Socioeconomic and Other Social Stressors and Biomarkers of Cardiometabolic Risk in Youth: A Systematic Review of Less Studied Risk Factors

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Abstract

**Background:** Socioeconomic disadvantage and other social stressors in childhood have been linked with cardiometabolic diseases in adulthood; however the mechanisms underlying these observed associations and the timing of their emergence are unclear. The aim of this review was to evaluate research that examined relationships between socioeconomic disadvantage and other social stressors in relation to less-studied cardiometabolic risk factors among youth, including carbohydrate metabolism-related factors, lipids, and central adiposity.

**Methods:** We searched PubMed and ISI Web of Science to identify relevant publications between 2001 and 2013. Studies were selected based on 4 criteria: (1) the study examined an association between at least one social or economic stressor and one relevant outcome prior to age 21; (2) the sample originated from a high-income country; (3) the sample was not selected based on a health condition; and (4) a central aim was to evaluate the effect of the social or economic stressor on at least one relevant outcome. Abstracts were screened and relevant publications were obtained and evaluated for inclusion criteria. We abstracted data from selected articles, summarized them by exposures and outcomes, and assigned an evidence grade.

**Results:** Our search identified 37 publications from 31 studies. Socioeconomic disadvantage was consistently associated with greater central adiposity. Research to date does not provide clear evidence of an association between childhood stressors and lipids or carbohydrate metabolism-related factors.

**Conclusions:** This review demonstrates a paucity of research on the relationship of socioeconomic disadvantage and other social stressors to lipid and carbohydrate metabolism-related factors in youth. Accordingly, it is not possible to form strong conclusions, particularly with regard to stressors other than socioeconomic disadvantage. Findings are used to inform priorities for future research. An improved understanding of these pathways is critical for identifying novel prevention targets and intervention opportunities to protect the long-term health of children and adolescents.


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Introduction

Cardiometabolic diseases are a leading cause of morbidity and mortality in the United States and the prevention of future cardiometabolic diseases is among the most significant public health challenges faced by contemporary society [1]. Several recent national policy statements point to childhood as a critical period for preventing cardiometabolic risk over the life course [2,3]. For example, a statement from the American Heart Association highlights emerging evidence that cardiometabolic physiological dysregulation begins in childhood [4,5] and that risk factor control in children is crucial [2]. A recent statement by the American Academy of Pediatrics (AAP) further identified the importance of the early social environment in setting up risk (or resilience) trajectories, and encouraged pediatric providers to assess family or community-level risk factors that may put children at risk for experiencing toxic social stress [3]. While there is increasing urgency to identify and address determinants of early biological risk factors for adult chronic diseases, our understanding of whether and how social adversity influences cardiometabolic risk factors that emerge early in life remains somewhat limited. Research in developmental biology has made a compelling case that early exposure to social disadvantage and toxic stress has lifelong consequences for health by virtue of biologically embed-
cardiovascular disease (CVD) [8–11]. Research suggests that such exposures may play a role in early risk of chronic disease later in life, including Type 2 diabetes and insulin resistance; (2) common lipid outcomes known to be associated with cardiometabolic risk, including total cholesterol, triglycerides, apolipoproteins A and B; and (3) central adiposity among children. A meta-analysis of the relevant literature was not possible at this time due to the heterogeneity of studies with regard to exposure and outcome measures, study design, covariates, and samples.

Methods

Inclusion Criteria

We applied four inclusion criteria, informed by previous systematic reviews. First, we required that the sample originated from a high-income country, according to the World Bank (Gross National Income per capita > US$12,480 in 2011); this criteria was established because the relationship between stressors and cardiometabolic outcomes may differ in poorer countries [13]. Second, we required that the sample was not selected based on a health condition, because our primary interest was to examine these associations in healthy children and adolescents. Third, studies were required to examine an association between at least one social or economic stressor and one relevant outcome (described below) prior to age 21. We defined childhood broadly in order to include as many studies as possible. Finally, we required that evaluating the effect of the social or economic stressor on the outcomes was central to the analysis (i.e., not simply included as a covariate to adjust for confounding).

Cardiometabolic Outcome Measures

We considered three categories of cardiometabolic indicators: (1) carbohydrate metabolism-related biomarkers, including acute and integrated markers of diabetes risk (e.g., glucose, HbA1c, insulin resistance); (2) common lipid outcomes known to be associated with cardiometabolic risk, including total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), cholesterol, triglycerides, apolipoproteins A and B; and (3) central
adiposity (e.g., waist circumference (WC), waist-hip ratio (WHR), waist standard deviation). We did not include metabolic syndrome, because it lacks consensus on definition and are not uniformly accepted as valid within pediatric and adolescent populations [29].

Socioeconomic and Other Social Stressors

In the absence of an explicit operational definition of social and economic stressors for child development research, we relied on a definition of “social context” articulated by Boyce and colleagues [30], which defines social context as “a set of interpersonal conditions, relevant to a particular behavior or disorder external to, but shaped and interpreted by, the individual child” (p. 146). In line with this broad definition, our review sought to include studies that have considered measures of contextual and material hardships, relative disadvantage, family SES, stressful experiences, and relationship stressors (i.e., with parents or peers).

