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ARTICLE

Socioeconomic status and inflammation: a meta-analysis

Keely A. Muscatell[1,2] · Samantha N. Brosso[1] · Kathryn L. Humphreys[3]

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Abstract

Socioeconomic status (SES), often conceptualized as income, education, or occupation, is associated with risk for disease morbidity and psychopathology. Recent research has focused on the potential biological mechanisms linking lower SES and poor outcomes; much of this work has examined the relationship between SES and markers of systemic inflammation. The strength of the estimated association between SES and inflammatory markers varies widely across individual studies. Thus, we used meta-analytic techniques to quantify the magnitude of this relationship. To accomplish this, PubMed and PsycINFO were searched for papers that reported on SES and two commonly measured systemic inflammatory markers, C-reactive protein (CRP) and interleukin-6 (IL-6). Peer-reviewed, empirical papers conducted in non-patient populations were included. Data from 43 papers ($N = 111{,}156$) reporting a total of 63 relevant effect sizes were included in analyses. SES, broadly defined, was significantly associated with both levels of CRP ($Z = 0.12$; 95% CI, 0.09–0.16) and IL-6 ($Z = 0.15$; 95% CI, 0.12–0.18); individuals with lower SES showed higher levels of systemic inflammation. Subanalyses demonstrated that studies operationalizing SES as either levels of income or educational attainment also found significant associations with both CRP and IL-6. Moderator analyses revealed that effect sizes varied based on sample characteristics and analysis approaches. Lower SES is associated with significantly elevated levels of inflammatory markers of disease risk. Thus, pro-inflammatory pathways are likely an important mechanism translating socioeconomic inequalities into mental and physical health disparities.

Introduction

Socioeconomic gradients in numerous negative physical and mental health outcomes are well-established [1, 2]. Indeed, factors such as poverty, low educational attainment, and neighborhood deprivation are associated with increased risk for psychopathology, including major depression [3] and schizophrenia [4], as well as poor physical health outcomes, including cardiovascular disease [5], diabetes [6], and all-cause mortality [7]. More recently, research has begun to investigate the biological mechanisms by which lower socioeconomic status (SES) confers risk for negative outcomes. Increases in systemic inflammation have emerged as one possible physiologic pathway. Levels of the inflammatory markers C-reactive protein (CRP) and interleukin-6 (IL-6) have been shown to prospectively predict a number of negative outcomes in pre-clinical and clinical studies, including depressive symptoms [8], likelihood of coronary events [9], ischemic stroke incidence [10], and all-cause mortality [11]. Further, inflammatory processes are upregulated in response to psychological stress [12], obesity [13], and among cigarette smokers [14], all of which are more prevalent in lower SES populations. Thus, increased levels of systemic inflammation may be a critical link between SES and health outcomes.

Associations between SES and inflammation were first reported nearly two decades ago [15–18]. Since then, numerous studies have examined associations between various indices of SES and levels of inflammatory markers. Estimates of the association between SES and inflammation vary widely across studies, likely due in part to the use of different measures of SES, different markers of

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✉ Keely A. Muscatell
kmuscatell@unc.edu

[1] Department of Psychology & Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

[2] Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

[3] Department of Psychology and Human Development, Vanderbilt University, Nashville, TN, USA

