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# Systemic Inflammation in Midlife: Race, Socioeconomic Status, and Perceived Discrimination

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**Introduction:** This study investigates social determinants of systemic inflammation, focusing on race, SES, and perceived discrimination.

**Methods:** Data on 884 white and 170 black participants were obtained from the Survey of Midlife in the U.S., a cross-sectional observational study combining survey measures, anthropometry, and biomarker assay. Data, collected in 2004–2009, were analyzed in 2016. Main outcome measures were fasting blood concentrations of C-reactive protein, interleukin 6, fibrinogen, and E-selectin. For each biomarker, series of multivariate linear regression models were estimated for the pooled sample and separately for blacks and whites. Full models included social determinants; psychological, lifestyle, and health factors; and demographic covariates.

**Results:** Bivariate analyses indicated higher concentrations of all inflammation markers among blacks compared with whites ($p<0.001$). In fully adjusted models using the pooled sample, racial differences persisted for interleukin 6 ($p<0.001$) and fibrinogen ($p<0.01$). For E-selectin and C-reactive protein, racial differences were explained after adjusting for covariates. Education was linked to lower fibrinogen concentration ($p<0.05$) in the fully adjusted model and C-reactive protein concentration ($p<0.01$) after adjusting for demographic factors and income. Lifetime perceived discrimination was related to higher concentrations of fibrinogen ($p<0.05$) in the fully adjusted model, and higher concentrations of E-selectin and interleukin 6 ($p<0.05$) after adjusting for socioeconomic status (SES) and demographic factors.

**Conclusions:** This study clarifies the contributions of race, SES, and perceived discrimination to inflammation. It suggests that inflammation-reducing interventions should focus on blacks and individuals facing socioeconomic disadvantages, especially low education.

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## INTRODUCTION

Systemic inflammation has received attention as a preventable factor in chronic conditions such as hypertension,[1] cardiovascular disease,[2,3] insulin resistance,[4] Type 2 diabetes,[3,5–7] and cancer.[8–10] Smoking,[11] alcohol consumption,[12] sedentary lifestyle,[13,14] and obesity,[4,15,16] are established factors in inflammation. Recent research, however, indicates that social determinants are as important—if not more important—as health behaviors for shaping health.[17,18] In fact, social determinants affect both the biological processes and health lifestyles of individuals.

Key social determinants of health include SES and race/ethnicity.[19–21] Higher inflammation levels among racial/ethnic minorities, especially blacks,[22–24] and individuals with lower SES[25,26] have been reported, but several investigations do not corroborate these findings.[1,27] Others argue that the role of SES in inflammation varies with SES measures[28] and racial/ethnic background.[29]

Perceived discrimination (PD) has been suggested as another social factor with relevance to inflammation. PD has been associated with inflammation among young

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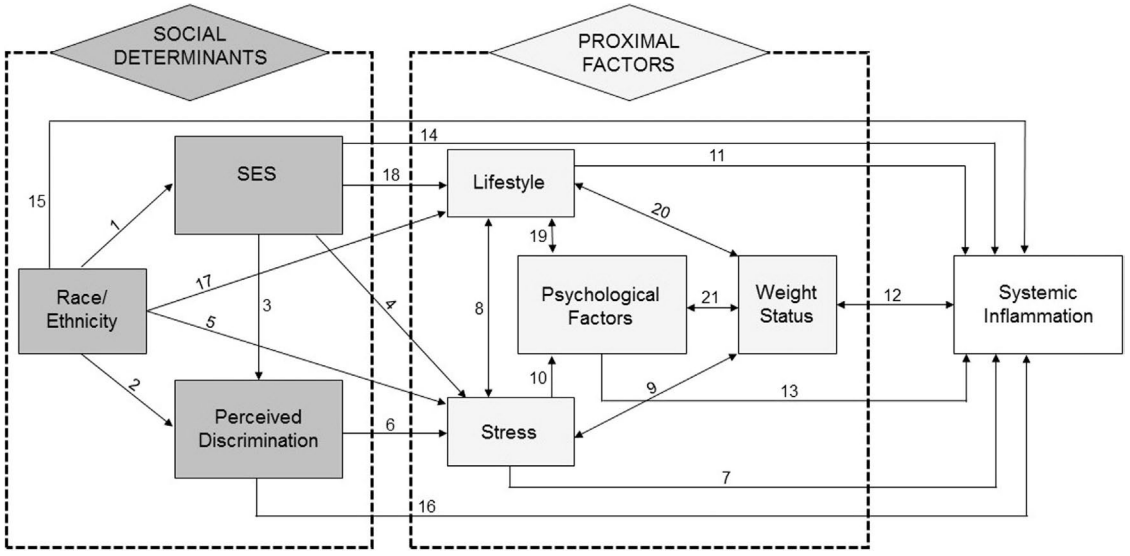


**Figure 1.** Social determinants of systemic inflammation: conceptual model.

adults,[30] midlife adults,[31] low-income black youths,[32] and older blacks,[33] although the Dallas Heart Study showed no relationship between PD and inflammation among blacks, Hispanics, and whites.[34] In other studies, the link between PD and inflammation was limited to specific subpopulations, including women anticipating a racial threat[35] and non-obese women.[36]

One important limitation of most prior research on inflammation is the lack of a theoretically grounded framework. To address this limitation, this study proposes a conceptual model of social determinants of inflammation (Figure 1) informed by fundamental cause theory (FCT), a sociological perspective. FCT postulates social determinants as key causes shaping health outcomes through multiple pathways that can evolve dynamically across life stages and historic periods in response to societal and technologic changes.[37–39]

