



Self-Reported Experiences of Discrimination and Inflammation Among Men and Women: The Multi-Ethnic Study of Atherosclerosis

Kiarri N Kershaw, *Northwestern University*
[Tene Lewis](#), *Emory University*
Ana V. Diez Roux, *Drexel University*
Nancy S. Jenny, *University of Vermont*
Kiang Liu, *Northwestern University*
Frank J. Penedo, *Northwestern University*
Mercedes Carnethon, *Northwestern University*

Journal Title: Health Psychology

Volume: Volume 35, Number 4

Publisher: American Psychological Association | 2016-04-01, Pages 343-350

Type of Work: Article | Post-print: After Peer Review

Publisher DOI: 10.1037/hea0000331

Permanent URL: <https://pid.emory.edu/ark:/25593/rz9zg>

Final published version: <http://dx.doi.org/10.1037/hea0000331>

Copyright information:

© 2016 American Psychological Association.

Accessed May 16, 2025 7:54 AM EDT



HHS Public Access

Author manuscript

Health Psychol. Author manuscript; available in PMC 2017 April 01.

Published in final edited form as:

Health Psychol. 2016 April ; 35(4): 343–350. doi:10.1037/hea0000331.

Self-reported experiences of discrimination and inflammation among men and women: The Multi-Ethnic Study of Atherosclerosis

Kiarri Kershaw¹, Tené T. Lewis², Ana V. Diez Roux³, Nancy S. Jenny⁴, Kiang Liu¹, Frank J. Penedo⁵, and Mercedes Carnethon¹

¹Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

²Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA 30322, USA

³Department of Epidemiology and Biostatistics, Drexel University School of Public Health, Philadelphia, PA 19104, USA

⁴Department of Pathology, University of Vermont College of Medicine, Burlington, VT 05405, USA

⁵Departments of Medical Social Sciences and Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

Abstract

Objective—To examine associations of lifetime and everyday discrimination with inflammation independent of sociodemographic characteristics.

Method—Cross-sectional associations of self-reported experiences of everyday discrimination and lifetime discrimination with interleukin-6 (IL-6) and C-reactive protein (CRP) were examined by gender in a multi-ethnic sample of 3099 men and 3468 women aged 45–84 years. Everyday discrimination, lifetime discrimination due to any attribution, and lifetime discrimination attributed to race/ethnicity were based on self-report, and IL-6 and CRP were assayed from blood samples.

Results—Among women, higher levels of all 3 discrimination measures were significantly associated with higher IL-6 in models adjusted for sociodemographic characteristics, recent infection, anti-inflammatory medication use, and hormone replacement therapy use. All associations were attenuated with adjustment for BMI. For men, everyday discrimination was inversely associated with IL-6 in all adjusted models. Lifetime discrimination was not related to IL-6 among men. Discrimination was unassociated with CRP in all models for both men and women.

Conclusions—The association between discrimination and inflammation varied by gender and marker of inflammation. These findings highlight the complex relationship between discrimination and CVD risk and point to areas in need of further research.

Keywords

discrimination; inflammation; gender

This article examines cross-sectional associations of discrimination with inflammation. Chronic exposure to psychosocial stressors like discrimination may result in chronic inflammation via dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis (Bailey Merz et al., 2002; Black, 2002; Lampert et al., 2008; McEwen, 1998; Sapolsky, Alberts, & Altmann, 1997). The HPA axis, one of the body's main stress-response systems, stimulates production of proinflammatory cytokines like interleukin-6 (IL-6) which in turn stimulates C-reactive protein (CRP), an acute-phase marker of systemic inflammation (Papanicolaou, Wilder, Manolagas, & Chrousos, 1998). Chronic inflammation in turn may lead to endothelial dysfunction and atherosclerosis, thus making it a potentially important physiologic contributor to existing racial/ethnic and socioeconomic disparities in cardiovascular disease (Arnett et al., 2011; Libby, Ridker, & Maseri, 2002; Pearson et al., 2003).

Few studies have examined associations of discrimination with inflammation, and findings are mixed (Albert et al., 2008; Cunningham et al., 2012; Friedman, Williams, Singer, & Ryff, 2009; Lewis, Aiello, Leurgans, Kelly, & Barnes, 2010). A study of older African-American adults (70% female) found that everyday experiences of discrimination (e.g., being treated with less respect than others or as if you are not smart) were associated with higher levels of C-reactive protein (CRP) after adjusting for sociodemographic characteristics (Lewis et al., 2010). In addition, a recent longitudinal study found white women reporting 3 or more major lifetime experiences of racial/ethnic discrimination and black women reporting 1–2 experiences had higher CRP levels compared with those who reported no major experiences of discrimination after adjusting for sociodemographic characteristics (Cunningham et al., 2012). However, they also found discrimination was inversely associated with CRP in black men and unassociated with CRP in white men. A study of non-Hispanic black, non-Hispanic white, and Hispanic adults living in Dallas found no association between lifetime racial/ethnic discrimination and CRP for any race/ethnic group (Albert et al., 2008). A study of chronic discrimination and E-selectin, a cell adhesion molecule expressed as part of the inflammatory response to endothelial damage, in a sample of whites found higher lifetime discrimination (due to any attribution) and higher everyday discrimination was associated with higher E-selectin in men; they found no association in women (Friedman et al., 2009).