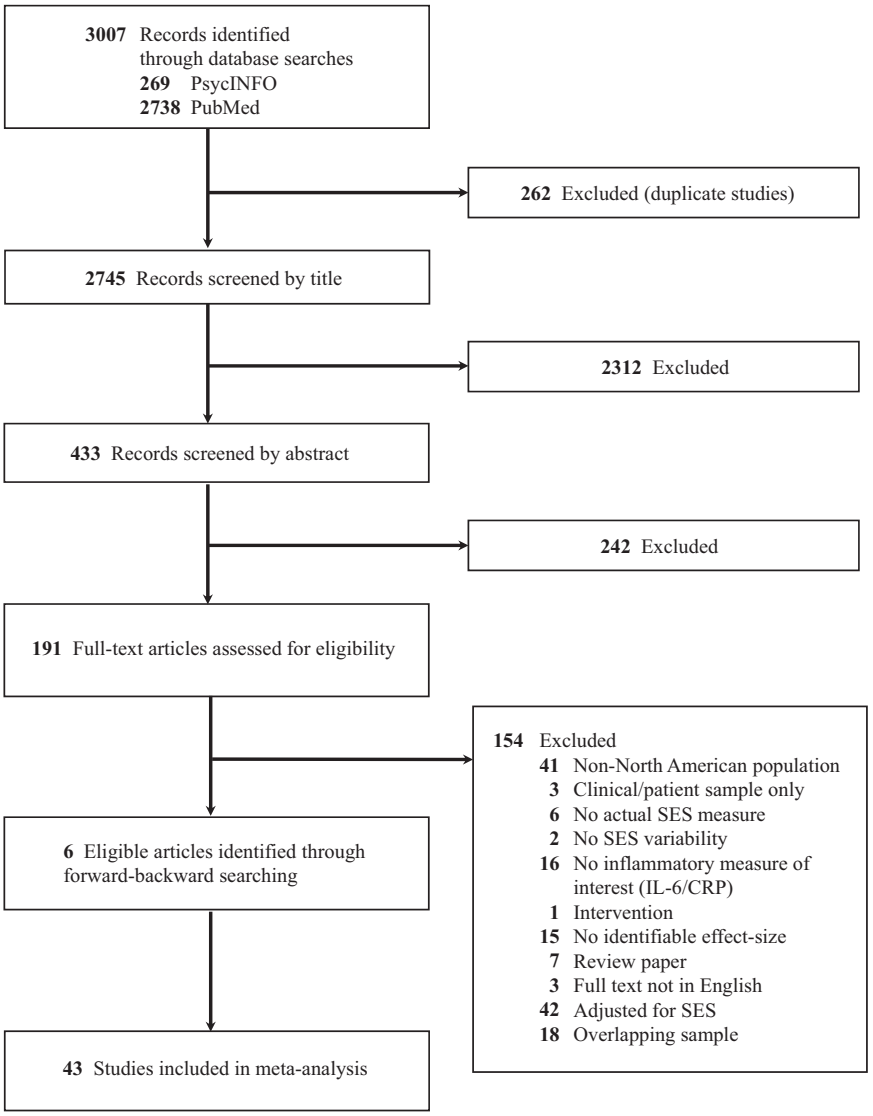

Fig. 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram for identification and inclusion of studies in the meta-analysis

inflammation, demographic characteristics of the samples, and other methodological factors. As such, the strength of the relationship between SES and inflammation is difficult to ascertain based on any single study from the current literature. Thus, the purpose of the present study was to use meta-analytic techniques to quantify the association between SES and the two most commonly assessed markers of systemic inflammation (i.e., CRP, IL-6). SES was broadly defined, including measures of objective (e.g., income, education, occupation), subjective (i.e., perceived social status), and neighborhood (e.g., average neighborhood income) SES. We also conducted analyses focusing exclusively on income and education, respectively. Finally, we explored potential moderators of SES -inflammation associations, focusing on sample characteristics and study design choices, to inform future research in this area.

Methods

Search strategy and selection criteria

We employed two primary search strategies (see Fig. 1 for PRISMA flowchart) to identify the 43 studies included. First, we conducted searches through PubMed and PsycINFO in April 2017 for studies that examined both SES and either CRP or IL-6 (see Supplementary Material for full search terms). Second, we reviewed the references of identified papers for possible additional studies, using forward and backward searching. Authors of journal articles that met the inclusion criteria but did not include the data required to calculate an effect size were contacted for additional information ($N = 11$).

Each study was required to satisfy the following criteria to be included in the overall meta-analysis: (a) assessed

