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Early life Adversity and Inflammation in African Americans and Whites in the Midlife in the United States Survey

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Abstract

Objectives—We sought to determine whether early life adversity (ELA) was predictive of inflammatory markers, and to determine the consistency of these associations across racial groups.

Methods—We analyzed data from 177 African Americans and 822 Whites aged 35 to 86 from two preliminary subsamples of the Midlife in the United States biomarker study. ELA was measured via retrospective self-report. We used multivariate linear regression models to examine the associations between ELA and CRP, IL-6, fibrinogen, E-selectin, and sICAM-1, independent of age, gender, and medications. We extended race-stratified models to test three potential mechanisms for the observed associations.

Results—Significant interactions between ELA and race were observed for all 5 biomarkers. Models stratified by race revealed that ELA predicted higher levels of log IL-6, fibrinogen, E-selectin, and sICAM-1 among African Americans (*p*-values <.05), but not among Whites. Some, but not all, of these associations were attenuated after adjustment for health behaviors and BMI, adult stressors, and depressive symptoms.

Conclusions—ELA was predictive of high concentrations of inflammatory markers at midlife for African Americans, but not Whites. This pattern may be explained by an accelerated course of age-related disease development for African Americans.

Keywords

childhood; early life adversity; inflammation; life course epidemiology; race/ethnicity; chronic disease risk

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A life course approach to chronic disease directs us to consider childhood origins of adult diseases (1). Research indicates that early life adversity (ELA) is associated with an increased risk for a broad range of diseases, including cardiovascular diseases (CVD), diabetes, cancers, and psychiatric disorders (2–4). Recently, researchers have begun to investigate physiologic mechanisms linking early life experiences to health later in life (5–7). One physiological pathway that is gaining interest as a potential link between ELA and increased risk of morbidity later in life is inflammation, as inflammatory processes are involved in a number of health conditions which might vary by level of life adversity. Large-scale epidemiologic studies provide support for an association between several blood markers of inflammation and age-related diseases, including CVD and cancer (8–11). A growing body of research demonstrates associations between social conditions in adulthood and inflammatory outcomes (12–15), and evidence is mounting that early life social conditions are also linked to levels of inflammatory burden later in life (5,6,16–18). To date, little is known about the extent to which the relationship of ELA with the health of African Americans (or Blacks, we use the terms interchangeably) in midlife differs for that of whites.

Among previous investigations of the association between ELA and inflammation, researchers have documented increased risk of inflammation associated with low socioeconomic position (SEP) in childhood (16–18), harsh family environment (6), and maltreatment (5). A limitation of this series of work is that most studies consider the influence of an isolated stressor; however, multiple stressors in childhood often co-occur (19). It is important to study multiple adversities simultaneously, because individuals exposed to a variety of stressors are at great risk of exhausting psychological and physiological resources to effectively cope with stress (20).

Childhood adversity experiences may vary by sociodemographic variables, including race/ethnicity. In the U.S., as a result of severe residential segregation, it is common for Black and White children to inhabit distinct environments (21). As a consequence, Blacks and Whites may be exposed to dramatically different types of stressors and stress-buffering resources throughout the life course. Researchers have hypothesized that African Americans may experience more rapid deterioration in health, relative to Whites, due to cumulative exposure to multiple sources of social and economic adversity. Accelerated aging theories, such as the *Weathering Hypothesis* (22,23), direct us to consider multiple sources of stressors over time, and draw attention to the role of differential exposure to stress in producing racial inequities in health. On this basis, application of a life course perspective to understanding racial health disparities is important.

In the present study, our first objective was to examine the association between a composite measure of ELA and concentration of 5 markers of inflammation known to be associated with CVD: C-reactive protein (CRP) (24), interleukin-6 (IL-6) (25), fibrinogen (26), endothelial leukocyte adhesion molecule-1 (E-selectin) (10), and soluble intercellular adhesion molecule-1 (sICAM-1) (27). These inflammatory markers were selected based on prior evidence of patterning by social exposures (5,17,28,29). We hypothesized that greater exposure to ELA would be associated with higher concentrations of each inflammatory marker. The second objective was to determine whether these associations were similar for Black and White respondents. On the basis of evidence for an accelerated course of disease progression among individuals exposed to a high burden of stressors (23,30), we hypothesized that the association between ELA and inflammation at midlife would be more pronounced for African Americans in our sample. In secondary analyses, we evaluated health, behavioral, and psychosocial risk factors that may serve as potential mechanisms by which ELA leads to higher levels of inflammation in midlife.