One reason for these mixed findings could be that the measure of discrimination differed across the studies, with two studies examining the correlates of lifetime discrimination, another focused on everyday discrimination, and yet another examining both types of discrimination. These different measures were designed to assess related, but distinct phenomena. Lifetime discrimination captures the accumulation of exposure to acute, major

stressors over time (e.g., being unfairly fired, being denied housing), while everyday discrimination reflects chronic exposure to more minor, day-to-day stressors (e.g. being treated with less respect, receiving poorer service in stores and restaurants) (Williams, Neighbors, & Jackson, 2003). Both represent salient sources of stress, and while stress theorists argue that, in general, chronic exposures to stress are more strongly linked to health outcomes than acute exposures (Cohen, Kessler, & Gordon, 1995), findings from Friedman et al. (2009) with E-selectin suggest that in the case of discrimination both types of discrimination may be equally predictive of inflammation. In addition, it remains unclear whether discrimination attributed to race/ethnicity in particular is associated with worse health outcomes. Many studies indicate the experience of discrimination is a stronger predictor of health than the attribution, but more research is needed in this area (Lewis, Cogburn, & Williams, 2015).

In this paper we examine associations of everyday and lifetime discrimination with IL-6 and CRP in participants of the Multi-Ethnic Study of Atherosclerosis study. Based on previous research showing gender and race/ethnic differences in the relationship between discrimination and inflammation (Cunningham et al., 2012; Friedman et al., 2009) as well as differences in health behaviors adopted to cope with stress (Block, He, Zaslavsky, Ding, & Ayanian, 2009; Kershaw, Mezuk, Abdou, Rafferty, & Jackson, 2010), we tested for interactions of discrimination with gender and race/ethnicity.

This research builds on the existing literature in several ways. No studies to our knowledge have assessed relationships of discrimination with multiple markers of inflammation and none have examined IL-6. IL-6 is hypothesized to contribute to the development of coronary heart disease via multiple mechanisms (Yudkin, Kumari, Humphries, & Mohamed-Ali, 2000). It induces CRP secretion in response to stress, but it has also been shown to predict CVD mortality independent of CRP (Harris et al., 1999). Thus, IL-6 and CRP represent related but distinct markers of inflammation. A better understanding of the impact of discrimination on different inflammatory markers may help elucidate the mechanisms underlying the impact of discrimination on CVD risk. In addition, few studies have compared multiple measures of discrimination. This approach allows for a deeper understanding of the impact of both lifetime discrimination and everyday discrimination on inflammation, as well as the role of attribution of discriminatory experiences.

Method

Sample and Design

This study used baseline data from the Multi-Ethnic Study of Atherosclerosis (MESA), an observational cohort study designed to examine the determinants of subclinical cardiovascular disease in 6814 adults aged 45–84 years (Bild et al., 2002). Participants free of clinical cardiovascular disease at baseline were recruited from six study sites (New York, New York; Baltimore City and County, Maryland; Forsyth County, North Carolina; Minneapolis, Minnesota; Chicago, Illinois; and Los Angeles County, California) between 2000 and 2002. The cohort was 38% non-Hispanic White, 28% non-Hispanic Black, 22% Hispanic, and 12% Chinese at baseline. At each site, random population samples were selected using various lists of area residents. Of the selected persons deemed eligible after

screening, 59.8% participated in the study. Additional details including other exclusion criteria are provided elsewhere (Bild et al., 2002). All participants provided written informed consent and the study was approved by Institutional Review Boards at each field center.

Baseline data were used because that is the only time point at which all exposure and outcome measures were assessed. Of the 6814 participants at baseline, 71 were excluded from analyses of everyday discrimination for missing data on everyday discrimination. In analyses of lifetime discrimination, 128 were excluded for missing data on lifetime discrimination due to any attribution and 129 for missing data on lifetime discrimination attributed to race/ethnicity and factors other than race/ethnicity. Another 176 were excluded from each model for missing data on other study covariates. An additional 169 were missing IL-6 and 32 were missing CRP, leaving 6398 participants for the IL-6 analyses (6341 and 6340 for lifetime discrimination attributed to any factor and race/ethnicity, respectively) and 6535 (6478 and 6477 for the lifetime discrimination exposures) participants for the CRP analyses. Participants who were excluded were more likely to have lower socioeconomic position, to be older, and to be Black.

Measures

Discrimination—Discrimination was assessed using two different scales: the everyday discrimination scale and the lifetime discrimination scale (Table 1). The lifetime discrimination scale was adapted from the Detroit Area Study (Williams, Yu, & Jackson, 1999). MESA participants were asked to report whether they were ever treated unfairly (yes/no) in the six domains listed in Table 1. For each “yes” response, participants indicated the perceived reason for the unfair treatment (race/ethnicity; gender; age; religion; physical appearance; sexual orientation; income level/social class; other). For these analyses, three summary scores were calculated for lifetime discrimination: one without regard to the attributed reason, one specifically attributed to race/ethnicity, and one attributed to factors other than race/ethnicity. For each score, one point was assigned for each “yes” response (range: 0–6; Cronbach’s alpha: 0.61).

The everyday discrimination scale was based on 9 questions adapted from The Detroit Area Study (Williams, Yan, Jackson, & Anderson, 1997). This measure was designed to capture day-to-day minor incidents of unfair treatment and has been widely used to measure discrimination across different race/ethnic groups (Gee, Spencer, Chen, & Takeuchi, 2007; Perez, Fortuna, & Alegria, 2008; Williams et al., 2003). Participants were asked to indicate the frequency of encounters in which they perceived that they were treated unfairly (e.g., treated with less courtesy than others, receive poorer service than others) on a day-to-day basis. The perceived reason for this unfair treatment was not assessed. Response options were on a 6-point scale: 1=almost every day; 2=at least once a week; 3=a few times a month; 4=a few times a year; 5=less than once a year; and 6=never. A summary score was created by summing across the nine items with higher scores indicating more everyday discrimination (range: 9–54; Cronbach’s alpha: 0.88). Discrimination was modeled continuously in these analyses.