Table 1 Systematic overview of articles included in the meta-analysis

Author [ref.]	Sample size	Sampling strategy	SES measure	Mean age (yrs)	Percent male	Percent White	Percent Black	Inflammatory markers examined
Appleton et al. [37]	392	Community	Household income in childhood	42	41%	80%	NR	CRP
Boylan et al. [38]	1,054	Population	Education[a]	58	45%	93%	NR	CRP, IL-6
Broyles et al. [39]	385	Community	Neighborhood poverty	11.8	49%	48%	49%	CRP
Carroll et al. [40]	112	Community	Composite SES	50.5	40%	89%	NR	IL-6
Chapman et al. [41]	103	Primary Care	Household income[ab]	52	23%	43%	NR	IL-6
Chiang et al. [42]	298	Community	Parental education	16.4	43%	29%	NR	CRP
Clark et al. [43]	24,664	Population	Household income[b]	53	0%	95%	2%	CRP
Cole et al. [44]	64	Community	Parental education	18.4	45%	41%	NR	CRP
Cozier et al. [45]	418	Population	Neighborhood SES composite[ab]	52.4	0%	0%	100%	CRP
Cushman et al. [46]	9080	Population	Education[a]	64.14	42%	59%	41%	CRP
Dowd et al. [47]	931	Community	Education[a]	70.4	42%	0%	0%	CRP
Dowd et al. [48]	3002	Population	Parental education	9.96	53%	62%	15%	CRP
Elliot et al. [49]	1152	Population	Composite SES	57.4	43%	80%	NR	CRP, IL-6
Fedewa et al. [50]	177	Community	Neighborhood SES composite	18.1	33%	66%	NR	CRP
Ford et al. [18]	13,748	Population	Education[a]	44.77	47%	76%	NR	CRP
Gallo et al. [51]	284	Community	Education; Income[ab]	49.74	0%	0%	0%	CRP, IL-6
Herd et al. [52]	510	Population	Education[ab]	68.13	50%	86%	8%	CRP
Hostinar et al. [53]	360	Community	Parental occupational status; current occupational status	36.47	45%	73%	NR	CRP, IL-6
Janicki-Deverts et al. [54]	1117	Population	Household income[b]	40.24	100%	62%	38%	CRP
John-Henderson et al. [24]	209	Community	Subjective social status	19.62	44%	25%	13%	IL-6
Joseph et al. [55]	71	Community	Education[a]	50.2	53%	68%	NR	CRP
Koster et al. [56]	782	Population	Household income[ab]	74.2	49%	58%	42%	CRP, IL-6
Loucks et al. [57]	2729	Population	Education[ab]	62.1	47%	N/A	NR	CRP, IL-6
Loucks et al. [58]	805	Population	Education[a]	74.26	47%	83%	17%	CRP, IL-6
Marsland et al. [59]	460	Population	Education[a]	44.6	52%	81%	18%	IL-6
McDade et al. [60]	188	Population	Education[ab]	59.5	45%	38%	34%	CRP
Miller et al. [61]	103	Community	Parental occupation	33.13	68%	35%	NR	CRP
Miller et al. [62]	145	Community	Parental education	17	0%	50%	NR	IL-6
Muennig et al. [63]	10,524	Population	Household income[ab]	NR	NR	NR	NR	CRP
Mwendwa et al. [64]	198	Community	Education[a]	45.56	48%	0%	100%	CRP, IL-6
Paalani et al. [65]	508	Population	Education[a]	68.8	37%	62%	38%	CRP, IL-6
Paul et al. [66]	219	Population	Income[b]	31.3	0%	55%	45%	CRP
Petersen et al. [67]	851	Population	Neighborhood SES	44.9	50%	77%	23%	CRP, IL-6
Pietras et al. [68]	941	Community	Household income[a]	14.99	49%	56%	45%	IL-6
Schmeer et al. [69]	404	Community	Parental education; family income to poverty ratio	10.9	53%	25%	6%	CRP
Schmeer et al. [70]	15,314	Population	Parental education	11	52%	61%	13%	CRP
Schreier et al. [71]	88	Community	Parental education	13	57%	51%	NR	CRP
Schreier et al. [72]	244	Community	Parental income[b]	14.57	49%	49%	NR	CRP, IL-6
Shanahan et al. [73]	13,257	Population	Household income[ab]	28.42	49%	67%	16%	IL-6

Table 1 (continued)

Author [ref.]	Sample size	Sampling strategy	SES measure	Mean age (yrs)	Percent male	Percent White	Percent Black	Inflammatory markers examined
Sin et al. [74]	872	Population	Household income[b]	57.85	43%	82%	14%	CRP, IL-6
Sturgeon et al. [75]	680	Community	Subjective social status	53.91	47%	74%	3.1%	CRP, IL-6
Taylor et al. [76]	3248	Population	Childhood SES (composite of parental education)	40.1	45%	55%	45%	CRP
Zhang et al. [77]	465	Community	Education[ab]	53	50%	50%	50%	CRP

NR not reported, *SES* socioeconomic status, *CRP* C-reactive protein, *IL-6* interleukin 6

[a]Article included in education sub-analysis

[b]Article included in income sub-analysis

SES; (b) assessed circulating levels of CRP and/or IL-6; (c) provided data to determine a relevant effect size; and (d) included only North American participants. We restricted the analysis to studies conducted with North American samples in an effort to account for the fact that socioeconomic influences on health vary strongly across countries and continents [19]. Studies were excluded if they focused on participants with an existing chronic condition or disease (e.g., diabetes) in order to eliminate studies that could bias the estimates, given that patients may be substantially non-representative in terms of their levels of inflammation.

Data extraction

Two trained raters (KAM, SNB) coded individual studies. When more than one relevant effect size was available, raters first selected the effect size with the fewest covariates included in the model, and second, the variable with the strongest association with the inflammatory marker of interest, as often the models included several variables that competed for explanatory variance (see Supplementary Information for more detail). Rater agreement for moderator codes was 96%. When raters provided contradictory judgments, disagreements were resolved via consensus.