Using the FCT, the proposed model specifies that SES, race, and PD act as key social determinants of inflammation. SES is a multidimensional construct consisting of income, education, and occupational prestige[40]; this study focuses more specifically on income and education as dimensions strongly associated with health outcomes in the U.S.[41,42] In the conceptual model, minority race contributes to lower SES[20] (Arrow 1) and to higher PD, which is also linked to lower SES[43–47] (Arrows 2 and 3). Proximal factors are those through which social determinants influence inflammation. Stress, an established mechanism leading to poor health,[48–50] is linked to all three social determinants specified in this model, with minorities, persons of lower SES, and those exposed to discrimination experiencing higher stress (Arrows 4–6). Stress harms health through overactivation of the biological stress response system, which may directly lead to increased inflammation (Arrow 7); furthermore, it contributes to unhealthy lifestyle and poorer psychological health (Arrows 8–10), which are also implicated in inflammation (Arrows 11–13).[11–14,51–54]

Figure 1 illustrates the complexity of relations among social determinants and inflammation. In addition to effects through proximal factors, the model allows for direct effects of unspecified mechanisms (Arrows 14–16). Reciprocal relationships reflect yet-unknown causal direction. Because of the model's complexity, comprehensive evaluation is outside the scope of this study. Instead, the study focuses on evaluating select components using three hypotheses:

1. Inflammation levels are higher among blacks compared with whites.
2. Inflammation levels decrease with higher SES.
3. Inflammation levels are higher among persons reporting PD.

This study sequentially evaluates the contribution of each group of proximal factors as suggested by the conceptual model, using a hierarchy-of-effects approach.[55] In addition to testing for the pooled sample, inflammation is modeled separately for blacks and whites because factors contributing to inflammation may vary by race/ethnicity.[29,30,51–54]

## METHODS

### Data Sample

Data were obtained from the Survey of Midlife in the U.S., an ongoing national survey using a random-digit-dial sample representative of non-institutionalized English-speaking residents of 48 contiguous U.S. states who are aged ≥35 years.[56] The present study was limited to 1,054 participants in the biomarker sub-study

that collected biological specimens (whites, $n$=884; blacks, $n$=170). Sub-study participants are similar to the national sample on age, sex, race, marital status, income, and health characteristics (subjective health, chronic conditions, activities of daily living, exercise, alcohol consumption, health insurance, physician visits) but are more educated and less likely to smoke.[57] Data collection took place between 2004 and 2009. Biological specimens and anthropometry were collected by trained staff during an overnight clinic stay. Demographic, social, and psychological indicators were measured using mail surveys and telephone interviews.

## Measures

Biomarkers of systemic inflammation included C-reactive protein (CRP), which is produced by hepatocytes in response to infection or injury[58]; interleukin 6 (IL-6), a proinflammatory cytokine; fibrinogen, a blood clotting factor involved in the coagulation response to vascular injury[59]; and soluble E-selectin, an endothelial adhesion molecule expressed as a result of endothelial damage.[60] Fibrinogen concentrations (mg/dL) and CRP concentrations (ug/mL) were measured in citrated plasma using immunoturbidometric assay. Soluble E-selectin concentrations (ng/mL) and IL-6 concentrations (pg/mL) were measured in serum using enzyme-linked immunosorbent assay. Standardized procedures were used for fasting blood samples collection and processing.

Race was self-reported and categorized as black and white. Dimensions of SES were years of education and annual household income from all sources, measured in U.S. dollars and log-transformed. Age in years and gender (woman=1, man=0) were also included.

The Daily Discrimination and Lifetime Discrimination scales[61] were used to measure PD. Consistent with the argument that PD is harmful to health regardless of the reason (race/ethnicity, gender, or others),[47] these scales measure PD experiences of any type. The Daily Discrimination scale asks respondents how often they experience each of nine types of discrimination (e.g., being treated with less courtesy, less respect, or receiving poorer service at restaurants because of race/ethnicity, gender, age, religion, physical appearance, sexual orientation, or other characteristics [*never*=1, *rarely*=2, *sometimes*=3, *often*=4]). The Daily Discrimination scale totals the responses; higher values indicate higher levels of perceived discrimination. The Lifetime Discrimination scale measures experiences of major discriminatory events in life domains including employment, education, health care, and housing. Examples include not being hired for a job or being prevented from renting or buying a home. Respondents are asked how many times in their lifetime they have experienced each event. Lifetime discrimination is calculated as a total of items for which respondents indicate experiencing the event at least once.

Measures of generalized anxiety and depressed affect were based on Wang et al.[62] The generalized anxiety scale consists of ten items, for example: *How often over the past 12 months were you restless because of your worry?*; the scale totals items for which *most days* was chosen. For depressed affect, respondents were asked: *During the past 12 months, was there ever a time when you felt sad, blue, or depressed for 2 weeks or more in a row?* (*yes*/*no*), and an additional seven items, for example, *During two weeks in past 12 months, when you felt sad, blue, or depressed, did you feel more tired out or low on energy than is usual?* (*yes*/*no*). The depressed affect scale totals *yes* answers on these seven items. This study also used three scales representing Negative Emotionality in Multidimensional Personality Questionnaire[63]: stress reactivity (three items; e.g., *minor setbacks sometimes irritate me too much*), aggression (four items; e.g., *when I get angry I am often ready to hit someone*), and alienation (three items; e.g., *I would be more successful if people did not make things difficult for me*). Items use a 1–4 response scale (false to true). A sum of responses is calculated for each scale.

Participants' BMI, a measure of weight status (calculated as $kg/m^2$), was based on anthropometric data. Two dichotomous indicators for weekly strenuous physical activity and weekly moderate physical activity were included (Appendix 1, available online), as well as two indicators of smoking capturing whether respondents ever smoked cigarettes regularly and whether they currently smoked cigarettes regularly (both *yes*/*no*). Because of potential effects on inflammation, current preventive use of aspirin was included. Finally, models controlled for chronic conditions during the past 12 months that had prevalence $\geq$5% in the sample and showed relationships with inflammation at $p<0.10$ in preliminary analyses. These conditions included high blood pressure/hypertension (henceforth hypertension), diabetes/high blood sugar (henceforth diabetes), joint/bone diseases, persistent skin trouble, teeth trouble, and sleep problems.

