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Article

Race by Sex Intersectional Differences in the Association between Allostatic Load and Depression in US Adults: 2005-2018

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Abstract **Objective:** Previous research has underscored the link between allostatic load—a comprehensive indicator of the cumulative physiological burden of chronic stress—and depression. However, there remains a significant gap in understanding how this relationship may differ across race and sex intersectional groups. This study aimed to investigate variations in the association between elevated allostatic load (AL>4) and depression among different race-sex intersectional groups within the general population. **Methods:** This cross-sectional secondary analysis utilized data from the National Health and Nutrition Examination Survey (NHANES) spanning 2005-2018. The analysis included variables such as race, sex, age, socioeconomic status, depression (measured via the Patient Health Questionnaire - PHQ), and allostatic load. Linear regression analyses were conducted to examine the interactions between race and sex with allostatic load, focusing on the likelihood of high depression as the outcome. **Results:** Across the pooled sample, an allostatic load greater than 4 was significantly associated with increased depression. Notably, an interaction effect was observed between race and AL>4 on depression among women, indicating that non-Hispanic Black women with a high allostatic load exhibited more pronounced depressive symptoms (Beta: 1.09, CI: 0.02-2.61). Conversely, among men, allostatic load greater than 4 neither correlated with nor interacted with race to influence depression levels. **Conclusion:** The study highlights the critical need to consider allostatic load as a key target for interventions that aim to reduce depression among Black women. These findings underscore the necessity for customized intervention strategies that address the nuanced race-sex disparities in the impact of allostatic load on mental health across populations.

Keywords: Depressive Symptoms, Allostatic Load, Racial Disparities, Women Health, Racism

1. Background

The Allostatic Load Model serves as a comprehensive framework for understanding the cumulative impact of chronic stress on individuals' and populations' physiological health [1,2]. Coined by Sterling, allostasis refers to the body's adaptive response to

environmental challenges, involving dynamic adjustments in physiological systems such as the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS) [1,2]. McEwen extended this concept and proposed the 'allostatic load model' that serves as a framework to investigate the physiological cost incurred by the body when exposed to prolonged or repeated stressors [3]. Chronic stress, according to this model, leads to dysregulation in key physiological systems, particularly the immune and cardiometabolic system, as well as HPA axis and SNS, resulting in maladaptive responses [4]. Manifestations of this dysregulation include alterations in cortisol levels and catecholamines, that negatively impact cardiovascular, immune, and metabolic functions over time [5]. The allostatic load model underscores the interconnectedness of stress and physiological responses, highlighting how prolonged stress exposure and adaptation contribute to systemic dysfunctions in the organism [6,7]. Beyond its initial formulation, researchers have shown that dysregulation in the HPA axis result in metabolic syndrome, which is associated with a cluster of undesired changes in the metabolic and cardiovascular symptoms [8,9].

However, the dysregulation outlined in the allostatic load model may extend beyond physiological domains [10]. This includes a proposed contribution to mental health issues, specifically mood disorders [11,12]. The link between allostatic load and depression is believed to be mediated through the impact of chronic stress on the HPA axis and downstream physiological systems [13]. Epidemiological research on allostatic load and its association with depression has the potential to yield valuable insights [1,12]. Studies that demonstrate significant connections between elevated allostatic load scores and increased depression indicate the allostatic load may have clinical utility in depression treatment and diagnosis [1,12]. Such research suggests that measurement of allostatic load may be useful in screening depression [14]. However, this research has seldom compared Black and White populations for the interplay between allostatic load and depression, despite that race may alter the intricate links between chronic stress, physiological adaptation, and mental health.