Data analysis

To ensure consistency in the directionality of the effect sizes, SES was coded to indicate that numerically higher SES values indicated lower SES. Effect size calculations were obtained using standard approaches, given each association available (e.g., r, two continuous variables; d, one continuous and one binary variable; odds ratio, two binary variables). Effect size values were transformed to *Z*s to place all estimates on a common scale and to be consistent with similar meta-analyses [20]. A *Z*-value of 0 indicated that SES had no association with inflammation. A positive *Z*-value indicated that lower SES was associated with higher levels of inflammation. A negative *Z*-value indicated that lower SES was associated with lower levels of inflammation. The 95% confidence interval (CI) for *Z* represents the relative precision of the measurement. Given that the available *N* for a particular effect size may have been lower than the total *N* in the study (e.g., due to inflammation not being assessed in all participants), estimates of effect size weight to calculate the 95% CI were based on the *N* from which the effect size was derived. These procedures produced 63 total effect sizes from 43 eligible studies. For analyses of SES broadly defined, 35 studies were included for CRP and 18 studies were included for IL-6.

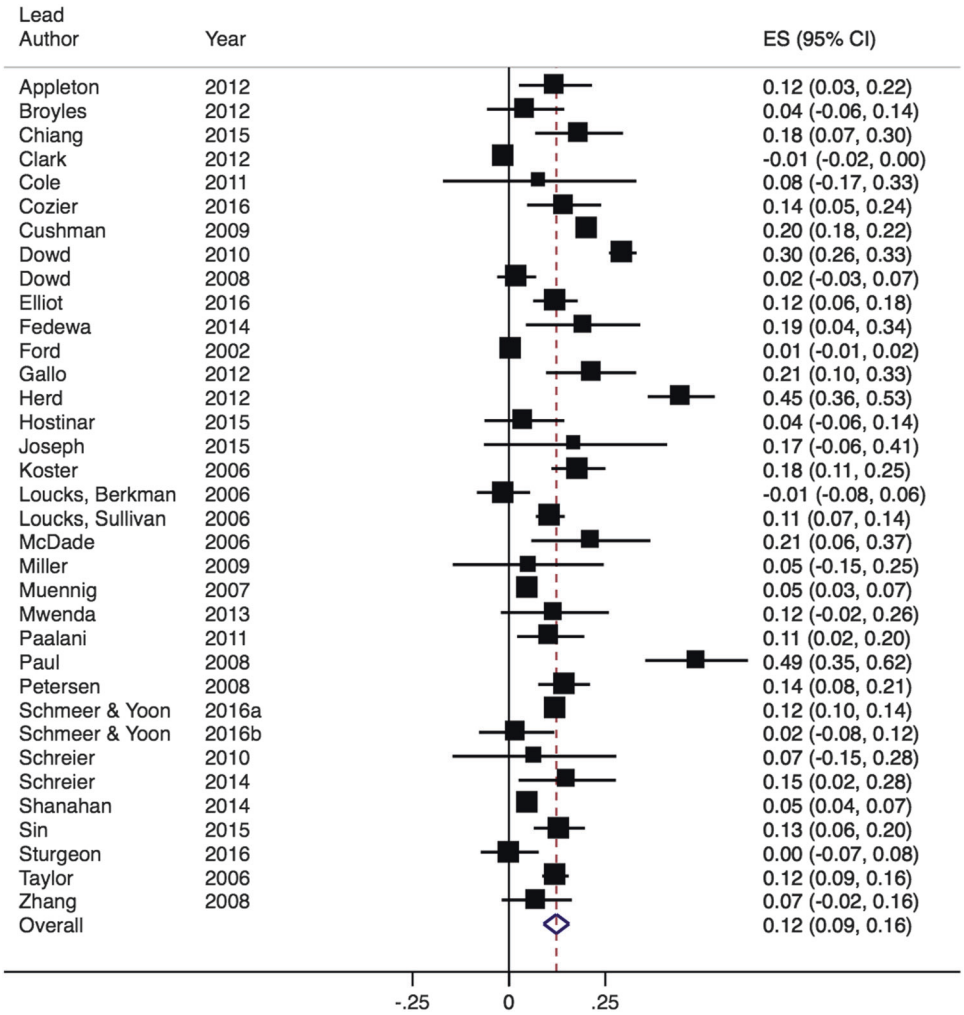

Fig. 2 Forest plot of effect sizes from studies examining the association between SES and CRP. Box sizes are indicative of study weight, with box center positioned at the point estimate of the effect. Horizontal lines indicate 95% CIs. Dashed vertical line indicates the estimated meta-analytic effect