## Statistical Analysis

First, descriptive statistics for the pooled sample and by race were obtained. *T*-tests were used to compare blacks with whites on continuous variables, and chi-square tests were performed for categorical variables. Next, series of multivariate linear regression models of each inflammation marker were estimated; robust estimators accounted for deviations from normality. Because CRP and IL-6 had skewed distributions, they were log-transformed for modeling purposes. Model 1 included race and demographic covariates (gender, age). Model 2 added income and education. Model 3 further added PD measures. Model 4 added psychological factors. Model 5 added lifestyle (smoking indicators, physical activity indicators, and BMI). Finally, Model 6 added health characteristics, including preventive use of aspirin and chronic conditions. After estimating multivariate models for the pooled sample, Models 2–6 were estimated separately by race.

# RESULTS

As shown in Table 1, blacks had higher concentrations of all four biomarkers of inflammation compared with whites ($p<0.001$).They had lower SES as indicated by fewer years of education and lower income, and scored higher on both measures of PD, as well as generalized anxiety, alienation, and BMI ($p$-values$<0.001$). They were also more likely to smoke regularly ($p<0.01$) and less likely to engage in weekly physical activity (vigorous, $p<0.05$; moderate, $p<0.001$). They had higher rates of diabetes, teeth problems ($p$-values$<0.001$), joint/bone disease, and sleep problems ($p$-values$<0.01$), but lower rates of hypertension ($p<0.001$) and preventive aspirin use ($p<0.05$). Demographically, blacks were younger ($p<0.001$) and more commonly women ($p<0.01$).

Table 2 summarizes results of multivariate models of inflammation markers for the pooled sample. Because of

**Table 1.** Characteristics of the Pooled Sample and by Racial Background

| Variable[a] | All ($n$=1,054) | Blacks ($n$=170) | Whites ($n$=884) |
|---|---|---|---|
| Systemic inflammation markers | | | |
| Fibrinogen, mg/dL (range, 94.0–857.0) | 348.36 (88.24) | **388.70 (101.67)**$^{***}$ | 340.61 (83.27) |
| E-selectin, ng/mL (range, 0.1–161.9) | 42.51 (22.01) | **49.19 (25.75)**$^{***}$ | 41.22 (20.99) |
| CRP, ug/mL (range, 0.1–59.3) | 3.11 (5.01) | **4.78 (6.90)**$^{***}$ | 2.79 (4.49) |
| IL-6, pg/mL (range, 0.2–21.8) | 2.97 (2.90) | **3.91 (3.05)**$^{***}$ | 2.79 (2.83) |
| SES | | | |
| Education, years (range, 2–20) | 14.75 (2.56) | **13.58 (2.75)**$^{***}$ | 14.98 (2.46) |
| Income, log $ (range, 0–30) | 10.27 (3.77) | **9.81 (3.45)**$^{***}$ | 10.36 (3.83) |
| Perceived discrimination | | | |
| Daily (range, 9–32) | 12.87 (4.60) | **14.65 (6.46)**$^{***}$ | 12.53 (4.07) |
| Lifetime (range, 0–11) | 1.23 (1.90) | **3.02 (2.82)**$^{***}$ | 0.88 (1.44) |
| Psychological factors | | | |
| Depression (range, 0–7) | 0.72 (1.85) | 0.88 (2.06) | 0.69 (1.81) |
| Anxiety (range, 0–10) | 0.15 (.94) | **0.41 (1.64)**$^{***}$ | 0.10 (.73) |
| Stress reactivity (range, 3–12) | 6.15 (2.31) | 6.45 (2.61) | 6.09 (2.24) |
| Aggression (range, 4–14) | 5.31 (1.66) | 5.36 (1.65) | 5.30 (1.66) |
| Alienation (range, 3–12) | 5.14 (1.89) | **6.04 (2.39)**$^{***}$ | 4.96 (1.73) |
| Lifestyle factors | | | |
| Ever regular smoker | 44.6 | **55.9**$^{**}$ | 42.4 |
| Currently regular smoker | 12.9 | **25.9**$^{***}$ | 10.4 |
| Vigorous physical activity | 30.5 | **22.4**$^{*}$ | 32.0 |
| Moderate physical activity | 44.1 | **30.6**$^{***}$ | 46.7 |
| BMI (range, 14.23–161.10) | 30.6 (13.99) | **34.59 (17.79)**$^{***}$ | 29.84 (13.01) |
| Health factors | | | |
| Preventive aspirin | 31.2 | **24.7**$^{*}$ | 32.5 |
| Chronic conditions | | | |
| Hypertension | 72.0 | **58.8**$^{***}$ | 75.0 |
| Diabetes | 10.0 | **18.8**$^{***}$ | 8.3 |
| Joint/bone diseases | 27.0 | **37.6**$^{**}$ | 25.0 |
| Persistent skin trouble | 9.1 | **7.1** | 9.5 |
| Teeth problems | 6.5 | **14.1**$^{***}$ | 5.1 |
| Sleep problems | 12.6 | **20.6**$^{**}$ | 11.1 |
| Demographic factors | | | |
| Age, y (range, 35–82) | 54.56 (11.62) | **51.27 (10.48)**$^{***}$ | 55.19 (11.73) |
| Woman | 56.6 | **67.6**$^{**}$ | 54.5 |

*Source:* Survey of Midlife in the U.S. (MIDUS II).
*Note*: Values are M (SD) for continuous variables and percentages for dichotomous variables. *T*-tests were used to compare blacks to whites on continuous variables. $\chi^2$ tests were used to compare blacks to whites on categorical variables. Boldface indicates statistical significance of the differences between blacks and whites ($^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$; two-tailed tests).
[a]Ranges are given for continuous variables only.
CRP, C-reactive protein; IL-6, interleukin 6; y, years.

