Associations between multiple indicators of discrimination and allostatic load among middle-aged adults

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ABSTRACT

The objective of this paper is to examine associations between multiple measures of discrimination (i.e., everyday, lifetime, and appraised burden) and components of allostatic load (AL). We drew on pooled cross-sectional data from the Biomarker Project of the Midlife in the United States study (n=2118). Ages ranged from 25 to 84 years and included mostly Black (n=389) and white (n=1598) adults. Quasi-Poisson models were fit to estimate prevalence ratios for each discrimination measure and high-risk quartiles across seven physiological systems (i.e., sympathetic and parasympathetic nervous system; HPA axis; inflammation; cardiovascular; metabolic glucose; and metabolic lipids) and overall AL scores. In fully adjusted models, everyday discrimination was associated with elevated lipids (aPR: 1.07; 95% CI 1.01, 1.13). Lifetime experiences of discrimination were associated with lower sympathetic nervous system (aPR: 0.82; 95% CI: 0.69, 0.98) and greater cardiovascular risk scores (aPR: 1.17; 95% CI: 1.02, 1.34) among those reporting three or more experiences, as well as increased inflammation (aPR: 1.13; 95% CI: 1.02, 1.25; aPR: 1.28; 95% CI: 1.14, 1.43), metabolic glucose (aPR: 1.35; 95% CI: 1.19, 1.54; aPR: 1.45; 95% CI: 1.24, 1.68), and metabolic lipids (aPR: 1.13; 95% CI: 1.03, 1.24; aPR: 1.28; 95% CI: 1.15, 1.43) scores for those reporting one to two and three or more experiences. Appraised burden yielded nuanced associations with metabolic glucose and parasympathetic nervous system scores. Everyday and lifetime experiences were also associated with higher overall AL, though burden of discrimination was only associated with AL among those reporting “a little” burden. While AL summary scores provide insight into the cumulative impacts of discrimination on health, there appear to be distinct physiologic pathways through which varying forms of discrimination contribute to AL and, ultimately, to poorer health. These unique pathways may be useful in identifying potential points of intervention to mitigate the impacts of discrimination on health inequities.

1. Introduction

Discrimination is defined as differential treatment directed towards marginalized and stigmatized groups by social institutions and individuals (Williams et al., 2019a, 2019b). An additional component of discrimination includes “patterns of dominance and oppression, viewed as expressions of a struggle for power and privilege.” (Krieger, 2001; Marshall, 1994) Different groups have been marginalized and discriminated against based on factors such as race/ethnicity, gender, disability status, and sexual orientation (Krieger, 2012, 2020; Williams and Mohammed, 2009). There is growing interest in understanding the mechanisms through which discrimination becomes embodied to affect health, including inflammatory pathways or stress responses (Cuevas et al., 2020; Goosby et al., 2018; Lockwood et al., 2018; Ong et al., 2017a; Priest, 2021). Efforts in this area are particularly salient given a growing body of research that documents associations between discrimination and several adverse health outcomes (Williams et al., 2019b; Williams and Mohammed, 2009; Pascoe and Smart Richman, 2017b).
The increased exposure to stressors such as discrimination as a result of social marginalization and devaluation is a critical component of the concept of allostatic load (AL). AL suggests that individuals from marginalized social groups frequently encounter sources of social stress which overwhelm available coping resources and physiological responses, resulting in adverse health outcomes (McEwen, 2000; Seeman et al., 2001; McEwen and Stellar, 1993). Introduced by McEwen & Stellar, AL is hypothesized as the cumulative “wear and tear” on multiple physiologic systems induced by exposure to chronic stress (McEwen and Stellar, 1993). Increased allostatic load has been associated with several adverse mental and physical health outcomes, including cardiovascular disease, poorer cognitive functioning, and mortality (Goosby et al., 2018; McEwen, 2000; Seeman et al., 2001). Indicators of multisystem physiological dysregulation, such as AL, have been employed to better understand the embodiment of discrimination. To date, studies have reported that experiences of discrimination are associated with higher AL, even after accounting for traditional risk factors (e.g., health behaviors) and sociodemographic covariates (Ong et al., 2017b; Brody et al., 2014; Vadiveloo and Mattei, 2017). Akin to other psychosocial stressors, discrimination is posited to increase allostatic load through changes to psychosocial and behavioral factors that additionally overwhelm biophysiological responses to stress (Williams et al., 2019b; Vadiveloo and Mattei, 2017; Cuevas et al., 2019). However, in understanding how discrimination becomes embodied, there remains a gap in understanding whether the strength of associations between discrimination and allostatic load are driven by specific subscales and whether these associations vary by measurement of discrimination.

In the stress literature, distinctions are drawn between acute stressors such as life events (e.g., divorce, death of a loved one, job loss), chronic, on-going stressors (e.g., a traffic-heavy commute or problems at work or in relationships), and appraisals (Cohen et al., 1995). These distinctions are mirrored in discrimination research where major lifetime events of discrimination are referred to as acute, defined experiences (e.g., unfairly fired or not hired for a job), compared to chronic or recurrent stressors such as everyday differential treatment (e.g., being treated with less respect or courtesy) (Williams et al., 2016; Lazarus, 1990). Measures of appraisals vary, though recent research has used measures of self-reported burden of discrimination, without relying on the attribution to a specific encounter. Although major lifetime events provide observable and more defined events to measure and provide context to the accumulated impact of discrimination over the lifecourse (Cohen et al., 1995; Williams et al., 2016), they may raise issues around statistical power given their infrequent occurrence. By contrast, chronic, everyday discrimination captures exposure to ongoing and relatively frequent events. While issues pertaining to measurement and assessment remain (Williams et al., 2016), these experiences may be no less “toxic” in their effects. For example, someone might not have (yet) experienced a major discrimination event in their life, but still be exposed to daily inequitable treatment. This persistent exposure to negative experiences and differential treatment through everyday experiences has been a strong predictor of the onset and progression of health outcomes (Lewis et al., 2006; Kershaw et al., 2016; Williams et al., 2003). Additionally, the inclusion of appraisals of burden of discrimination in recent literature provides evidence that the additional consideration of burden and stress from discrimination are beneficial to understanding discrimination as a contributor to adverse health outcomes (Davis et al., 2005; Sim et al., 2012; Panteso et al., 2018). This evidence suggests that the inclusion of appraisals of burden may also be useful in understanding the implications of discrimination on wellbeing. Illustrating the scope and range in impacts of measures of discrimination is of particular importance since all stressors may not equally contribute to or share plausible associations with allostatic load measures (Cohen et al., 1995; Lazarus, 1990; Rodriguez et al., 2019).