Moderator analyses

When heterogeneous effect sizes were detected, we tested whether important demographic and methodological factors, selected on the basis of prior meta-analytic work in this area and recommended control variables for studies examining inflammation [21], moderated the observed association between SES and inflammation. The following characteristics of each sample were coded: average age (examined linearly and categorically [i.e., under 18 years vs. 18 years or older]); gender composition (% male); racial diversity (% White) and (% Black); and mean body mass index (BMI). Methodological characteristics of each study were coded as follows: whether SES was a continuous or binary variable; if binary, was an extreme group approach used (e.g., lowest quintile of income compared with the highest quintile); developmental period of SES assessment (e.g., childhood vs. adulthood); whether SES was a focus of the study (vs. a covariate in analyses pertaining to another topic); whether the SES measure was subjective (vs. objective); year in print; covariate present in analysis (Yes/No: age, sex, race/ethnicity, BMI, cigarette smoking, chronic health conditions, and medication use); sample source (i.e., community sample vs. population-based sample); study design (i.e., retrospective vs. cross-sectional vs. longitudinal); inflammatory source (i.e., plasma vs. serum vs. blood spots); transformation of inflammatory marker before analysis (i.e., to adjust for skew); if the inflammatory marker was treated as a continuous or binary variable (see Table 1 and Supplementary Material).

Random-effects models were constructed using the Z estimate and the lower and upper bounds for the 95% CI. Publication bias was assessed via Egger's [22] and Begg's [23] tests. Heterogeneity of effect sizes was estimated using the standard Cochran's Q Test, which approximates a chi-square distribution with $k-1$ degrees of freedom, where k is the number of effect sizes and indicates the degree of consistency of findings across studies. When the p-value associated with the Q statistic was ≤0.10, indicating heterogeneity in the effect sizes, pre-specified random-effects meta-regression moderator analyses were conducted to determine whether the study characteristics described above

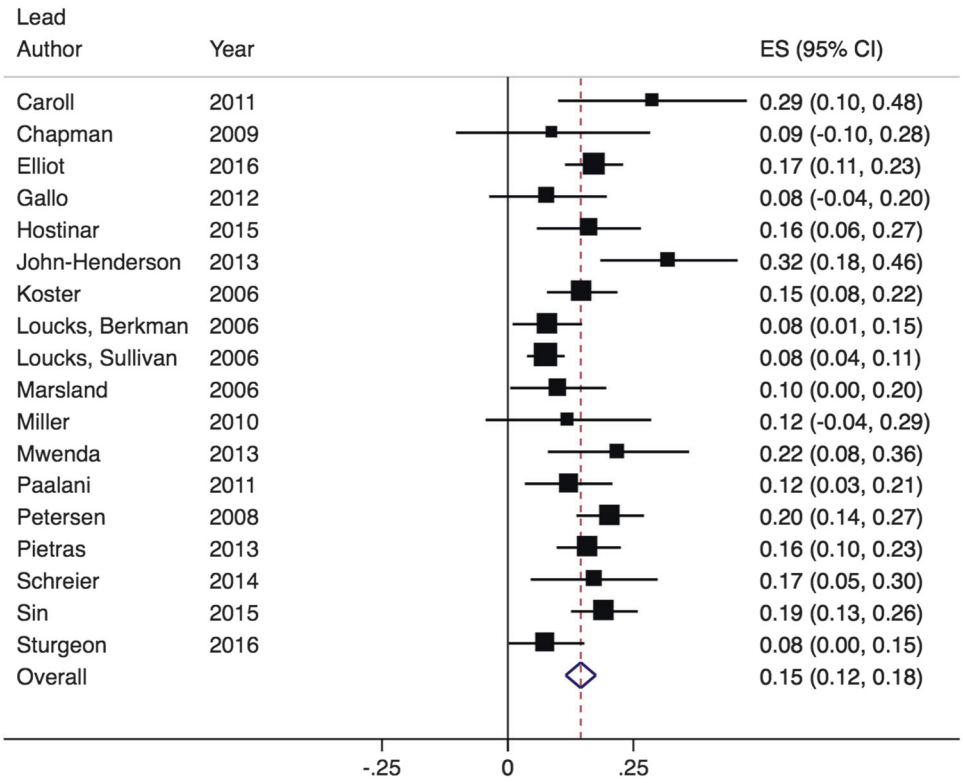

Fig. 3 Forest plot of effect sizes from studies examining the association between SES and IL-6. Box sizes are indicative of study weight, with box center positioned at the point estimate of the effect. Horizontal lines indicate 95% CIs. Dashed vertical line indicates the estimated meta-analytic effect

could explain variability across studies. We tested each moderator separately using simple regressions (i.e., the *metareg* command). Analyses were performed using STATA 14.2 (StataCorp, 2015).

Results

Table 1 and Supplemental Table 1 provide descriptive information for each study, including demographic and methodological moderators coded and outcomes obtained.