Search Strategy and Data Extraction

We conducted systematic searches of PubMed and ISI Web of Science (including Science Citation Index Expanded, Social Sciences Citation Index, and Arts and Humanities Citation Index) to identify relevant studies published in English between January 2001 and January 2013. Our PubMed search was guided by Medical Subject Heading terms and keywords, including but not limited to: body fat distribution, waist-hip ratio, blood glucose, lipids/blood, insulin resistance, socioeconomic factors, social environment and interpersonal relations (see Appendix S1); this search returned 1304 abstracts. A similar strategy was developed for ISI Web of Science, and this search returned 773 abstracts. After we removed duplicate abstracts (n = 351), we screened each abstract according to the four criteria outline above. Of note, we carefully examined studies that focused on composite outcomes (e.g., allostatic load, metabolic syndrome, insulin resistance syndrome) in order to establish whether the study reported associations for component factors as well; if so, the study was eligible for inclusion. After applying our criteria, the PubMed and ISI Web of Science searches yielded 36 relevant studies, and one additional study was identified within a reference section of an identified article (see Figure S1). We reviewed these 37 studies and extracted information related to design, sample, measures, statistical methods, stratification and control variables, and findings. The reported findings are based on models adjusted for standard covariates, including age, sex, and race/ethnicity, when provided, and when effect modification was considered, we include that information.

Evidence Grade

We assessed the strength of the evidence by rating four components of each study’s methodology, including study design, sample size, covariates, and exposure measures. For study design, we awarded one point for longitudinal or prospective designs (i.e., repeated measures on the same individual, or following an individual over time with a time lag between the exposure and outcome). For sample size, we awarded one point to studies that had an n greater than 500 [31]. For covariates, we awarded one point to studies that provided results adjusted for at least basic demographics including age and sex. Finally, if a study examined more than one exposure measure (e.g., SES measured using both parental income and education), we awarded one point, as this provided more information about the consistency and generalizability of associations. Studies that received at least three points were identified as “high quality” for the purpose of this review.

Results

Tables 1 and 2 summarize the 37 publications (originating from 31 samples), organized by outcomes. Most studies (32 of 37) examined at least one SES exposure. Table 1 presents studies with SES-related exposures, and Table 2 presents studies with non-SES exposures (“other social stressors”), which may or may not be influenced by SES.

Socioeconomic Status-Related Exposures and Cardiometabolic Risk Markers

Carbohydrate Metabolism-related Outcomes. Table 1 provides a summary of the eight cross-sectional and three prospective studies of SES and carbohydrate metabolism-related outcomes, including insulin, glucose, HbA1c, insulin sensitivity, acute insulin response to glucose, and insulin resistance. Six of the eleven studies evaluated more than one relevant outcome, and the most common SES measure used was parental education. All eleven studies reported findings adjusted for basic covariates (i.e., at a minimum, age and sex). Overall, the findings lack consistency. Of the eleven studies, three were null [32–34], one study found an association in the expected direction (only one exposure and one relevant outcome considered) [35], two studies had conditional findings (whereby the direction of associations varied by country [36] and race [37]) and six studies had mixed findings (three resulted from different associations of the same measure of SES with two different outcome measures, and the other three resulted from discrepant findings with different measures of SES and the same outcomes). When we consider the 3 prospective studies on their own [35,38,39], the findings are more consistent (i.e., none of these studies had null findings) and provide some evidence for an association between socioeconomic disadvantage and elevated risk. Four of the eleven studies that examined carbohydrate metabolism-related factors were classified as higher-quality based on our evidence rating [35,36,38,40], and each provided some positive evidence for an association.

Lipid Outcomes. Fourteen studies examined SES in relation to lipid outcomes (i.e., total cholesterol, LDL and HDL cholesterol, triglycerides, apolipoproteins A and B); twelve of these studies were cross-sectional and two studies were prospective [41,42]. Most studies considered a single SES exposure, however the majority evaluated more than one lipid outcome. All fourteen studies reported results adjusted for basic covariates (i.e., at a minimum, age and sex). These studies do not indicate a consistent association between SES and lipid outcomes among youth. Of the fourteen studies, seven were null for all associations that were examined [32,34,40,41,43–45], and two showed associations in the direction opposite to the expected direction [42,46]. Considering the other five studies, four had high mixed results due to differences in the association of SES with multiple lipid outcomes [37,47–49]; one had mixed results due to discrepant findings resulting from different measures of SES [50], and in one of these studies, the mixed results also varied by race [37]. Of note, there were not observable patterns across the studies that produced mixed results. Five of the fourteen studies that examined SES in relation to lipid outcomes were rated as higher quality [34,41,42,44,50], and four of these studies had null results.

Central Adiposity. Our search identified twelve cross-sectional and five prospective studies which examined SES with central adiposity (measured by WC, WHR, waist standard deviation, and trunk fat (kg)). The majority of these studies incorporated only one measure of SES, and parental education was the most common measure. Sixteen of the seventeen studies reported associations from models adjusted for basic covariates...
### Table 1. Studies examining socioeconomic status and cardiometabolic biomarkers in youth, January 2001 through January 2013.

