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Social Inequalities in Inflammation: Age Variations in Older Persons

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Abstract

Objective—Systemic inflammation is an important risk factor for cardiovascular diseases and inequalities by race/ethnicity, gender, and education have been documented. However, there is incomplete knowledge as to how these disparities present across age, especially in late life. This study assesses whether differences in C-reactive protein (CRP), a marker of inflammation, are contingent on age among older persons.

Method—Data are from the 2006/2008 Health and Retirement Study ($n = 10,974$) biomarker assessment. CRP was regressed on interactions between age and other status characteristics.

Results—Racial/ethnic differences in inflammation do not vary significantly by age. However, gender and education differences are greatest at younger ages and then narrow steadily with increasing age.

Discussion—There is considerable heterogeneity in how disparities in inflammation present across age and characteristics such as race/ethnicity, gender, and education. Understanding status differences in the influence of age on factors affecting late-life health is useful for health disparities research.

Keywords

inflammation; health disparities; race/ethnicity; gender; education

Cardiovascular diseases (CVDs) have been and continue to be the leading cause of death among older adults in the United States (Jemal, Ward, Hao, & Thun, 2005; Xu, Murphy, & Kochanek, 2015). More than one third of Americans have at least one form of CVD and more than half of these persons are aged 60 and older (Mozaffarian et al., 2014). CVDs also affect quality of life, contributing to functional disabilities. Because CVDs place a substantial burden on individual and population health, medical and public health researchers and practitioners are calling for greater attention to efforts toward prevention.

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The early identification of adverse physiological changes in functioning that lead to CVDs and place populations at greatest risk is essential to the primary prevention of CVDs.

Biological risk factors, or biomarkers, reflect changes in physiological functioning and, therefore, are considered important indicators of and potential risk factors for the onset and progression of disease. Biomarkers such as C-reactive protein (CRP) are useful for detecting emergent CVDs and monitoring disease progression because CVDs are preceded by a lengthy deterioration in cardiovascular functioning—deterioration that is manifest by elevated levels of inflammation. CRP is an acute-phase protein produced by the liver in response to increasing levels of circulating inflammatory factors; thus, CRP functions as a marker of systemic inflammation (Black, Kushner, & Samols, 2004). Acute inflammatory responses are usually short-lived and linked to acute physical or psychosocial stressors that result in transiently elevated CRP levels. Excessive and prolonged inflammation, however, is likely due to the accumulation of social, behavioral, and environmental exposures over the life course that compromise physiological functioning and lead to dysregulation and chronically elevated biomarkers (McEwen, 1998), including CRP.

CRP is associated with other risk factors for CVDs, such as diabetes (Effoe, Correa, Chen, Lacy, & Bertoni, 2015), obesity (Yudkin, Kumari, Humphries, & Mohamed-Ali, 2000), and hypertension (Sesso, Wang, Buring, Ridker, & Gaziano, 2007), and with unhealthy behaviors, such as smoking (Tracy et al., 1997) and physical inactivity (Majka et al., 2009). It also is predictive of cardiovascular events, including death from coronary heart disease (Cushman et al., 2005). Systemic inflammation is hypothesized to naturally increase with age (Franceschi & Campisi, 2014), but socially disadvantaged populations may experience disproportionately large increases that result in much greater risk for CVD. Among older adults, non-Hispanic Blacks (hereafter Blacks) have higher CRP levels than non-Hispanic Whites (hereafter Whites) and Hispanics (Albert, 2007); however, differences in inflammation between Hispanics and other groups may vary by country of origin (Crimmins, Kim, Alley, Karlamangla, & Seeman, 2007). Overall, women tend to have higher levels of CRP than men of similar ages (Lakoski et al., 2006), and individuals with less than a high school education have higher CRP levels than their more educated counterparts (Friedman & Herd, 2010).

It is unclear, however, whether differences in CRP by race/ethnicity, gender, and education change with age among older adults or why these variations occur. Widening CRP differentials across age groups may be due to the continued accumulation of health-damaging exposures among disadvantaged populations and of health-sustaining resources among advantaged populations (Dannefer, 2003). Therefore, racial minorities may experience much higher CRP levels in old age compared with Whites, for example, because they have amassed over time a disproportionate amount of adverse social and economic exposures that compromise health and well-being. Alternatively, CRP differentials may narrow with increasing age because of differential mortality, the “catching up” of socially advantaged subgroups in terms of poor health (i.e., age-as-leveler hypothesis), or a combination of both processes (Ferraro & Farmer, 1996). Yet again, the magnitude of gaps between more and less privileged social groups may remain the same across age groups, if

the damage done in earlier life is sufficient for determining late-life health differentials that may be resistant to change.