Sample

The sample for our analysis was comprised of two preliminary subsamples from the Midlife in the United States (MIDUS) biomarker study: one from participants who were enrolled in the original MIDUS longitudinal sample, and the other from a city-specific sample of African Americans from Milwaukee, WI. The original MIDUS participants (N=7108, aged 25 to 74 at baseline) were recruited between January 1995 to September 1996 from a national random-digit-dial sample of non-institutionalized adults living in the 48 contiguous states (31). This sample included siblings for some respondents, and some pairs of twins. Between January 2004 and August 2005 a follow-up of 4963 MIDUS I respondents took place (70% response rate; referred to as MIDUS II). At this time, a supplement sample of 592 African Americans from Milwaukee, WI was recruited to participate. This subsample increased the participation of African Americans in MIDUS and facilitated analyses of biopsychosocial influences on health in a highly segregated American city that was in geographic proximity to one of the clinic sites. The research team also had prior experience in bringing African Americans from Milwaukee to Madison, WI for biological data collection.

Respondents from the MIDUS II and Milwaukee samples were eligible to participate in the biomarker study if they participated in the telephone interview (or home interview for Milwaukee) and mail surveys, and lived in the continental U.S.; this required an overnight at one of three General Clinical Research Centers (GCRC). As of July 2008, a total of 1038 individuals participated in biological assessments, 999 of whom comprise the sample for these analyses. There were 39 non-Black minority participants from the MIDUS II cohort excluded from this analysis because this group was not large enough to create independent samples by racial category. The sample of 999 individuals includes 822 Whites and 26 Blacks from MIDUS II, and 151 Blacks from the Milwaukee sample.

Data collection for the MIDUS, Milwaukee, and biomarker studies was approved by Institutional Review Boards at the University of Wisconsin, Madison, as well as the University of California, Los Angeles, and Georgetown University, which served as additional sites of data collection for the biomarker sub-study. All participants provided informed consent.

For both the MIDUS II and Milwaukee samples, individuals who participated in the GCRC assessment were significantly more likely to have a college degree relative to non-participants; no significant differences were observed for age, gender, marital status, or employment status. For the African American respondents only, the mean ELA score was modestly but significantly higher for individuals who participated in the biomarker study relative to those who did not (by approximately one-quarter of a standard deviation).

Measures

Inflammatory Markers

Fasting serum samples were assayed for CRP, IL-6, fibrinogen, E-selectin, and sICAM-1, according to manufacturer guidelines (Dade Behring Inc., Deerfield, IL for CRP and fibrinogen; R&D Systems, Minneapolis, MN for IL-6, E-selectin, and sICAM-1). Citrated plasma CRP and fibrinogen were assayed using immunonephelometric assay; IL-6 was assayed using enzyme-linked immunosorbent assay (ELISA), and, E-selectin and sICAM-1 were assayed using high-sensitivity ELISA. For all biomarkers, the laboratory coefficients of variance were <11%. In regression models, CRP and IL-6 were log-transformed to improve normality of the distributions, and all inflammatory markers were modeled as continuous variables. In addition, we created a summary score to capture overall inflammatory burden. We assigned one point for each inflammatory marker above the sample median (range: 0 to

5), following an approach used in previous publications (16). A score was only created for individuals with valid observations for all 5 outcomes (n=978).