Inflammatory markers—CRP (mg/L) was measured by nephelometry (BNII nephelometer, Dade Behring, Deerfield, IL). The intra-assay and inter-assay analytical coefficients of variation for CRP ranged from 2.3%–4.4% and from 2.1%–5.7%, respectively. IL-6 (pg/mL) was measured by ultrasensitive enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN) with an analytical coefficient of variation of 6.3%. The distributions of both IL-6 and CRP were highly skewed, so they were log-transformed for the analyses.

Covariates—Sociodemographic variables included in the analyses were age, education (categorized as high school diploma/GED certificate or less; some college but no degree; and college or more completed), income (quartiles), and employment status (dichotomized as employed, homemaker, or retired vs. unemployed). Anti-inflammatory medication use was defined as reporting currently using non-steroidal anti-inflammatory agents, oral anti-inflammatory agents, or aspirin at least 3 days per week. Hormone replacement therapy use was dichotomized as current versus not current. Recent infection was defined as reporting an acute infection within the 2 weeks prior to the baseline interview including fever, cold or flu, urinary infection, sinusitis, gout flare-up, and arthritis flare-up.

Diabetes was defined as having a fasting glucose ≥ 126 mg/dl or being on insulin or oral hypoglycemic medications (American Diabetes, 2004). Hypertension was defined as having a diastolic blood pressure ≥ 90 mm Hg, a systolic blood pressure ≥ 140 mm Hg, or reported use of blood pressure-lowering medications (“The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure,” 1997). Plasma total cholesterol (mg/dl) was measured by the cholesterol-oxidase method (Paramsothy et al., 2010) and statin medication use was based on self-report. BMI (kg/m^2) was modeled continuously using measured height (in m) and weight (in kg). Physical activity was categorized as high (≥ 1000 MET-minutes per week of energy expenditure from recreational activity), intermediate (< 1000 MET-minutes per week), or physically inactive based on the 2008 Physical Activity Guidelines for Americans (U.S. Department of Health and Human Services). Cigarette smoking was categorized as current, former, and never (reference), and alcohol use was dichotomized as current vs. not current. Depressive symptoms were assessed continuously using the 20-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977). The potential range for this scale is 0 to 60.

Data Analysis

Descriptive statistics for selected participant characteristics were generated. Linear regression on the log-transformed inflammatory markers was used to estimate percent differences in the geometric mean of inflammatory markers associated with a standard deviation increase in each discrimination measure before and after adjusting for confounders and mediators. Four models were fit for each outcome. Model 1 adjusted for age, income, education, employment status, recent infection, anti-inflammatory medication use, and current hormone replacement therapy use as potential confounders. Models 2–4 sequentially adjusted for behavioral and biological factors that could act either as confounders or mediators of the discrimination-inflammation relationship. The cross-sectional study design

precludes us from definitively making this distinction, but we have modeled these separately as potential factors on the causal pathway linking discrimination to inflammation. Model 2 adjusted for lifestyle factors including current smoking, current alcohol use, physical inactivity, and depressive symptoms. Model 3 further adjusted for BMI, and Model 4 adjusted for diabetes, hypertension, total cholesterol, and statin medication use. Moderation of associations of discrimination with inflammation by race/ethnicity and gender was assessed by testing discrimination*gender and discrimination*race/ethnicity interaction terms in models adjusted for Model 1 covariates.

Statistical mediation was assessed for any Model 2–4 covariates that attenuated associations of discrimination with inflammation using the PROCESS macro for SAS (Hayes, 2013). Ordinary least squares regression was used to estimate indirect effects of discrimination on inflammation through the potential mediator(s). Bootstrapping of the sampling distribution of the indirect effects was used to derive bias-corrected 95% confidence intervals (CIs) and assess statistical significance. Bootstrap estimates were based on 10,000 draws with replacement from the current sample. Statistical significance was determined at the level of $\alpha=0.05$. One potential concern is that the numerous statistical tests performed in this study (two types of discrimination and two measures of inflammation) may result in p-values less than 0.05 by chance, even if all of our null hypotheses are really true. To account for this, findings were also evaluated for statistical significance after adjustment for multiple tests using Bonferroni's method ($\alpha=0.05/4=0.0125$). All analyses were carried out using SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

Our tests of interaction terms of discrimination with race/ethnicity and discrimination with gender revealed the majority of associations varied by gender but not race/ethnicity. Only lifetime discrimination of any attribution varied significantly by race/ethnicity, and that was only for CRP (lifetime discrimination*race/ethnicity interaction, $p = 0.23$ for IL-6 and 0.01 for CRP). Associations did not vary significantly by race/ethnicity for everyday discrimination for IL-6 or CRP (everyday discrimination*race/ethnicity interaction, $p = 0.51$ and 0.79, respectively). Associations of everyday and lifetime discrimination of any attribution with IL-6 varied significantly by gender (everyday discrimination*gender interaction, $p = 0.0004$; lifetime discrimination*gender interaction, $p = 0.04$). The relationship between everyday discrimination and CRP also varied significantly by gender (everyday discrimination*gender interaction, $p = 0.02$); there was no significant variation by gender in the association between lifetime discrimination of any attribution and CRP (lifetime discrimination*gender interaction, $p = 0.23$). Given the more consistent differences in discrimination-inflammation associations by gender, gender-specific estimates are provided for all analyses.

