMR, cardiometabolic risk; SES, socioeconomic status.
early adversity (16–20). Only a few studies have investigated a more comprehensive measure of childhood risk exposure in relation to health-related outcomes. One such study created an index that captured a range of prospectively assessed measures of poverty, residential crowding, noise, and exposure to violence (21), which was associated with poorer self-regulatory behaviors leading to weight gain in adolescence. In the most comprehensive study to date, the Dunedin Multidisciplinary Health and Development Study provided a prospective assessment of exposure to low SES, maltreatment, and social isolation in childhood, which revealed associations with depression, inflammation, and metabolic risk at age 32 years (22). They found that low SES and very high social isolation were associated with higher relative risks for developing high metabolic risk markers of 2.11 and 1.96, respectively, whereas childhood maltreatment had no significant association with the risk of developing high metabolic risk markers. These findings were particularly striking because they revealed that having multiple adverse exposures was associated with worse health outcomes, and that consequences of early social adversity may be evident even prior to manifest disease development (22).

Further work is needed to determine the consistency of associations across a range of biological systems, whether they continue to be evident in middle adulthood, and whether adverse exposures related to socioeconomic and family stability factors (which may be more prevalent and less severe than exposures previously considered) are also related to poorer health trajectories. The current study addresses these gaps by investigating whether a multidimensional measure of childhood social disadvantage is associated with cardiometabolic risk (CMR) and chronic disease status in adulthood. We used prospective data with more than 40 years of follow-up from a subset of participants from the New England Family Study. We hypothesized that exposure to greater social disadvantage in early childhood would lead to dysregulation across a range of cardiometabolic markers and would increase the risk of chronic disease. We also hypothesized that these associations may be due in part to other factors patterned by early experience including adult health behaviors, adult SES, and depression.

METHODS

Study cohort

Our study sample was drawn from the New England Family Study, an adult continuation of the Boston, Massachusetts, and Providence, Rhode Island, sites of the Collaborative Perinatal Project. This project is a longitudinal study originally designed to follow children born to pregnant women enrolled between 1959 and 1966 to identify neurodevelopmental consequences of pregnancy complications (23, 24). Detailed data on medical history and social environment were obtained from mothers at the time of enrollment and again at when their children were 7 years of age. Data on birth outcomes, growth, and childhood mental and physical disorders were obtained several times between birth and age 7 years. Institutional review board approvals were obtained from the Harvard School of Public Health (Boston, Massachusetts) and Brown University (Providence, Rhode Island).

For this study, we drew on the 618 participants of the EdHealth Study (25), an adult follow-up study of the New England Family Study conducted in 2005–2007 (Web Figure 1 available at http://aje.oxfordjournals.org/). EdHealth participants were drawn from a larger (n = 1,674) New England Family Study follow-up study (the Brown-Harvard Transdisciplinary Tobacco Use Research Center (26)), and were selected with preference for racial/ethnic minorities and those with low or high educational level as required by the aims of the project. These 618 subjects participated in a 3-hour in-person interview that included assessment of adult SES, psychological functioning, and physical health, at an average age of 42.5 years of age. Analyses considering chronic disease as the outcome were conducted with 566 participants who had complete data on chronic diseases and demographic characteristics and who were not missing data on more than 3 social disadvantage measures. For analyses of CMR, 42 of the original 618 subjects were excluded because they did not interview in person and, thus, did not complete physiological assessments. Of the remaining 576 participants, 430 agreed to participate in a clinical assessment in which a blood sample and anthropometric measurements were taken by trained study personnel. This sample was further restricted to 387 participants (90% of eligible individuals with a blood sample) in which successful measures were obtained across all tested biomarkers, and none was missing data on more than 3 social disadvantage variables. Those who provided a blood sample were significantly younger than those who did not, but they did not differ significantly by race/ethnicity, sex, or educational attainment (16). Those missing answers to more than 3 childhood adversity questions had significantly higher CMR scores and significantly higher incidence of chronic disease, and were thus included in sensitivity analyses (Web Appendix 1). The final analytical sample includes some siblings, who cluster into 312 families for CMR analyses and 436 families for chronic disease analyses.