SES and CRP

We first examined SES among all studies that included a measure of this construct in relation to CRP levels. Among these, *Z*s ranged from −0.01 to 0.49 (see Fig. 2). The random-effects meta-analysis found that lower SES was associated with higher CRP ($Z = 0.12$; 95% CI, 0.09–0.16) and significantly differed from zero, $Z = 7.32$, $p < 0.001$. Significant heterogeneity was observed across studies ($Q(34) = 747.01$, $p < 0.001$; $I^2 = 95\%$). The bias statistic from both Egger's and Begg's publication bias tests was not significant ($p > 0.10$).

Within studies that used uniform definitions of SES based on income or education attainment, we found a similar magnitude of association between lower income and lower education and higher CRP ($Z = 0.11$ for income; $Z = 0.12$ for education; both $p < 0.05$; see Supplementary Material).

SES and IL-6

We also examined SES among all studies that included a measure of this construct in relation to IL-6. Among these, *Z*s ranged from 0.08 to 0.32 (see Fig. 3). The random-effects meta-analysis found that lower SES was associated with higher IL-6 ($Z = 0.15$; 95% CI, 0.12–0.18) and significantly differed from zero, $Z = 9.50$, $p < 0.001$. There was evidence of significant heterogeneity across studies ($Q(17) = 36.89$, $p = 0.003$; $I^2 = 54\%$). The bias statistic from both Egger's and Begg's publication bias tests was not significant ($p > 0.10$).

Again, within studies that used uniform definitions of SES based on income or education attainment, we found a similar magnitude of association between lower income and lower education and higher IL-6 ($Z = 0.12$ for income; $Z = 0.11$ for education; both $p < 0.05$; see Supplementary Material).

Moderators of the association between SES and CRP

We explored whether the moderators described previously were associated with heterogeneity of effect sizes for the

analyses with significant Q statistics (see Supplementary Material for full moderator results). For the association between SES and CRP, four moderators were significantly associated with variation in effect sizes: (1) whether SES was treated as a continuous or binary variable [Coef. = 0.10, SE = 0.04, $t = -2.45$, $p = 0.020$]; (2) whether BMI was included as a covariate in analyses [Coef. = −0.11, SE = 0.05, $t = -2.38$, $p = 0.023$]; (3) whether cigarette smoking was included as a covariate in analyses [Coef. = −0.13, SE = 0.04, $t = -2.97$, $p = 0.005$]; and (4) whether CRP values were transformed prior to analysis [Coef. = 0.08, SE = 0.04, $t = 2.06$, $p = 0.047$]. Meta-analyses within each set of studies indicated that the estimated effect size among those that used a binary assessment of SES was half as large ($Z = 0.09$; 95% CI, 0.06–0.12; $n = 26$) compared with those that used a continuous assessment of SES ($Z = 0.20$; 95% CI, 0.11–0.28; $n = 9$), though both produced effect sizes that were significantly different from zero ($ps < 0.001$). Studies that did not covary for BMI ($Z = 0.15$; 95% CI, 0.11–0.19; $n = 29$) had a larger estimated effect size than those that did ($Z = 0.03$; 95% CI, −0.01–0.06; $n = 5$), and only those that did not covary for BMI produced an effect size that significantly differed from zero ($p < 0.001$). Studies that did not covary for cigarette smoking ($Z = 0.15$; 95% CI, 0.11–0.18; $n = 30$) had a larger estimated effect size than those that did ($Z = 0.01$; 95% CI, −0.01–0.04; $n = 5$), and only those that did not covary for smoking produced an effect size that significantly differed from zero ($p < 0.001$). Analyses comparing studies that did and did not transform CRP showed larger estimated effect sizes among studies that transformed CRP prior to analyses ($Z = 0.15$; 95% CI, 0.10–0.20; $n = 23$) compared with those that did not transform ($Z = 0.07$; 95% CI, 0.02–0.12; $n = 12$), though both produced effect sizes that were significantly different from zero ($ps < 0.01$).