Mean discrimination scores were slightly higher for men than women (Table 2). A greater percentage of women were in the lowest socioeconomic category than men; women were also less likely to be currently employed. Current smoking and current alcohol use were more prevalent among men than women, while physical inactivity and BMI were higher for women. Geometric mean IL-6 and CRP were both higher among women than men.

Among women, IL-6 levels were 3.0% higher (95% CI: 0.7%, 5.2%) for each standard deviation increase in everyday discrimination score after adjusting for age, race/ethnicity, education, income, employment status, recent infection, anti-inflammatory medication use, and current hormone replacement therapy use (Table 3). This association attenuated with further adjustment for BMI (1.1%; 95% CI: -1.0%, 3.2%). BMI was a significant mediator of the everyday discrimination-IL-6 relationship ($a*b = 0.03$; 95% CI: 0.02, 0.04). Higher everyday discrimination was significantly associated with higher BMI (not shown in table; $\beta = 0.44$; 95% CI: 0.29, 0.58), and higher BMI was significantly associated with higher IL-6 (not shown; 4.4%; 95% CI: 4.1%, 4.7%). Findings were essentially unchanged in models further adjusted for diabetes, hypertension, total cholesterol, and statin medication use. In contrast, for men, IL-6 levels were 2.6% lower (95% CI: -4.9%, -0.2%) for each standard deviation increase in everyday discrimination score in Model 1. Although the point estimates only changed slightly across models, this association was not significant after adjustment for multiple tests in initial models, but became stronger ($p < 0.0125$) in models adjusted for BMI and biological CVD risk factors.

Higher reported lifetime discrimination due to any attribution was associated with higher IL-6 among women after adjusting for age, race/ethnicity, education, income, employment status, recent infection, anti-inflammatory medication use, and current hormone replacement therapy use (Model 1, 4.6%; 95% CI: 2.3%, 7.0%). As with everyday discrimination, this association was attenuated with adjustment for BMI (Model 3, 2.3%; 95% CI: 0.1%, 4.6%). Higher lifetime discrimination was significantly associated with higher BMI (not shown in table; $\beta = 0.43$; 95% CI: 0.29, 0.56). BMI was a statistically significant mediator of associations of lifetime discrimination due to any attribution ($a*b = 0.03$; 95% CI: 0.02, 0.04). Findings for lifetime discrimination attributed to race/ethnicity ($a*b = 0.03$; 95% CI: 0.02, 0.04) and lifetime discrimination attributed to other factors ($a*b = 0.02$; 95% CI: 0.003, 0.04) were similar but associations did not remain statistically significant with adjustment for BMI. Higher lifetime discrimination attributed to race/ethnicity ($\beta = 0.28$; 95% CI: 0.14, 0.41) and other factors ($\beta = 0.31$; 95% CI: 0.18, 0.45) were both related to higher BMI. Lifetime discrimination was not associated with IL-6 among men.

Among women, none of the discrimination measures were significantly associated with CRP levels (Table 4). For men, all point estimates were stronger for associations between everyday discrimination and CRP compared to IL-6, but none reached statistical significance. In addition, neither measure of lifetime discrimination was significantly associated with CRP in men.

Discussion

In a multi-ethnic cohort, everyday experiences of discrimination and lifetime discrimination were associated with higher IL-6 in women. This positive association appeared to be mediated by BMI. Everyday discrimination was inversely related to IL-6 among men, but there was no association between lifetime discrimination and IL-6. Discrimination was unassociated with CRP in both men and women.

Among women, the relationship between discrimination and IL-6 was similar in magnitude and significance across the measures of discrimination. This is consistent with a review of previous research by (Lewis et al., 2015) which found similar associations of both racial and nonracial discrimination with health. These results support the theory that experiences of discrimination are more salient predictors of health than the attributions of these experiences. In contrast, findings were not consistent for men, with everyday discrimination being the only measure significantly associated with IL-6.

In addition, while higher everyday discrimination was associated with higher IL-6 among women, it was linked to lower IL-6 among men. Reasons for the gender difference in associations of everyday discrimination with IL-6 are not clear. It may reflect gender differences in the extent to which these everyday experiences of discrimination are appraised as stressful. Unfortunately measures were not available to assess this possibility. These divergent findings may also be indicative of gender differences in the choice of stress-coping behaviors (Block et al., 2009; Grunberg & Straub, 1992). More specifically, it is possible that experiences of discrimination decrease protective psychological or behavioral activities in women, but increase these same behaviors in men. For example, a laboratory study in healthy, non-smoking men and women found the introduction of acute stressor resulted in some increased food consumption among women but lower consumption among men (Grunberg & Straub, 1992). This may also explain why adjusting for BMI only attenuated the relationship between everyday discrimination and IL-6 in women.

The significant associations between discrimination and IL-6 among women in the current study was independent of a number of factors known to be associated with inflammation including sociodemographic characteristics, recent infection, medication use, and depressive symptoms. However, they were largely accounted for with adjustment for BMI. Due to the cross-sectional nature of this study, it cannot be determined whether the attenuated association found for women indicates BMI is a confounder or a mediator. BMI could be acting as a confounder, given that it is a strong correlate of inflammatory cytokines like IL-6 and CRP (Barinas-Mitchell, Cushman, Meilahn, Tracy, & Kuller, 2001; Visser, Bouter, McQuillan, Wener, & Harris, 1999). Alternatively, BMI could be acting as a mediator if women who are exposed to everyday discrimination gain weight as a result (e.g., by eating unhealthy foods to cope with the stress of discrimination (Adam & Epel, 2007; Dallman et al., 2003)).