<table>
<thead>
<tr>
<th>Carbohydrate Metabolism</th>
<th>Country; Study name if &gt; 1 article</th>
<th>Design, n</th>
<th>Ages *</th>
<th>Stressor **</th>
<th>Outcomes</th>
<th>Findings *</th>
<th>Expected direction?</th>
<th>Evidence Grade</th>
<th>Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchan et al., 2012</td>
<td>Scotland</td>
<td>Cross-sectional, n = 107</td>
<td>16.4 (± 0.7)</td>
<td>Free school meal eligibility; Scottish Index of Multiple Deprivation</td>
<td>Insulin; glucose</td>
<td>Among boys, lower SES was associated with higher glucose. Among girls, lower SES was associated with higher glucose and lower insulin.</td>
<td>Mixed, based on outcome; conditional, by sex</td>
<td>+</td>
<td></td>
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<tr>
<td>Goodman et al., 2005</td>
<td>U.S.A; Princeton School District Study</td>
<td>Cross-sectional, n = 758</td>
<td>13–19</td>
<td>Highest parental education</td>
<td>Insulin; glucose; HbA1c; insulin resistance</td>
<td>Lower education associated with higher insulin, higher glucose, and greater insulin resistance.</td>
<td>Mixed, based on outcomes</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Goodman et al., 2007</td>
<td>U.S.A; Princeton School District Study</td>
<td>Longitudinal, n = 1167</td>
<td>13–19</td>
<td>Highest parental education; income</td>
<td>Insulin resistance</td>
<td>Lower education associated with baseline insulin resistance, and worsening insulin resistance over time; effect especially strong for obese youth.</td>
<td>Mixed, based on exposures</td>
<td>++++</td>
<td></td>
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<tr>
<td>Goodman et al., 2010</td>
<td>U.S.A; Princeton School District Study</td>
<td>Longitudinal, n = 1222</td>
<td>13–19</td>
<td>Highest parental education</td>
<td>Insulin</td>
<td>Education associated with higher insulin at follow-up, adjusting for baseline.</td>
<td>Yes</td>
<td>+++</td>
<td></td>
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<tr>
<td>Gower et al., 2003</td>
<td>U.S.A</td>
<td>Longitudinal, n = 125</td>
<td>5–16</td>
<td>Hollingshead index</td>
<td>Insulin; insulin sensitivity; acute insulin response to glucose</td>
<td>SES associated with acute insulin response to glucose.</td>
<td>Mixed, based on outcomes</td>
<td>++</td>
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<tr>
<td>Lawlor et al., 2005</td>
<td>Denmark, Estonia, Portugal</td>
<td>Cross-sectional, n = 3189</td>
<td>9–15</td>
<td>Maternal and paternal education; income</td>
<td>Insulin resistance</td>
<td>Varied by country: Danish children from poorer and less educated families had greater insulin resistance; in Estonia and Portugal, children from poorer and less educated parents had lower insulin resistance.</td>
<td>Conditional, by country</td>
<td>+++</td>
<td></td>
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<tr>
<td>Thomas et al., 2012</td>
<td>England</td>
<td>Cross-sectional, n = 4804</td>
<td>9–11</td>
<td>Highest parental occupation</td>
<td>HbA1c; glucose; insulin resistance</td>
<td>In White students, lower occupation was associated with greater insulin resistance; in Black students, lower occupation was associated with lower insulin resistance (no associations for South Asians).</td>
<td>Conditional, by race; and, mixed based on outcome</td>
<td>++</td>
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<tr>
<td>van den Berg et al, 2012</td>
<td>The Netherlands</td>
<td>Cross-sectional, n = 1308</td>
<td>5–6</td>
<td>Maternal education; self-report income adequacy</td>
<td>Glucose; insulin resistance</td>
<td>Low maternal education was associated with higher glucose and insulin resistance.</td>
<td>Mixed, based on exposure</td>
<td>+++</td>
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<tr>
<td>Wennlof et al., 2005</td>
<td>Sweden</td>
<td>Cross-sectional, n = 969</td>
<td>9–15</td>
<td>Maternal education</td>
<td>Insulin; glucose</td>
<td>Null.</td>
<td>No</td>
<td>++</td>
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<td>Lipids</td>
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<td>Alberty et al., 2009</td>
<td>Slovakia</td>
<td>Cross-sectional, n = 788</td>
<td>7–17</td>
<td>Income</td>
<td>Fasting TC minus HDL</td>
<td>Greater household income positively associated with greater non-HDL cholesterol.</td>
<td>No</td>
<td>++</td>
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<tr>
<td>Country; Study name if &gt; 1 article</td>
<td>Design, n</td>
<td>Ages a</td>
<td>Stressor b</td>
<td>Outcomes</td>
<td>Findings c</td>
<td>Expected direction?</td>
<td>Evidence Grade d</td>
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<tr>
<td>Buchan et al., 2012 Scotland</td>
<td>Cross-sectional, n = 107</td>
<td>16.4 (± 0.7)</td>
<td>Free school meal eligibility; Scottish Index of Multiple Deprivation</td>
<td>Fasting HDL; LDL</td>
<td>Null.</td>
<td>No</td>
<td>+</td>
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<tr>
<td>Goodman et al., 2005 U.S.A; Princeton School District Study</td>
<td>Cross-sectional, n = 758</td>
<td>13–19</td>
<td>Highest parental education</td>
<td>Fasting HDL; LDL; TG</td>
<td>Lower education associated with higher LDL and lower HDL.</td>
<td>Mixed, based on outcome</td>
<td>++</td>
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<tr>
<td>Howe et al., 2010 England; ALSPAC</td>
<td>Cross-sectional, n = 7772</td>
<td>10</td>
<td>Maternal education</td>
<td>Non-fasting TC; HDL; TG; apolipoproteins A and B</td>
<td>Education was associated with apolipoprotein B.</td>
<td>Mixed, based on outcome</td>
<td>++</td>
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<tr>
<td>Kant et al., 2012 USA; NHANES 2003–2006</td>
<td>Cross-sectional, n = 2700</td>
<td>2–19</td>
<td>Poverty-income ratio; education of head of household</td>
<td>Fasting TC; HDL; LDL; TG</td>
<td>Null.</td>
<td>No</td>
<td>+++</td>
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<tr>
<td>Khanolkhar et al., 2012 Sweden</td>
<td>Cross-sectional, n = 1204</td>
<td>5–14</td>
<td>Maternal and paternal education; maternal and paternal occupational class</td>
<td>TC; ratio of apolipoproteins A and B (fasting status not specified)</td>
<td>Few inconsistent associations were observed for both TC and ratio of apolipoproteins A and B for both maternal and paternal occupational class.</td>
<td>Mixed, based on exposure</td>
<td>+++</td>
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<tr>
<td>Kvaavik et al., 2012 Norway</td>
<td>Prospective, n = 498</td>
<td>11–15</td>
<td>Maternal and paternal education</td>
<td>TC; TG (fasting for some participants)</td>
<td>Null.</td>
<td>No</td>
<td>+++</td>
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<tr>
<td>McGrindle et al., 2010 Canada</td>