Moderators of the association between SES and IL-6

Turning to SES and IL-6, four moderators predicted significant variability in effect sizes: (1) year in print (Coef. = 0.01, SE = 0.003, $t = 2.62$, $p = 0.019$); (2) whether SES was a subjective or objective assessment (Coef. = 0.18, SE = 0.08, $t = 2.23$, $p = 0.041$); (3) whether age was included as a covariate in analyses (Coef. = −0.07, SE = 0.02, $t = -2.99$, $p = 0.009$); and (4) whether IL-6 levels were transformed prior to analysis (Coef. = 0.07, SE = 0.02, $t = 2.79$, $p = 0.013$). Greater effect sizes were found among studies published more recently. Only one study included used a subjective measure of SES [24]. With it excluded, the estimated effect size that was just slightly smaller than the full set of studies ($Z = 0.14$; 95% CI, 0.11–0.17; $n = 17$), and produced an effect size that was significantly different from zero ($p < 0.001$). Studies that did not covary for age in analyses ($Z = 0.16$; 95% CI, 0.13–0.19; $n = 13$) had larger effect sizes than those that did ($Z = 0.11$; 95% CI, 0.07–0.15; $n = 5$), and both produced effect sizes that were significantly different from zero ($ps < 0.001$). Lastly, studies that transformed IL-6 ($Z = 0.16$; 95% CI, 0.13–0.19) demonstrated a stronger association than those studies that did not transform IL-6 ($Z = 0.10$; 95% CI, 0.06–0.15; $n = 4$), though both sets significantly differed from zero ($ps < 0.001$).

Discussion

In the first known meta-analysis to examine the association between SES and levels of systemic inflammation, we quantified the effects from 43 published papers comprising of over 110,000 participants, yielding 63 relevant effect sizes. These analyses produced several key findings. First, we found a significant association between SES, broadly defined, and circulating levels of both CRP and IL-6, such that individuals with lower SES showed higher levels of these inflammatory markers. This is notable given that elevated levels of systemic inflammation are a risk factor for disease development and psychopathology [8, 10, 11], and yet studies included in the meta-analysis excluded samples selected on the basis of any mental or physical health problem. In other words, these data suggest the possibility that low SES may set individuals on a pro-inflammatory trajectory that can be observed in the general population rather than only among individuals currently experiencing a chronic disease. Second, analyses among studies using narrower definitions of SES (i.e., income and educational attainment) revealed remarkably similar, significant effects of both factors relating to CRP and IL-6. Indeed, the 95% CIs of the effect sizes for the associations between income and CRP, income and IL-6, education and CRP, and education and IL-6 were all overlapping, indicating no statistically significant differences between the magnitude of these associations. Thus, this study provides evidence that despite potential meaningful differences in these indices [25], both low income and low levels of education are related to higher levels of systemic inflammation. Finally, there was significant heterogeneity in effects across studies, and moderator analyses shed some light on important factors that may contribute to this heterogeneity, which we expand upon below. Taken together, these meta-analytic results indicate that there is a consistent association, albeit on average a small effect, between SES and inflammatory markers of risk for negative outcomes. Though the evidence is not causal, our findings provide support for the notion that upregulation of inflammatory processes may play a part in contributing to known socioeconomic disparities in disease morbidity and psychopathology.

In contextualizing the magnitude of the relationship between SES and inflammatory markers observed here, it is useful to consider the effects observed in other recent meta-analyses that have examined the association between psychosocial/behavioral factors and inflammation. For example, the estimated overall weighted association between SES and inflammatory markers ($Z = 0.12$ and $Z = 0.15$ for CRP and IL-6, respectively) appears somewhat stronger than the association found for childhood trauma and inflammation ($Z = 0.10$ and 0.08 for CRP and IL-6, respectively) [20] and similar to the effects of depression ($d = 0.15$ and 0.25 for CRP and IL-6, respectively) [26] and sleep disturbance ($d = 0.12$ and 0.20 for CRP and IL-6, respectively) [27] on inflammatory markers. Compared with these other markers of distress, SES is the least direct in its impact, yet the association between SES and systemic inflammation is similar in strength, suggesting that SES may be an important contributor to levels of inflammation.

While the present meta-analysis provides greater confidence in the association between SES and inflammation, this approach is not designed to test *why* low SES is associated with inflammation. Moderator analyses may provide some insight, however, as studies that controlled for BMI and/or cigarette smoking showed a much smaller association between SES and CRP than those that did not control for these factors (which was not found for analyses examining IL-6). Obesity and smoking are two possible mediators, or mechanisms, linking SES and levels of CRP, as the SES–CRP link is attenuated if SES-related differences in obesity and smoking are eliminated (though other factors are likely important as well [28]). This result is consistent with another recent meta-analysis in this area [29], which also found that BMI explained significant variability in the association between childhood SES and adult CRP. Taken together, these findings provide further support for the usefulness of population health initiatives aimed at weight management and smoking cessation to help reduce health disparities across the SES spectrum [30, 31], and targeted prevention programs may be useful in reducing elevated CRP among those at highest risk.