Early Life Adversity

ELA was measured using retrospective report of events or conditions experienced in childhood and adolescence, collected in surveys that were completed prior to recruitment for biological assessment. It is a composite score reflecting 3 domains of stress. First, stressful events during childhood/adolescence were measured using a 9-item inventory; events included school failure, being sent away from home for doing something wrong, parental unemployment when wanting to work, parental alcohol problems, parental drug problems, dropped out of school, expelled/suspended from school, receipt of welfare, moved to new neighborhood/town 2 or more times. Second, self-report rating of relationship with parents during childhood was evaluated using 2 items (1 item for mother, 1 item for father), using a 5-point scale. Third, frequency of verbal and physical assault by parents was evaluated using 6 items from the Conflict Tactics Inventory (32); 3 items referred to interactions with mother, 3 items referred to interactions with father. The items captured frequency of verbal and emotional abuse, and moderate and extreme acts of physical violence on a 4-point scale (never to often). Because the 3 domains of ELA were each measured on a different scale (i.e., had different ranges of values), we standardized the domain scores into z-scores, and then created a z-scored composite of the 3 domains. The composite score was standardized for the full sample of all MIDUS and Milwaukee participants.

Demographic Covariates

Demographic covariates were selected based on the prior literature (33). Self-reported race and gender were coded using indicator variables, and a linear covariate for age was used. Educational attainment was measured using a three category variable: high school degree or less, some college (no degree), and associates/bachelors degree. We adjusted for use of 4 classes of medications (as inventoried by staff at the GCRC): use of anti-hypertensive, lipid-lowering, corticosteroid, and antidepressant medications was indicated with dummy variables. We adjusted for use of these medications based on research showing that these medications affect circulating markers of inflammation (34–37).

Covariates in Extended Models

Secondary analyses were conducted to determine if any observed associations between ELA and elevated inflammation were independent of body mass index (BMI), health behaviors (smoking, exercise), stressful life events in adulthood, and depressive symptoms. These factors were selected based on research suggesting that individuals exposed to ELA have increased risk of these experiences and conditions (2,3,38,39), and other research showing that these factors may act as pathways through which ELA is associated with elevated inflammation (5, 6,16,40). In addition, in the extended models, we adjusted for self-reported physician-diagnosed history of CVD (stroke or heart attack), diabetes mellitus, and cancer because it is possible that the onset of these conditions may have temporally preceded elevations in inflammation.

Body Mass Index and Health Behaviors

BMI (kg/m^2) was measure by GCRC staff and modeled continuously. Vigorous exercise, reflective of cardiorespiratory fitness, was defined as self-report of vigorous activity at least 3 times per week, and was modeled using a dichotomous variable. Smoking status was a 3-category variable (current, previous, or never).

Adult Stress Events

A measure of adult stress events was created using responses from the MIDUS stressful life event inventory, created for the purpose of the MIDUS study. The inventory includes acute stressors similar those included in standard stressful life event measures (e.g., child died, parent died, sexual assault, bankruptcy, combat experience) (41). The inventory asked participants to identify the age at which each event occurred. Separate scores were created for: (1) stressful events in the past 5 years (20 events), and (2) stressful events more than 5 years ago (23 events). If the respondent endorsed an event but no age was specified, the event was categorized as occurring more than 5 years ago. Similar to the procedure used to create the ELA composite score, the 2 inventory scores were standardized into z-scores, and the 2 standardized scores were summed. The summated value was then standardized into a z-score.

Depressive Symptoms

A continuous measure of depressive symptoms in the past week was created using the 20-item Center for Epidemiological Studies Depression Inventory (CES-D) (42).

Statistical Analyses

Analyses were performed using SAS 9.2. Descriptive statistics were generated for all variables (means and standard deviations for continuous variables; proportions for discrete variables). Linear regression models were used to estimate the effect of ELA on inflammation, using separate models for each outcome. All models were adjusted for age, gender, and medication use. First, we ran a series of baseline models to examine the effect of ELA on each inflammatory marker. We tested for effect modification by race using an interaction term, and then constructed race-stratified models when appropriate.

To test hypotheses about possible mechanisms that may underlie the association between ELA and inflammation, we extended race-stratified models. The stratified models were adjusted for educational attainment to control for SEP, in addition to age, gender, medication use, and prior history of CVD, diabetes, and cancer. We assessed the potential role of BMI and health behaviors, adult stress events, and depressive symptoms by considering the percent change in the size of the ELA coefficient when these covariates were included.