Measures

Childhood social disadvantage. A childhood social disadvantage index was constructed by using 10 adverse family stability and socioeconomic exposures following methods used in prior research (21). The family stability exposures included living away from home for more than 3 months between birth and age 7 years, sibling death between birth and age 7 years, moving more than 3 times between birth and age 7 years, change in parental marital status (i.e., divorce, married, separated, widowed) between birth and age 7 years, and being raised by a single mother at age 7 years. The socioeconomic exposures included manual occupation of the main household wage earner at the subject’s birth and at age 7 years, having a father who was unemployed for more than 6 months in the past year when the subject was 7 years of age, crowded housing density (>1.5 people/room) at age 7 years, household income less than or equal to the poverty threshold at birth or age 7 years, and highest parental educational level of less than high school at the subject’s birth. All exposures were measured via questionnaires.
given to participants’ mothers when children were less than 1 year of age and again at age 7 years, and all were treated as binary variables (yes/no) according to whether they were present at the time specified. For each participant, the index was defined as the mean of (nonmissing) binary variables and categorized into the following 3 groups: least disadvantaged (mean $<0.2$, corresponding to 0–1 adverse exposures), moderately disadvantaged (0.2$\leq$ mean $<0.5$, corresponding to 2–4 adverse exposures), and most disadvantaged (mean $\geq0.5$, corresponding to $\geq5$ adverse exposures). Alternate grouping into tertiles showed similar results. The index was also used as a continuous measure (multiplied by 10 for interpretability).

To independently test the 2 exposure domains, we also divided into tertiles showed similar results. The index was also used as a continuous measure (multiplied by 10 for interpretability). 

Cardiometabolic risk score. Following the approach used in similar studies (27, 28), we constructed a CMR score from 8 biomarkers measured in adulthood. For each biomarker, a binary score was created by assigning a value of 1 if the biomarker exceeded clinically defined criteria for high risk of cardiometabolic disease, and 0 otherwise. The CMR score was defined as the sum of these binary scores. The biomarkers include the following: systolic and diastolic blood pressure (indicators of cardiovascular function); triglycerides, high- and low-density lipoprotein, hemoglobin A1c, and waist circumference (indicators of metabolic function); and C-reactive protein (indicator of inflammation). Criteria for high risk are listed in Table 1 as defined in prior studies for C-reactive protein (29), cholesterol (30), and all other measures (27). Any participant taking physician-prescribed medications for blood pressure, diabetes, or hypercholesterolemia (assessed via inspection of medication bottles by study staff) was classified as being at high risk for those indicators. Five individuals with C-reactive protein levels higher than 30 mg/L were removed, because these values indicate serious current infection (31, 32); 1 individual whose diastolic blood pressure exceeded systolic blood pressure was removed. Details on the measurement of each biomarker are provided in Web Appendix 2.

Chronic disease score. To capture a more clinically diagnostic measure of adult health, we also created a chronic disease score as a count of how many of 8 chronic diseases each individual reported ever having diagnosed by a doctor or health professional in adulthood. Chronic diseases included severe migraine in the past 3 months or ever having been diagnosed with heart disease, chronic obstructive pulmonary disease, cancer, nonpregnancy diabetes, hypertension, hypercholesterolemia, or arthritis. Participants who reported taking medications for diabetes, blood pressure, or cholesterol were classified as being diagnosed with the relevant disease. This chronic disease score partially overlaps with the CMR score; however, they are separable and distinct indicators. For example, among individuals in the highest quartile of CMR, 11% did not report any chronic disease, whereas among those with the lowest CMR value (i.e., 0), 47% reported at least 1 chronic disease.

Covariates. We considered covariates according to whether they reflected factors from adulthood or childhood, or whether they were potential pathway variables. The adult covariates included age (mean centered) at adult follow-up; sex; self-identified race (white or other); and study site (Boston or Providence). Childhood covariates included small for gestational age; intelligence quotient at age 7 years (based on the Wechsler Intelligence Scale for Children (33)); and child chronic diseases (any or none). Child chronic disease was a summary measure indicating whether the child experienced 1 or more chronic physical health conditions from birth to age 7 years as identified by a study pediatrician or maternal report (34). Childhood chronic disease and small for gestational age, which are often correlated with childhood intelligence quotient, may be confounders, because these factors can reduce a parent’s ability to maintain employment and can also lead to worse health in adulthood (35).