<td>Cross-sectional, n = 20719</td>
<td>14–15</td>
<td>School district income</td>
<td>Non-fasting TC</td>
<td>Null.</td>
<td>No</td>
<td>++</td>
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<tr>
<td>Murasko, 2008 U.S.A.; NHANES 1999–2004</td>
<td>Cross-sectional, n = 4788 (HDL), n = 2137 (LDL)</td>
<td>12–17</td>
<td>Income</td>
<td>HDL; LDL (fasting for some participants)</td>
<td>Greater household income associated with reduced probability of low HDL, and association more pronounced for females.</td>
<td>Mixed, based on outcome</td>
<td>++</td>
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<tr>
<td>Thomas et al., 2012 England</td>
<td>Cross-sectional, n = 4804</td>
<td>9–11</td>
<td>Highest parental occupation</td>
<td>Fasting TG; HDL</td>
<td>In White students, lower SES was associated with higher TG; in Black students, lower SES was associated with lower TG.</td>
<td>Conditional, by race; mixed, based on exposure</td>
<td>++</td>
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<tr>
<td>van den Berg et al., 2012 The Netherlands</td>
<td>Cross-sectional, n = 1308</td>
<td>5–6</td>
<td>Maternal education; self-report income adequacy</td>
<td>Fasting TC; HDL; TG</td>
<td>Null.</td>
<td>No</td>
<td>+++</td>
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<tr>
<td>Van Lente et al., 2001 Ireland</td>
<td>Prospective, n = 509</td>
<td>12</td>
<td>Occupation</td>
<td>Non fasting TC; HDL; TC/HDL</td>
<td>Among boys at age 15 (but not girls), HDL was greater among youth with parents that had manual occupations, and TC/HDL was lower in this group.</td>
<td>No</td>
<td>+++</td>
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<tr>
<td>Wennlof et al., 2005 Sweden</td>
<td>Cross-sectional, n = 969</td>
<td>9–15</td>
<td>Maternal education</td>
<td>Fasting TC; HDL; TG</td>
<td>Null.</td>
<td>No</td>
<td>++</td>
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<td><strong>Central Adiposity</strong></td>
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<tr>
<td>Ali et al., 2011 USA; NHANES 1998–2008</td>
<td>Cross-sectional, n = 16,085</td>
<td>6–24</td>
<td>Poverty-income ratio</td>
<td>Waist-to-height ratio &gt; 0.5</td>
<td>Among boys ages 6–11 and girls ages 12–17, lower poverty-income ratio was associated with higher prevalence of central obesity.</td>
<td>Conditional, by sex and age</td>
<td>++</td>
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<tr>
<td>Country; Study name if &gt; 1 article</td>
<td>Design, n</td>
<td>Ages</td>
<td>Stressor</td>
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<td>Findings</td>
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<tr>
<td>Bjelland et al., 2010 Norway</td>
<td>Cross-sectional, n = 1483</td>
<td>11</td>
<td>Highest parental education</td>
<td>WC; WHR</td>
<td>Lower education associated with higher WC and WHR.</td>
<td>Yes</td>
<td>++</td>
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<tr>
<td>Brown et al., 2012 U.S.A.</td>
<td>Cross-sectional, n = 123</td>
<td>5.6 (kindergarten) and 8.7 (3rd grade)</td>
<td>Maternal and paternal education</td>
<td>WC; WHR</td>
<td>Among 3rd grade girls, lower paternal education was associated with higher WC and WHR.</td>
<td>Conditional, by sex; mixed, based on exposure</td>
<td>++</td>
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<tr>
<td>Brug et al., 2012 Belgium, Greece, Hungary, Nether-lands, Norway, Slovenia, Spain</td>
<td>Cross-sectional, n = 7234</td>
<td>10–12</td>
<td>Highest parental education</td>
<td>WC</td>
<td>Across countries, lower parental education was associated with higher WC.</td>
<td>Yes</td>
<td>+</td>
<td></td>
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</tr>
<tr>
<td>Buchan et al., 2012 Scotland</td>
<td>Cross-sectional, n = 107</td>
<td>16.4 (± 0.7)</td>
<td>Free school meal eligibility; Scottish Index of Multiple Deprivation</td>
<td>WC</td>
<td>Null.</td>
<td>No</td>
<td>+</td>
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<tr>
<td>Goodman et al., 2005 U.S.A.; Princeton School District Study</td>
<td>Cross-sectional, n = 758</td>
<td>13–19</td>
<td>Highest parental education; income</td>
<td>WC</td>
<td>Lower education associated with higher WC.</td>
<td>Mixed, based on exposure</td>
<td>+++</td>
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<tr>
<td>Jimenez-Pavon et al., 2010 Spain</td>
<td>Cross-sectional, n = 1795</td>
<td>12.5–18.5</td>
<td>Maternal and paternal education; occupation</td>
<td>WC</td>
<td>Higher education was associated with lower WC in boys but not girls; no association for profession status.</td>
<td>Conditional, by sex; mixed, based on exposure</td>
<td>+++</td>
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<tr>
<td>Kendzor et al., 2012 U.S.A.</td>
<td>Prospective, n = 1356</td>
<td>15</td>
<td>Household income trajectory from birth to 15</td>
<td>WC</td>
<td>Downward income trajectory and stable low income from birth to age 15 were associated with greater WC.</td>
<td>Yes</td>
<td>+++</td>
<td></td>
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<tr>
<td>Kosziel &amp; Jankowska, 2002 Poland</td>
<td>Cross-sectional, n = 2016</td>
<td>14</td>
<td>Maternal education</td>
<td>WHR</td>
<td>Lower education associated with higher WHR among girls (not boys).</td>
<td>Conditional</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moore et al., 2002 U.S.A.</td>
<td>Longitudinal, n = 235</td>
<td>8.8 (±2)</td>
<td>Hollingshead index</td>
<td>WC; WHR</td>
<td>Lower SES associated with greater increase in WC over time.</td>
<td>Mixed, based on outcome</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ness et al., 2006 England; ALSPAC</td>
<td>Prospective, n = 5917</td>
<td>9.9 (± 0.33)</td>
<td>Lowest parental social class</td>
<td>Trunk fat (kg)</td>
<td>Null.</td>
<td>No</td>
<td>+++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ortega et al., 2012 Estonia, Sweden</td>
<td>Longitudinal, n = 949</td>
<td>9–15</td>
<td>Maternal education</td>
<td>WC</td>
<td>High maternal education was associated with decreased odds of remaining in the top quartile of WC over the 6 years follow-up.</td>
<td>Yes</td>
<td>+++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Okosun et al., 2006 U.S.A.</td>
<td>Cross-sectional, n = 5020</td>
<td>6–11</td>
<td>Highest parental education</td>
<td>WC</td>
<td>Lower education associated with higher probability of WC &gt;95th percentile.</td>
<td>Yes</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thomas et al., 2012 England</td>
<td>Cross-sectional, n = 4804</td>
<td>9–11</td>
<td>Highest parental occupation</td>
<td>WC</td>
<td>Among White students, lower SES was associated with greater WC.</td>
<td>Conditional, by race</td>
<td>++</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 1. Cont.