Based on several theoretical perspectives, it is plausible that the link between allostatic load and depression varies between Black and White men and women. According to the Environmental Affordance Model [15,16], Black individuals may develop coping mechanisms in response to chronic stress that increase their metabolic and physiological risks while concurrently preserving their mental health. This model suggests that the coping strategies employed by Black individuals might differ from those of White individuals, impacting the manifestation of physiological and mental health outcomes [17]. Flourishing Hypothesis [18] posits that Black individuals may possess coping mechanisms that effectively mitigate the impact of stress and physiological strain, preventing these factors from culminating in depression [19-22]. This perspective underscores the resilience and adaptability of Black individuals in the face of adversity, potentially influencing the connection between allostatic load and depression in this population [23,24]. Furthermore, the Minorities' Diminished Returns theory [25,26] posits that the impact of the presence or absence of resources and risk factors on outcomes is less pronounced for minority groups. This theory can also be extended to suggest that factors such as socioeconomic status or chronic diseases related to depression may exert a different influence on Black individuals in comparison to White individuals. In line with this argument, the effects of chronic diseases on depression are shown to be weaker for Black than White men and women [27-30]. Consequently, this implies that the connection between allostatic load and depression may be less straightforward for Black individuals, as their health outcomes are shaped by an intricate interplay of various factors. Finally, the Black Mental Health Paradox [31,32] adds another layer to this discussion, proposing that, despite facing numerous stressors, Black men and women exhibit a lower likelihood of experiencing depression, indicating a unique form of resilience [33,34]. Taken together, these theoretical frameworks suggest that the connection between allostatic load and

depression may be weaker for Black individuals compared to their White counterparts. Still, understanding these nuanced dynamics is crucial for tailoring interventions and addressing mental health disparities across diverse racial groups.

Considerable empirical evidence also suggests that race by sex differences may exist in the association between depression and physiological changes. In their analysis of the National Health and Nutrition Survey (NHANES) data, Jokela and colleagues compared Black and White adults for the association between C-Reactive Protein (CRP) and depression. While CRP was positively associated with all 9 depressive symptoms in separate models, it was associated with only sleep disturbance, fatigue, and appetite changes in models adjusting for the other 8 symptoms. Authors concluded that this line of work has the potential to clarify the pathophysiology of inflammation-related depression and inform the development of new depression interventions targeting inflammation [35]. In another study, the directionality of the depression-inflammation relationship was assessed in Black people. The study followed 263 healthy older men and women as a part of the Pittsburgh Healthy Heart Project in a 6-year prospective cohort study Baseline depression was a predictor of 6-year change in IL-6, even after adjustment for demographic, biomedical, and behavioral factors as well as other negative emotions. In contrast, baseline IL-6 did not predict 6-year change in depression. This analysis provided evidence for a weak bidirectional relationship between depression and CRP in Black people [36]. Another analysis of NHANES 2005–2010 examined the associations of nine allostatic load biomarkers with depression in Black and White adults aged 18–64 years (n = 6431). High c-reactive protein was associated with depression among White women (adjusted odds ratio (aOR) = 1.7) and men (aOR = 1.8) but not Black women (aOR = 0.8) or men (aOR = 0.9) [37].

2. Aims

This study leverages data from the National Health and Nutrition Examination Survey (NHANES) [38,39] to explore whether the relationship between allostatic load and depression in the general population of adults varies across diverse race by sex groups.

3. Methods

3.1. Study Design and Settings

This study conducted a secondary analysis using data from the National Health and Nutrition Examination Survey (NHANES), a publicly available from the National Center for Health Statistics. NHANES gathers data to provide national estimates of the health and nutrition status of the U.S. population.

3.2. Data Collection Method

NHANES has been collecting data biennially since 1999, with an average response rate of 73.2% recorded between 2005-2018 [40,41]. The survey methodology involved in-person interviews, standardized physical examinations, and laboratory tests. Participants were chosen from various counties across the U.S., representing both metropolitan and nonmetropolitan areas in all four regions. NHANES has detailed documentation available outlining the sample design, estimation, and analytic guidelines [42].

3.3. Study Population and Sampling

The analytical sample comprised 22,650 participants, including 5463 men, and 6593 women. These participants were 20 years and older and had taken part in NHANES between 2005 and 2018.

