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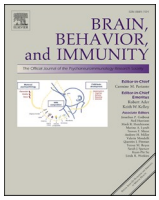

Full-length Article

Discrimination and C-reactive protein across the life course: Findings from three national US cohorts

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A B S T R A C T

Discrimination is increasingly recognized as a chronic social stressor that may contribute to physiological dysregulation. While cross-sectional research has linked discrimination exposure to elevated systemic inflammation (e.g., C-reactive protein [CRP]), less is known about how these associations unfold across the lifespan. To examine the relationship between systemic inflammation and repeated exposure to interpersonal discrimination among non-Hispanic White and Black adults, we analyzed harmonized data from three US population-based cohorts spanning young adulthood (National Longitudinal Study of Adolescent to Adult Health; Add Health), mid-adulthood (Midlife in the United States Study; MIDUS), and older adulthood (Health and Retirement Study; HRS). In each cohort, interpersonal discrimination was assessed at two time points using a self-reported item asking whether participants had been treated with less respect or courtesy than others. Based on responses across waves, we created a harmonized exposure variable with three categories: no exposure (discrimination not reported at either time point), intermittent exposure (reported at one time point only), and chronic exposure (reported at both baseline and follow-up). In adjusted models accounting for baseline CRP, sex, race, education, and change in body mass index, chronic exposure to discrimination was significantly associated with increases in CRP over time in the young adult cohort (Add Health). Specifically, individuals reporting chronic discrimination in Add Health showed greater increases in inflammation relative to those reporting no exposure (B = 0.87 mg/L, 95% CI: 0.19 to 1.54). No significant associations were observed in MIDUS or HRS. These findings suggest that chronic interpersonal discrimination may have a particularly strong impact on inflammatory processes during early adulthood, pointing to a potential sensitive period in which psychosocial stressors have long-term consequences for inflammatory homeostasis.

1. Introduction

Perceived discrimination (hereafter, discrimination) refers to unfair treatment directed at individuals because of social characteristics such as race, gender, or social class.(Williams and Mohammed, 2009) Discrimination has been implicated as a social determinant of disease. (Lewis et al., 2015; Paradies et al., 2015; Williams et al., 2019) It is theorized that experiences of discrimination signal social threat, such as danger, rejection, or devaluation, and contribute to feelings of social exclusion, (Richman and Leary, 2009; Neblett, 2019) which in turn can elicit threat-related cognitive and emotional responses. (Fani et al., 2021; Clark et al., 2018) These psychological responses can activate physiological stress systems that are adaptive for short-term response to threats but may undermine long-term health. Chronic exposure to discrimination may thus contribute to cumulative physiological burden, increasing vulnerability to disease.

Emerging evidence supports the general hypothesis that discrimination is associated with biological weathering processes, particularly elevated inflammatory responses. Systematic reviews have found that exposure to discrimination is linked to higher levels of circulating inflammatory markers (particularly C-reactive protein; CRP). (Cuevas et al., 2020; Lawrence et al., 2022) However, most current data are cross-sectional, and the causal relations and longitudinal dynamics of this association remain poorly understood. Although discrimination may increase the risk of low-grade systemic inflammation, proinflammatory cytokines can also signal the brain to heighten sensitivity to the social environment, potentially amplifying perceptions of social threat and negative social interactions. (Eisenberger et al., 2017) The use of repeated measures of both discrimination and inflammation can improve understanding of how cumulative exposure to this threat

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shapes inflammatory homeostasis (the body's regulation of immune activity to maintain physiological stability) over time.

Existing research has largely focused on middle-aged adults, a population at increased risk for morbidity and mortality. Nevertheless, Geronimus et al. (Geronimus et al., 2006) have shown that physiological dysregulation can begin accumulating as early as young adulthood. Moreover, studies consistently report age differences in discrimination, with young adults experiencing higher levels than their middle-aged and older counterparts. (Lewis et al., 2015; Sims et al., 2009; Potter et al., 2019; Lewis and Van Dyke, 2018) As proposed by Lewis et al., (Lewis et al., 2015) this pattern may reflect selective survival among older adults, shifts in how discrimination is experienced or perceived across the life course, or cohort differences whereby older generations faced more severe or less easily captured forms of discrimination. Whether the association between discrimination and inflammation varies across developmental stages remains unclear. A life course analysis of these relationships would significantly advance our understanding of how discrimination becomes biologically embedded over time.