Few studies have examined age variations in disparities in inflammation among older adults and none have used multiple indicators of social status. Therefore, the current study assesses the extent to which population differences in inflammation by race/ethnicity, gender, and education change with age by formally testing whether these differences are conditional on age. Our hypotheses are guided by the theory of cumulative advantage/disadvantage (Dannefer, 2003). We expect to find that Blacks have higher levels of CRP than Whites and Hispanics and that these differences widen with age among older persons. Differences between Hispanics and Whites are hypothesized to be minimal and constant with age, an instance of the “Hispanic paradox” of favorable health outcomes among Hispanics despite their low socioeconomic status (SES). We additionally expect to find widening education differences in CRP due to the accumulation of risks with age among persons with relatively low levels of education. Even though women tend to have higher CRP levels than men overall, our analysis of gender is exploratory because the relationship between inflammation and sex-related physiological changes that occur at advanced ages is not well understood. We also assess the extent to which sociodemographic characteristics, health behaviors, and current physical and mental health status explain age variations in these disparities because inflammation is known to be associated with individual characteristics and lifestyle factors that affect health.

Our study contributes to a growing body of research documenting social disparities in the biological foundations of disease, and advances research in this area by testing how disparities vary with age and the explanations for these variations. This information can be constructive for designing health interventions, particularly interventions aimed at eliminating health disparities and improving the health of the least advantaged social groups in older adulthood.

Method

Data and Sample

The Health and Retirement study (HRS) is an ongoing biannual survey of a nationally representative sample of older Americans aged 51 and older. In 2006, a random half-sample ($n = 9,067$) was selected for assessments of physical measures, biological markers, and psychosocial factors. The remainder ($n = 7,857$) was assigned the same assessments in 2008. We pooled data from the half-samples to increase the sample size and statistical power. Additional details on the HRS are reported elsewhere (Heeringa & Connor, 1995; Sonnega et al., 2014).

In total, 12,099 individuals were selected and eligible for the assessments and had a sampling weight. Individuals were dropped if they did not identify as White, Black, or Hispanic because of small sample sizes in other groups (combined $n = 242$). Of the remaining 11,857 individuals, 10,794 (93%) had complete data on all variables in our models; incomplete cases were more likely to be older, Black, female, less educated, sedentary, and in poor health. The University of Michigan granted approval of the HRS

study and obtained written consent. Our study is exempt from review by the institutional review board because all data are publicly available and de-identified.

Study Measures

The specific methods used to collect blood samples and assay CRP are reported by the HRS elsewhere (Crimmins et al., 2013). High-sensitivity assays were used to help detect low but persistent CRP levels in blood serum. CRP is measured in units of micrograms per milliliter ($\mu\text{g/mL}$); we log-transformed the variable to improve its skewed distribution. Self-reported race/ethnicity is categorized as Whites (omitted reference), Blacks, and Hispanics of all races. Age is measured in years and males are the reference for gender. Less than high school is the reference for three educational dummy variables of high school, some college, and college or higher. Household income is the combined total from all sources for the respondent and his or her spouse/partner in thousands of dollars; in regression analyses, this variable is log-transformed to improve its distribution. Marital status is coded as married or partnered (reference), separated/divorced, widowed, or never married. Employment status is coded as employed (reference), retired, or other (e.g., unemployed).

We also examine health behaviors and physical risk factors that are related to CVDs and inflammation (Albert, Glynn, & Ridker, 2004; Ford, 2002; Imhof et al., 2001; Kasapis & Thompson, 2005; Majka et al., 2009; Tracy et al., 1997). Non-smokers are the reference for current and former smokers. Non-drinkers are the reference for moderate and heavy drinkers, classifications that are based on gender-specific national guidelines (National Institute on Alcohol Abuse and Alcoholism, 2015). Measures of light, moderate, and vigorous physical activity are categorized as active (i.e., reported frequency of once a month or higher) or inactive (i.e., reported never engaging in physical activity; reference). Adipose tissue is a source of proteins and other factors that contribute to inflammation (Berg & Scherer, 2005) and is operationalized as waist circumference measured in inches and body mass index (BMI) in kilograms of weight divided by height in squared meters.

Depressive symptoms are also linked to acute and chronic inflammatory processes in older persons (Penninx et al., 2003) and are measured with a count of eight depressive symptoms in the past week using a modified version of the Center for Epidemiologic Studies–Depression (CES-D) Scale (Radloff, 1977). Finally, chronic health conditions, such as high blood pressure (Bautista, 2003), diabetes (Barzilay et al., 2001), heart disease (Cushman et al., 2005), stroke (Cao et al., 2003), cancer (Heikkilä, Ebrahim, & Lawlor, 2007), and lung diseases (Gan, Man, Senthilselvan, & Sin, 2004), are associated with elevated CRP levels as is the presence of multiple chronic conditions (Friedman, Christ, & Mroczek, 2015). Therefore, we control for the number of conditions a person has among the six conditions previously listed.