Potential pathway variables were assessed using adult questionnaires. Smoking was measured in pack-years. Consumption of fried foods outside the home (in days/week consumed) was extracted from a 25-item food frequency questionnaire designed to detect Western dietary patterns. Several other dietary factors were also considered in analyses, including fruit/vegetable and alcohol consumption, but were not included in final models because of lack of association with any outcomes. Physical activity was assessed from a single question about vigorous exercise (in minutes) in a usual week; moderate exercise was also considered but not included in final analyses. Years of self-reported educational attainment (range, 0–21) were used as a measure of adult SES. Depression was measured via lifetime diagnosis of a major depressive episode, derived from a questionnaire that used the Diagnostic and Statistical Manual of Mental Disorders IV criteria. The number of participants reporting a major depressive episode in our study is relatively high compared with the national average, perhaps because the sample included more women and was somewhat enriched for individuals with less education.

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<td><strong>Biomarker</strong></td>
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<td>Diastolic</td>
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<td>Triglycerides*, mg/dL</td>
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<td>Low-density lipoprotein, mg/dL</td>
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<td>Hemoglobin A1c, %</td>
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<td>C-reactive protein, mg/L</td>
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<td>Waist circumference, cm</td>
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* Participants taking medication for high blood pressure, diabetes, or hypercholesterolemia were also classified as at high risk for the associated biomarkers.

* Criteria for triglycerides and high-density lipoprotein are drawn from National Cholesterol Education Program (30), criteria for C-reactive protein are from the work of Ridker (29), and criteria for the remaining biomarkers are drawn from the work of King et al. (27).
Statistical analyses

For both CMR and chronic disease scores, we fit Poisson mixed models with random effects for family. These models allow for easily interpretable estimates of the multiplicative effect of each predictor on a mean count score and are consistent with other work using similar outcomes (27). These models also allow for overdispersion and assume that within-family observations (i.e., siblings) are correlated (36). We note that Poisson models are only approximate because they allow for predicted values outside the possible ranges; however, this proved to be a minimal concern in our analysis. Substantive findings did not differ (though associations were even stronger) when linear regressions were considered.

For each outcome, the following 4 primary models were fit: unadjusted, minimally adjusted, fully adjusted, and a pathway model. The minimally adjusted model includes adult covariates; the fully adjusted model adds childhood covariates to the second model; and the pathway model adds adult pathway variables to the fully adjusted model. Formal mediation analyses were not undertaken given that pathway variables were measured concurrently with the health outcomes; rather, we examined how the regression coefficient for social disadvantage changed when it was the sole predictor versus when potential pathway variables were added to the model. In all primary models, social disadvantage was treated as a 3-level categorical variable. Other models using social disadvantage as a continuous measure were considered, and substantive findings were similar. See Web Appendix 1 for the continuous model and other sensitivity analyses.

All analyses were conducted in SAS, version 9.3, software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Sample characteristics

At adult follow-up, the mean age of subjects was 42.5 years (range, 38–48); 60% of participants were women, and 78% were white. Childhood social disadvantage ranged within the sample, whereby 9.0% had high (≥5 factors),
36.4% had moderate (2–4 factors), and 54.6% had low (≤1 factor) levels of social disadvantage. Frequencies of individual social disadvantage factors are shown in Web Table 1. Distributions of all covariates across the 3 social disadvantage levels are shown in Table 2. Those in the most versus the least socially disadvantaged group were significantly more likely to be nonwhite and to have had lower childhood intelligence quotients. As adults, they were more likely to have achieved fewer years of education and to engage in fewer healthy behaviors. Sample means for the CMR and chronic disease scores were 1.80 (range, 0–8) and 1.3 (range, 0–7), respectively; sample frequencies of each chronic disease and the chronic disease score can be found in Web Table 2.