To address these gaps, we leveraged longitudinal data from three large U.S. population health research cohorts with harmonized psychosocial and biomarker data from early adulthood (the National Longitudinal Study of Adolescent to Adult Health; Add Health), midadulthood (the Midlife in the United States Study; MIDUS), and older adulthood (the Health and Retirement Study; HRS). These datasets span a broad range of adult experience ranging from 24 to 90 in age, and all three studies include comparable measures of discrimination and systemic inflammation (CRP), enabling cross-cohort analyses that enhance the generalizability of findings and allow for the examination of potential variation in the discrimination-inflammation association across stages of adult development. For consistency across cohorts, analyses focused on non-Hispanic White and non-Hispanic Black adults.

2. Methods

2.1. Data sources

Add Health is a nationally representative cohort of individuals initially enrolled as adolescents in grades 7–12 during the 1994–1995 school year and followed into early midlife. (Harris et al., 2019) The Add Health study was designed to examine social, behavioral, and biological influences on health across the life course. We used data from Wave IV (2008; N = 4,543), when participants were first asked about experiences of discrimination and provided extensive biomarker data. At Wave IV, participants were on average 28 years old (range 24–32). To align with the timeframes of MIDUS and HRS, we used Wave IV as the baseline and Wave V (2016–2018) as Time 2, when both discrimination and biomarker data were again collected through in-home interviews and venous blood draws approximately 8–10 years later.

MIDUS is a national longitudinal study launched in 1995–1996 to examine the role of sociodemographic, psychosocial, and behavioral factors in shaping physical and mental health in a sample of noninstitutionalized, English-speaking U.S. adults. (Brim and Ryff, 2004; Ryff and Krueger, 2018) MIDUS 2 (2004–2005) included a biomarker subsample of 1,255 participants (aged 35 to 86), including a Black American oversample from Milwaukee. MIDUS 2 served as the baseline for our analyses, with MIDUS 3 (2017–2022), which repeated biomarker assessments, serving as Time 2.

The Health and Retirement Study (HRS) is an ongoing, nationally representative longitudinal study of U.S. adults aged 50 and older that began in 1992. In 2006, HRS incorporated an enhanced face-to-face interview that included a psychosocial questionnaire (Clarke et al., 2008) and biomarker assessment. (Williams, 1999) We used psychosocial data from the 2008 wave (N = 8,608) to serve as baseline measures, and appended biomarker data from the 2016 wave as Time 2. Detailed information about study design, recruitment, and sampling can be found elsewhere. (Sonnega et al., 2014; Heeringa and Connor, 1995; Fisher and Ryan, 2018).

2.2. Measures

2.2.1. Discrimination and the harmonizing procedure

Discrimination was measured using versions of the validated and widely used Everyday Discrimination Scale (EDS). (Williams, 1999) The original EDS consists of nine items assessing the frequency of day-to-day interpersonal mistreatment, such as being treated with less courtesy or respect than others, receiving poorer service at restaurants or stores, being insulted or harassed, or having others act afraid of the respondent. MIDUS included all nine original items; HRS administered a six-item version; and Add Health used a two-item adaptation derived from the EDS (i.e., being treated with less courtesy and less respect). Across all three cohorts, the EDS items did not specify a particular timeframe, instead asking participants how often these experiences occurred in their day-to-day life. In MIDUS and Add Health, the EDS items used four response options: 1 = never, 2 = rarely, 3 = sometimes, and 4 = often. HRS employed a five-point frequency scale: 1 = almost every day, 2 = at least once a week, 3 = a few times a month, 4 = a few times a year, and 5 = less than once a year, and 6 = never. To harmonize the measure across studies, we summed the first two items from the MIDUS scale, which assess being treated with less courtesy and less respect than others. In HRS, we used only the first item, which combines these two experiences into a single question. This approach aligns with the single-item discrimination measure used in Add Health. The two-item EDS, as well as the two-item combined scale in Add Health, has been shown to demonstrate high construct, predictive, and convergent validity relative to the full nine-item version, and functions similarly across racial and ethnic groups. (Benner et al., 2022; Lewis et al., 2012; Kim et al., 2014) We then created a harmonized discrimination exposure variable across all three cohorts: individuals were coded as 'never' if they reported no exposure to discrimination at either time point, 'intermittent' if they reported exposure at one time point only, and 'chronic' if they reported exposure at both baseline and follow-up.