Statistical Analysis

To account for the complex sampling design, we conducted all analyses using the survey (svy) commands in Stata® 13. We used multiple linear regression models of log-CRP to estimate a main effects model including age, race/ethnicity, gender, and education. We then tested three variants of this model that add the interaction of age separately with race/

ethnicity, gender, and education. An adjusted Wald test was used to evaluate the significance of each conditional relationship relative to the main effects model. Post hoc comparisons of linear combination of coefficients (i.e., comparing the coefficients for Blacks and Hispanics) were conducted using the Stata `lincom` command. We estimated a second set of conditional models including the remaining demographic, behavioral, and health-related variables to determine which of these factors, if any, contribute to age variations in disparities in inflammation.

Results

Table 1 presents characteristics of the sample. The majority is White, female, and has at least a high school degree. The average household income is slightly more than US\$72,000; most of the sample is retired (53%) and most are married (67%). In general, members of the sample engage in healthful behaviors as evidenced by low rates of current smoking and heavy drinking, and high rates of physical activity. The average waist circumference and BMI of the sample correspond with being overweight and at increased risk for CVDs, and respondents reported an average of at least one depressive symptom and one chronic condition.

The main effects model (Table 2, Model 1) shows that log-CRP levels are higher among Blacks than Whites and Blacks also have higher levels than Hispanics (post hoc test: $b = 0.253$, $SE = 0.064$, $p < .001$); Hispanics, however, do not differ significantly from Whites. Women have higher levels than men, and there is a graded decrease in log-CRP across successively higher levels of education. Age is inversely associated with log-CRP, and a sensitivity analysis testing nonlinearity with a quadratic age variable was not significant.

Model 2 added variables for the interaction between race/ethnicity and age. This interaction is not statistically significant, Wald test: $F(2, 55) = 0.73$; $p = .49$, which suggests that racial/ethnic differences in log-CRP are not conditional on age: There is an overall decline in log-CRP for all groups and the magnitudes of the Black–White and Black–Hispanic differentials do not change with increasing age.

In the next model, we tested the interaction between gender and age (Table 2, Model 3). This model shows a significant conditional relationship between gender and age, adjusted Wald test: $F(1, 56) = 28.14$, $p < .001$, which is depicted in Figure 1. We see that, on average, log-CRP levels are higher among women than men at younger ages. However, a crossover occurs between ages 75 and 80 such that log-CRP levels are higher for men than women among the oldest-old.

Likewise, the conditional relationship between education and age (Table 2, Model 4) is statistically significant, adjusted Wald test: $F(3, 54) = 6.05$, $p < .01$. In Figure 2, we see that at younger ages, individuals with less than a high school education start off with the highest log-CRP levels, followed by those with a high school degree, some college, and a college degree or higher, respectively. However, the difference between the two lowest and the two highest groups narrows with increasing age. The difference between high school and some college converge between ages 65 and 70, while the differences between high school and

college and between less than high school and some college converge later, at age 85 and 95, respectively. The difference between the least and most advantaged education groups—that is, less than high school versus college or higher—converge at even later ages. It should be noted, however, that there are relatively few people in the upper age range: Individuals ages 85 and old comprise less than 7% of the sample, making estimates imprecise.

In Table 3, we assess whether these differences are explained by other sociodemographic characteristics, health behaviors, and measures of physical and mental health status. We present regression coefficients from the main effects model to examine changes in the race difference after accounting for these variables (Panel A). We also present coefficients from conditional models of the interaction between gender and age (Panel B), and education and age (Panel C). For each panel of Table 3, Model 1 includes only the key independent variables—age, race/ethnicity, gender, and education—and reproduces values presented in Table 2, while Model 2 includes the explanatory variables (not shown). The models used to estimate the fully adjusted coefficients (i.e., Model 2) are presented in their entirety in Supplemental Table S1.

After accounting for sociodemographic characteristics, health behaviors, and physical and mental health status, racial/ethnic differences in log-CRP are reduced by more than half, but remain statistically significant (Panel A). Net of the explanatory variables included in Model 2, the gender-age interaction is still significant. However, compared with Model 1, the gender difference is larger and decreases more rapidly with age as evidenced by a slower rate of decline in log-CRP among women ($b = -.015$ in Model 1 vs. $b = -.013$ in Model 2) and a faster rate of increase among men ($b = 0.005$ in Model 1 vs. $b = 0.008$ in Model 2). Age variations in education differences are completely accounted for by these explanatory variables (Panel C, Model 2).