<table>
<thead>
<tr>
<th>Country; Study name if &gt;1 article</th>
<th>Design, n</th>
<th>Ages</th>
<th>Stressor</th>
<th>Outcomes</th>
<th>Findings</th>
<th>Expected direction?</th>
<th>Evidence Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbohydrate Metabolism</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wake et al., 2007</td>
<td>Cross-sectional, n=4938</td>
<td>4-5</td>
<td>Maternal education; occupation; income; area-level disadvantage</td>
<td>WC</td>
<td>Null.</td>
<td>No</td>
<td>+++</td>
</tr>
<tr>
<td>Wardle et al., 2006</td>
<td>Longitudinal, n=5863</td>
<td>11-12</td>
<td>Area-level deprivation</td>
<td>WC; waist standard deviation</td>
<td>Higher area-level socioeconomic deprivation associated with trajectory of WC and waist standard deviation.</td>
<td>Yes</td>
<td>+++</td>
</tr>
<tr>
<td>Yin et al., 2005</td>
<td>Cross-sectional, n=303</td>
<td>12-24</td>
<td>Community-level economic disadvantage</td>
<td>WC</td>
<td>Community disadvantage associated with higher WC.</td>
<td>Yes</td>
<td>++</td>
</tr>
</tbody>
</table>

*aAge at baseline outcome measurement; bRefers to parent SES status; cOnly significant findings are reported; describes adjusted model findings, if provided (e.g., control variables of age, sex, race/ethnicity). dThe strength of the evidence was evaluated based on four components of each study’s methodology, including study design, sample size, covariates, and exposure measures. LDL = Low density lipoprotein cholesterol; HDL = High density lipoprotein cholesterol; TG = Triglycerides; TC = Total cholesterol; Apo = Apolipoprotein; WC = Waist circumference; WHR = Waist-hip ratio; ALSPAC = Avon Longitudinal Study of Parents and Children.