The measurement of allostatic load, as originally presented by Seeman et al., included 10 biomarkers across different physiologic systems (i.e., DHEA, epinephrine, cortisol, norepinephrine, cholesterol, systolic and diastolic blood pressure, and glycosylated hemoglobin, BMI and waist-hip ratio) (Seeman et al., 2001). However, the operationalization of AL has since been expanded given that additional biomarkers have been found to contribute to AL and, when added, act as better predictors of outcomes such as mortality and physical functioning (Guidi et al., 2021). Allostatic load can capture: the stress response via sympathetic and parasympathetic nervous system and hypothalamic-pituitary-adrenal axis (HPA) axis activity, inflammation via several markers of inflammation (e.g., C-reactive protein), metabolic glucose and lipid profiles, and indicators of cardiovascular health. Given that no gold standard exists, variations in the number of biomarkers used to assess each component and which subscales are represented in the measure have been documented (Beckie, 2012). Additionally, statistical concerns regarding the use of a summary score of highly correlated measures (e.g., BMI, waist-hip ratio) have been raised (Rodriquez et al., 2019). As previous researchers have identified, including a composite score of measures that may not be relevant to the exposure-outcome association increase measurement error (Rodriquez et al., 2019; Beckie, 2012) and do not present plausible biological pathways through which embodiment occurs for specific outcomes (Rodriquez et al., 2019). It is plausible, for example, that the associations between discrimination and mental health could be mediated through one component of AL, such as inflammation or HPA axis measures (Berger and Sarnyai, 2015), but not dysregulation in lipid metabolism. In fact, recent work has found evidence that specific subscales have stronger associations with mental health outcomes (Carbone, 2021). Focus on specific indicators used to create AL summary scores, including individual biomarkers used to compose AL measures, can facilitate an enhanced understanding of the physiological pathways underpinning the embodiment of experiences of discrimination and guide future research.

The present analysis sought to understand patterning in associations between multiple measures of general experiences of discrimination, without attribution, AL subscales, and overall AL scores. Our objectives included, first, examining associations between everyday, lifetime, and burden of discrimination and allostatic load subscales and overall allostatic load scores. Given findings from previous literature that has documented differences in relationships with allostatic load by race (Rodriquez et al., 2019; Guidi et al., 2021; Beckie, 2012), we also evaluated whether the above associations were modified by race. Last, we sought to understand whether the above associations between discrimination and allostatic load were modified by other included measures of discrimination (e.g., lifetime*everyday, everyday*burden). We hypothesized that, individually, each measure of discrimination is associated with increased high-risk scores across seven physiologic indicators of AL. Additionally, we posited that effect modification will exist between each measure of discrimination, as well as between the individual measures and race.

### 2. Methods

We use pooled cross-sectional data from the Biomarker Substudies of the Midlife in the United States (MIDUS) Study for our analysis. MIDUS is a longitudinal study of a national probability sample of households in the 48 contiguous states with a telephone. Approximately 7000 non-institutionalized U.S. residents aged 25 to 74 at the time of interview (1995–96) were included (Brim et al., 2004; Dienberg Love et al., 2010). MIDUS I data includes extensive measurement of sociodemographic and psychosocial factors (e.g., discrimination). Additional detail regarding the sampling and data collection strategies of the MIDUS study are described elsewhere (Dienberg Love et al., 2010).

In follow up interviews of the initial MIDUS I wave (MIDUS II; data collected from 2004–09), MIDUS investigators also added African American participants from Milwaukee, WI (n = 592) in an effort to
increase the racial diversity of the sample (Dienberg Love et al., 2010). Data collection in MIDUS II and the Milwaukee waves included measures captured in the initial assessment, however they also captured cognitive, biomarker, and neuro-physiological assessments on a subsample of respondents. In 2011–14, MIDUS investigators recruited and collected data on a Refresher sample of approximately 3500 adults to replenish the original MIDUS I wave. Similar data, including psychological, social factors, were collected in this cohort as were collected in MIDUS II. A subsample of the Refresher wave was also selected for cognitive, biomarker, and neuro-physiological assessments.

For the present analyses, multiple measures of discrimination, including lifetime burden of discrimination are examined in relationship to AL, using pooled cross-sectional data from the Biomarker Substudy of the MIDUS II (n = 1255) and the MIDUS Refresher waves (n = 863). All participants were eligible for inclusion. This analysis of publicly available, de-identified data was exempt from IRB review.