2.2.2. Systemic inflammation

All three studies assessed CRP as a biomarker of systemic inflammation at both baseline and follow-up. In Add Health, CRP concentrations were reported in milligrams per liter (mg/L), whereas in MIDUS and HRS, CRP was reported in micrograms per milliliter (μg/mL); these units are numerically equivalent. In Add Health, CRP was measured from dried blood spots at Wave IV using a high-sensitivity enzyme-linked immunosorbent assay (ELISA) and from plasma and serum at Wave V using a high-sensitivity particle-enhanced immunonephelometric assay on the Siemens BNII / BN Prospec System (Siemens Healthcare Diagnostics). In MIDUS, CRP assay methods differed across waves. In MIDUS 2, CRP was measured using the BNII nephelometer (Dade Behring/Siemens, Inc.), and values below the detectable range were reanalyzed using a high-sensitivity immunoelectrochemiluminescence assay (Meso Scale Diagnostics). In MIDUS 3, CRP was quantified using an immunoelectrochemiluminescence assay on the Meso Scale Discovery platform using the V-PLEX Plus Human CRP Kit. To improve comparability across MIDUS waves, MIDUS 2 CRP values were transformed to the MIDUS 3 assay scale using the regression-based adjustment recommended in the MIDUS biomarker documentation (MIDUS 3-harmonized CRP) = ((MIDUS 2 CRP) + 0.0841)/0.7828. In HRS, CRP was quantified in serum using a particle-enhanced immunonephelometric assay on the BNII nephelometer (Dade Behring/Siemens, Inc.)Change in inflammation was operationalized as the difference in CRP values between follow-up and baseline: (CRP at Time 2) minus (CRP at Time 1). Cohort-specific protocols for blood collection, laboratory assays, and quality control procedures are described in detail in publicly available documentation. (Whitsel et al., 2012; Crimmins et al., 2013; Ryff et al., 2017).

2.2.3. Covariates

The primary models included covariates that were consistently available and similarly defined across all three cohorts: race (non-Hispanic Black and non-Hispanic White), self-reported biological sex (female and male), educational attainment (high school or less, some college, college and above), and change in body mass index (BMI) between baseline and follow-up. To further account for individual differences in inflammatory status and to reduce potential regression to the mean, we included CRP at Time 1 as a covariate.

2.3. Statistical analysis

Analyses were limited to Black and White participants, as these were the only racial groups with sufficient sample sizes across all cohorts to support reliable estimation. The final analytic sample sizes were as follows: Add Health (n = 2,816), MIDUS (n = 624), and HRS (n = 2,061). The primary analysis used linear regression models to assess the association between change in CRP and perceived discrimination. Model 0 adjusted for CRP at Time 1 to account for initial inflammatory levels and potential regression to the mean. Model 1 additionally adjusted for sociodemographic covariates: race, sex, and educational attainment. To explore a potential pathway, Model 2 further included change in BMI from Time 1 to Time 2. Guided by the vulnerability hypothesis, (Cuevas et al., 2020; Sternthal et al., 2011) which posits that marginalized groups may be more sensitive to the health effects of psychosocial stressors, we tested whether associations between discrimination and changes in CRP varied by race and sex. Specifically, we included interaction terms between race and both intermittent and chronic discrimination (Model 3), as well as interaction terms between sex and both intermittent and chronic discrimination (Model 4). Due to sample size (Supplemental Table 1), we did not test a three-way interaction between discrimination, race, and, sex. (Gelman et al., 2021) All analyses for Add Health and HRS were weighted using biomarker sample weights to adjust for survey design effects and nonresponse. The MIDUS biomarker studies did not include survey weights. To account for potential within-family clustering, we adjusted standard errors (SEs) using robust variance estimation clustered by family membership. This approach aligns with prior research. (Yang et al., 2016) Statistical significance was defined as $p < 0.05$. Cases with missing data on any variables included in the models were excluded using listwise deletion. All analyses were conducted in R version 4.4.1 (R Core Team, R Foundation for Statistical Computing).

Table 1
Weighted demographic and health characteristics of participants across three study cohorts: the National Longitudinal Study of Adolescent to Adult Health (Add Health), the Midlife in the United States Study (MIDUS), and the Health and Retirement Study (HRS).