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### Discussion

Given increasing understanding that a child’s early experiences has profound effects on risk for chronic diseases later in life [63] and the escalating societal burden of cardiometabolic [69] diseases in the United States, it is important to identify and intervene on social stressors and biomarkers of cardiometabolic risk in youth. Our search identified six studies that examined a possible relationship between social stressors and cardiometabolic risk factors in children and adolescents. These studies assessed associations between social stressors and measures of cardiometabolic risk, such as waist circumference, triglycerides, and total cholesterol (Table 1). A number of studies examined the relationships between social stressors and markers of cardiometabolic risk, with notable exceptions in the literature, including those that assessed the relationships between stressors and cardiometabolic risk factors in children and adolescents. A number of studies have shown that social stressors, such as maternal stress and depression, are associated with increased risk for cardiometabolic disorders in children and adolescents [64,65].

Our search identified six studies that examined a possible relationship between social stressors and cardiometabolic risk factors in children and adolescents. These studies assessed associations between social stressors and measures of cardiometabolic risk, such as waist circumference, triglycerides, and total cholesterol (Table 1). A number of studies examined the relationships between social stressors and markers of cardiometabolic risk, with notable exceptions in the literature, including those that assessed the relationships between stressors and cardiometabolic risk factors in children and adolescents. A number of studies have shown that social stressors, such as maternal stress and depression, are associated with increased risk for cardiometabolic disorders in children and adolescents [64,65].
Table 2. Studies examining social stressors and cardiometabolic biomarkers in youth, January 2001 through March 2012.

<table>
<thead>
<tr>
<th>Country</th>
<th>Design, n</th>
<th>Ages</th>
<th>Stressor</th>
<th>Outcomes</th>
<th>Findings</th>
<th>Expected direction?</th>
<th>Evidence Grade d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marin et al., 2007</td>
<td>Cross-sectional, n = 104</td>
<td>15–19</td>
<td>Stressful events; interpersonal stress</td>
<td>Insulin; glucose</td>
<td>Null.</td>
<td>No</td>
<td>+</td>
</tr>
<tr>
<td>Ravaja, N., et al. (2001).</td>
<td>Longitudinal, n = 451</td>
<td>9 years</td>
<td>Self-rated maternal child rearing</td>
<td>Insulin</td>
<td>Among girls (but not boys), mother's low tolerance towards the child predicted higher insulin.</td>
<td>Conditional, by sex</td>
<td>++</td>
</tr>
<tr>
<td>Buchmann et al., 2010</td>
<td>Prospective, n = 207</td>
<td>19</td>
<td>Rearing practices; maternal responsiveness</td>
<td>Fasting HDL; LDL; TG; TC; Apo A1, B C3, and E</td>
<td>Adverse rearing and poor responsiveness associated with lower HDL and apolipoprotein A1.</td>
<td>Mixed, by outcome</td>
<td>+++</td>
</tr>
<tr>
<td>Ravaja, N., et al. (2001).</td>
<td>Longitudinal, n = 451</td>
<td>9 years</td>
<td>Self-rated maternal child rearing</td>
<td>Fasting HDL; triglycerides</td>
<td>Among boys (but not girls), hostile maternal child-rearing attitudes predicted HDL. Among girls (but not boys), strict disciplinary style of the mother predicted higher TG.</td>
<td>Conditional, and mixed by outcome</td>
<td>++</td>
</tr>
<tr>
<td>Buchmann et al., 2001</td>
<td>Germany</td>
<td>Prospective, n = 207</td>
<td>19</td>
<td>Rearing practices; maternal responsiveness</td>
<td>WHR</td>
<td>Null.</td>
<td>No</td>
</tr>
<tr>
<td>Kim et al., 2008</td>
<td>Cross-sectional, n = 106</td>
<td>13–15</td>
<td>Maternal and paternal rearing practices</td>
<td>WC</td>
<td>Maternal authoritative style associated with smaller WC; maternal control associated with greater WC.</td>
<td>Mixed, by exposure.</td>
<td>++</td>
</tr>
<tr>
<td>Midei &amp; Matthews, 2009</td>
<td>Longitudinal, n = 213</td>
<td>14–16</td>
<td>Lack of supportive relationships</td>
<td>WHR</td>
<td>Fewer supportive relationships predicted increased WHR over time.</td>
<td>Yes</td>
<td>++</td>
</tr>
<tr>
<td>Yin et al., 2005</td>
<td>Cross-sectional, n = 303</td>
<td>12–24</td>
<td>Stressful events</td>
<td>WC</td>
<td>Stressful life events associated with higher WC.</td>
<td>Yes</td>
<td>++</td>
</tr>
</tbody>
</table>