2.1. Measures

Experiences of discrimination. Experiences of discrimination were captured via self-administered questionnaires across three levels: (1) lifetime (Williams et al., 2008), (2) everyday (Williams et al., 1997), and (3) burden of discrimination. Items included in the lifetime and everyday measures are outlined in Supplemental Table 1. Lifetime experiences of discrimination were captured using the Major Experiences of Discrimination scale (Williams et al., 2008) measure which captures how many times over the lifecourse respondents were discriminated against as a result of their “race, ethnicity, gender, age, religion, physical appearance, sexual orientation or other characteristics” in 11 areas (e.g., discouraged to seek higher education, denied a scholarship). Similar to previous MIDUS studies examining discrimination, responses for lifetime experiences of discrimination were coded as none (i.e., a response to 0 of all 11 items), 1–2 instances (i.e., a response greater than 0 to any 1–2 of the 11 items), and 3 or more (Friedman et al., 2009). Internal reliability was acceptable within this sample (α = 0.77).

Responses to experiences of everyday discrimination were captured using the Everyday Discrimination Scale (Williams et al., 1997). This measure the frequency of routine experiences of discrimination such as being treated with less respect than others across 9 areas, including items related to being treated with less respect than others. For each item, respondents answered with the frequency of occurrence in their day-to-day life – 1 = often, 2 = sometimes, 3 = rarely, or 4 = never. Responses were reverse coded, such that 0 = never, 1 = rarely, 2 = sometimes, 3 = often and averaged. The mean of the frequency responses across the 9 items were used as the everyday discrimination score (Sims et al., 2012). This measure exhibited excellent reliability within the present sample (α = 0.95).

Capturing appraisals of the burden of discrimination, participants responded to two survey items inquiring: “Overall, how much has discrimination interfered with you having a full and productive life?” and “Overall, how much harder has your life been because of discrimination and did not respond to these questions were coded as “no discrimination reported” and grouped in the “none” category. The measures together exhibit good internal reliability (α = 0.91).

Allostatic load. Using information from 24 available biomarkers, MIDUS collects variables related to AL across seven physiological systems: (1) sympathetic nervous system (SNS) activity via overnight urinary norepinephrine & noradrenaline measures; (2) parasympathetic nervous system (PNS) activity via heart rate variability data, including two time-domain measures: root-mean square difference of the successive R-R intervals (RMSSD) and standard deviations of R-R intervals (SDRR); and two spectral frequency measures (low and high frequency heart rate variability (LFRHR; HFRHR, respectively); (3) HPA activity via urine cortisol data and blood DHEA; (4) inflammatory markers via blood-level measures of interleukin-6 (IL-6), fibrinogen, C-reactive protein (CRP), E-Selectin, and intercellular Adhesion Molecule 1 (ICAM-1); (5) cardiovascular indicators via systolic blood pressure, pulse pressure, and pulse; (6) metabolic glucose via HbA1c; glucose, and insulin resistance; and (7) metabolic lipids via BMI, waist-to-hip ratio (WHR), triglycerides, and high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol (Dienberg Love et al., 2010; Gruenewald et al., 2012). Detailed information regarding data collection of biomarkers has been previously published (Dienberg Love et al., 2010; Gruenewald et al., 2012), however we provide a brief summary of data collection procedures in the supplement (Supplemental Table 2).

An overall AL score was computed as the sum of the seven subscales (i.e., SNS, PNS, HPA, inflammation, cardiovascular, glucose, and lipids), using a high-risk quartile defined for each subscale. Subscale scores were computed for respondents with at least half of the measured biomarkers for each subscale. Risk scores were created for each subscale ranging from 0 to 1 indicating the proportion of system indicators that fell into high-risk quartile ranges based on the sample distribution (Gruenewald et al., 2012). The overall AL score (range: 0–7) is a sum of the averaged subscale scores and was calculated where 6 of the 7 subscale scores were present. Additional insight into variable creation for AL is available in supplemental materials from an analysis by Gruenewald and colleagues (Gruenewald et al., 2012). The primary outcomes of interest are average high-risk levels across each AL subscale; however, the secondary outcome includes the overall AL score. Supplemental analyses include an outcomes-wide analysis of each of the 24 available biomarkers.

Covariates. Models included measures of socioeconomic status (including measures of educational attainment (high school or less; some college; college or more), income (total household income per year; $25,000 or less; >$25,000 to $40,000; >$40,000 to $55,000; >$55,000 to $70,000; >$70,000), and current employment status (employed [i.e., working now; self-employed]; retired; not working [i.e., unemployed; homemaker; students; on leave or disabled]), age, self-reported race [Black; Other (including Indigenous, Asian, Native Hawaiian); white], sex (male; female), wave of data collection (i.e., MIDUS II, Refresher), and modifiable health behaviors (Sims et al., 2012). Modifiable health behaviors include cigarette use (ever and current smoker status) and alcohol consumption (never, sometimes, and current affirmative response to at least one drink in the past month) (Sims et al., 2012).

2.2. Statistical analysis

Descriptive statistics of the overall sample (i.e., means and percentages) were calculated. Models were fit using quasi-Poisson regression given that risk scores follow a binomial distribution and allostatic load is a sum of these values ranging from 0 to 7. Modified Poisson models have been identified as an approach to estimate prevalence ratios (or relative risk, in prospective studies) (Zou, 2004) and provide an estimate that is easier to interpret compared to logistic regression (prevalence odds ratio) (Barros and Hirakata, 2003). Baseline models assessed independent associations between lifetime discrimination, everyday discrimination, and appraised burden and each AL subscale and overall AL scores. Two multivariable regression models were run, beginning with a model adjusted for age, sex, and race. The second multivariable model
Additionally accounted for a fuller set of covariates and potential mediators of the association (i.e., educational attainment, income, employment status, wave of data collection, cigarette use and alcohol consumption). Socioeconomic variables (educational attainment, income, and employment status) are viewed as potentially confounding the association between experiences of discrimination and markers of AL. On the other hand, health behaviors such as smoking, and drinking are viewed as potential mediators of the association between experiences of discrimination and AL.