Childhood social disadvantage and CMR

In the unadjusted model, children with the highest level of social disadvantage were estimated to have 1.61 (95% confidence interval: 1.13, 1.55) times the expected number of cardiometabolic risk factors as children with the lowest level of social disadvantage. In the model adjusted for adult covariates, the estimate increased to 1.69 (95% confidence interval: 1.19, 2.39) (Table 3). The association of social disadvantage with CMR appears to be graded, whereby medium levels of disadvantage were associated with somewhat higher CMR scores, and high disadvantage was associated with the highest CMR scores. This trend was supported by models using a continuous measure of disadvantage (Web Appendix 2). Associations were slightly higher with the addition of childhood covariates. Adding all pathway variables to the model with all childhood covariates.

<table>
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<tr>
<th>Table 4. Poisson Mixed Model for Social Disadvantage and Adult Chronic Disease Within the EdHealth Study (n = 566), Baseline in 1959–1966, Follow-up in 2005–2007, Boston, Massachusetts, and Providence, Rhode Island</th>
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<td>Covariate</td>
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<td>Social disadvantage</td>
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<td>Childhood Covariates</td>
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<td>Chronic disease</td>
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<td>Childhood IQ</td>
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<td>Pathways</td>
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<td>Education, years</td>
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<td>Major depressive episode</td>
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<td>Vigorous exercise</td>
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<td>Fried food consumption</td>
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<td>Smoking (pack-years)</td>
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Abbreviations: CI, confidence interval; IQ, intelligence quotient; IRR, incident rate ratio.

* P < 0.05; **P < 0.01.
* The unadjusted model and all subsequent models are adjusted for random effect of family; this model contains 436 family clusters.
* The minimally adjusted model is adjusted for social disadvantage, as well as adult covariates of age, race, sex, and study site; this model contains 436 family clusters.
* The fully adjusted model additionally adjusts for childhood covariates; this model contains 430 family clusters.
* The pathway model additionally adjusts for adult potential pathways, such as education, depression, and adult health behaviors (i.e., smoking, diet, exercise); this model contains 417 family clusters.
* The IRR indicates the multiplicative effect of the predictor on the number of cardiometabolic risk factors in adulthood.
* In models where childhood IQ was standardized, results were nearly identical.
* Vigorous exercise includes activities done for at least 10 minutes at a time that can cause large increases in breathing or heart rate.
adult and child covariates slightly increased the estimate for high social disadvantage relative to the fully adjusted model (Table 3). None of the pathway variables was significantly associated with CMR. In analyses considering the 2 components of the social disadvantage score separately, family stability, but not childhood SES, was significantly associated with CMR (Web Table 3).

**Childhood social disadvantage and chronic disease**

Children with the highest social disadvantage had 1.42 times the expected number of chronic diseases in unadjusted models (Table 4) relative to children with the lowest level of social disadvantage. After we controlled for adult covariates, this estimate was relatively unchanged, and it remained significant after additional adjustment for childhood covariates (Table 4). A graded trend was again evident, such that the highest level of disadvantage was most strongly associated with the outcome, with a moderate association evident for intermediate levels of disadvantage. When all pathway variables were added, only depression maintained a significant association with elevated chronic disease scores, and the estimate for high social disadvantage was attenuated to non-significance. When we considered the component indices, both family stability and childhood SES were significantly associated with chronic disease (Web Table 4). Additional sensitivity analyses examining alternative models of disadvantage, including associations with individual biomarkers and chronic diseases, are described in Web Appendix 2.

**DISCUSSION**

The results of this prospective study suggest that children who experience high levels of childhood social disadvantage are more likely to have cardiometabolic dysregulation across multiple biological systems and also to be diagnosed with a higher number of chronic diseases more than 4 decades later. Because these cardiometabolic changes are already detectable in midadulthood, we anticipate these associations may grow stronger over time as individuals begin to exhibit more age-related diseases. In fact, even at midadulthood, we found associations with a greater number of chronic diseases for those exposed to high levels of childhood social disadvantage.