Characteristic	Add Health	MIDUS	HRS
	n = 2,816	n = 624	n = 2,061
Age (Time 1), Mean (SE) [Min, Max]	28.7 (1.7) [25.0, 34.0]	51.7 (9.9) [34.0, 80.0]	63.9 (8.6) [42.0, 90]
Age (Time 2), Mean (SE) [Min, Max]	37.7 (1.8) [33.0, 44.0]	61.2 (9.8) [43.0, 89.0]	72.1 (8.6) [50.0, 98.0]
Change in age, Mean (SE) [Min, Max]	8.9 (0.8) [7.0, 13.0]	9.4 (0.9) [8.0, 12.0]	8.2 (0.5) [7.0, 9.0]
Sex, No. (%)			
Male	1055 (46.6%)	284 (45.5%)	783 (38.0%)
Female	1761 (53.4%)	340 (54.5%)	1278 (62.0%)
Race, No. (%)			
non-Hispanic Black	611 (18.3%)	110 (17.6%)	237 (6.4%)
non-Hispanic White	2205 (81.7%)	514 (82.4%)	1824 (93.6%)
Educational attainment (Time 1), No. (%)			
<High school	484 (19.6%)	146 (23.4%)	1037 (45.0%)
Some college	1153 (43.1%)	188 (30.1%)	484 (24.9%)
College and above	1179 (37.3%)	290 (46.5%)	540 (30.2%)
BMI (Time 1), Mean (SE)	29.4 (7.9)	29.3 (6.2)	29.6 (5.9)
BMI (Time 2), Mean (SE)	31.1 (7.8)	29.8 (6.6)	29.6 (5.9)
Change in BMI, Mean (SE)	1.7 (4.8)	0.4 (3.2)	−0.1 (3.5)
Blood c-reactive protein (mg/L or μg/mL) (Time 1), Mean (SE)	5.0 (9.1)	3.8 (5.8)	3.9 (9.4)
Blood c-reactive protein (mg/L or μg/mL) (Time 2), Mean (SE)	4.1 (6.1)	4.0 (5.7)	3.3 (4.1)
Change in blood c-reactive protein (μg/mL), Mean (SE)	−0.9 (9.2)	0.2 (6.6)	−0.7 (9.9)
Discrimination, No. (%)			
Never	364 (11.6%)	250 (40.1%)	707 (33.5%)
Intermittent	922 (33.8%)	183 (29.3%)	640 (31.3%)
Chronic	1530 (54.7%)	191 (30.6%)	714 (35.3%)

The statistics for the MIDUS were not weighted because weights were not available. Standard deviations are shown instead of standard errors for MIDUS.

3. Results

Descriptive characteristics of the three study cohorts are summarized in Table 1. The mean age of participants was 28.7 years (SE = 1.7) in Add Health, 51.7 years (SD = 9.9) in MIDUS, and 63.9 years (SE = 8.6) in HRS. Across cohorts, the samples were predominantly non-Hispanic White, comprising 81.7% of Add Health, 82.4% of MIDUS, and 93.6% of HRS participants. Chronic exposure to discrimination was most commonly reported in Add Health (54.7%), compared to 30.6% in MIDUS and 35.3% in HRS. In Add Health, average CRP levels at baseline were 5.0 mg/L (SE = 9.1); in MIDUS, 3.8 μg/mL (SD = 5.8); and in HRS, 3.9 μg/mL (SE = 9.4).

Results from the bivariate analyses are shown in Supplemental Tables 2–4. In MIDUS, discrimination status significantly varied by education level (Supplemental Table 3): those in the never group had a higher proportion with a college degree or higher (50.4%) compared to the intermittent (45.9%) and consistent (41.9%) groups ($p = 0.018$). In HRS (Supplemental Table 4), discrimination status significantly varied by age ($p < 0.001$), with those in the consistent group being younger at baseline (mean age = 62.3) than those in the intermittent (mean age = 63.4) and never groups (mean age = 66.1). The remaining bivariate comparisons were not statistically significant (all $p > 0.05$).