*aAge at baseline outcome measurement; b Only significant findings are reported; describes adjusted model findings, if provided (e.g., control variables of age, sex, race/ethnicity). c The strength of the evidence was evaluated based on four components of each study's methodology, including study design, sample size, covariates, and exposure measures. LDL = Low density lipoprotein cholesterol; HDL = High density lipoprotein cholesterol; TG = Triglycerides; TC = Total cholesterol; Apo = Apolipoprotein; WC = Waist circumference; WHR = Waist-hip ratio.

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identify how and when disease processes are initiated to develop
effective prevention and early intervention strategies. In this
systematic review, we identified 37 published articles of socioeconomic
disadvantage and other social stressors in relation to three
potential mechanisms that may connect early socioeconomic
disadvantage and other social stressors to adult cardiometabolic
disease: carbohydrate metabolism-related factors, lipids, and waist
circumference. The clearest evidence emerged for the relation
between socioeconomic disadvantage and central adiposity, which
is consistent with findings from recent reviews of childhood
experiences and overweight and obesity [13–15]. While this
finding is important given that central fat may be particularly
harmful for long-term health [70], it is not unexpected and
unfortunately does not shed new light on other pathways by which
social stressors may contribute to development of cardiometabolic
diseases. In fact, what this review most clearly demonstrates is that
surprisingly, research on the relationship between stressors and
carbohydrate and lipid metabolism-related risks is too sparse to be
able to form strong conclusions, particularly with regard to non-
SES social exposures. Further, the few published studies we found
rarely assessed identical exposures and outcomes or used a similar
study design. A review of only the prospective or higher-quality
studies also showed inconsistent associations between socioeconomic
or other social stressors and carbohydrate and lipid
metabolism-related factors, without any discernible patterns that
could explain the discrepant associations.

While we found relatively few studies on social stressors and
carbohydrate and lipid-related risks, considerable research has
examined stressful social environments in relation to cognitive,
behavioral, and other physical health outcomes in children [71],
particularly overweight and obesity [14,15,72–75]. Although
obesity is an important risk factor to consider, indicators from other
physiological parameters that may respond to stress are
worthy of investigation because they may provide additional
insight on the mechanisms that underlie cardiometabolic disorders
[76]. Increasing research has documented that the distribution of
body fat contributes to diabetes and cardiovascular risk among
adults independent of general assessments of adiposity [70,77].
Other research using NHANES participants aged 12–19 found
that in linear regression models adjusted for age, survey period,
and race-ethnicity, body fat percentage only explained 2–20% of
the variance in lipid concentrations [78]. Such findings suggest that it is important to examine the relationship between stressful experiences and cardiometabolic risk factors beyond basic
consideration of adiposity in youth. Research on how socioeconomic
disadvantage and other social stressors affect a variety of
cardiometabolic risk markers early in life will improve our
understanding of how stress experiences become biologically
embedded and lead to metabolic alterations and weight change,
and may elucidate new pathways and opportunities for earlier
interventions to prevent cardiometabolic disorders.

Comparison of the findings from the present review to previous
reviews considering similar exposures (social disadvantage
and other social stressors) in relation to overweight and obesity
[14,15,72,73] and inflammatory biomarkers [75] suggests that
studies on the outcomes we consider are fewer and also less
consistent. For example, in a review of 45 studies from developed
countries (1990 to 2005), Shrewsbury and colleagues [72] found
inverse associations between SES and adiposity in 42% of studies,
mixed or conditional associations in 31%, and null associations in
27%. These associations were most consistent when parental
education was used as the indicator of SES (i.e., 75% of studies
that examined education as the exposure found an inverse
association). In our review, education was not more consistently
associated with outcomes relative to other SES indicators.
However, because only a few studies examined parental educa-
tional attainment in relation to each specific outcome, additional
research is needed to determine if education is in fact a particularly
strong predictor of these cardiometabolic factors as well. Carter
and colleagues [15] examined 27 studies (1999 to 2009) of the
relationship between neighborhood characteristics and child
adiposity. Across studies, area-level socioeconomic disadvantage
was positively associated with adiposity, and there was some
evidence that greater social capital was inversely associated with
adiposity [15]. In our review, only 3 studies considered area-level
environmental features [45,56,57] (and 2 of the 3 examined
central adiposity [56,57]); therefore we do not have enough studies
to determine whether area-level measures are consistent predictors
of other cardiometabolic outcomes.