Discussion

Among older Americans, we find that the associations between several social status characteristics and inflammation are conditional on age, with race/ethnicity being a notable exception. Based on cumulative disadvantage theory, we hypothesized a widening of racial/ethnic difference at more advanced ages. Although there are racial/ethnic differences in CRP, the conditional relationship with age is not significant. The lack of a significant interaction between race/ethnicity and age is counter to our hypothesis and the results from one recent study (Herd, Karraker, & Friedman, 2012). Previous research has emphasized differences between Blacks and Whites, but we additionally find that Blacks differ from Hispanics. The SES of Blacks and Hispanics is similarly low, on average, suggesting that SES may not be a driving force of inflammation for Hispanics or for both Hispanics and Blacks. The lack of difference in CRP between Hispanics and Whites may be part of the more general “Hispanic Paradox,” although empirical support for this phenomenon in other studies is mixed and may vary by Hispanic subgroup (Crimmins et al., 2007). The diminished racial/ethnic differences with the addition of the physical and behavioral risk factors and chronic conditions suggest that unhealthy lifestyles may account in part for observed differences.

Our study also shows that women have higher CRP levels than men and that the extent of the gender difference is contingent on age: It is most pronounced at younger ages, narrows and then converges during early old age. The higher levels of CRP among women would seemingly place women at greater risk for CVDs and a shortened life span because inflammation is positively associated with mortality (Ridker, 2007). However, women are more likely than men to seek and receive preventive care and treatment (Bertakis, Azari, Helms, Callahan, & Robbins, 2000), which may contribute to their greater longevity.

The convergence of and eventual crossover in CRP levels among women and men is consistent with other research (Yang & Kozloski, 2011) and appears to be due to both a decrease among women and increase among men (See Figure 1). This patterning of the gender gap in CRP by age may explain why age is negatively associated with CRP in the full sample (see Table 2) to the extent that the positive association between age and CRP among men is offset by the negative association among women.

The gendered pattern of CRP may be due to biological processes (Short, Yang, & Jenkins, 2013). Sex hormones have been shown to mediate differences in immune responses; male sex hormones tend to reduce the immune response while female sex hormones stimulate it (Schuurs & Verheul, 1990). Age-related declines in the production of sex hormones (e.g., menopause) may effectively decrease the immune response among women. However, sensitivity analyses including an indicator for menopausal status did not change our substantive findings.

Biological processes leading to gender differences in CRP may also be coupled with social and behavioral processes. Gendered social experiences lead to parallel differences in acquired risks and behaviors (Rieker & Bird, 2005), for example, that are embodied in biology and subsequently manifest as gender differences in health (Krieger, 2005). In other words, men and women have followed different life-course trajectories with cumulative effects that manifest in mid to late life. They age differently both biologically and with regard to social experiences (e.g., differences in response to spousal bereavement; Lee & Carr, 2007), which may lead to disparate trajectories of inflammation in late life.

Alternately, selection effects due to the longer survival of healthy persons (e.g., persons with low CRP levels) may contribute to the gender gap. Given higher mortality rates for U.S. men for most major causes of death (Xu, Kochanek, Murphy, & Arias, 2014), selection is likely to be greater among men than women. However, if this were the case, then we would expect a stable or widening gender difference due to relatively low CRP levels among older men, the opposite of what we observed. This interpretation, however, uses age as a proxy for aging, a limitation demonstrating the need for longitudinal research on biomarkers.

Our study provides some evidence that the association between education and inflammation is also conditional on age. Although the interaction with education is significant, it appears to be driven primarily by the least and most educated groups, specifically declines in CRP among those with less than a high school education and increases among those with a college education. Selective mortality may contribute to decreases in the magnitude of the disparity and the nonsignificant difference at older ages may be due to limitations in sample

size. However, the presence of a significant difference between those with less than a high school degree and those with a college degree at earlier ages may reflect earlier cumulative effects of social disadvantage over the life course among persons with little formal education (Dannefer, 2003; Ferraro & Shippee, 2009).

Overall, we find that populations that have been marginalized historically and more frequently exposed to adversity and discrimination have higher CRP at younger ages than their more privileged counterparts. Disparities by gender and education narrow at older ages, which could be due to selection or to the “equalizing” of access to social resources (e.g., social welfare programs) that occur with advanced age, an instance of the age-as-leveler hypothesis. That said, the stability of race difference in CRP across age that are not accounted for by other individual characteristics and lifestyle factors suggests that social and environmental risks unique to race and independent of age, such as racism, may be responsible for the persistence of the race gap. In other words, the equalization of access to social and economic resources that accompanies age and the selective pressures favoring the healthy may be inconsequential with regard to racial disparities in inflammation. Future research should more explicitly test this statement and explain why age-patterns of racial disparities in inflammation differ from those based on other indicators of social status.