space limitations, only Models 2, 3, and 6 are displayed; Models 1, 4, and 5 appear in Appendix 2 (available online). In Model 3, which included race, SES, PD, and demographic covariates, blacks had higher concentrations of fibrinogen ($p>0.001$), IL-6 ($p>0.001$), CRP ($p<0.01$), and E-selectin ($p<0.05$), lending support to Hypothesis 1. In fully adjusted models (Model 6), higher levels of IL-6 ($p<0.001$) and fibrinogen ($p<0.01$) among blacks persisted, though the coefficients underwent attenuation. For E-selectin, the black–white difference was explained after including PD, SES, psychological characteristics, and lifestyle factors in Model 5 (Table 1); for CRP, the difference was explained when health factors were controlled in Model 6. Hypothesis 2, which argues that inflammation decreases with SES, was supported for education but not for income in the pooled sample. Individuals with higher education had lower concentrations of fibrinogen ($p<0.05$ in Model 6) and

**Table 2.** Coefficients from Linear Regression Models for Systemic Inflammation Markers: Pooled Sample ($n$=1,054)

| | Fibrinogen[a] | | | E-selectin[b] | | | CRP[c] | | | IL-6[d] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** |
| Demographic factors | | | | | | | | | | | | |
| Age, y | **1.13**$^{***}$ (0.25) | **1.17**$^{***}$ (0.25) | **1.07**$^{***}$ (0.28) | **−0.19**$^{**}$ (0.05) | **−0.17**$^{**}$ (0.06) | **−0.23**$^{**}$ (0.07) | 0.005 (0.003) | 0.01 (0.003) | 0.001 (0.003) | **0.01**$^{***}$ (0.002) | **0.01**$^{***}$ (0.002) | **0.01**$^{***}$ (0.002) |
| Woman | **29.51**$^{***}$ (5.15) | **28.33**$^{***}$ (5.14) | **30.18**$^{**}$ (5.46) | **−4.25**$^{**}$ (1.35) | **−4.54**$^{**}$ (1.34) | **−4.15**$^{**}$ (1.40) | **0.37**$^{***}$ (0.07) | **0.36**$^{***}$ (0.07) | **0.07**$^{***}$ (0.39) | 0.06 (0.04) | 0.05 (0.05) | 0.07 (0.05) |
| Social determinants | | | | | | | | | | | | |
| Race, black | **45.49**$^{***}$ (8.34) | **34.53**$^{***}$ (9.51) | **29.25**$^{**}$ (9.71) | **7.25**$^{**}$ (2.10) | **4.52**$^{*}$ (2.28) | 2.52 (2.34) | **0.45**$^{***}$ (0.10) | **0.36**$^{**}$ (0.11) | 0.16 (0.12) | **0.43**$^{***}$ (0.06) | **0.36**$^{***}$ (0.07) | **0.28**$^{***}$ (0.07) |
| SES | | | | | | | | | | | | |
| Education, y | **−2.59**$^{**}$ **(**1.07) | **−2.86**$^{**}$ (1.09) | **−2.34**$^{*}$ (1.10) | −0.43 (0.027) | −0.46 (0.27) | −0.21 (0.28) | **−0.04**$^{**}$ (0.01) | **−0.04**$^{**}$ (0.02) | −0.03 (0.02) | −0.01 (0.01) | −0.02 (0.01) | −0.001 (0.01) |
| Income, log $ | 0.82 (0.56) | 0.91 (0.56) | 0.82 (0.57) | 0.11 (0.014) | 0.13 (0.13) | 0.08 (0.15) | 0.01 (0.01) | 0.01 (0.01) | 0.01 (0.01) | 0.0004 (0.01) | 0.001 (0.01) | −0.003 (0.01) |
| Perceived discrimination | | | | | | | | | | | | |
| Daily | | −0.06 (0.69) | −0.42 (0.73) | | 0.18 (0.18) | 0.07 (0.19) | | 0.01 (0.01) | 0.003 (0.01) | | 0.002 (0.01) | −0.01 (0.01) |
| Lifetime | | **5.18**$^{**}$ (1.95) | **4.52**$^{*}$ (1.90) | | **1.14**$^{*}$ (0.47) | 0.81 (0.48) | | 0.04 (0.02) | 0.02 (0.02) | | **0.03**$^{*}$ (0.01) | 0.02 (0.01) |
| Psychological factors | | | | | | | | | | | | |
| Depressed affect | | | 0.46 (1.71) | | | 0.10 (0.43) | | | −0.01 (0.02) | | | 0.02 (0.02) |
| General anxiety | | | −2.33 (2.66) | | | **−1.71**$^{**}$ (0.62) | | | 0.05 (0.04) | | | 0.001 (0.03) |
| Stress reactivity | | | −0.88 (1.37) | | | −0.33 (0.38) | | | −0.01 (0.02) | | | −0.02 (0.01) |
| Aggression | | | 0.14 (1.89) | | | 0.32 (0.47) | | | −0.01 (0.02) | | | 0.02 (0.01) |
| Alienation | | | 1.31 (1.68) | | | 0.53 (0.47) | | | 0.02 (0.02) | | | 0.03 (0.01) |
| Lifestyle factors | | | | | | | | | | | | |
| Ever regular smoker | | | −3.30 (6.11) | | | 1.51 (1.52) | | | 0.04 (0.08) | | | 0.07 (0.05) |
| Currently regular smoker | | | 0.78 (9.05) | | | 2.18 (2.63) | | | 0.06 (0.21) | | | 0.01 (0.07) |
| Vigorous physical activity | | | 1.88 (6.63) | | | −1.98 (1.64) | | | −0.07 (0.09) | | | **−0.12**$^{*}$ (0.06) |