All analyses were conducted using R (R Core Team, 2013). Effect modification on the multiplicative scale was assessed using interaction terms. In fully adjusted models, interaction terms between race and each measure of discrimination were assessed for significance. We then examined interactions between the included measures of discrimination (e.g., everyday-lifetime) in fully adjusted models.

Imputation of all missing data was conducted using the built-in multivariate imputation by chained equations technique available in the “mice” package in R (van Buuren et al., 2015). Imputations were conducted over 5 iterations, using proportional odds models for ordinal categorical variables (i.e., income, educational attainment, lifetime discrimination, burden of discrimination) and polytomous logistic regression for nominal categorical variables (i.e., race). Numeric variables were imputed using predictive mean modeling (i.e., allostatic load risk scores, individual biomarkers, everyday discrimination, count of lifetime experiences of discrimination). Variables with the greatest level of missing data were burden of discrimination (11.5%) and para-sympathetic nervous system subscale scores (14.3%). Remaining variables had less than 10% missingness, with exact levels summarized in Table 1.

Sensitivity analyses. Sensitivity analyses were conducted to assess the robustness of findings to how measures of discrimination were coded, particularly given that there is no “gold standard” regarding operationalizing the included discrimination measures (Williams et al., 2016). Everyday discrimination was assessed categorically, where respondents reporting 0 experiences were coded as none, the top quartile of experiences were coded as high, and remaining non-zero responses were coded as some. This may capture a threshold effect of everyday discrimination. Lifetime discrimination was assessed as a count of experiences. Additionally, each burden appraisal was assessed individually to capture whether each item had unique associations with the AL subscales and overall AL scores.

E-values were calculated to assess the robustness of the associations to potential unmeasured confounding (VanderWeele and Ding, 2017). The E-value is defined as “the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the treatment and outcome to fully explain away a specific treatment-outcome association, conditional on the measured covariates” (VanderWeele and Ding, 2017) with larger values indicating considerable unmeasured confounding would be necessary to explain away the observed outcome.

E-values were calculated for statistically significant findings from fully adjusted models using:

\[ E-value = RR + \sqrt{RR \times (RR - 1)} \]

where RR = relative risk values greater than 1. (VanderWeele and Ding, 2017) Prevalence ratios were used to calculate E-values.

2.3. Supplemental analyses

To illustrate the potential differences in associations between measures of discrimination and measures used to define the AL scores, we employed an outcome-wide analysis (VanderWeele, 2017) assessing associations between everyday, lifetime, and burden of discrimination with each of the 24 biomarkers used to create AL indicators. Utilizing an outcome-wide approach provides additional insight into the potentially

Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Summary data of the MIDUS participants (overall and by wave).</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>MIDUS 2</td>
</tr>
<tr>
<td>Age [n (sd)]</td>
<td>53.02 (12.56)</td>
</tr>
<tr>
<td>Race [n (%)]</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>393 (16.8)</td>
</tr>
<tr>
<td>Other</td>
<td>129 (6.1)</td>
</tr>
<tr>
<td>White</td>
<td>1596 (75.4)</td>
</tr>
<tr>
<td>Sex [n (%)]</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1163 (54.9)</td>
</tr>
<tr>
<td>Male</td>
<td>955 (45.1)</td>
</tr>
<tr>
<td>Employment Status [n (%)]</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>1470 (69.4)</td>
</tr>
<tr>
<td>Retired</td>
<td>423 (20.0)</td>
</tr>
<tr>
<td>Not employed</td>
<td>225 (10.6)</td>
</tr>
<tr>
<td>Educational Attainment [n (%)]</td>
<td></td>
</tr>
<tr>
<td>High school or less</td>
<td>499 (23.6)</td>
</tr>
<tr>
<td>Some college</td>
<td>456 (21.5)</td>
</tr>
<tr>
<td>College or more</td>
<td>1163 (54.9)</td>
</tr>
<tr>
<td>Income [n (%)]</td>
<td></td>
</tr>
<tr>
<td>$&lt;25,000</td>
<td>428 (20.2)</td>
</tr>
<tr>
<td>$25,001 - $40,000</td>
<td>254 (12.0)</td>
</tr>
<tr>
<td>$40,001 - $55,000</td>
<td>233 (11.0)</td>
</tr>
<tr>
<td>$55,001 - $70,000</td>
<td>253 (11.9)</td>
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<tr>
<td>$&gt;70,000</td>
<td>950 (44.9)</td>
</tr>
<tr>
<td>Smoking status [n (%)]</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>616 (29.1)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>589 (27.8)</td>
</tr>
<tr>
<td>Prior</td>
<td>645 (30.5)</td>
</tr>
<tr>
<td>Current</td>
<td>268 (12.7)</td>
</tr>
<tr>
<td>Alcohol consumption [n (%)]</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>109 (5.1%)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>619 (29.2)</td>
</tr>
<tr>
<td>Current</td>
<td>1390 (65.6)</td>
</tr>
<tr>
<td>Everyday discrimination [m (sd)]</td>
<td>0.89 (0.88)</td>
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<tr>
<td>Lifetime discrimination [n (%)]</td>
<td></td>
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<tr>
<td>None</td>
<td>1123 (53.0)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>601 (28.4)</td>
</tr>
<tr>
<td>3 or more</td>
<td>394 (18.6)</td>
</tr>
<tr>
<td>Burden of discrimination [n (%)]</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>849 (40.1)</td>
</tr>
</tbody>
</table>