Although our study is 1 of the first to test for associations between prospective and nuanced measures of childhood SES and family stability with CMR and chronic disease, our results are largely consistent with those of prior studies (7, 17, 37, 38). Our findings are similar to those reported in the longitudinal Dunedin Multidisciplinary Health and Development Study, in which exposure to low SES or childhood isolation was found to elevate risk for clustering of metabolic risk factors (22, 39). It is notable that, even with a measure of social disadvantage that may capture less severe aspects of the early social environment than maltreatment per se, we found a similar magnitude of risk associated with both CMR and chronic disease as that found in the Dunedin Multidisciplinary Health and Development Study.

Our measure of social disadvantage uniquely extends beyond standard proxies of SES to incorporate multiple measures of family-level SES, as well as aspects of family stability. In the current sample, the measure of family stability alone accounted for more variation in CMR and chronic disease than the childhood SES measures. Whether this is because implicit SES is better captured by family stability measures but not vice versa, or because of the particularly damaging nature of these factors, remains to be determined. These findings suggest that stability in the family environment is critical to setting children on a healthy trajectory early in life; further identifying key processes behind these associations may help inform more targeted prevention efforts.

Our use of an additive index to capture multiple risk factors of social disadvantage provided a more accurate representation of the early social environment and may better represent the ecology of risk than analyses of each individual factor (40). We also obtained more precise estimates (with narrower confidence intervals) for the cumulative health indices than for nearly all of the individual health-related biomarkers (Web Table 4), consistent with findings from other studies that have summarized across multiple biological risk factors to provide insight into systemic imbalance (41, 42).

We also note that the association between disadvantage and chronic disease was partly attenuated by depression. These findings suggest that a poor early social environment may lead to worse mental health, which in turn may produce worse health outcomes in adulthood. However, because depression was measured concurrently with adult health outcomes, we cannot conclusively determine the causal pathways (e.g., poor cardiometabolic health could have led to depression). It is worth noting that a high level of social disadvantage remained significantly associated with cardiometabolic health even after accounting for these adult pathways, suggesting a role for other unmeasured factors, or a potentially direct biological pathway independent of lifestyle variables. Although the biological mechanisms linking stress and CMR are yet unknown, it is possible that chronic activation of the sympathetic nervous system can lead to hemodynamic changes, such as increased blood pressure (43). Additionally, epigenetic changes may occur in genes that affect CMR, such as angiotensinogen or glucocorticoid receptors (44).

Several limitations should be noted. Our analyses focused on measures of social disadvantage related to common adversities such as childhood SES and family stability, but we recognize that other unmeasured adverse experiences likely contribute to adult health outcomes (22). That said, absence of other more traumatic adverse experiences, such as child abuse, could have led to an underestimate of the relationship between social disadvantage and cardiometabolic health, because a more comprehensive measure of social disadvantage, including more severe experiences, may reveal stronger associations with health outcomes. The inclusion of more information on adversities and child health measures, as well as a larger sample size, may have added greater precision to our findings. Accuracy of chronic disease outcomes and medication use may be limited by self-reporting and may be potentially misclassified because of variation in access to medical care. However, the highest reports of all of these variables were found in the most disadvantaged group (data not shown), despite potentially lower access to medical care. The stronger association we found with CMR relative to chronic diseases

may indicate a reduced risk of misclassification with this more objective measure. Finally, generalizability was potentially limited to participants born in urban centers in New England.

Strengths of our study include prospective measures of childhood disadvantage that avoid recall bias and allow detailed assessment of the early social environment in a well-characterized sample with a substantial period of follow-up. Additionally, our biomarker measures are not subject to reporting bias, providing more objective insight into whether biological processes are related to childhood social disadvantage. In conclusion, our study builds upon an emerging literature in which adverse early social experiences become biologically embedded to influence lifetime health. These findings can be leveraged toward changing public health policy, interventions, and clinical practice by shifting focus from individual health behaviors in adulthood to increased efforts to develop policies and interventions to reduce stressors in early childhood. In particular, as we find family stability measures to matter even more than childhood SES, future interventions and public health programs may want to broaden their reach to include children with shifting environments, in addition to the traditional focus on children in poverty.

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