The sample included 103 pairs of twins, and no sibling pairs: 101 pairs of twins were White and 2 were Black. For models that included White participants, we ran models using (1) ordinary regression, and (2) generalized estimating equations (GEE) to account for clustering. We observed that the findings were nearly identical. Given that there were only 2 sets of twins in the African American sample, GEE was not appropriate for models that included only African American participants. Therefore, in order to test the potential effect of the 2 twin pairs in the African American sample within race-stratified models, we compared models using the full sample to models that excluded the 2 sets of twins: we observed that the results were unchanged. Informed by these sensitivity analyses documenting that our findings are not affected by the presence of twins, we present the findings from the single-level models in order to present a consistent modeling strategy for all analyses.

Missing Data

Information from the mail survey was used in the measures of ELA and adult stress events and some surveys were returned with incomplete information. We used multiple imputation to estimate missing values for the measures within the composite scores of ELA and adult stress events. Multiple imputation is a strategy that can reduce bias, and is preferred to complete case analysis because it does not assume that data is missing completely at random and makes full

use of available data (43). IVEware (44) was used to create 10 imputed datasets and PROC MIANALYZE was used for the regression models to analyze the imputed data.

Results

Table 1 presents characteristics of the White and African American participants. The mean age of the sample was 57.86 years (range: 35–86). African American participants were younger, less educated, and more likely to be female than White participants. On average, the African American respondents had a higher ELA score, but this difference was not statistically significant ($p=0.08$). The mean inflammation values for the Black respondents were significantly higher for CRP, IL-6, fibrinogen, and E-selectin relative to the White respondents (all p -values $<.01$); there was not a significant difference by race for sICAM-1 ($p=0.96$).

Table 2 presents multiple regression models adjusted for age, gender, and medication use. In the first set of models, we tested our hypothesis that individuals exposed to high levels of ELA have increased risk for elevated markers of inflammation in adulthood. ELA was significantly associated with elevated concentration of sICAM-1 ($b=9.17$, $p<.05$), but not with any of the other outcomes. In a second set of models, which included an interaction term to examine effect modification by race, all 5 inflammatory outcomes and the summary score showed a significant interaction between ELA and race. These models indicated that higher inflammation level was associated with ELA for the African American respondents, relative to the White respondents, for each outcome. Therefore, we used race-stratified models for the remainder of our analysis.

Table 3 presents race-stratified models, adjusted for age, gender, medications, and educational attainment. For the White sample, the models did not indicate a main effect of ELA for any of the inflammatory markers or the summary score. However, for the Black sample, models indicated that ELA had a significant positive association with log IL-6 ($b=0.11$, $SE=0.05$; $p<.05$), fibrinogen ($b=15.66$, $SE=7.03$; $p<.05$), E-selectin ($b=3.54$, $SE=1.70$; $p<.05$), sICAM-1 ($b=29.49$, $SE=12.90$; $p<.05$), and the summary score ($b=0.25$, $SE=0.10$; $p<.05$). The association for log CRP was marginally significant in the expected direction ($b=0.14$, $SE=0.09$; $p=0.12$), therefore it was retained for consideration in the extended models.

In Table 4, we present extended models to examine whether the observed associations between ELA and the inflammatory outcomes in the Black sample were independent of potentially relevant variables. The models were organized to consider the impact of adjustment for (1) BMI, smoking, and vigorous exercise, (2) adult stressful life events, and (3) depressive symptoms. The baseline (comparison) model (Model 1) in this analysis is adjusted for age, gender, medications, educational attainment, and prior history of CVD, diabetes or cancer. The effect estimates in Model 1 show statistically significant associations between ELA and IL-6, fibrinogen, E-selectin, sICAM-1, and the summary score, adjusting for the covariates noted above. Model 2, which includes covariates for vigorous exercise, smoking status, and BMI, shows that significant positive associations between ELA and fibrinogen, E-selectin, sICAM-1 and the summary score were maintained; however, the association between ELA and log IL-6 was no longer statistically significant. The percent change in the size of the ELA parameter estimates were largest for log IL-6, fibrinogen, and the summary score when exercise, smoking status, and BMI were included in the models (8–16%), whereas the estimated coefficients for E-selectin and sICAM-1 were relatively similar to Model 1.