(continued on next page)
Table 1

<table>
<thead>
<tr>
<th>Discrimination Type</th>
<th>Overall</th>
<th>MIDUS 2</th>
<th>MIDUS Refresher</th>
<th>Percent missinga</th>
</tr>
</thead>
<tbody>
<tr>
<td>A little</td>
<td>220</td>
<td>188</td>
<td>32 (3.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10.4)</td>
<td>(15.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some</td>
<td>367</td>
<td>169</td>
<td>198 (22.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(17.3)</td>
<td>(13.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A lot</td>
<td>682</td>
<td>116 (9.2)</td>
<td>566 (65.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(32.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Allotopic Load Subscale</th>
<th>Model 1b</th>
<th>Model 2b</th>
<th>Model 3c</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNS</td>
<td>1.05 (0.99, 1.12)</td>
<td>1.05 (0.96, 1.08)</td>
<td>1.04 (0.96, 1.09)</td>
</tr>
<tr>
<td>PNS</td>
<td>1.02 (0.95, 1.09)</td>
<td>1.01 (0.99, 1.08)</td>
<td>1.00 (0.98, 1.09)</td>
</tr>
<tr>
<td>HPA</td>
<td>1.01 (0.96, 1.00)</td>
<td>1.01 (0.96, 1.09)</td>
<td>1.00 (0.96, 1.10)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>1.05 (1.00, 1.10)</td>
<td>1.04 (0.97, 1.09)</td>
<td>1.04 (0.98, 1.10)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1.03 (0.97, 1.15)</td>
<td>1.01 (0.98, 1.12)</td>
<td>1.01 (0.98, 1.14)</td>
</tr>
<tr>
<td>Metabolic Glucose</td>
<td>1.06 (0.99, 1.15)</td>
<td>1.06 (0.98, 1.15)</td>
<td>1.05 (0.97, 1.15)</td>
</tr>
<tr>
<td>Metabolic Lipids</td>
<td>1.03 (0.98, 1.07)</td>
<td>1.01 (1.01, 1.15)</td>
<td>1.01 (1.02, 1.13)</td>
</tr>
<tr>
<td>Overall AL Score</td>
<td>1.04 (1.01, 1.07)</td>
<td>1.01 (1.02, 1.10)</td>
<td>1.05 (1.02, 1.09)</td>
</tr>
</tbody>
</table>

Abbreviations: SNS – sympathetic nervous system; PNS – parasympathetic nervous system; HPA axis – hypothalamic-pituitary-adrenal.

a Percent missing in observed data.
b Adjusted for sex, race, age, and wave.

c Adjusted for education, employment status, and wave.

d Mediators (i.e., health behaviors, SES measures). Increased everyday discrimination was also associated with higher AL scores.

3. Results

Overall sample descriptive statistics are provided in Table 1. The mean age of the overall sample was 53 years. Most participants were white (75.4%) and female (54.9%). Nearly 27% of respondents reported no everyday discrimination. Experiencing lifetime discrimination in three or more areas was reported by 18% of respondents and 32% of respondents appraised discrimination as contributing a “lot” of burden to living a full and productive life and in making life harder.

Interactions among lifetime, everyday, and burden of discrimination were not statistically significant for any of the outcomes (p > 0.05); nor was race an effect modifier of discrimination measures in fully adjusted models. Findings are reported for each measure. We place emphasis on findings from model 3 although it accounts for potential mediators between discrimination and physiologic markers.

3.1. Everyday discrimination

Among the full sample, increases in average frequency of everyday discrimination was associated with increased prevalence of high-risk scores in the metabolic lipids subscales in models accounting for race, age, and sex (Table 2). Associations between everyday discrimination and metabolic lipids risk scores remained after accounting for potential mediators (i.e., health behaviors, SES measures). Increased everyday discrimination was also associated with higher AL scores.

3.2. Lifetime discrimination

Compared to those who reported no lifetime discrimination, experiencing one to two and three or more experiences was associated with high-risk scores in the inflammation, metabolic glucose, and metabolic lipid subscales in partially adjusted models (Table 3). These associations remained after further adjustment. Associations between reporting three or more experiences of lifetime discrimination and SNS and cardiovascular risk scores were also observed. The association between three or more lifetime experiences of discrimination was protective of SNS risk scores. Reporting both one to two and three or more experiences of lifetime discrimination was associated with higher AL scores. No associations were observed for PNS and HPA risk scores.

3.3. Burden of discrimination

Associations between the appraisals of burden of discrimination and AL are presented in Table 4. Respondents categorized as experiencing “a little” burden of discrimination had greater prevalence of higher metabolic glucose risk scores compared to those who reported “none” in fully adjusted models. Elevated PNS risk scores were prevalent among those reporting “some” burden of discrimination as compared to those reporting none. Associations between appraised burden and overall AL scores were significant for those reporting “a little” burden in the fully adjusted model, though not for other groups.

3.4. Sensitivity analyses

When coded categorically, there appeared to be a threshold effect of experiencing high everyday discrimination compared to respondents reporting no experiences in fully adjusted models (Supplemental Table 5). Associations between count of experiences of lifetime discrimination and AL were directionally similar to associations observed when experiences were assessed categorically, though estimates were smaller (Supplemental Table 6). Increases in experiences of lifetime discrimination remained associated with increased inflammation, metabolic glucose, and metabolic lipid subscales and overall AL scores. Assessing burden of discrimination questions independently also revealed unique associations with AL subscales and overall AL scores.
Appraisals of life being harder because of discrimination were associated with the prevalence of higher PNS and metabolic lipid subscale risk scores (Supplemental Table 7). Appraisals of discrimination as having interfered in having a full and productive life were associated with scores (Supplemental Table 7). Appraisals of discrimination as having increased PNS, inflammation, metabolic glucose, and metabolic lipid subscale risk scores, as well as overall AL scores (Supplemental Table 8).