Limitations and Strengths

The cross-sectional nature of these data is a substantial shortcoming of the study that limits conclusions about aging and inferences of causality. Although this is of limited concern for fixed characteristics, such as race/ethnicity and gender, the directionality of the association between inflammation and other covariates, such as depressive symptoms (Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008), is less certain and could be reversed or reciprocal. In addition, we analyzed only one biomarker rather than multiple markers or an index of inflammation as some studies have done (Short et al., 2013; Yang & Kozloski, 2011), although still other studies have examined only CRP (see for review, Nazmi & Victora, 2007).

A notable strength of the study is the large, diverse, and nationally representative sample of older persons, which allows generalization to the older U.S. population. Whereas existing research has focused on Blacks and Whites, this study additionally examined Hispanics, an understudied population, particularly with regard to age variations in biomarkers. Using biomarkers in population-based research is advantageous because they are not prone to recall bias, unlike self-reports of health outcomes. CRP, in particular, is relatively easy to assess within clinics and on a population-level, and has a known clinical cut-point for high-risk of CVDs (Ridker, 2003). Moreover, due to its association with multiple health outcomes, CRP captures the emergence of physiological dysregulation before the onset of CVD or related conditions such as diabetes (Effoe et al., 2015). These characteristics make CRP a desirable candidate for monitoring the health of at-risk populations with the goal of preventing the development and progression of chronic disease.

Conclusion

Our study has demonstrated that some health disparities in inflammation are conditional on age within the older population and that these disparities may be masked when heterogeneity by age is not taken into consideration. We have expanded research on race/ethnicity to include the Hispanic population, finding that Hispanics share the White advantage with regard to inflammation even though Hispanics have similar levels of SES as Blacks. This is a critical contrast because it suggests that we must look beyond SES for an explanation of racial/ethnic differences in inflammation. Our findings point to markedly different patterns of age-related change in inflammation between women, who experience declines in inflammation with age, and men, who exhibit increases with age. In addition, we present evidence that the education gradient in inflammation compresses with age due to a decline in inflammation among persons with the least amount of education.

Racial/ethnic differences in inflammation persist net of demographic and socioeconomic controls, suggesting that future research should identify potential mediators of the relationship between race/ethnicity and inflammation. That these differences are compressed when behavioral and physical risk factors and chronic conditions are taken into consideration suggests that some part may be due to lifestyle. Differential exposure to stressors associated with the aging experience and minority status may be one mechanism contributing to racial/ethnic disparities in CRP. Similarly, the convergence of levels of CRP by gender at older ages merits further investigation and should be examined longitudinally. Investigations of the effects of social and age-related stressors, such as caregiving stress, would be productive directions for future research because these stressors are patterned by gender and associated with CVDs related to inflammation (Lee, Colditz, Berkman, & Kawachi, 2003).

Health disparities research often focuses on single indicators of social status and treats other characteristics—especially age—as statistical controls, implicitly assuming that any difference in health for the primary characteristic are constant across the others. Our study shows that this assumption is not always warranted and that disparities in health may not be constant across age, even within the older population. Age reflects past histories and experiences that lead to current circumstances and living conditions that influence health, and these histories and experiences differentially unfold over the life course based on social status. For this reason, an examination of the intersection of age with other status characteristics offers a more complete representation of how social status shapes the distribution of health across the diverse subgroups that collectively comprise the older U.S. population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Albert MA. Inflammatory biomarkers, race/ethnicity and cardiovascular disease. *Nutrition Reviews*. 2007; 65:S234–S238. doi:10.1111/j.1753-4887.2007.tb00369.x. [PubMed: 18240555]
- Albert MA, Glynn RJ, Ridker PM. Effect of physical activity on serum C-reactive protein. *The American Journal of Cardiology*. 2004; 93:221–225. [PubMed: 14715354]
- Barzilay JI, Abraham L, Heckbert SR, Cushman M, Kuller LH, Resnick HE, Tracy RP. The relation of markers of inflammation to the development of glucose disorders in the elderly: The Cardiovascular Health Study. *Diabetes*. 2001; 50:2384–2389. [PubMed: 11574423]
- Bautista L. Inflammation, endothelial dysfunction, and the risk of high blood pressure: Epidemiologic and biological evidence. *Journal of Human Hypertension*. 2003; 17:223–230. [PubMed: 12692566]
- Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. *Circulation Research*. 2005; 96:939–949. [PubMed: 15890981]
- Bertakis KD, Azari R, Helms LJ, Callahan EJ, Robbins JA. Gender differences in the utilization of health care services. *Journal of Family Practice*. 2000; 49:147–152. [PubMed: 10718692]
- Black S, Kushner I, Samols D. C-reactive protein. *Journal of Biological Chemistry*. 2004; 279:48487–48490. [PubMed: 15337754]
- Cao JJ, Thach C, Manolio TA, Psaty BM, Kuller LH, Chaves PHM, Cushman M. C-reactive protein, carotid intima-media thickness, and incidence of ischemic stroke in the elderly: The Cardiovascular Health Study. *Circulation*. 2003; 108:166–170. [PubMed: 12821545]
- Crimmins EM, Faul J, Kim JK, Guyer H, Langa KM, Ofstedal MB, Weir D. Documentation of biomarkers in the 2006 and 2008 Health and Retirement Study. Survey Research Center, University of Michigan; Ann Arbor: 2013.
- Crimmins EM, Kim JK, Alley DE, Karlamangla A, Seeman T. Hispanic paradox in biological risk profiles. *American Journal of Public Health*. 2007; 97:1305–1310. [PubMed: 17538054]
- Cushman M, Arnold AM, Psaty BM, Manolio TA, Kuller LH, Burke GL, Tracy RP. C-reactive protein and the 10-year incidence of coronary heart disease in older men and women: The Cardiovascular Health Study. *Circulation*. 2005; 112:25–31. [PubMed: 15983251]
- Dannefer D. Cumulative advantage/disadvantage and the life course: Cross-fertilizing age and social science theory. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*. 2003; 58:S327–S337.
- Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: When the immune system subjugates the brain. *Nature Reviews Neuroscience*. 2008; 9:46–56. [PubMed: 18073775]
- Effoe VS, Correa A, Chen H, Lacy ME, Bertoni AG. High-sensitivity C-reactive protein is associated with incident Type 2 diabetes among African Americans: The Jackson Heart Study. *Diabetes Care*. 2015; 38:1694–1700. [PubMed: 26068864]
- Ferraro KF, Farmer MM. Double jeopardy, aging as leveler, or persistent health inequality? A longitudinal analysis of white and black Americans. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*. 1996; 51:S319–S328.
- Ferraro KF, Shippee TP. Aging and cumulative inequality: How does inequality get under the skin? *The Gerontologist*. 2009; 49:333–343. [PubMed: 19377044]
- Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among us adults. *Epidemiology*. 2002; 13:561–568. [PubMed: 12192226]
- Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*. 2014; 69(Suppl. 1):S4–S9.