Model 3 included a covariate for adult stress events; in this series of models, only sICAM-1 and the summary score maintained significant associations with ELA; the significance of the associations between ELA with IL-6, fibrinogen, and E-selectin dropped below $p=0.05$. Relative to the baseline model, the parameter estimates were reduced by 10%, 17%, 25% and 13%, respectively, for IL-6, fibrinogen, E-selectin, and summary score. The coefficient for

sICAM-1 did not change. In Model 4, we included a covariate for depressive symptoms: the parameter estimates for the association between ELA with fibrinogen and the summary score remained significant at $p < .05$, whereas the other associations were no longer statistically significant. For this model including depressive symptoms, the coefficient estimate for the association between ELA and E-selectin was substantially attenuated in comparison to Model 1 (reduced by 28%).

This series of extended models suggests that the association between ELA and inflammation may partially operate through the influence of ELA on health behaviors and particularly, BMI. In general, the coefficients for adult stress events and depressive symptoms were not significant in these adjusted models, yet inclusion of these covariates causes the effect of ELA to drop from significance for several of the inflammatory markers. This may suggest that these variables have a small role for some of the observed associations that cannot be detected in our small sample.

Of note, for the majority of the inflammatory markers that have significant associations with ELA, standard cut-points for clinically meaningful risk are not yet established. However, the extended models can provide insight on biological significance by allowing for a comparison between the estimated coefficients for ELA and the estimated coefficients for BMI, a known risk factor for a wide range of chronic diseases (45). For each of the outcomes considered, each one unit increase in ELA (i.e., equivalent to the standard deviation) is associated with an increase in inflammatory score that is larger than the increase associated with each one unit increase in BMI (see Table 4, Model 2).

Supplemental Analyses

In order to rule out concern that the associations between ELA and inflammation were caused by the dominant influence of one component of our ELA measure, we performed post-hoc analyses to determine if there was a single necessary component for the patterns observed. We replicated our models using ELA measures that included only 2 of the 3 scales that comprised our measure (data not shown). In these analyses, the statistical interaction effects were largely unchanged for all 3 variations, demonstrating that there is not a dominant component causing the effect modification by race. In the race-stratified models with the African American sample, the coefficient estimates for the partial ELA scores were generally smaller than the estimates obtained with the original measure, which demonstrates the value of integrating multiple forms of adversity. In addition, we examined a complete-case analysis and found comparable results to those obtained using multiple imputed data sets.

Discussion

The data from the MIDUS provide a unique opportunity to examine the association between ELA and inflammation, and to compare the impact of ELA on these markers for African Americans and Whites in the sample. In comparison to prior investigations of the association between adversity in childhood and later inflammation, the pattern of our results is generally consistent with previous findings for the African Americans in our sample, but not for the White participants (5,6,16–18).

Previous research related to the association between ELA and inflammation that has utilized racially-heterogeneous samples (6,16) show inconsistent findings with regard to uniformity of effects across racial groups. In some studies, results are consistent for African Americans and Whites (6), whereas in other studies this is not the case (16). For example, Pollitt and colleagues (16) found significant associations between cumulative exposure to low SEP and elevated fibrinogen and white blood cells for White participants; however, results were weaker and less consistent for African American participants. We were only able to identify one study with a

similar pattern to our findings (although the exposure was in adulthood rather than childhood): in a study of chronic stress burden, Troxel and colleagues (46) found that a composite stress index and unfair treatment were associated with higher carotid intima-media thickness among Blacks, but not Whites.