Table 2 presents findings from multivariable models assessing the relationship between discrimination exposure and change in CRP across the three cohorts. In Add Health, chronic exposure to discrimination was significantly associated with increasing CRP over the 8 to 10-year year interval between assessments. In the model controlling for CRP at Time 1, individuals with chronic exposure showed greater increases in CRP relative to those with no exposure (B = 0.91 mg/L, 95% CI: 0.20 to 1.61). This association remained statistically significant after adjusting for demographic covariates including sex, race, and educational attainment (B = 0.91 mg/L, 95% CI: 0.21 to 1.60), and persisted even after accounting for BMI (B = 0.87 mg/L, 95% CI: 0.19 to 1.54). In contrast, no significant associations were observed between discrimination exposure and change in CRP in MIDUS or HRS, regardless of model specification. No significant associations were observed for the intermittent exposure group across the three cohorts.

3.1. Differences by race and sex

To assess whether the association between discrimination and change in CRP differed by race, we included interaction terms between race and discrimination in Model 3 (Supplemental Table 5). Across all three cohorts, there was no evidence the association between discrimination and change in CRP varied by race. We also examined similar discrimination by sex interactions and found no evidence that the

Table 2
Weighted association between discrimination and change in blood C-reactive protein (mg/L or μg/mL) across three study cohorts.

	Model 0		Model 1		Model 2	
	B (95% CI)	p-value	B (95% CI)	p-value	B (95% CI)	p-value
National Longitudinal Study of Adolescent to Adult Health (Add Health)						
Discrimination						
Never (reference)						
Intermittent	0.43 (−0.28 to 1.16)	0.23	0.58 (−0.12 to 1.29)	0.11	0.54 (−0.13 to 1.22)	0.25
Chronic	**0.91 (0.20 to 1.61)**	**0.010**	**0.91 (0.21 to 1.60)**	**0.010**	**0.87 (0.19 to 1.54)**	**0.010**
Race						
non-Hispanic White (reference)						
non-Hispanic Black			**0.81 (0.05 to 1.56)**	**0.04**	0.71 (−0.01 to 1.43)	0.05
Midlife in the United States Study (MIDUS)						
Discrimination						
Never (reference)						
Intermittent	0.01 (−0.97 to 1.00)	0.98	0.06 (−0.89 to 1.01)	0.90	0.07 (−0.88 to 1.01)	0.89
Chronic	0.63 (−0.39 to 1.65)	0.23	0.49 (−0.52 to 1.50)	0.34	0.50 (−0.51 to 1.51)	0.34
Race						
non-Hispanic White (reference)						
non-Hispanic Black			**1.94 (0.60 to 3.28)**	**0.005**	**1.84 (0.51 to 3.16)**	**0.006**
Health and Retirement Study (HRS)						
Discrimination						
Never (reference)						
Intermittent	−0.19 (−0.65 to 0.26)	0.40	−0.20 (−0.65 to 0.25)	0.39	−0.19 (−0.63 to 0.26)	0.41
Chronic	0.03 (−0.45 to 0.50)	0.91	0.05 (−0.43 to 0.52)	0.85	0.04 (−0.43 to 0.52)	0.86
Race						
non-Hispanic White (reference)						
non-Hispanic Black			**1.01 (0.26 to 1.76)**	**0.010**	**1.08 (0.34 to 1.83)**	**0.004**

Bold indicates $p < 0.05$.
Model 0 controlled for c-reactive protein at Time 1.
Model 1 controlled for c-reactive protein at Time 1, sex, race, and educational attainment.
Models 2 controlled for c-reactive protein at Time 1, sex, race, educational attainment, and change in body mass index.
The statistics for the MIDUS were not weighted because weights were not available.

association between discrimination and changes in CRP varied by sex (Supplemental Table 5).

3.2. Exploratory analyses

We examined whether an increase in exposure (no exposure at Time 1 but exposure at Time 2) or a decrease in exposure (exposure at Time 1 but no exposure at Time 2) was associated with change in CRP relative to no exposure in both time points. In Add Health, 19.1% of participants experienced increased exposure to discrimination, while 14.7% experienced a decrease (Supplemental Table 6). In MIDUS, 12.7% showed increased exposure and 16.7% showed decreased exposure. In HRS, 14.0% experienced an increase in discrimination and 17.3% experienced a decrease. We found no evidence that either increased or decreased exposure to discrimination was associated with change in CRP (Supplemental Tables 7 and 8).