*(continued on next page)*

**Table 2.** Coefficients from Linear Regression Models for Systemic Inflammation Markers: Pooled Sample ($n$=1,054) *(continued)*

| | Fibrinogen[a] | | | E-selectin[b] | | | CRP[c] | | | IL-6[d] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** |
| Moderate physical activity | | | −9.65<br>(6.15) | | | −0.98<br>(1.55) | | | −0.16<br>(0.08) | | | −0.07<br>(0.05) |
| BMI | | | **0.63**$^{*}$<br>(0.24) | | | 0.02<br>(0.04) | | | **0.01**$^{***}$<br>(0.003) | | | **0.01**$^{***}$<br>(0.0002) |
| Health factors | | | | | | | | | | | | |
| Preventive aspirin | | | 5.13<br>(6.51) | | | −1.21<br>(1.65) | | | 0.13<br>(0.08) | | | 0.02<br>(0.05) |
| Hypertension | | | −6.43<br>(6.72) | | | −2.34<br>(1.62) | | | −**0.24**$^{**}$<br>(0.08) | | | −**0.18**$^{**}$<br>(0.05) |
| Diabetes | | | 16.14<br>(9.75) | | | **8.75**$^{**}$<br>(2.84) | | | **0.31**$^{**}$<br>(0.11) | | | 0.06<br>(0.07) |
| Joint/bone diseases | | | −8.06<br>(6.72) | | | 1.68<br>(1.65) | | | 0.09<br>(0.08) | | | −0.01<br>(0.05) |
| Persistent skin trouble | | | 14.01<br>(10.17) | | | 0.94<br>(2.69) | | | −0.08<br>(0.12) | | | 0.12<br>(0.08) |
| Teeth problems | | | 17.93<br>(11.90) | | | 4.21<br>(3.81) | | | 0.26<br>(0.15) | | | 0.04<br>(0.09) |
| Sleep problems | | | 3.89<br>(9.00) | | | 0.18<br>(2.33) | | | 0.13<br>(0.12) | | | 0.07<br>(0.07) |
| Intercept | **292.40**$^{***}$ | **290.03**$^{***}$ | **284.89**$^{***}$ | **59.31**$^{***}$ | **55.32**$^{***}$ | **57.42**$^{***}$ | 0.38 | 0.24 | 0.46 | 0.15 | 0.09 | 0.12 |
| Model F | **17.94**$^{***}$ | **15.08**$^{***}$ | **5.69**$^{***}$ | **8.24**$^{***}$ | **7.82**$^{***}$ | **3.33**$^{***}$ | **14.10**$^{***}$ | **11.66**$^{***}$ | **7.82**$^{***}$ | **23.16**$^{***}$ | **17.30**$^{***}$ | **8.77**$^{***}$ |
| $R^2$, % | 9.45 | 10.44 | 13.23 | 3.83 | 5.06 | 8.74 | 6.36 | 6.86 | 14.10 | 8.85 | 9.46 | 15.68 |

*Source:* Survey of Midlife in the U.S. (MIDUS II).
*Note*: Values are coefficients unless otherwise noted; standard errors appear in parentheses. Robust estimators are used. Boldface indicates statistical significance ($^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$; two-tailed tests).
[a]mg/dL.
[b]ng/mL.
[c]log ug/mL.
[d]log pg/mL.
CRP, C-reactive protein; IL-6, interleukin 6; y, years.

CRP ($p<0.01$ in Model 3); a trend toward lower E-selectin was evident as well ($p<0.10$ in Model 3). Lifetime perceived discrimination was related to higher concentrations of fibrinogen ($p<0.05$ in Model 6), E-selectin ($p<0.05$ in Model 3), and IL-6 ($p<0.05$ in Model 3). These results support Hypothesis 3, which predicts increased inflammation with PD.

Tables 3 and 4 shows multivariate model estimates separately for whites and blacks. Results for whites were similar to the pooled sample and generally supportive of Hypothesis 2; one exception concerns income, which showed a positive relation to E-selectin ($p<0.05$ in Model 6). Models for blacks supported the hypothesized inverse relationships between education and CRP ($p<0.05$, Model 3) and between income on E-selectin ($p<0.01$, Model 6). Hypothesis 3, however, was not supported for blacks, except for a marginally significant relationship between fibrinogen and lifetime perceived discrimination in Model 3 ($p<0.10$).

BMI showed a positive relationship with three inflammation markers in the pooled sample (Table 2, Model 6), including fibrinogen ($p<0.05$), CRP ($p<0.001$), and IL-6 ($p<0.001$). Among whites, CRP concentrations decreased with moderate physical activity, and IL-6 concentrations decreased with vigorous physical activity ($p$-values $<0.05$, Model 6, Table 3).

Among psychological factors, general anxiety was associated with higher CRP ($p<0.05$, Model 6, Table 4) and lower E-selectin ($p<0.01$) in blacks; there were also trends toward increased E-selectin with higher depressed affect and lower alienation in this racial group ($p$-values $<0.10$). Among whites, stress reactivity was linked to lower IL-6 ($p<0.05$, Model 6, Table 3), whereas alienation was linked to higher E-selectin ($p<0.05$, Model 6, Table 3). E-selectin concentrations further increased among blacks and whites who reported having diabetes ($p<0.05$, Model 6, Tables 3 and 4); among whites, diabetes was further linked to higher CRP ($p<0.01$, Model 6, Table 3). In whites, hypertension was inversely associated with IL-6 ($p<0.01$, Model 6, Table 3) and marginally with CRP ($p<0.10$); an inverse relationship between hypertension and CRP was also evident among blacks ($p<0.01$, Model 6, Table 4).

In models for the pooled sample (Table 2), older individuals had higher fibrinogen ($p<0.001$) and IL-6 ($p<0.001$), but lower E-selectin ($p<0.01$). Older whites had higher CRP ($p<0.05$, Model 3, Table 3), but the opposite was true for blacks ($p<0.01$ in Model 6, Table 4). Older blacks also had lower E-selectin ($p<0.05$, Model 3, Table 4). White women had higher fibrinogen and CRP ($p<0.001$, Model 6, Table 3), but lower E-selectin ($p$-values $<0.01$) compared with white men. Black women had higher fibrinogen and CRP ($p$-values $<0.01$, Model 6, Table 4), as well as higher IL-6 concentrations ($p<0.05$, Model 3, Table 4) compared with black men.