Robustness of the observed associations between measures of discrimination and AL subscale risk and overall scores to unmeasured confounding are presented using E-values in Supplemental Table 9. We report these values for model 3. These reflect the minimum association an unmeasured confounder would have to have with both the measure of discrimination and AL outcome – beyond measured covariates – to explain away the observed associations from fully adjusted models (VanderWeele and Ding, 2017).

3.5. Supplemental analyses

Post hoc analyses used an outcome-wide approach to understand differences in patterning of associations between measures of discrimination and AL subscales. Findings from these fully adjusted analyses are presented in supplemental tables (Supplemental Tables 10–12). Associations meeting the adjusted p-value level of significance to account for multiple testing (p < 0.0007) are highlighted in red.
After accounting for multiple testing, we found that everyday discrimination was associated with lower HDL levels. Additionally, reporting 3 or more experiences of lifetime discrimination was associated with elevated IL-6, CRP, insulin resistance (HOMA-IR), BMI, WHR, and triglycerides, while reporting one to two experiences of lifetime discrimination was associated with greater glucose and HOMA-IR. None of the associations between the burden of discrimination measures met the criteria of the adjusted p-value.

4. Discussion

In this cross-sectional analysis of MIDUS participants, we observed that associations between discrimination and AL subscales varied by the discrimination measure used. These findings suggest that there may be distinct mechanisms through which chronic and acute major lifetime experiences or appraisals of discrimination contribute to AL and, ultimately, poorer mental and physical health outcomes. Though we did not examine these unique relationships in reference to specific health endpoints, these findings could be extended to examine whether these patterns between discrimination measures and allostatic load subscales or indicators are more predictive of certain physical and mental health outcomes. For example, in a latent class analysis of allostatic load and mental health, Carbone (2021) found that individuals meeting the criteria for depression measures were more likely to be clustered in metabolic and inflammatory dysregulation and parasympathetic dysregulation categories as compared to the baseline cluster (e.g., low overall dysregulation, except for metabolic lipids) (Carbone, 2021). Our results, in combination with these recent findings, suggest directions for future exploration of embodiment and the processes through which embodiment occurs.

We extend the findings of previous literature that documented associations between discrimination and AL using individual measures or composite scores of multiple measures of discrimination (Ong et al., 2017b; Brody et al., 2014; Vadiveloo and Mattei, 2017; Cuevas et al., 2019; Currie et al., 2020; Van Dyke et al., 2020) by also noting that associations between discrimination, individual physiologic markers, and AL subscale risk scores vary by type of discrimination assessed and how measures are operationalized. We highlight the main findings of this analysis in a summary table below.

A summary of associations between measures of discrimination and allostatic load subscales and overall allostatic (AL) scores from fully adjusted models

<table>
<thead>
<tr>
<th></th>
<th>SNS</th>
<th>PNS</th>
<th>HPA</th>
<th>Inflammation</th>
<th>Metabolic Glucose</th>
<th>Metabolic Lipids</th>
<th>Cardiovascular</th>
<th>Overall AL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everyday</td>
<td>Null</td>
<td>Null</td>
<td>Null</td>
<td>NULL</td>
<td>Null</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lifetime</td>
<td>Null</td>
<td>Null</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Burden</td>
<td>+</td>
<td>Null</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

We did not find evidence that the included measures of discrimination were associated with HPA axis scores. Associations were observed for everyday discrimination and metabolic lipid risk scores and overall AL score. By contrast, lifetime experiences of discrimination were primarily associated with intermediate- and long-term physiological indicators—such as inflammation, cardiovascular, and metabolic glucose and lipid measures. We also observed greater lifetime discrimination to be protective of SNS risk scores. However, this relationship does not align with previous assessments of discrimination (both general experiences and racial discrimination) and SNS indicators where null or positive associations have been observed (Ong et al., 2017b; Brody et al., 2014). Increased reports of lifetime discrimination were associated with higher risk scores for inflammatory markers (specifically, CRP and IL-6), metabolic glucose (i.e., glucose and HOMA-IR), and metabolic lipid (i.e., BMI, WHR, and triglyceride levels) subscales. Appraised burden of discrimination was associated with PNS, metabolic glucose, and metabolic lipids risk scores and overall AL scores. The variations in associations by measures contribute to evidence of the criterion validity of each measure, where lifetime and appraised burden of discrimination may capture the enduring impact of major events or burden of discrimination on long-term health outcomes, while everyday discrimination captures the implications of broader, day-to-day exposures of stress.

Health behaviors (i.e., smoking and alcohol use) were included as potential mediators of associations between discrimination and AL outcomes. Some findings were robust to these adjustments, including the outcome-wide assessments where measures of discrimination remained associated with several individual physiological markers. However, it is important to note that the included health behaviors and covariates do not represent the totality of variables that may mediate the effects of discrimination on indicators of AL and AL scores. Additionally, given the cross-sectional nature of our analyses, we cannot rule out the possibility of reverse causation, whereby components of AL may affect experiences and appraisals of discrimination.

Additionally, we observed no interaction on the multiplicative scale between measures of discrimination or between individual measures and race and AL. Previous work has found larger (though not statistically different) within-group associations between pervasive discrimination and AL among African American respondents compared to whites when relative threshold categorization was used (e.g., high/low) (Van Dyke et al., 2020). Our findings may reflect 1) small samples of African American participants and participants that identified as “Other” racial groups or 2) that interactions between measures or race may occur on the additive scale.