3.3. Sensitivity analyses

Because we used listwise deletion, a reduction in sample size was expected. To assess the extent of this reduction, we examined the proportion of participants with complete data. Among those with CRP data at both time points, 6.7% (Add Health) and 4.0% (MIDUS) were missing data on one or more variables included in the models. However, about 24% of participants in the HRS sample with CRP data were missing responses. To address this, we conducted sensitivity analyses in which missing values on the discrimination measure were treated as a separate analytic category. This approach reduced the proportion of missing cases in HRS to 7.9%. Including a missing-data category led to an increase in sample size but did not materially alter the results in HRS (Supplemental Tables 9–12).

4. Discussion

This study drew on three US population-based cohorts spanning early, middle, and older adulthood to examine whether exposure to discrimination is associated with change in systemic inflammation over time among non-Hispanic White and non-Hispanic Black adults. Results from young adulthood (Add Health) showed that chronic exposure to discrimination (i.e., reporting discrimination at both longitudinal assessments) was significantly associated with increases in plasma CRP levels over time. This association remained even after accounting for sociodemographic factors and changes in BMI. In contrast, we found no evidence of an association between discrimination and changes in inflammation among middle-aged (MIDUS) or older adults (HRS). These data suggest that early adulthood may be a particularly critical period in which exposure to discrimination might become embedded in the homeostasis of systemic inflammatory biology.

Our findings contribute to a growing body of research documenting the physiological consequences of discrimination. (Cuevas et al., 2020; Lawrence et al., 2022; Lockwood et al., 2018; Lewis et al., 2014) While previous studies have reported associations between discrimination and systemic inflammation, (Lawrence et al., 2022) many have relied on cross-sectional designs and predominantly focused on individuals in midlife. By leveraging harmonized longitudinal data from three nationally representative cohorts, this study extends prior work by incorporating repeated assessments of both discrimination and inflammation. This approach allowed us to evaluate how exposure to discrimination relates to within-person changes in biological functioning over time across three life course stages. Further, by modeling within-person change, these estimates are fairly robust, as they help account for time-invariant characteristics, both observed and unobserved, that may confound the association between CRP and discrimination (e.g., stable personality traits, early life adversity, or other unmeasured sources of heterogeneity). The presence of significant associations in early adulthood aligns with life course frameworks that emphasize the formative role of early exposures in shaping long-term health trajectories. (Halfon and Hochstein, 2002; Cole et al., 2020) The heightened biological reactivity observed among younger adults may reflect both developmental vulnerabilities and more frequent encounters with discrimination at this life stage. (Hope et al., 2015; Grey et al., 2024; Lee et al., 2020; Boyce, 2016) In contrast, the lack of significant associations in middle-aged and older cohorts may suggest age-related differences in physiological sensitivity or psychosocial adaptation. (Lewis and Van Dyke, 2018; Brinkhof et al., 2023; Mitchell et al., 2021; Wilson and Gentzler, 2021) With age, individuals may develop more effective

coping strategies or cognitive reframing techniques that buffer the physiological impact of discriminatory experiences. It is also possible that inflammatory responses to discrimination that embed during young adulthood may simply be maintained at a stable level over time in older adulthood, reflecting a persistent insult that manifests as both higher initial levels of CRP and similarly higher levels at the later follow-up time points. Cohort differences may also arise from demographic or contextual factors, such as wealth, chronic health conditions, social support, neighborhood environments, or other structural and social variables that influence both exposure to discrimination and inflammatory responses. Future research should examine these factors to better understand cohort differences and identify conditions that may buffer or exacerbate the physiological effects of discrimination.

Beyond physiological adaptation, cohort differences may also reflect broader social and historical processes. (Lewis et al., 2015) Younger adults may be more attuned to subtle, everyday slights captured by current discrimination measures, in part because greater societal dialogue about social justice has increased awareness of microaggressions and expectations for fair treatment. It is also plausible that older adults experienced more overt or traumatic forms of discrimination earlier in life, so contemporary experiences of disrespect or being treated with less courtesy may be perceived differently or feel less severe compared with past experiences. These generational differences in both exposure and interpretation underscore the need for measurement approaches that are historically and contextually grounded, capable of capturing the evolving manifestations of discrimination across time and cohorts.