In addition to providing insights important for clinicians and public health professionals, results of moderator analyses can also be used to guide decisions for future research examining the relation between SES and inflammation. For example, we observed stronger effect sizes for studies that transformed CRP and IL-6 before analysis to account for the skew in such data, suggesting that using non-transformed inflammatory marker data may lead to underestimations of their relation with SES. This is perhaps due to the fact that the use of untransformed data does not meet statistical assumptions of normality, thus possibly producing biased estimates. Further, for studies examining the relation between SES and CRP, we observed stronger effect sizes among studies that treated SES as a continuous measure compared with those that used a binary SES measure (e.g., comparing those with and without a high school degree). This result suggests that levels of CRP vary across the entire SES spectrum and not just when comparing groups, including extreme groups (e.g., comparing those who did not complete high school to those with a graduate degree). Thus, results from these moderator analyses suggest that future work should ensure adequate transformation of inflammatory data prior to analysis and should conceptualize SES as a continuous measure (particularly among studies using CRP) [1].

Turning to IL-6, we found that year in print, whether age was controlled for analyses and whether SES was a subjective or objective measure, moderated the magnitude of the association between SES and IL-6; with most recent papers, effects that did not control for age, and subjective SES measures, respectively, yielding stronger associations. While moderator analyses are useful, the lack of consistency of moderator variables for analyses examining CRP versus IL-6 are interesting to note but difficult to interpret, as the difference may reflect true variation in the nature between SES and each marker, or perhaps differences related to the studies that provided each marker, as there were more studies that examined CRP than IL-6. Further, CRP is generally a more stable indicator of chronic inflammatory activation [32] and thus may be more strongly related to behavioral factors like smoking and BMI. Moving forward, examination of the moderators identified here in large epidemiological studies of a single cohort that assesses both CRP and IL-6 would be most informative about the potential specificity of each moderator and to gain confidence in the patterns observed here.

We did not find evidence that the magnitude of the association between SES and CRP or IL-6 was moderated by a number of demographic and study design factors that are thought to be important for research in this area (e.g., sex, race, age, and BMI makeup of the sample, SES in childhood vs. adulthood, if inflammation was measured in pediatric or adult samples, type of study design, sample recruitment strategy, source of inflammation for assay, and if inflammation was measured on a continuum or with a cut-off). It will be important for future work in this area to continue to measure these factors and examine if the association between SES and inflammation exists for all individuals and across all types of studies, given the limited ability for broad study-level patterns to inform individual-level mechanistic processes.

A number of limitations of this study should be noted. First, only studies that included non-patient samples were included in the analysis, so we cannot draw conclusions regarding the association between SES and inflammation in specific disease states. Second, we restricted our

analysis to studies conducted with North American samples in an effort to account for the fact that socioeconomic influences on health vary strongly across countries and continents [19]. Future work could examine the association between SES and inflammation as a function of country-level economic inequality, given that inequality has shown to influence health over-and-above individual-level SES factors [33]. Third, our subanalyses focused on income and educational attainment, given that these were the most commonly-assessed measures of SES in this literature. However, there is growing appreciation of the role that neighborhood-level SES [34], as well as subjective perceptions of SES [35], may play in influencing health; as more studies accumulate in this area, we will be able to examine the association between these (and other) alternative indicators of SES and their associations with inflammation. Fourth, we undoubtedly missed studies in which SES and inflammation were examined, as many studies include SES as a covariate, and these may not have been surfaced in our search strategy. Importantly, however, we found no difference in studies in which SES was a primary focus or merely a covariate. Further, we only examined the association between SES and CRP/IL-6, and thus cannot speak to the magnitude of the relationship between SES and other markers of inflammation (e.g., TNF-α). Finally, due to inconsistencies in the literature in the use, conceptualization, and measurement of psychological stress [36], we did not explore stress as a possible moderator of the link between SES and inflammation. This would be a valuable contribution for future meta-analyses in this area.

In sum, there is a significant association between SES and levels of inflammation (both CRP and IL-6). These results are important for our understanding of how social inequalities may become health inequalities. As next steps, it will be important to explore mechanistic pathways (i.e., psychological and biological) by which SES may influence inflammation. Results from moderator analyses presented here suggest that the association between SES and CRP may be explained in-part by SES disparities in obesity and smoking, demonstrating the importance of behavioral processes in contributing to this link. In addition, researchers should consider building upon theoretical foundations to explore the potential pathways of psychosocial stress, social comparison, and scarcity perceptions, as well as the more proximal biological mechanisms that may link SES and inflammation (e.g., sympathetic nervous system activation). Interventions that improve SES can be leveraged to test causal assumptions about the effect of SES on inflammatory markers. Such mechanistic and causal insights would allow for directed interventions at a population level with the potential to improve mental and physical health for all individuals, regardless of SES background.

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Compliance with ethical standards

Conflict of interest Dr. Humphreys received financial support from NIH, the Brain and Behavior Research Foundation, the Klingenstein Third Generation Foundation, and the Jacobs Foundation. Dr. Muscatell and Ms. Brosso declare that they have no conflict of interest.

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