Our formal test for mediation showed BMI was a statistically significant mediator for all 3 measures of discrimination, and there is some evidence in the literature supporting the role of weight gain as a mediator. Cross-sectional studies have shown perceived everyday discrimination is associated with obesity (Hunte, 2011; Hunte & Williams, 2009) and visceral fat accumulation (Lewis, Kravitz, Janssen, & Powell, 2011). In addition, a prospective study found higher levels of perceived everyday and lifetime racism was related to weight gain (Cozier, Wise, Palmer, & Rosenberg, 2009). Another longitudinal study found increases in self-reported discrimination were associated with increases in waist circumference and BMI in black women, but not in white women or men (Cunningham et al., 2013).

Findings for CRP were weaker than findings for IL-6 among both men and women. One explanation for this is that greater variability in CRP levels among participants compared with IL-6 levels, led to less precise estimates. This may explain findings for men in particular, given the point estimates for associations of discrimination with CRP were generally stronger than those for IL-6, but the confidence intervals were also wider. However, for women, point estimates for associations of each discrimination measure with CRP were much weaker than associations with IL-6. Further work is needed using multiple markers of inflammation to better understand reasons for these differences.

Although we found associations of discrimination with inflammation varied by gender, we found little evidence of heterogeneity by race/ethnicity. Prior findings in MESA describe higher reporting of lifetime and everyday discrimination in blacks than other race/ethnic groups but no differences in the associations of discrimination with hypertension (Mujahid, Diez Roux, Cooper, Shea, & Williams, 2011) and poor health behaviors (Borrell et al., 2010). This suggests experiences of discrimination have a similar impact on the health of different race/ethnic groups but that the differential prevalence of these experiences may make discrimination more detrimental to the health of blacks.

This study has several strengths and limitations. An important strength of this study is that discrimination was measured using two previously validated psychometric instruments that have been commonly used in population-based studies (Williams et al., 1997). In addition, although this study was cross-sectional, inflammation is an asymptomatic condition, and thus was less likely to bias study findings by influencing individuals' recall of experiences of discrimination. It also reduces the likelihood that differential missing data by race/ethnicity, age, and SEP was associated with our study outcome, which means our findings are less susceptible to nonresponse bias. This is particularly true given this population is free of clinical cardiovascular disease.

A major limitation of the cross-sectional design of this study is that it does not allow for an assessment of whether experiences of discrimination influence changes in inflammation over time. Another limitation is that differences in the appraisal of exposure to discrimination could not be measured, which may help explain the gender differences. In addition, the MESA cohort is not necessarily representative of all populations, which may limit generalizability. Specifically, the fact that they are all free of clinical cardiovascular disease may mean they are healthier than the general population.

Few studies have examined associations of discrimination with markers of inflammation. These findings provide some evidence supporting inflammation as a pathway linking discrimination to poor cardiovascular health among women, with BMI potentially representing a key upstream determinant of both inflammation and cardiovascular health disparities. Given the well-documented disparities in obesity by race/ethnicity and SEP among women, it is essential to elucidate how discrimination influences BMI and what resources may be used to buffer the adverse health impact of discrimination. Further work is needed to better understand the mechanisms linking discrimination to different markers of inflammation and to uncover explanations for gender differences in these relationships.

Acknowledgments

This research was supported by contracts N01-HC-95159 through N01-HC-95169 from the National Heart, Lung, and Blood Institute and by grants UL1-RR-024156 and UL1-RR-025005 from NCRR. The authors thank the other investigators, the staff, and the participants of the Multi-Ethnic Study of Atherosclerosis (MESA) for their valuable contributions. A full list of participating MESA investigators and institutions can be found at <http://www.mesa-nhlbi.org>.