Theories of accelerated biological aging (23), which posit that differential exposure to adversities engender racial health disparities, may offer a possible explanation for this pattern. An implication of this notion is that physiological aging is accelerated in contexts of high exposure to adversity (47), and therefore statistical adjustment for chronological age cannot account for accelerated physiologic aging. Of note, the associations between ELA and some of the markers of inflammation were maintained for the African American sample in the race-stratified models even after adjustment for CVD, diabetes, and cancer (Table 4, Model 1); it is possible that because the sample is still in midlife, an accelerated course of aging may not have yet resulted in disease outcomes. Longer follow-up is needed in order to determine the potential role of accelerated aging in the associations observed here: a theory of accelerated aging will only be applicable if the association between ELA and inflammation is eventually observed for White participants as well. Research indicates that patterns consistent with accelerated aging are most pronounced in urban areas with high poverty concentration (23); this is important to note, given that a large majority of Blacks in our sample originates from Milwaukee, WI, a highly segregated city. Future studies should seek to identify the specific aspects of the social environment related to institutionalized discrimination that may have produced additional risk for the African American participants (e.g., neighborhood environment, work conditions).

There are several limitations to the present study. First, our measure of ELA was self-report and retrospective, which may lead to measurement inaccuracies. The questions used to generate the ELA assessments were only assessed at a single time-point, and therefore repeated measurement reliability of these retrospective measures cannot be assessed. Second, there are limitations associated with the sampling design. The majority of the African American respondents (85%) were recruited as part of the Milwaukee supplement sample; therefore, our analyses are largely describing White respondents originally recruited as part of a national sample, and African American respondents from Milwaukee, WI. In addition, for the African American participants only, the sample who participated in biological assessments had a slightly higher mean ELA summary score relative to African American respondents who did not participate in the biological assessment. Thus, the generalizability of our findings is unknown. An important next step is to repeat this analysis in more representative samples.

Third, although we hypothesize that depression may be on the pathway between ELA and inflammation, because depression and inflammation were measured concurrently, we do not have information about temporal ordering between these variables. Finally, due to limited sample size in the stratified models, we could not adjust for all covariates one might include in an ideal context (e.g., blood pressure, lipids); therefore, it is important to repeat this study in a larger sample that can accommodate additional covariates. Two strengths of this study include the broad set of inflammatory markers considered, and the application of a life course perspective to research on racial disparities in health in midlife. This study contributes to a growing body of research from MIDUS linking ELA to health (48,49); it expands on previous work by examining early experiences in relation to biomarkers of risk, and comparing the magnitude of these associations by race.

In conclusion, the present study found that ELA predicted markers of inflammation for the African Americans respondents, but not for the White respondents. A potential explanation for this pattern is that the African Americans in our sample, who were chronologically younger, are on an accelerated course of disease progression relative to Whites. Future research should

investigate how social trajectories following ELA may differ for African Americans and Whites, and work to identify exposures and behaviors throughout the life course that may exacerbate or attenuate the negative effect of ELA on later health.

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ACRONYMS

BMI	body mass index
CRP	C-reactive protein
CVD	cardiovascular diseases
E-selectin	endothelial leukocyte adhesion molecule-1
ELA	early life adversity
ELISA	enzyme-linked immunosorbent assay
GCRC	general clinical research center
IL-6	interleukin-6
MIDUS	Midlife in the United States survey
SEP	socioeconomic position
sICAM-1	soluble intercellular adhesion molecule-1

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Table 1

Characteristics of White and Black study participants (N=999); Study of Midlife in the U.S. (MIDUS)