In sensitivity analyses, we found that the operationalization of discrimination measures affected some of the observed associations for everyday and burden of discrimination measures. In understanding how stressors result in adverse health outcomes, these findings suggest that there may be a threshold effect of everyday experiences of discrimination where these experiences may go beyond individual, collective, and structural resources available to mitigate the negative impacts of everyday differential treatment (Van Dyke et al., 2020). For example, we found that persons high in everyday discrimination have increased prevalence of high PNS, cardiovascular, and metabolic lipids risk scores and overall AL scores. These findings, and results from the outcome-wide analysis, provide evidence of the importance of further consideration and theoretical guidance to how we operationalize discrimination measures when evaluating it as a stressor and/or contributor to health inequities.

4.1. Discrimination and allostatic load scores

Our findings of positive associations between discrimination measures and overall AL scores are supported by previous work. Three cross-sectional studies have found discrimination to be associated with AL in samples of Indigenous Canadian, Puerto Rican, and African American adults (Ong et al., 2017b; Cuevas et al., 2019; Currie et al., 2020). The analysis by Cuevas et al. yielded nuanced findings, however, with results indicating inverse associations between general experiences of everyday discrimination and AL scores, while lifetime discrimination was associated with greater AL in a sample of Puerto Rican adults in the Boston metro area (Cuevas et al., 2019). This difference in results may reflect differences in biomarkers used to compose the AL measure. Longitudinal work assessing the frequency of racist events among African American adolescents by Brody et al. the frequency of everyday discrimination among middle-aged women by Upchurch and colleagues, and weight discrimination among adults in the MIDUS sample by Vadiveloo and Mattei also provides evidence of the persistent effects of discrimination on increased AL (Brody et al., 2014; Vadiveloo and Mattei, 2017; Upchurch et al., 2015). Pervasive discrimination, operationalized as the sum of tertiles across general experiences of everyday, lifetime, and workplace discrimination, was also associated with AL scores in a recent
analyses using MIDUS data (Van Dyke et al., 2020). When assessing the components of pervasive discrimination independently, Van Dyke et al. observed associations between lifetime and everyday discrimination with AL scores, though not workplace discrimination.

4.2. Discrimination and subscale-specific findings

Subscale-specific findings provide empirical justification for the distinct associations between measures or types of discrimination and AL subscale components. Studies in this area that have examined the relationship between measures of discrimination and specific indicators have yielded similar findings for most associations observed. Work by Wagner and colleagues which examined the physiological implications of lifetime exposure to racial discrimination using the Schedule of Racist Events scale observed no associations between discrimination and plasma norepinephrine levels (Wagner et al., 2015). Null associations between discrimination and epinephrine levels may reflect the differences between plasma and urinary assessments of epinephrine and norepinephrine and the timing of sample draws (Lundberg, 2003). Depending on how the stressor is conceptualized to impact SNS activity, plasma hormonal measures of SNS may reflect acute responses to stress, but require more invasive methods to capture that may influence levels (i.e., venipuncture), while urinary measures provide an opportunity to assess SNS activity over a longer period of time (Lundberg, 2003; Lundberg and Fink, 2000). In contrast to the present analysis, however, prior research found associations between discrimination and markers of PNS activity (Ong et al., 2017b; Wagner et al., 2015; Hill et al., 2017). Hill et al. found greater ethnic discrimination (summary score up to 17 using the Perceived Ethnic Discrimination Questionnaire-Community Version) to be associated with decreased HFHRV – one of the indicators used to calculate the parasympathetic nervous system risk score (Hill et al., 2017).

Our results indicated no associations between measures of discrimination and AL axis risk scores. Research has found inconsistent associations between discrimination and indicators of HPA axis dysregulation (i.e., cortisol, DHEAs) (Busse et al., 2017), with some studies reporting null findings (Ratner et al., 2013) and others finding positive (Zeiders et al., 2012; Huynh et al., 2017) or indirect associations (Lee et al., 2018). Previous findings suggest that associations between differentiation and HPA axis risk scores and indicators are sensitive to the timing of discrimination (i.e., acute, chronic) and may yield elevated changes to HPA axis activity or blunted responses (Busse et al., 2017).

Most studies examining associations between discrimination and inflammation markers have found increased experiences to be associated with greater inflammation, with CRP and IL-6 being the most frequently assessed biomarkers (Cuevas et al., 2020). Similar to previous findings (Cuevas et al., 2020; Stepanikova et al., 2017), we observed that lifetime discrimination is associated with increased levels of inflammatory risk scores with specific associations with IL-6 and CRP. We found no associations with everyday discrimination and overall inflammation risk scores. Our findings are similar to an analysis of everyday and lifetime discrimination with inflammation markers by Stepanikova and colleagues, though their results differ slightly. The authors found lifetime discrimination to be associated with fibrinogen, E-selectin, and IL-6, but not with CRP and no associations between everyday discrimination and the above inflammation biomarkers (Stepanikova et al., 2017). Work by Van Dyke et al. found pervasive discrimination to be associated with inflammation, metabolic glucose and metabolic lipid subscales (Van Dyke et al., 2020). These results are similar to our findings regarding lifetime discrimination, though everyday discrimination was also associated with metabolic lipid risk scores and appraised burden with metabolic glucose risk scores.

Last, our findings regarding associations between discrimination and cardiovascular risk scores were consistently null across everyday and burden measures, though not lifetime discrimination. Our results are consistent with studies that have observed null associations between discrimination and some cardiovascular outcomes (Dolezsar et al., 2014). However, the literature in this area remains mixed, with varying associations seen by operationalization of discrimination (e.g., implicit biases, internalized, interpersonal, institutional, domain-specific), gender, and type of outcome used to assess cardiovascular risk (Lewis et al., 2014).