- Friedman EM, Christ SL, Mroczek DK. Inflammation partially mediates the association of multimorbidity and functional limitations in a national sample of middle-aged and older adults: The MIDUS Study. *Journal of Aging and Health*. 2015; 27:843–863. [PubMed: 25649677]
- Friedman EM, Herd P. Income, education, and inflammation: Differential associations in a national probability sample (The MIDUS Study). *Psychosomatic Medicine*. 2010; 72:290–300. doi: 10.1097/PSY.0b013e3181cfe4c2. [PubMed: 20100883]
- Gan WQ, Man SFP, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: A systematic review and a meta-analysis. *Thorax*. 2004; 59:574–580. [PubMed: 15223864]
- Heeringa SG, Connor JH. Sample design and methods for the Health and Retirement Survey. Statistical Design Group, Survey Research Center, University of Michigan; Ann Arbor: 1995.
- Heikkilä K, Ebrahim S, Lawlor DA. A systematic review of the association between circulating concentrations of C reactive protein and cancer. *Journal of Epidemiology & Community Health*. 2007; 61:824–833. [PubMed: 17699539]
- Herd P, Karraker A, Friedman E. The social patterns of a biological risk factor for disease: Race, gender, socioeconomic position, and C-reactive protein. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*. 2012; 67:503–513.
- Imhof A, Froehlich M, Brenner H, Boeing H, Pepys MB, Koenig W. Effect of alcohol consumption on systemic markers of inflammation. *The Lancet*. 2001; 357:763–767.
- Jemal A, Ward E, Hao Y, Thun M. Trends in the leading causes of death in the United States, 1970–2002. *Journal of the American Medical Association*. 2005; 294:1255–1259. [PubMed: 16160134]
- Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: A systematic review. *Journal of the American College of Cardiology*. 2005; 45:1563–1569. [PubMed: 15893167]
- Krieger N. Embodiment: A conceptual glossary for epidemiology. *Journal of Epidemiology & Community Health*. 2005; 59:350–355. [PubMed: 15831681]
- Lakoski SG, Cushman M, Criqui M, Rundek T, Blumenthal RS, D'Agostino RB Jr, Herrington DM. Gender and C-reactive protein: Data from the Multiethnic Study of Atherosclerosis (MESA) cohort. *American Heart Journal*. 2006; 152:593–598. doi:10.1016/j.ahj.2006.02.015. [PubMed: 16923436]
- Lee M-A, Carr D. Does the context of spousal loss affect the physical functioning of older widowed persons? A longitudinal analysis. *Research on Aging*. 2007; 29:457–487.
- Lee S, Colditz GA, Berkman LF, Kawachi I. Caregiving and risk of coronary heart disease in U.S. women: A prospective study. *American Journal of Preventative Medicine*. 2003; 24:113–119.
- Majka DS, Chang RW, Vu T-HT, Palmas W, Geffken DF, Ouyang P, Liu K. Physical activity and high-sensitivity C-reactive protein: The Multi-Ethnic Study of Atherosclerosis. *American Journal of Preventive Medicine*. 2009; 36:56–62. doi:10.1016/j.amepre.2008.09.031. [PubMed: 19013748]
- McEwen BS. Stress, adaptation, and disease: Allostasis and allostatic load. *Annals of the New York Academy of Sciences-Paper Edition*. 1998; 840:33–44.
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Turner MB. Heart disease and stroke statistics—2015 update: A report from the American Heart Association. *Circulation*. 2014; 131:e29–e322. [PubMed: 25520374]
- National Institute on Alcohol Abuse and Alcoholism. Drinking levels defined. 2015. Retrieved from <http://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking>
- Nazmi A, Victora CG. Socioeconomic and racial/ethnic differentials of C-reactive protein levels: A systematic review of population-based studies. *BMC Public Health*. 2007; 7 Article 212.
- Penninx BW, Kritchewsky SB, Yaffe K, Newman AB, Simonsick EM, Rubin S, Pahor M. Inflammatory markers and depressed mood in older persons: Results from the Health, Aging and Body Composition Study. *Biological Psychiatry*. 2003; 54:566–572. [PubMed: 12946885]
- Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1:385–401.
- Ridker PM. Clinical application of c-reactive protein for cardiovascular disease detection and prevention. *Circulation*. 2003; 107:363–369. [PubMed: 12551853]