References

- Adam TC, Epel ES. Stress, eating and the reward system. *Physiol Behav.* 2007; 91(4):449–458.10.1016/j.physbeh.2007.04.011 [PubMed: 17543357]
- Albert MA, Ravenell J, Glynn RJ, Khera A, Halevy N, de Lemos JA. Cardiovascular risk indicators and perceived race/ethnic discrimination in the Dallas Heart Study. *Am Heart J.* 2008; 156(6):1103–1109.10.1016/j.ahj.2008.07.027 [PubMed: 19033005]
- American Diabetes, A. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2004; 27(Suppl 1):S5–S10. [PubMed: 14693921]
- Arnett DK, McClelland RL, Bank A, Bluemke DA, Cushman M, Szalai AJ, Lima JA. Biomarkers of inflammation and hemostasis associated with left ventricular mass: The Multiethnic Study of Atherosclerosis (MESA). *Int J Mol Epidemiol Genet.* 2011; 2(4):391–400. [PubMed: 22200000]
- Bairey Merz CN, Dwyer J, Nordstrom CK, Walton KG, Salerno JW, Schneider RH. Psychosocial stress and cardiovascular disease: pathophysiological links. *Behav Med.* 2002; 27(4):141–147.10.1080/08964280209596039 [PubMed: 12165968]
- Barinas-Mitchell E, Cushman M, Meilahn EN, Tracy RP, Kuller LH. Serum levels of C-reactive protein are associated with obesity, weight gain, and hormone replacement therapy in healthy postmenopausal women. *Am J Epidemiol.* 2001; 153(11):1094–1101. [PubMed: 11390329]
- Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Tracy RP. Multi-ethnic study of atherosclerosis: objectives and design. *Am J Epidemiol.* 2002; 156(9):871–881. [PubMed: 12397006]
- Black PH. Stress and the inflammatory response: a review of neurogenic inflammation. *Brain Behav Immun.* 2002; 16(6):622–653. [PubMed: 12480495]
- Block JP, He Y, Zaslavsky AM, Ding L, Ayanian JZ. Psychosocial stress and change in weight among US adults. *Am J Epidemiol.* 2009; 170(2):181–192.10.1093/aje/kwp104 [PubMed: 19465744]
- Borrell LN, Diez Roux AV, Jacobs DR Jr, Shea S, Jackson SA, Shrager S, Blumenthal RS. Perceived racial/ethnic discrimination, smoking and alcohol consumption in the Multi-Ethnic Study of Atherosclerosis (MESA). *Prev Med.* 2010; 51(3–4):307–312.10.1016/j.ypmed.2010.05.017 [PubMed: 20609433]
- Cohen, S.; Kessler, RC.; Gordon, LU. *Measuring stress: A guide for health and social scientists.* New York, NY: Oxford University Press; 1995.
- Cozier YC, Wise LA, Palmer JR, Rosenberg L. Perceived racism in relation to weight change in the Black Women’s Health Study. *Ann Epidemiol.* 2009; 19(6):379–387.10.1016/j.annepidem.2009.01.008 [PubMed: 19364665]
- Cunningham TJ, Berkman LF, Kawachi I, Jacobs DR Jr, Seeman TE, Kiefe CI, Gortmaker SL. Changes in waist circumference and body mass index in the US CARDIA cohort: fixed-effects associations with self-reported experiences of racial/ethnic discrimination. *J Biosoc Sci.* 2013; 45(2):267–278.10.1017/s0021932012000429 [PubMed: 22856616]
- Cunningham TJ, Seeman TE, Kawachi I, Gortmaker SL, Jacobs DR, Kiefe CI, Berkman LF. Racial/ethnic and gender differences in the association between self-reported experiences of racial/ethnic discrimination and inflammation in the CARDIA cohort of 4 US communities. *Soc Sci Med.* 2012; 75(5):922–931.10.1016/j.socscimed.2012.04.027 [PubMed: 22682683]
- Dallman MF, Pecoraro N, Akana SF, La Fleur SE, Gomez F, Houshyar H, Manalo S. Chronic stress and obesity: a new view of “comfort food”. *Proc Natl Acad Sci U S A.* 2003; 100(20):11696–11701.10.1073/pnas.1934666100 [PubMed: 12975524]

- Friedman EM, Williams DR, Singer BH, Ryff CD. Chronic discrimination predicts higher circulating levels of E-selectin in a national sample: the MIDUS study. *Brain Behav Immun.* 2009; 23(5):684–692.10.1016/j.bbi.2009.01.002 [PubMed: 19171188]
- Gee GC, Spencer MS, Chen J, Takeuchi D. A nationwide study of discrimination and chronic health conditions among Asian Americans. *Am J Public Health.* 2007; 97(7):1275–1282.10.2105/AJPH.2006.091827 [PubMed: 17538055]
- Grunberg NE, Straub RO. The role of gender and taste class in the effects of stress on eating. *Health Psychol.* 1992; 11(2):97–100. [PubMed: 1582385]
- Harris TB, Ferrucci L, Tracy RP, Corti MC, Wacholder S, Ettinger WH Jr, Wallace R. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. *Am J Med.* 1999; 106(5):506–512. [PubMed: 10335721]
- Hayes, AF. Introduction to mediation, moderation and conditional process analysis: A regression-based approach. New York, NY: Guilford Press; 2013.
- Hunte HE. Association between perceived interpersonal everyday discrimination and waist circumference over a 9-year period in the Midlife Development in the United States cohort study. *Am J Epidemiol.* 2011; 173(11):1232–1239.10.1093/aje/kwq463 [PubMed: 21354988]
- Hunte HE, Williams DR. The association between perceived discrimination and obesity in a population-based multiracial and multiethnic adult sample. *Am J Public Health.* 2009; 99(7):1285–1292.10.2105/AJPH.2007.128090 [PubMed: 18923119]
- Kershaw KN, Mezuk B, Abdou CM, Rafferty JA, Jackson JS. Socioeconomic position, health behaviors, and C-reactive protein: a moderated-mediation analysis. *Health Psychol.* 2010; 29(3): 307–316.10.1037/a0019286 [PubMed: 20496985]
- Lampert R, Bremner JD, Su S, Miller A, Lee F, Cheema F, Vaccarino V. Decreased heart rate variability is associated with higher levels of inflammation in middle-aged men. *Am Heart J.* 2008; 156(4):759 e751–757.10.1016/j.ahj.2008.07.009 [PubMed: 18926158]
- Lewis TT, Aiello AE, Leurgans S, Kelly J, Barnes LL. Self-reported experiences of everyday discrimination are associated with elevated C-reactive protein levels in older African-American adults. *Brain Behav Immun.* 2010; 24(3):438–443.10.1016/j.bbi.2009.11.011 [PubMed: 19944144]
- Lewis TT, Cogburn CD, Williams DR. Self-reported experiences of discrimination and health: scientific advances, ongoing controversies, and emerging issues. *Annu Rev Clin Psychol.* 2015; 11:407–440.10.1146/annurev-clinpsy-032814-112728 [PubMed: 25581238]
- Lewis TT, Kravitz HM, Janssen I, Powell LH. Self-reported experiences of discrimination and visceral fat in middle-aged African-American and Caucasian women. *Am J Epidemiol.* 2011; 173(11): 1223–1231.10.1093/aje/kwq466 [PubMed: 21354991]
- Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. *Circulation.* 2002; 105(9):1135–1143. [PubMed: 11877368]
- McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med.* 1998; 338(3):171–179.10.1056/NEJM199801153380307 [PubMed: 9428819]
- Mujahid MS, Diez Roux AV, Cooper RC, Shea S, Williams DR. Neighborhood stressors and race/ethnic differences in hypertension prevalence (the Multi-Ethnic Study of Atherosclerosis). *Am J Hypertens.* 2011; 24(2):187–193.10.1038/ajh.2010.200 [PubMed: 20847728]
- Papanicolaou DA, Wilder RL, Manolagas SC, Chrousos GP. The pathophysiologic roles of interleukin-6 in human disease. *Ann Intern Med.* 1998; 128(2):127–137. [PubMed: 9441573]
- Paramsothy P, Knopp RH, Bertoni AG, Blumenthal RS, Wasserman BA, Tsai MY, Heckbert SR. Association of combinations of lipid parameters with carotid intima-media thickness and coronary artery calcium in the MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol.* 2010; 56(13):1034–1041.10.1016/j.jacc.2010.01.073 [PubMed: 20846602]
- Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO 3rd, Criqui M, American Heart, A. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation.* 2003; 107(3):499–511. [PubMed: 12551878]