Calculated E-values for the observed findings (range: 1.28 to 2.19; the lowest possible E-value is 1) suggest that our findings may be robust to unmeasured confounding (Chen and VanderWeele, 2018). For example, an unmeasured confounder would have to have a prevalence ratio of 1.34 with everyday discrimination and prevalence of high-risk metabolic lipid scores to explain away the observed association beyond the included covariates. Potential factors that may be confounders include negative affect and neuroticism, though studies that have included these measures in assessing the effects of discrimination on health outcomes found associations to persist even after accounting for these factors (Van Dyke et al., 2020; Smart Richman et al., 2010; Hübner et al., 2005). However, these factors are not exhaustive and do not negate the possibility of unmeasured confounding impacting our results.

This analysis is not without its limitations. First, given the cross-sectional design, the temporality of the associations between experiences and appraisals of discrimination and AL markers is uncertain. However, the advantage of using biomarkers as the outcome is that reverse causality (i.e., values of biomarkers affecting self-reports of discrimination) as well as common-source bias seem less likely. While we may capture major forms of institutional discrimination through items available in the lifetime discrimination measure, we only capture experiences of discrimination that people are able to recognize and are willing to report. This does not speak to forms of structural racism or other forms of oppression that exist and result in material, opportunity, and political deprivation whether or not an individual was aware of such experiences and reported them as discriminatory or harmful (Krieger, 2011, 2012; Williams and Mohammed, 2009; Bailey et al., 2017). There is a growing body of evidence that social factors such as structural racism, through interconnected and mutually reinforcing practices, policies, and patterns, directly and indirectly affect health and wellbeing (Bailey et al., 2017). Though we include appraised burden of discrimination which provides some insight into the potential impacts and perceptions of discrimination as a barrier or hindrance without reliance on the report of or reaction to a specific experience, it still relies on self-report. Additionally, we focus on general reports of discrimination, without considerations of attribution of experiences (e.g., race, gender). While there is substantial evidence documenting that the material, social, and economic impacts of discrimination differ by race, for example; where Black or other marginalized racial groups carry a disproportional burden (Williams et al., 2019a, 2019b; Williams and Mohammed, 2009; Bailey et al., 2017), there has not been clarity on whether assigning an attribution, or primary reason, for experiences of discrimination to race more negatively impacts health (Lewis et al., 2006; Kessler et al., 1999; Roberts et al., 2008; Guyll et al., 2001). However, studies have found differential health impacts of discrimination reported among Black adults compared to white adults (Guyll et al., 2001; Troxel et al., 2003). The role attribution of experiences of discrimination should continue to be explored in future work.

Also, while the MIDUS I wave is a nationally representative sample of US adults, the proposed analysis is a subsample of MIDUS participants including the longitudinal (MIDUS II) and the Milwaukee waves. The overall percentage of Black respondents in the national MIDUS study were small and, as a result, most of the Black population in the MIDUS study was recruited in the Milwaukee wave. As such, it means that the Milwaukee wave is less representative, however the data provides insight into the experiences of Black Americans living in highly segregated cities. Researchers found that participants in the MIDUS II Biomarker Substudy were similar to participants in the full sample, except for higher levels of educational attainment, were less likely to
smoke, and were more likely to use alternative therapies (Dienberg Love et al., 2010). Additionally, small sample sizes of Black (n = 386) and “Other” (n = 128) individuals limits the power to capture interactions between race and discrimination measures; however, future work should assess whether interactions between multiple measures and race occur on the additive scale instead of multiplicative (Bauer, 2014). Additionally, future research should employ other considerations for modeling multiple experiences of marginalization and inequitable treatment, such as latent class analysis (Bauer, 2014).

Our analysis also has several strengths in that it adds to literature examining the impacts of racial discrimination by using and comparing the effects of multiple measures of discrimination on AL subscales, individual biomarkers, and overall scores. These findings extend the existing body of literature by finding that associations between multiple measures of discrimination and AL vary by measure used (i.e., everyday, lifetime, appraisals of burden) and subscale. These unique pathways may be useful in identifying potential points of intervention, though efforts should include rectifying harms from all forms of discrimination through institutional (e.g., policy) and cultural interventions (e.g., policing, lending, or education) can be intervened upon through legal action (Krieger, 2012; Massey, 2015; Nielsen and Nelson, 2005) as well as through organizing and building political support (Bailey et al., 2017). To further the understanding of pathways that drive associations between individual measures of discrimination and AL subscales, we employed an outcomes-wide analysis to capture specific indicators that shed light on the biological pathways through which multiple forms of discrimination may uniquely impact health. We also add to assessments of discrimination by capturing the appraisal of experiences of discrimination as a barrier to living a full life and making life harder, outside of reference to a specific event/experience. Last, we also identified that associations between measures of discrimination and AL outcomes can vary based on how discrimination is used in the analysis.

These findings provide points of focus for future research, specifically around the pathways through which discrimination adversely impacts health and the importance and theoretical implications of how discrimination is operationalized. While most stressful events do not affect health (Williams and Mohammed, 2009), identifying salient experiences of discrimination that are likely to have implications for population health remains important for current and future work – in an effort to understand and intervene upon discriminatory processes that unfairly disadvantage some and unfairly advantage others (Jones, 2014).

Author credit

Jourdyn A. Lawrence: conceptualization, methodology, writing – original draft; writing – review & editing. Ichiro Kawachi; Kellee White; Mary T. Bassett; David R. Williams: conceptualization; writing – original draft; writing – review & editing; supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2022.114866.

References


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