## DISCUSSION

Among the examined social determinants (race, SES, and PD), race was most consistently linked to inflammation, with blacks showing higher levels of all examined biomarkers. For fibrinogen and IL-6, racial differences tended to persist in fully adjusted models, whereas for E-selectin and CRP, racial differences were explained after including covariates. Consistent with research highlighting the importance of education for health,[41] inverse associations between inflammation markers and educational attainment were observed, especially among whites, and an inverse association between income and E-selectin was found for blacks. For whites, there was an increase—not a decrease—of E-selectin with income, suggesting that higher income may have protective effects for blacks but not for whites. PD, the third social determinant considered in this study, was related to increased concentrations of most biomarkers of inflammation, but only for lifetime discrimination, not daily discrimination. In supplementary analyses (data not shown), bivariate associations between daily discrimination and inflammation markers were statistically significant but dissipated after controlling for lifetime discrimination. The reasons for this are unclear. Daily discrimination represents relatively minor events, such as being given poor service in a restaurant. Nevertheless, chronic exposure to such experiences may influence responses to major lifetime discriminatory events and other race-related stressors once they occur, increasing physiologic and perceived stress and consequently harming health. More research is needed to disentangle these processes.

Importantly, the hypotheses proposed in this study received weaker support for blacks than for whites. This could be because of fewer blacks in the sample and lower statistical power, but the possibility that different mechanisms contribute to inflammation among different racial populations cannot be ruled out, especially in light of prior studies, in which education, weight status, and depressive symptoms showed weaker associations with inflammation among blacks compared with whites.[29,51–53,64] By contrast, the results of this study were less consistent with prior research, suggesting that the effects of PD on health are mediated by psychological factors. Few statistically significant relationships between psychological factors and inflammation emerged. The absence of positive associations between stress reactivity and inflammation biomarkers was especially surprising, given the known

**Table 3.** Coefficients from Linear Regression Models for Systemic Inflammation Markers by Racial Background

| | Whites ($n$=884) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fibrinogen[a] | | | E-selectin[b] | | | CRP[c] | | | IL-6[d] | | |
| **Variable** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** |
| Demographic factors | | | | | | | | | | | | |
| Age, y | **0.16**$^{***}$ (0.25) | **1.20**$^{***}$ (0.25) | **1.17**$^{***}$ (0.29) | **−0.15**$^{**}$ (0.06) | **−0.12**$^{*}$ (0.06) | **−0.19**$^{**}$ (0.07) | **0.01**$^{*}$ (0.003) | **0.01**$^{*}$ (0.004) | 0.002 (0.004) | **0.02**$^{***}$ (0.002) | **0.01**$^{***}$ (0.002) | **0.01**$^{***}$ (0.002) |
| Woman | **24.93**$^{***}$ (5.43) | **23.11**$^{***}$ (5.37) | **26.91**$^{***}$ (4.65) | **−4.66**$^{**}$ (1.43) | **−5.21**$^{**}$$^{*}$ (1.43) | **−4.56**$^{**}$ (1.50) | **0.34**$^{***}$ (0.08) | **0.32**$^{***}$ (0.08) | **0.37**$^{***}$ (0.08) | 0.03 (0.05) | 0.004 (0.05) | 0.04 (0.05) |
| Social determinants | | | | | | | | | | | | |
| SES | | | | | | | | | | | | |
| Education, y | **−2.87**$^{*}$ (1.20) | **−3.06**$^{*}$ (1.23) | −2.33 (1.22) | −0.54 (0.29) | −0.48 (0.29) | −0.23 (0.29) | **−0.04**$^{*}$ (0.02) | **−0.04**$^{*}$ (0.02) | −0.02 (0.02) | −0.013 (0.01) | −0.01 (0.01) | 0.0004 (0.01) |
| Income, log $ | 0.71 (0.48) | 0.76 (0.50) | 0.62 (0.51) | **0.31**$^{**}$ (0.10) | **0.33**$^{*}$ (0.11) | **0.31**$^{*}$ (0.12) | 0.02 (0.01) | 0.02 (0.01) | 0.01 (0.01) | −0.001 (0.01) | −0.0003 (0.01) | −0.003 (0.01) |
| Perceived discrimination | | | | | | | | | | | | |
| Daily | | −0.39 (0.78) | −0.59 (0.81) | | 0.37 (0.20) | 0.23 (0.22) | | 0.01 (0.01) | 0.002 (0.01) | | 0.01 (0.01) | 0.001 (0.01) |
| Lifetime | | **5.39**$^{*}$ (2.47) | 4.47 (2.35) | | **1.21**$^{*}$ (0.61) | 0.70 (0.62) | | 0.05 (0.03) | 0.03 (0.03) | | **0.06**$^{**}$ (0.02) | **0.04**$^{*}$ (0.02) |
| Psychological factors | | | | | | | | | | | | |
| Depressed affect | | | −0.51 (1.82) | | | −0.27 (0.43) | | | −0.01 (0.02) | | | 0.02 (0.02) |
| General anxiety | | | −1.17 (2.99) | | | −1.37 (0.96) | | | 0.002 (0.05) | | | −0.02 (0.03) |
| Stress reactivity | | | −1.74 (1.46) | | | −0.66 (0.40) | | | −0.01 (0.02) | | | **−0.03**$^{*}$ (0.01) |
| Aggression | | | 1.13 (2.01) | | | 0.41 (0.49) | | | 0.003 (0.03) | | | 0.02 (0.02) |
| Alienation | | | 1.79 (1.93) | | | **1.14**$^{*}$ (0.54) | | | 0.01 (0.03) | | | 0.02 (0.02) |
| Lifestyle factors | | | | | | | | | | | | |
| Ever regular smoker | | | −2.03 (6.31) | | | 2.29 (1.61) | | | 0.05 (0.09) | | | 0.07 (0.05) |
| Currently regular smoker | | | 2.58 (9.91) | | | −1.02 (2.83) | | | 0.03 (0.14) | | | −0.04 (0.08) |