- Ridker PM. Inflammatory biomarkers and risks of myocardial infarction, stroke, diabetes, and total mortality: Implications for longevity. *Nutrition Reviews*. 2007; 63(Suppl. 3):S253–S259.
- Rieker PP, Bird CE. Rethinking gender differences in health: Why we need to integrate social and biological perspectives. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*. 2005; 60(Special Issue 2):S40–S47.
- Schuurs A, Verheul H. Effects of gender and sex steroids on the immune response. *Journal of Steroid Biochemistry*. 1990; 35:157–172. [PubMed: 2407902]
- Sesso HD, Wang L, Buring JE, Ridker PM, Gaziano JM. Comparison of interleukin-6 and C-reactive protein for the risk of developing hypertension in women. *Hypertension*. 2007; 49:304–310. doi: 10.1161/01.HYP.0000252664.24294.ff. [PubMed: 17159088]
- Short SE, Yang YC, Jenkins TM. Sex, gender, genetics, and health. *American Journal of Public Health*. 2013; 103:S93–S101. [PubMed: 23927517]
- Sonnega A, Faul JD, Ofstedal MB, Langa KM, Phillips JW, Weir DR. Cohort profile: The Health and Retirement Study (HRS). *International Journal of Epidemiology*. 2014; 43:576–585. [PubMed: 24671021]
- Tracy RP, Psaty BM, Macy E, Bovill EG, Cushman M, Cornell ES, Kuller LH. Lifetime smoking exposure affects the association of C-reactive protein with cardiovascular disease risk factors and subclinical disease in healthy elderly subjects. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 1997; 17:2167–2176.
- Xu JQ, Kochanek KD, Murphy SL, Arias E. Mortality in the United States, 2012. *NCHS Data Brief*. 2014; 168:1–8.
- Xu JQ, Murphy S, Kochanek K. Deaths: Final data for 2013. *National Vital Statistics Reports*. 2015; 64(2)
- Yang Y, Kozloski M. Sex differences in age trajectories of physiological dysregulation: Inflammation, metabolic syndrome, and allostatic load. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*. 2011; 66:493–500.
- Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: Is interleukin-6 the link? *Atherosclerosis*. 2000; 148:209–214. doi:10.1016/S0021-9150(99)00463-3. [PubMed: 10657556]

Figure 1.
Predicted mean log-CRP by gender and age, Health and Retirement Study, 2006/2008.
Note. CRP = C-reactive protein.

Figure 2.
Predicted mean log-CRP by education and age, Health and Retirement Study, 2006/2008.
Note. CRP = C-reactive protein.

Table 1Sample Characteristics (Weighted): Health and Retirement Study, United States, 2006/2008 ($n = 10,794$).