- Perez DJ, Fortuna L, Alegria M. Prevalence and Correlates of Everyday Discrimination among U.S. Latinos. *J Community Psychol*. 2008; 36(4):421–433.10.1002/jcop.20221 [PubMed: 19960098]
- Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Measurement*. 1977; 1(3):385–401.
- Sapolsky RM, Albers SC, Altmann J. Hypercortisolism associated with social subordination or social isolation among wild baboons. *Arch Gen Psychiatry*. 1997; 54(12):1137–1143. [PubMed: 9400351]
- The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med*. 1997; 157(21):2413–2446. [PubMed: 9385294]
- U.S. Department of Health and Human Services. Physical activity guidelines for Americans. 2008. Retrieved July 20, 2013, from <http://www.health.gov/paguidelines>
- Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. *JAMA*. 1999; 282(22):2131–2135. [PubMed: 10591334]
- Williams DR, Neighbors HW, Jackson JS. Racial/ethnic discrimination and health: findings from community studies. *Am J Public Health*. 2003; 93(2):200–208. [PubMed: 12554570]
- Williams DR, Yan Y, Jackson JS, Anderson NB. Racial Differences in Physical and Mental Health: Socio-economic Status, Stress and Discrimination. *J Health Psychol*. 1997; 2(3):335–351.10.1177/135910539700200305 [PubMed: 22013026]
- Williams, DR.; Yu, Y.; Jackson, JS. Race, stress, and physical health. In: Contrada, RJ.; Ashmore, RD., editors. *Self, social identity, and physical health*. New York, NY: Oxford University Press; 1999. p. 71-100.
- Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: is interleukin-6 the link? *Atherosclerosis*. 2000; 148(2):209–214. [PubMed: 10657556]

Table 1

Questionnaire Items for Everyday and Life Discrimination Scales

Everyday discrimination*	You are treated with less courtesy than other people
	You are treated with less respect than other people
	You receive poorer service than other people at restaurants or stores
	People act as if they think you are not smart
	People act as if they are afraid of you
	People act as if they think you are dishonest
	People act as if they're better than you
	You are called names or insulted
	You are threatened or harassed
Lifetime discrimination	Do you think you have ever been unfairly fired or denied a promotion?
	For unfair reasons, do you think you have ever not been hired for a job?
	Have you ever been unfairly stopped, searched, questioned, physically threatened or abused by the police?
	Have you ever been unfairly discouraged by a teacher or advisor from continuing your education?
	Have you ever been unfairly prevented from moving into a neighborhood because the landlord or a realtor refused to sell or rent you a house or apartment?
	Have you ever moved into a neighborhood where neighbors made life difficult for you or your family?

* Responses are to the following question: In your day-to-day life, how often have any of the following things happened to you?

Table 2

Selected characteristics of study participants.

	Men (n=3099) ^a	Women (n=3468) ^b	t-value or χ^2 ^c	p-value
Everyday discrimination, mean (SD)	14.7 (6.2)	14.3 (5.8)	-2.84	0.005
Lifetime discrimination (any attribution), mean (SD)	0.8 (1.1)	0.6 (1.0)	-7.37	<0.0001
Lifetime discrimination (attributed to race/ethnicity), mean (SD)	0.4 (0.9)	0.2 (0.7)	-8.14	<0.0001
Lifetime discrimination (attributed to factors other than race/ ethnicity), mean (SD)	0.4 (0.8)	0.4 (0.7)	-2.14	0.03
Age (years), mean (SD)	62.1 (10.2)	61.9 (10.2)	-0.48	0.63
High school diploma or equivalent, %	31.2	40.0	54.99	<0.0001
Income < \$16,000, %	14.7	23.3	78.38	<0.0001
Currently working, %	59.1	48.7	9.62	<0.0001
Current smoker, %	14.3	11.7	226.56	<0.0001
Current alcohol user, %	63.4	48.9	138.37	<0.0001
Physically inactive, %	21.0	24.2	70.1	<0.0001
BMI (kg/m ²), mean (SD)	27.9 (4.4)	28.7 (6.2)	6.42	<0.0001
Depressive symptoms score, mean (SD)	6.4 (6.6)	8.6 (8.3)	12.12	<0.0001
Anti-inflammatory medication use, %	33.9	35.2	1.21	0.27
Diabetes, %	13.9	11.3	10.36	0.001
Hypertension, %	42.5	46.1	8.37	0.004
Total cholesterol (mg/dl), mean (SD)	188.3 (35.0)	199.5 (35.6)	12.86	<0.0001
Statin medication use, %	14.8	14.9	0.02	0.88
Current hormone replacement therapy use, %	-	28.4	-	-
Recent infection, %	23.9	35.7	108.0	<0.0001
IL-6 (pg/mL), geometric mean (IQR)	1.18 (0.73 – 1.79)	1.28 (0.82 – 1.94)	4.76	<0.0001
CRP (mg/L), geometric mean (IQR)	1.49 (0.70 – 3.14)	2.38 (1.04 – 5.62)	16.51	<0.0001