3.4. Measures

3.4.1. Outcome variables

Depression Assessment: The NHANES used the nine-item version of the Public Health Questionnaire (PHQ-9) to evaluate depressive symptoms. The PHQ-9, derived from the Primary Care Evaluation of Mental Disorders (PRIME-MD), measures depression severity on a graded scale. Administered as a self-report by the patient, it has demonstrated reliability and validity. A threshold score of greater than 9 on the PHQ-9 indicates an 88% sensitivity [43] and specificity, making it suitable for clinical application. Scores on the PHQ-9 correspond to different levels of depression severity on the DSM-IV scale, ranging from mild to severe [44]. Participants rated the frequency of various depressive symptoms they experienced over the preceding two weeks on a 4-point scale. The sum of these ratings across the nine items yielded a total score, with a maximum score of 27 [45]. To facilitate logistic modeling, a binary variable was created using a cutoff score of 10 or higher (=1 for PHQ ≥ 10, =0 for PHQ < 10), a threshold commonly employed in previous research [46,47].

3.4.2. Main Independent Variable

Allostatic Load Score (AL): The allostatic load score was computed following the methodology suggested by Chyu and Upchurch (2011), using eight biomarkers: systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), pulse rate (beats/min), body mass index (kg/m2), glycohemoglobin (%), direct HDL-cholesterol (mg/dL), total cholesterol (mg/dL), and serum albumin (g/dL) [48]. Biomarkers exceeding the 75th percentile were categorized as high risk, except for HDL-cholesterol and serum albumin, where values below the 25th percentile were deemed high risk [49]. This established methodology has been widely applied in various research studies [50,51].

3.4.3. Control Variables

In our analysis, we included various control variables to address potential factors that could influence the study outcomes. These control variables encompass demographic and socioeconomic status (SES), healthcare access, and health behaviors. For demographic and SES factors, we considered variables such as age, sex, marital status (1 = married, 0 = unmarried, including divorced, separated, widowed, or never married), educational attainment (less than high school, high school, or general equivalency diploma, more than high school), and the Poverty Income Ratio (PIR). PIR, which serves as an income proxy, is calculated by dividing family (or individual) income by the poverty guidelines specific to each survey year [52]. By incorporating family income, family size, and poverty thresholds, PIR offers a more accurate measure of socioeconomic status. We categorized PIR into low, medium, and high tertile based on specific ranges. To address healthcare access, we included having a regular healthcare provider. Overall, these control variables allowed us to consider and adjust for various factors that could impact the study outcomes.

3.4.4. Race and Sex

Race and sex were both self-identified. Race was non-Hispanic White or non-Hispanic Black. Sex was male vs female.

3.5. Statistical Analysis

The objective of this study was to investigate the relationship between depressive symptoms, Allostatic Load (AL), Poverty Income Ratio (PIR), and other socioeconomic indicators in individuals aged 20 years and older. To achieve this aim, the study implemented two analytical approaches.

First, descriptive analyses were carried out to compare variables such as the PHQ-9 scale, PHQ-categories, elevated AL (AL≥4), demographic factors, SES markers, and healthcare access between men and women. Independent t-tests were utilized to compare these variables across gender groups.

Secondly, to evaluate the association between depressive symptoms and the individual-level factors mentioned earlier, the study conducted weighted linear regression analyses on participants with depression (PHQ-9>10). To investigate how race influenced the relationship between depression and elevated AL, race categories were interacted with AL values. The models were adjusted for race, age, marital status, education, PIR category, and having a routine healthcare provider.

Weighted analyses were performed using NHANES individual-level sampling weights for the years 2005-2018 [53]. Statistical significance was set at $p<0.05$, with all tests being two-sided. The statistical analyses were conducted using STATA statistical software, version 15.

4. Results

4.1. Descriptive Data

Table 1 displays the weighted means and standard deviations for all variables incorporated in the models. The sample had an average age of 48.5 (SD: 13) years, with around 50% being college-educated. They predominantly belonged to the middle class or lower, as indicated by a Poverty-to-Income Ratio (PIR) of 2.28 (SD: 1.60). 88% of the participants had a regular healthcare provider. In terms of race, 17% of the population were non-Hispanic Black, while 83% were non-Hispanic White.

Regarding health outcomes, the PHQ-9 scale averaged at 14 (3.16). 63% of the population experienced moderate depressive symptoms, 27% had moderate-severe symptoms, and around 10% reported severe depression. Elevated Allostatic Load (AL≥4) was present in 43% of the study population, with non-Hispanic Black individuals exhibiting a higher prevalence compared to non-Hispanic White individuals (47.5% vs. 42.4%). Notable differences between men and women were observed in the Poverty-to-Income Ratio (PIR), with 34% of men having a high PIR compared to 27% of women. Further details can be found in Table 1.