There has been increasing interest in whether childhood
adversity influences risk of low level chronic inflammation [79–
81], with more studies focusing on CVD-relevant inflammatory
and other immune-related biomarkers in youth relative to those
focusing on lipids or carbohydrate metabolism-related factors.
Inflammatory processes have been identified as another plausible
mechanism by which socioeconomic disadvantage and other social
stressors increase later risk for cardiometabolic diseases [7]. A
recent systematic review of 20 published studies of social adversity
and inflammation in youth suggests a trend towards positive
associations [75]. At present, it is unclear whether heightened
inflammatory markers in response to childhood adversity appear
earlier in development compared to elevations in carbohydrate
metabolism-related factors or lipids (which may become evident
later, perhaps as a downstream consequence of adiposity).
Additional studies are needed in order to establish whether the
different strength of findings across domains of outcomes (i.e.,
adiposity, inflammation, carbohydrate metabolism-related mark-
ers, lipids) are a function of more limited research available on
carbohydrate metabolism-related markers and lipids or because in
fact these alterations are less evident early in life.

Our review suggests a number of priorities for future research.
First, our review reveals a striking paucity of longitudinal studies to
examine the effects of socioeconomic disadvantage and other
social stressors on carbohydrate metabolism-related factors, lipids,
and central adiposity. From cross-sectional studies, it is not
possible to assess when cardiometabolic risk factors begin to
emerge in response to social disadvantage or other stressors.
Therefore, the next generation of life course research aiming to
identify social and biological mechanisms by which socioeconomic
disadvantage and other social stressors are embedded to influence
adult health, will require investment in longitudinal cohorts with
extensive data collection on social conditions and experiences and
health outcomes at multiple time points. Although longitudinal
studies are more time-intensive and expensive than cross-sectional
studies, they address concerns about the temporal ordering
between exposures and outcomes, and provide insight into
whether there are particular periods of development when these
cardiometabolic biomarkers are especially sensitive to, or resilient
against, certain social exposures. Longitudinal studies will further
allow investigators to identify if effects of social stress depend on
developmental stage (i.e., sensitive periods) and at what point in
the life course they are detectable.

Second, our review shows there are many types of social
stressors (e.g., child maltreatment, parent psychopathology,
personal intimate partner violence) that have not been examined
in relation to the markers considered in this review, but that have
shown to be relevant to other physiological outcomes (such as BMI
[82] or inflammation [79,80]) in youth. Thus, there is a need for
future studies to assess a wider variety of types and severity (ranging from minor to severe, acute and chronic) of social stressors and compare effects within the same sample, to identify which are most toxic in relation to cardiometabolic factors. For example, a review by Berge and colleagues [73] reported strong evidence that parenting style is associated with child BMI [73]. However, our review only identified one study that reported substantial evidence that parenting style is associated with child BMI in relation to insulin and lipid levels [65]. Therefore, additional research that considers parenting style and other types of social stressors, in relation to a broader set of cardiometabolic risk markers would be fruitful.

Third, several researchers have begun to examine childhood stressors in relation to cumulative biological risk scores (e.g., allostatic load) [47,83–85] and cardiovascular risk phenotypes (e.g., metabolic syndrome [86]) in youth. These approaches may be valuable for identifying meaningful dysregulation when the effect of an exposure on one specific biomarker is small or inconsistent, but there is a distinguishable effect when you consider a number of related physiological indicators. Additional research is needed to assess whether composite approaches (incorporating individual or multiple systems) within pediatric populations are meaningful for long-term health outcomes, and if composite approaches provide any advantages for understanding the effects of early adversity for later risk of cardiometabolic disorders.

It is important to acknowledge several limitations to the present review. First, several studies used the same sample to examine more than one type of outcome, or the same outcome at a later time point; this could make the literature appear to be more consistent than it actually is. Related, several studies that considered more than one outcome did not calculate a family-wide error, which may compromise the validity of the statistical associations we report. However, in light of the sparse research in this area, we included all unique findings that exist. Finally, this review is limited to studies published in English, and we cannot account for publication bias towards studies with significant results.

In conclusion, scientific understanding of the biological pathways that connect early life experiences to cardiometabolic risk in adulthood remains limited. With improved understanding of the relationship between social adversity and less-studied cardiometabolic risk factors such as glucose, insulin, and lipids among youth, we may begin to identify key intervention opportunities to protect the health of children and adolescents, and the adults they will become.

Supporting Information

Figure S1 Prisma 2009 Flow Diagram (TIF)

Appendix S1 Pubmed Search Strategy. (DOC)

Appendix S2 Prisma 2009 Checklist. (DOC)

Acknowledgments

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Author Contributions

Conceived and designed the experiments: NS EG KK LK. Analyzed the data: NS LK KK EG. Wrote the paper: NS LK EG KK.

References