	White Respondents (n=822) Mean (SD) or %	African American Respondents (n=177) Mean (SD) or %	p-value
Age	58.66 (11.65)	54.15 (10.71)	<0.001
Gender			
Male	47.20	32.77	0.001
Female	52.80	67.23	
Inflammatory Markers			
CRP (ug/mL)	2.75 (4.52)	4.93 (6.97)	<.0001
IL-6 (pg/mL)	2.73 (2.81)	4.11 (3.45)	<.0001
Fibrinogen (mg/dL)	336.00 (84.82)	386.80 (100.70)	<0.001
E-selectin (ng/mL)	38.44 (18.38)	43.75 (22.98)	0.001
sICAM-1 (ng/mL)	305.70 (98.74)	305.10 (177.80)	0.96
Summary score ^a	2.35 (1.51)	3.13 (1.39)	<0.001
Early life adversity (z-score)	0.01 (1.00)	0.17 (1.06)	0.08
Stress Events (z-score)	-0.13 (0.86)	0.39 (1.18)	<0.001
Relationship with Parents (z-score)	0.13 (1.00)	-0.20 (0.98)	<0.001
Verbal/Physical Abuse (z-score)	0.01 (1.01)	0.16 (1.10)	0.09
Education			
≤High school degree	24.09	46.89	<0.001
Some College	22.38	26.55	
Associates/Bachelors Degree	53.53	26.55	
Adult stress events (z-score)	-0.03 (0.96)	0.82 (1.29)	<0.001
Past 5 years (z-score)	-0.06 (0.92)	0.58 (1.50)	<0.001
6+ years ago (or unidentified; z-score)	0.01 (0.99)	0.61 (1.16)	<0.001
Health behaviors			
Current Smoker	11.21	29.94	<0.001
Ex-smoker	33.86	33.33	
Never Smoker	54.93	36.72	
Vigorous exercise ≥3 times/week	25.87	14.11	<0.001
BMI	29.14 (5.95)	33.35 (8.89)	<0.001
CVD diagnosis (% yes)	14.23	13.56	0.82
Diabetes diagnosis (% yes)	10.34	24.29	<0.001
Prior cancer diagnosis (% yes)	14.96	10.17	0.10
CES-D symptoms	7.99 (7.78)	12.46 (10.02)	<0.001
Current medications (% yes)			
Blood pressure medication	34.55	47.46	0.001
Cholesterol medication	29.93	18.64	0.002
Corticosteroid medication ^b	12.17	9.60	0.34
Anti-depressant medication	15.45	7.91	0.009

^aThe summary score ranges from 0 to 5; 1 point is given for each maker above the sample median.

^bCorticosteroid medication includes adrenals, estrogens, antiestrogens and estrogen agonistsantagonists.

Unstandardized ordinary least square regression coefficients (and standard errors) for inflammatory outcomes; Study of Midlife in the U.S. (MIDUS)

Table 2

	Log CRP ($\mu\text{g/mL}$) b(SE)	Log IL-6 (pg/mL) b(SE)	Fibrinogen (mg/dL) b(SE)	E-selectin (ng/mL) b(SE)	sICAM-1 (ng/mL) b(SE)	Summary ^a b(SE)
<i>Model 1. Baseline Models^b</i>						
Early life adversity (z-score)	0.01 (0.04)	0.01 (0.02)	2.48 (2.77)	0.84 (0.63)	9.17 (3.74)*	0.04 (0.05)
Race:						
African American	0.46 (0.10)***	0.47 (0.06)***	51.00 (7.39)***	4.73 (1.65)***	-1.42 (10.02)	0.75 (0.13)***
White (reference)	1.00	1.00	1.00	1.00	1.00	1.00
<i>Model 2. Including Interaction Term^b</i>						
Early life adversity (z-score)	-0.03 (0.04)	-0.02 (0.03)	-1.07 (3.09)	0.21 (0.70)	2.93 (4.16)	-0.03 (0.05)
Race:						
African American	0.43 (0.09)***	0.45 (0.06)***	48.71 (7.43)***	4.30 (1.67)**	-5.74 (10.05)	0.70 (0.13)***
White (reference)	1.00	1.00	1.00	1.00	1.00	1.00
Early Adversity x Race						
African American	0.22 (0.09)*	0.16 (0.06)**	17.52 (6.76)**	3.13 (1.53)*	31.23 (9.16)**	0.34 (0.12)**
White (reference)	1.00	1.00	1.00	1.00	1.00	1.00

^aThe summary score ranges from 0 to 5; 1 point is given for each marker above the sample median.

^bModels 1 and Model 2 include the presented covariates, in addition to age, gender, and medication use (blood pressure, cholesterol, steroid, and anti-depressant medications). Unstandardized coefficients and standard errors are from separate linear regression models.