SD, standard deviation; BMI, body mass index; IL-6, interleukin-6; CRP, C-reactive protein; IQR, interquartile range

^a n=3012 for IL-6 and n=3085 for CRP^b n=3386 for IL-6 and n=3450 for CRP^c t-value for continuous covariates and χ^2 for categorical covariates

Table 3

Percent difference (95% CI) in interleukin-6 associated with a standard deviation increase in everyday and lifetime discrimination scores according to gender

	Model 1 ^a	Model 2 ^b	Model 3 ^c	Model 4 ^d
Everyday Discrimination				
Men	-2.6 (-4.9, -0.2) *	-2.7 (-5.1, -0.4) *	-2.8 (-5.0, -0.6) **	-2.8 (-5.0, -0.6) **
Women	3.0 (0.7, 5.2) **	2.8 (0.5, 5.1) *	1.1 (-1.0, 3.2)	1.3 (-0.9, 3.4)
Lifetime Discrimination (any attribution)				
Men	1.2 (-1.0, 3.5)	1.2 (-1.0, 3.4)	0.9 (-1.1, 3.0)	0.9 (-1.2, 3.0)
Women	4.6 (2.3, 7.0) **	4.5 (2.2, 6.9) **	2.3 (0.1, 4.6) *	2.3 (0.7, 4.5) *
Lifetime discrimination (attributed to race/ethnicity)				
Men	0.3 (-1.9, 2.5)	0.1 (-2.0, 2.3)	0.4 (-1.6, 2.4)	0.2 (-1.8, 2.3)
Women	3.8 (1.1, 6.4) **	3.6 (1.0, 6.3) **	1.4 (-1.1, 3.8)	1.4 (-1.1, 3.8)
Lifetime discrimination (attributed to factors other than race/ethnicity)				
Men	1.5 (-0.7, 3.7)	1.6 (-0.7, 3.8)	0.9 (-1.2, 3.0)	1.0 (-1.1, 3.1)
Women	3.0 (0.8, 5.3) **	3.0 (0.7, 5.2) **	1.9 (-0.2, 4.0)	1.9 (-0.2, 3.9)

* p<0.05;

** p<0.0125

^a Adjusted for age, race/ethnicity, income, education, employment status, current hormone replacement therapy use, recent infection, and anti-inflammatory medication use

^b Adjusted for Model 1, cigarette smoking, current alcohol use, physical activity, and depressive symptoms

^c Adjusted for Model 2 and body mass index

^d Adjusted for Model 3, diabetes, hypertension, total cholesterol, and statin medication use

Table 4

Percent difference (95% CI) in C-reactive protein associated with a standard deviation increase in everyday discrimination score according to gender

	Model 1 ^a	Model 2 ^b	Model 3 ^c	Model 4 ^d
Everyday Discrimination				
Men	-3.9 (-7.8, 0.1)	-3.5 (-7.6, 0.5)	-3.7 (-7.5, -0.003)	-3.5 (-7.2, 0.3)
Women	1.8 (-2.0, 5.7)	2.2 (-1.7, 6.1)	-1.0 (-4.6, 2.7)	-0.9 (-4.6, 2.8)
Lifetime Discrimination (any attribution)				
Men	1.5 (-2.3, 5.2)	1.6 (-2.2, 5.4)	1.3 (-2.2, 4.9)	1.3 (-2.2, 4.8)
Women	1.6 (-2.4, 5.7)	1.8 (-2.3, 5.9)	-1.9 (-5.7, 1.9)	-1.9 (-5.6, 1.9)
Lifetime discrimination (attributed to race/ethnicity)				
Men	2.5 (-1.1, 6.1)	2.5 (-1.1, 6.1)	3.2 (-0.1, 6.6)	3.0 (-0.4, 6.3)
Women	1.2 (-3.2, 5.6)	1.4 (-3.1, 5.8)	-2.6 (-6.7, 1.6)	-2.5 (-6.6, 1.6)
Lifetime discrimination (attributed to factors other than race/ethnicity)				
Men	-0.6 (-4.4, 3.2)	-0.5 (-4.3, 3.4)	-1.7 (-5.3, 1.9)	-1.5 (-5.0, 2.1)
Women	1.1 (-2.7, 4.9)	1.1 (-2.7, 5.0)	-0.5 (-4.0, 3.1)	-0.5 (-4.0, 3.1)

^aAdjusted for age, race/ethnicity, income, education, employment status, current hormone replacement therapy use, recent infection, and anti-inflammatory medication use

^bAdjusted for Model 1, cigarette smoking, current alcohol use, physical activity, and depressive symptoms

^cAdjusted for Model 2 and body mass index

^dAdjusted for Model 3, diabetes, hypertension, total cholesterol, and statin medication use