*(continued on next page)*

**Table 3.** Coefficients from Linear Regression Models for Systemic Inflammation Markers by Racial Background *(continued)*

| | Whites ($n$=884) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fibrinogen[a] | | | E-selectin[b] | | | CRP[c] | | | IL-6[d] | | |
| **Variable** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** |
| Vigorous physical activity | | | 0.07<br>(7.02) | | | −2.04<br>(1.70) | | | −0.09<br>(0.10) | | | **−0.15**$^{*}$<br>(0.06) |
| Moderate physical activity | | | −10.17<br>(6.44) | | | −0.71<br>(1.61) | | | **−0.20**$^{*}$<br>(0.09) | | | −0.08<br>(0.06) |
| BMI | | | 0.48<br>(0.31) | | | 0.09<br>(0.05) | | | **0.01**$^{**}$<br>(0.004) | | | **0.01**$^{**}$<br>(0.002) |
| Health factors | | | | | | | | | | | | |
| Preventive aspirin | | | 4.27<br>(6.95) | | | −1.45<br>(1.72) | | | 0.13<br>(0.09) | | | 0.03<br>(0.06) |
| Hypertension | | | −4.67<br>(7.48) | | | −1.18<br>(1.70) | | | −0.18<br>(0.10) | | | **−0.19**$^{**}$<br>(0.06) |
| Diabetes | | | 14.77<br>(11.18) | | | **6.76**$^{*}$<br>(3.27) | | | **0.37**$^{**}$<br>(0.13) | | | 0.04<br>(0.09) |
| Joint/bone diseases | | | 14.02<br>(7.31) | | | 2.92<br>(1.73) | | | 0.04<br>(0.09) | | | −0.01<br>(0.06) |
| Persistent skin trouble | | | 15.98<br>(10.65) | | | −0.54<br>(2.49) | | | −0.01<br>(0.12) | | | 0.13<br>(0.09) |
| Teeth problems | | | 20.87<br>(15.09) | | | 7.70<br>(4.57) | | | 0.19<br>(0.19) | | | 0.09<br>(0.11) |
| Sleep problems | | | 5.84<br>(10.29) | | | 0.29<br>(2.44) | | | 0.13<br>(0.14) | | | 0.05<br>(0.09) |
| Intercept | **298.34**$^{***}$ | **299.59**$^{***}$ | **286.24**$^{***}$ | **56.94**$^{***}$ | **48.50**$^{***}$ | **45.83**$^{***}$ | 0.18 | 0.00 | 0.09 | 0.11 | 0.06 | 0.15 |
| Model F | **12.96**$^{***}$ | **9.14**$^{***}$ | **3.74**$^{***}$ | **7.23**$^{***}$ | **6.39**$^{***}$ | **2.99**$^{***}$ | **8.31**$^{***}$ | **6.72**$^{***}$ | 4.40 | **14.40**$^{***}$ | **11.75**$^{***}$ | **5.65**$^{***}$ |
| $R^2$, % | 5.63 | 6.37 | 9.38 | 2.53 | 4.13 | 8.44 | 3.43 | 4.00 | 10.54 | 5.75 | 7.27 | 13.86 |

*Source:* Survey of Midlife in the U.S. (MIDUS II).
*Note*: Values are coefficients unless otherwise noted; standard errors appear in parentheses. Robust estimators are used. Boldface indicates statistical significance ($^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$; two-tailed tests).
[a]mg/dL.
[b]ng/mL.
[c]log ug/mL.
[d]log pg/mL.
CRP, C-reactive protein; IL-6, interleukin 6; y, years.

**Table 4.** Coefficients from Linear Regression Models for Systemic Inflammation Markers by Racial Background

| | Blacks ($n$=170) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fibrinogen[a] | | | E-selectin[b] | | | CRP[c] | | | IL-6[d] | | |
| **Variable** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** |
| Demographic factors | | | | | | | | | | | | |
| Age, y | 0.75 (0.91) | 0.69 (0.94) | 0.33 (1.08) | **−0.42**$^{*}$ (0.16) | **−0.44**$^{*}$ (0.17 | −0.34 (0.24) | −0.01 (0.01) | −0.01 (0.01) | **−0.03**$^{**}$ (0.01) | 0.01 (0.01) | 0.01 (0.01) | 0.01 (0.01) |
| Woman | **57.45**$^{***}$ (15.02 | **62.13**$^{***}$ (14.51) | **49.25**$^{**}$ (16.82) | −2.39 (4.13) | −1.67 (4.24) | −2.42 (4.58) | **0.64**$^{**}$ (0.19) | **0.67**$^{***}$ (0.19) | **0.52**$^{**}$ (0.19) | **0.29**$^{*}$ (0.12) | **0.29**$^{*}$ (0.12) | 0.23 (0.13) |
| Social determinants | | | | | | | | | | | | |
| SES | | | | | | | | | | | | |
| Education, y | −1.96 (2.34) | −3.14 (2.40) | −2.85 (2.85) | 0.05 (0.68) | −0.18 (0.72) | 0.01 (0.75) | **−0.06**$^{*}$ (0.03) | **−0.07**$^{*}$ (0.03) | −0.05 (0.03) | −0.02 (0.02) | −0.02 (0.02) | −0.01 (0.02) |
| Income, log $ | 1.98 (2.82) | 2.36 (2.49) | 1.75 (2.92) | **−1.10**$^{*}$ (0.54) | **−0.99**$^{*}$ (0.49) | **−1.41**$^{**}$ (0.45) | 0.01 (0.01) | 0.01 (0.01) | 0.03 (0.02) | 0.02 (0.01) | 0.02 (0.01) | 0.02 (0.01) |
| Perceived discrimination | | | | | | | | | | | | |
| Daily | | 0.68 (1.50) | −0.11 (1.75) | | −0.16 (0.40) | −0.08 (0.37) | | 0.01 (0.02) | −0.01 (0.02) | | 0.004 (0.01) | −0.01 (0.01) |
| Lifetime | | 5.57 (3.28) | 4.91 (3.52) | | 1.26 (0.83) | 1.04 (0.81) | | 0.03 (0.04) | 0.02 (0.04) | | 0.01 (0.02) | −0.001 (0.03) |
| Psychological factors | | | | | | | | | | | | |
| Depressed affect | | | 5.58 (5.49) | | | 2.39 (1.32) | | | 0.06 (0.05) | | | 0.04 (0.04) |
| General anxiety | | | −5.11 (5.83) | | | **−3.20**$^{**}$ (1.15) | | | **0.10**$^{*}$ (0.05) | | | 0.03 (0.05) |
| Stress reactivity | | | 2.47 (3.81) | | | 1.29 (0.98) | | | −0.04 (0.04) | | | 0.02 (0.03) |
| Aggression | | | −6.04 (5.43) | | | −0.99 (1.59) | | | −0.10 (0.07) | | | −0.02 (0.04) |
| Alienation | | | −1.19 (3.76) | | | −1.53 (0.91) | | | 0.06 (0.04) | | | 0.02 (0.03) |
| Lifestyle factors | | | | | | | | | | | | |
| Ever regular smoker | | | −14.13 (18.83) | | | −3.80 (4.18) | | | −0.01 (0.20) | | | −0.02 (0.12) |
| Currently regular smoker | | | 1.95 (21.96) | | | 10.07 (6.51) | | | −0.02 (0.22) | | | 0.16 (0.14) |