* $P < .05$;

** $P < .01$;

*** $P < .001$

Unstandardized ordinary least square regression coefficients (and standard errors) for inflammatory outcomes in race-stratified models; Study of Midlife in the U.S. (MIDUS)

Table 3

	Log CRP (ug/mL) b(SE)	Log IL-6 (pg/mL) b(SE)	Fibrinogen (mg/dL) b(SE)	E-selectin (ng/mL) b(SE)	sICAM-1 (ng/mL) b(SE)	Summary ^a b(SE)
<i>White Sample^b</i>						
Early life adversity (z-score)	-0.04 (0.04)	-0.02 (0.03)	-1.96 (3.01)	0.17 (0.67)	2.86 (3.56)	-0.04 (0.05)
<i>African American Sample^b</i>						
Early life adversity (z-score)	0.14 (0.09)	0.11 (0.05) [*]	15.66 (7.03) [*]	3.54 (1.70) [*]	29.49 (12.90) [*]	0.25 (0.10) [*]

^aThe summary score ranges from 0 to 5; 1 point is given for each marker above the sample median.

^bModels adjusted for age, gender, education, and medication use (blood pressure, cholesterol, steroid, and anti-depressant medications). Unstandardized coefficients and standard errors are from separate linear regression models.

^{*} P<.05;
^{**} P<.01;
^{***} P<.001

African American sample, models extended to include health behaviors, adult stress events, and depressive symptoms; Study of Midlife in the U.S. (MIDUS)

Table 4

	Log CRP (ug/mL) b(SE)	Log IL-6 (pg/mL) b(SE)	Fibrinogen (mg/dL) b(SE)	E-selectin (ng/mL) b(SE)	sICAM-1 (ng/mL) b(SE)	Summary ^a b(SE)
<i>Model 1. Baseline (Comparison) Model^b</i>						
Early life adversity (z-score)	0.13 (0.09)	0.10 (0.05)*	15.69 (7.10)*	3.69 (1.72)*	28.32 (13.02)*	0.24 (0.10)*
<i>Model 2. Health Behaviors^b</i>						
Early life adversity (z-score)	0.10 (0.08)	0.09 (0.05)	13.19 (6.56)*	3.80 (1.72)*	29.11 (13.01)*	0.22 (0.09)*
Current smoker	0.10 (0.22)	0.29 (0.14)*	20.26 (18.55)	4.03 (4.72)	46.92 (36.01)	0.37 (0.25)
Ex-smoker	0.10 (0.21)	0.08 (0.13)	-4.99 (17.00)	-5.75 (4.40)	-14.67 (33.57)	-0.22 (0.23)
Never smoked (ref)	1.00	1.00	1.00	1.00	1.00	1.00
Vigorous exercise	-0.38 (0.25)	-0.01 (0.16)	-19.76 (20.56)	-4.79 (5.34)	-58.90 (40.75)	-0.76 (0.28)*
BMI	0.06 (0.01)***	0.03 (0.01)***	4.84 (0.84)***	0.04 (0.22)	-0.11 (1.65)	0.06 (0.01)***
<i>Model 3. Stressful Events in Adulthood^b</i>						
Early life adversity (z-score)	0.10 (0.10)	0.09 (0.06)	12.98 (7.75)	2.77 (1.86)	29.33 (14.16)*	0.21 (0.10)*
Adult stress events (z-score)	0.07 (0.08)	0.03 (0.05)	5.97 (6.83)	2.08 (1.60)	-2.30 (12.30)	0.07 (0.09)
<i>Model 4. Depressive Symptoms^b</i>						
Early life adversity (z-score)	0.13 (0.09)	0.11 (0.06)	16.21 (7.40)*	2.66 (1.80)	27.01 (13.87)	0.22 (0.10)*
CES-D Symptoms	0.00 (0.01)	0.00 (0.01)	-0.08 (0.85)	0.42 (0.20)*	0.56 (1.58)	0.01 (0.01)

^aThe summary score ranges from 0 to 5; 1 point is given for each marker above the sample median.

^bModels 1, 2, 3 and 4 include the covariates presented, in addition to age, gender, education, medication use (blood pressure, cholesterol, steroid, and anti-depressant medications), and indicator variables for prior history of CVD, diabetes and cancer. Unstandardized coefficients and standard errors are from separate linear regression models.

* P<.05;

** P<.01;

*** P<.001