The mechanisms underlying young adults' heightened vulnerability to the physiological effects of discrimination remain unclear. In our analysis, the association between chronic discrimination and increased inflammation persisted even after accounting for changes in BMI, which is a potential mediator of stress-related biological processes. Future research should investigate whether health behaviors such as smoking, alcohol use, physical activity, and sleep quality help to explain the observed associations, particularly in this age group. These behaviors may serve as behavioral conduits through which discrimination exerts its impact on inflammatory processes. The average CRP levels were higher in Add Health than in MIDUS or HRS at baseline, despite the younger age of the cohort. This may reflect unmeasured age-related social stressors (e.g., student debt or job instability) or health behaviors, such as smoking or poor sleep, and methodological differences in CRP measurement, including the use of dried blood spot assays in Add Health versus serum-based assays in MIDUS and HRS. Future research should use consistent methodological approaches across cohorts and incorporate other age-relevant social stressors and behavioral factors to better understand how discrimination contributes to inflammation across the life course. Emerging evidence also points to the importance of molecular mechanisms, including immune-related gene expression, as potential pathways linking discrimination to chronic disease risk. Studies have shown that individuals reporting discrimination exhibit upregulation of pro-inflammatory genes, (Bird et al., 2024; Thames et al., 2019; Li et al., 2020) suggesting that social stressors can become biologically embedded at the genomic level. Incorporating gene expression data into future longitudinal research could deepen understanding of the biological embedding of discrimination. Additionally, further work is needed to examine the multidimensional nature of discrimination, including the attribution (e.g., racial, gender-based) and source (e.g., peers, institutions). Although existing studies have found limited evidence that attribution modifies health effects (Lewis et al., 2015; Harrington et al., 2025), it remains an open question whether the identity of the perpetrator or context of the discriminatory event matters in shaping physiological responses.

This study has limitations that should be acknowledged. First, although we harmonized measures of discrimination across the three cohorts to allow for comparison, differences in item wording and response formats may have influenced how participants reported their experiences. To facilitate harmonization, we created a simplified binary measure of discrimination exposure, which does not capture the severity of the exposure. Second, while health behaviors such as smoking, alcohol use, physical activity, and sleep are plausible pathways linking discrimination to inflammation, variation in the availability and measurement of these variables across cohorts prevented us from including them in the analysis. Third, our analytic sample was limited to non-Hispanic Black and White participants, which restricts the generalizability of the findings to other racial and ethnic groups who may experience and respond to discrimination differently. Furthermore, the samples in this study were predominantly non-Hispanic White, particularly in MIDUS, and low statistical power in the non-Hispanic Black subgroup may have limited our ability to detect differences. Therefore, findings should be interpreted with caution, and future research should examine more racially and ethnically diverse samples. Although the condensed version of the EDS demonstrates strong construct validity with the full nine-item version, it does not capture the other ways discrimination operates in daily life as reflected in the remaining items of the full scale and in other discrimination measures. As a result, we may underestimate the true influence of discrimination on CRP over time. Moreover, the condensed version may not adequately reflect the context-specific nature of discriminatory experiences, particularly for middle-aged and older adults. It is possible that the form, meaning, and effects of discrimination evolve over the life course and the EDS does not fully capture the lived experiences of older individuals. Future research should prioritize the development of age-appropriate instruments that can more accurately capture the ways discrimination is experienced and internalized at different stages of adulthood.

5. Conclusions

Chronic exposure to interpersonal discrimination across two time points is associated with increases in systemic inflammation during young adulthood. These findings highlight the importance of early-life psychosocial exposures in shaping long-term physiological risk. To inform effective intervention strategies, more research is needed to identify the biobehavioral mechanisms that link discrimination to inflammation, including health behaviors and molecular pathways that may mediate this relationship.

CRediT authorship contribution statement

Adolfo G. Cuevas: Writing – original draft, Conceptualization. **Xiaoyan Zhang:** Writing – original draft, Formal analysis, Data curation. **Jemar R. Bather:** Writing – original draft, Formal analysis, Data curation. **Alisha A. Crump:** Writing – review & editing, Formal analysis. **José A. Pagán:** Writing – original draft, Conceptualization. **Shu Xu:** Writing – original draft, Methodology, Conceptualization. **Kathleen Mullan Harris:** Writing – original draft, Supervision, Conceptualization. **Steven W. Cole:** Writing – original draft, Supervision, Conceptualization.

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Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2026.106816.

Data availability

Data will be made available on request.

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