Table 1. Descriptive Analysis of Outcome and Control Variables in Women 20 year and over, NHANES: 2005-2018

	All (n=22,650)		**Men (n=5,463)**		**Women (n=6,593)**		
	Mean	SD	Mean	SD	Mean	SD	p
PHQ-9 Scale	14.05	(3.16)	14.04	(3.33)	14.06	(3.06)	0.3454
PHQ Category							
Moderate	63.04	(40.63)	63.10	(41.65)	63.00	(40.06)	0.8646
Mod-Severe	27.36	(37.52)	27.47	(38.53)	27.30	(36.97)	0.9324
Severe	9.60	(24.79)	9.43	(25.22)	9.70	(24.55)	0.6502
AL Score	3.32	(1.36)	3.17	(1.33)	3.41	(1.36)	0.2186
Elevated AL(ALS>4)	43.31	(41.70)	40.70	(42.40)	44.76	(41.26)	0.2660
Elevated AL(ALS>4) x White	42.4	(37.3)	40.4	(38.3)	43.6	(36.7)	0.4471
Elevated AL(ALS>4) x Black	47.5	(59.1)	42.2	(60.8)	50.1	(57.9)	0.1342
Race/Ethnicity							
White NH	83.25	(31.43)	84.93	(30.88)	82.31	(31.66)	0.1059
Black NH	16.75	(31.43)	15.07	(30.88)	17.69	(31.66)	0.1059
Age (Year)	48.54	(13.00)	48.74	(12.97)	48.43	(13.01)	0.4243
Female	64.12	(40.37)	0.00		100.00		
Married	47.26	(42.02)	49.69	(43.15)	45.90	(41.35)	0.2584
Education							

	All (n=22,650)		Men (n=5,463)		Women (n=6,593)		
	Mean	SD	Mean	SD	Mean	SD	p
<High school (HS)	21.37	(34.50)	21.88	(35.68)	21.09	(33.85)	0.5001
HS graduate/GED	28.69	(38.07)	30.24	(39.64)	27.82	(37.18)	0.3667
More than HS	49.93	(42.08)	47.88	(43.11)	51.08	(41.48)	0.1743
Poverty to income ratio							
Low	34.21	(39.93)	31.51	(40.10)	35.71	(39.76)	0.2388
Medium	36.12	(40.43)	34.61	(41.06)	36.96	(40.05)	0.4698
High	29.67	(38.45)	33.87	(40.85)	27.33	(36.98)	0.0363
Routine place to receive care	88.21	(27.14)	84.93	(30.88)	90.04	(24.84)	0.0113

AL: Allostatic Load NH: Non-Hispanic

4.2. Estimating the association between selected health outcome and PIR groups

Table 2 displays the results from the adjusted regression models for depressed men and women (PHQ≥10), with Poverty-to-Income Ratio (PIR) as the only predictor. In comparison to those with high PIR, individuals with low PIR showed a beta coefficient of 0.94 (CI: 0.47-1.4), and those with medium PIR had a beta coefficient of 0.76 (CI: 0.22-1.3). The interaction between Allostatic Load (AL) and race did not demonstrate significance in this analysis.

Table 2. Weighted Regression Estimates on the Association between Depressive Symptoms and AL in US Population 20 Year and Older, 2005-2018