*(continued on next page)*

**Table 4.** Coefficients from Linear Regression Models for Systemic Inflammation Markers by Racial Background *(continued)*

| | Blacks ($n$=170) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fibrinogen[a] | | | E-selectin[b] | | | CRP[c] | | | IL-6[d] | | |
| **Variable** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** | **Model 2** | **Model 3** | **Model 6** |
| Vigorous physical activity | | | 7.39<br>(24.70) | | | −0.08<br>(5.25) | | | −0.13<br>(0.32) | | | −0.04<br>(0.18) |
| Moderate physical activity | | | 4.65<br>(22.01) | | | −2.42<br>(4.68) | | | 0.29<br>(0.29) | | | 0.06<br>(0.17) |
| BMI | | | 0.91<br>(0.50) | | | −0.11<br>(0.09) | | | **0.01**$^{**}$<br>(0.01) | | | **0.01**$^{**}$<br>(0.003) |
| Health factors | | | | | | | | | | | | |
| Preventive aspirin | | | 0.77<br>(21.91) | | | −3.76<br>(5.01) | | | 0.08<br>(0.24) | | | −0.11<br>(0.14) |
| Hypertension | | | −13.98<br>(17.33) | | | −6.60<br>(5.36) | | | **−0.49**$^{**}$<br>(0.18) | | | −0.12<br>(0.11) |
| Diabetes | | | 22.14<br>(19.16) | | | **14.10**$^{*}$<br>(5.84) | | | 0.24<br>(0.19) | | | 0.12<br>(0.14) |
| Joint/bone diseases | | | 14.51<br>(16.54) | | | −5.42<br>(4.63) | | | 0.27<br>(0.18) | | | −0.05<br>(0.11) |
| Persistent skin trouble | | | −18.29<br>(38.72) | | | 4.16<br>(11.32) | | | −0.79<br>(0.43) | | | −0.01<br>(0.24) |
| Teeth problems | | | 13.93<br>(20.99) | | | −2.25<br>(7.00) | | | 0.40<br>(0.27) | | | −0.09<br>(0.16) |
| Sleep problems | | | 3.53<br>(23.98) | | | −0.29<br>(6.09) | | | 0.24<br>(0.24) | | | 0.19<br>(0.14) |
| Intercept | **318.50**$^{***}$ | **304.19**$^{*-**}$ | **351.47**$^{*-**}$ | **82.54**$^{***}$ | **83.52**$^{***}$ | **100.13**$^{*-**}$ | **1.84**$^{**}$ | **1.67**$^{*}$ | **2.96**$^{**}$ | **0.81***  | **0.86**$^{*}$ | 0.32 |
| Model F | **3.85**$^{**}$ | **5.00**$^{**}$ | **1.65**$^{*}$ | **3.26**$^{*}$ | **3.44**$^{**}$ | **2.26**$^{**}$ | **4.00**$^{**}$ | **3.46**$^{**}$ | 4.88 | **2.10** | 1.45 | **1.94**$^{*}$ |
| $R^2$, % | 7.90 | 11.07 | 17.87 | 4.81 | 6.16 | 22.65 | 8.52 | 9.80 | 29.92 | 5.34 | 5.48 | 17.50 |

*Source:* Survey of Midlife in the U.S. (MIDUS II).
*Note*: Values are coefficients unless otherwise noted; standard errors appear in parentheses. Robust estimators are used. Boldface indicates statistical significance ($^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$; two-tailed tests).
[a]mg/dL.
[b]ng/mL.
[c]log ug/mL.
[d]log pg/mL.
CRP, C-reactive protein; IL-6, interleukin 6; y, years.

role of stress in physical and mental health. One explanation is that the measure of stress reactivity does not capture the level of stress exposure; instead, it measures a relatively stable personality characteristic representing how a person responds emotionally once stress has occured.[63] Future research should assess stress exposure more directly to clarify its influence on inflammation.

### Limitations

This study has a cross-sectional, observational design, which prevents assessing changes over time and causally interpreting results, though specifically for race and education, it seems unlikely that they might change in response to changes in inflammation among midlife individuals. Racial identification tends to be stable over the life course, and education is typically completed during young adulthood. Nevertheless, inflammation may reduce SES by contributing to poorer health, which may limit earnings, productivity, and career advancement. This study addressed two dimensions of PD but it did not capture institutional, implicit, and covert discrimination. Finally, this investigation focused on blacks and whites; in future studies, it will be important to assess inflammation among Latinos and Native Americans, who have high prevalence of cardiovascular disease[65] and diabetes[66] and may be at risk of perceived discrimination.

## CONCLUSIONS

As systemic inflammation is implicated in many chronic diseases, evidence of the role of social determinants in inflammation highlights the social origins of chronic disease during midlife and informs scholarship seeking to pinpoint the processes leading to health disparities. Better understanding is the first step toward preventive interventions to reduce the health risks among vulnerable populations, including racial/ethnic minorities, individuals at risk for discrimination, and those facing socioeconomic disadvantages. Notably, this work suggests the importance of systemic interventions that address large-scale social determinants of health, including system-level factors that underlie discrimination and lead to disparities in income and education.

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## SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.amepre.2016.09.026.

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