Study variables	<i>M (SE) or %</i>
Age (years)	66.0 (0.19)
Race/ethnicity	
White	83.8
Black	8.9
Hispanic	7.3
Female	53.5
Education	
Less than high school	16.1
High school degree/GED	35.2
Some college	23.8
College or more	24.9
Household income (US\$1,000)	72.3 (2.10)
Employment status	
Full/part time	36.3
Retired	53.1
Other	10.6
Marital status	
Married/partnered	67.0
Separated/divorced	13.4
Widowed	16.0
Never married	3.6
Smoking status	
Never smoked	43.1
Former smoker	42.4
Current smoker	14.5
Alcohol consumption	
Non-drinker	62.3
Moderate	30.0
Heavy	7.7
Any vigorous activity	41.9
Any moderate activity	82.1
Any light activity	91.9
Waist circumference (inches)	39.9 (0.10)
Body mass index (kg/m ²)	28.3 (0.09)
Depressive symptoms (range = 0-8)	1.4 (0.03)
Number of conditions (range = 0-6)	1.2 (0.01)

Note: SE = standard error.

Table 2

Minimally Adjusted Unconditional and Conditional Models for Log-CRP: Health and Retirement Study, United States, 2006/2008 ($n = 10,794$).

Study Variables	Model 1		Model 2		Model 3		Model 4	
	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>
Key predictors								
Race/ethnicity (reference = White)								
Black	0.268***	0.045	0.400	0.303	0.266***	0.045	0.264***	0.046
Hispanic	0.015	0.041	0.383	0.316	0.016	0.041	0.0002	0.043
Female (reference = male)	0.196***	0.023	0.196***	0.023	1.154***	0.185	0.199***	0.024
Education (reference = less than high school)								
High school degree/GED	-0.195***	0.040	-0.197***	0.041	-0.189***	0.040	-0.171	0.270
Some college	-0.251***	0.035	-0.253***	0.035	-0.246***	0.035	-0.824*	0.309
College or more	-0.521***	0.044	-0.522***	0.044	-0.520***	0.044	-1.416***	0.300
Age (years)	-0.003*	0.001	-0.003	0.001	0.005*	0.002	-0.008**	0.003
Race-age interaction								
Black $\times$ Age			-0.002	0.004				
Hispanic $\times$ Age			-0.006	0.005				
Gender-age interaction								
Female $\times$ Age					-0.015***	0.003		
Education-age interaction								
High school degree/GED $\times$ Age							-0.001	0.004
Some college $\times$ Age							0.008	0.004
College or more $\times$ Age							0.014**	0.004
Constant	1.058***	0.095	1.028***	0.100	0.509**	0.159	1.396***	0.214
Model fit statistics								
R^2 -adjusted	0.035		0.036		0.039		0.038	
F -statistic	$F(7, 50) = 42.31$ ***		$F(9, 48) = 32.18$ ***		$F(8, 49) = 39.96$ ***		$F(10, 47) = 32.76$ ***	
Wald Test	—		$F(2, 55) = 0.73$		$F(1, 56) = 28.14$ ***		$F(3, 54) = 6.05$ **	

Note. *b* = unstandardized regression coefficient. Wald test is based on comparison to Model 1. CRP = C-reactive protein. Weighted data.

* $p < .05$.
** $p < .01$.
*** $p < .001$.

Table 3

Coefficients From Unadjusted and Adjusted Conditional Models of Log-CRP: Health and Retirement Study, United States, 2006/2008 ($n = 10,794$).

Panel A				
Study variables	Model 1^a		Model 2^b	
	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>
Main effects of Race and Age				
Race/ethnicity (reference = White)				
Black	0.268 ***	0.045	0.131 **	0.042
Hispanic	0.015	0.041	0.021	0.046
Age (years)	-0.003 *	0.001	0.001	0.002
Panel B				
Study variables	Model 1^c		Model 2^b	
	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>
Gender-age interaction				
Female (reference = male)	1.154 ***	0.185	1.208 ***	0.178
Age (years)	0.005 *	0.002	0.008 ***	0.002
Female × Age	-0.015 ***	0.003	-0.013 ***	0.003
Panel C				
Study variables	Model 1^d		Model 2^b	
	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>
Education-age interaction				
Education (reference = less than high school)				
High school degree/GED	-0.171	0.270	0.118	0.228
Some college	-0.824 *	0.309	-0.316	0.283
College or more	-1.416 ***	0.300	-0.442	0.273
Age (years)	-0.008 **	0.003	0.0001	0.003
Education × Age				
High school × Age	-0.001	0.004	-0.003	0.003
Some college × Age	0.008	0.004	0.003	0.004
College × Age	0.014 **	0.004	0.004	0.004

Note. *b* = unstandardized regression coefficient. CRP = C-reactive protein; BMI = body mass index. Weighted data.

^aModel includes variables for gender and education.

^bModel adds variables for marital status, employment, income, smoking, alcohol consumption, physical activity, BMI, waist circumference, depressive symptoms, and number of chronic conditions.

^cModel includes variables for race/ethnicity and education.

^dModel includes variables for race/ethnicity and gender.

*
 $p < .05$.

**
 $p < .01$.

 $p < .001$.