	All		All with interaction	
	Coeff.	**95% CI**	**Coeff.**	**95% CI**
Elevated AL (>4)	-0.1554	[-0.652]-[0.341]	-0.273	[-0.845]-[0.299]
Race/Ethnicity (Ref. WNH)				
Black NH	-0.081	[-0.570]-[0.408]	-0.4104	[-1.017]-[0.196]
Age (Year)	-0.0017	[-0.016]-[0.013]	-0.0019	[-0.016]-[0.013]
Female	-0.0551	[-0.495]-[0.384]	-0.0594	[-0.497]-[0.378]
Married	-0.0551	[-0.495]-[0.384]	-0.0594	[-0.497]-[0.378]
Poverty to income ratio (Ref. High PIR)				
Low	0.9422***	[0.472]-[1.412]	0.9378***	[0.469]-[1.407]
Medium	0.7572**	[0.221]-[1.293]	0.7635**	[0.231]-[1.296]
Education (Ref. <High school (HS)				
HS graduate/GED	-0.3089	[-0.927]-[0.309]	-0.3054	[-0.924]-[0.313]
More than HS	-0.3126	[-0.875]-[0.250]	-0.3156	[-0.877]-[0.246]
Routine place to receive care	0.6465	[-0.004]-[1.297]	0.6469	[-0.003]-[1.296]
Interaction (AL Race)				
AL in BNH	NA	NA	0.7021	[-0.118]-[1.522]
Constant	13.3438***	[12.273]-[14.415]	13.4125***	[12.315]-[14.510]
R-sq	0.016		0.0172	

** p<0.05, ** p<0.01, *** p<0.001* AL: Allostatic Load NH: Non-Hispanic

Table 3 illustrates the outcomes of the adjusted models for men and women. In men, the sole predictor of high depressive symptoms was medium-Poverty-to-Income Ratio (PIR), with a beta coefficient of 1.14 (CI: 0.12-2.17). On the other hand, when considering

women, those with low PIR exhibited higher depressive symptoms, showing a beta coefficient of 1.16 (CI: 0.56-1.76). Additionally, non-Hispanic Black women with elevated Allostatic Load (AL) reported higher depressive symptoms (Beta: 1.09, CI: 0.02-2.61).

Table 3. Weighted Regression Estimates on the Association between Depressive Symptoms and AL by Sex

	Women		**Women with interaction**		**Men**		**Men with interaction**	
	Coeff.	**95% CI**	**Coeff.**	**95% CI**	**Coeff.**	**95% CI**	**Coeff.**	**95% CI**
Elevated AL(ALS>4)	0.0294	[-0.560]-[0.618]	-0.1665	[-0.858]-[0.525]	-0.3997	[-1.155]-[0.355]	-0.3474	[-1.214]-[0.519]
Race/Ethnicity (Ref. WNH)								
Black NH	0.0706	[-0.496]-[0.637]	-0.4657	[-1.211]-[0.279]	-0.4656	[-1.180]-[0.249]	-0.3177	[-1.302]-[0.666]
Age (Year)	-0.0092	[-0.025]-[0.007]	-0.0093	[-0.025]-[0.006]	0.0121	[-0.013]-[0.037]	0.0123	[-0.013]-[0.038]
Female								
Married	0.0000	[0.000]-[0.000]	0.0000	[0.000]-[0.000]	0.0000	[0.000]-[0.000]	0.0000	[0.000]-[0.000]
Poverty to income ratio (Ref. High PIR)								
Low	1.1614***	[0.558]-[1.765]	1.1503***	[0.548]-[1.752]	0.4747	[-0.480]-[1.429]	0.4739	[-0.481]-[1.428]
Medium	0.5775	[-0.037]-[1.192]	0.5825	[-0.025]-[1.190]	1.1444*	[0.117]-[2.172]	1.1382*	[0.106]-[2.170]
Education (Ref. <High school (HS))								
HS graduate/GED	-0.5699	[-1.269]-[0.130]	-0.5722	[-1.270]-[0.126]	0.2023	[-0.825]-[1.230]	0.1964	[-0.830]-[1.223]
More than HS	-0.5131	[-1.165]-[0.138]	-0.5186	[-1.169]-[0.132]	-0.0641	[-1.051]-[0.923]	-0.0643	[-1.052]-[0.923]
Routine place to receive care	0.5452	[-0.333]-[1.423]	0.5667	[-0.305]-[1.438]	0.5079	[-0.538]-[1.554]	0.5141	[-0.530]-[1.558]
Interaction (AL Race)								
AL in BNH	NA	NA	1.0928*	[0.025]-[2.161]	NA	NA	-0.3468	[-1.682]-[0.989]
Constant	13.8572***	[12.645]-[15.070]	13.9401***	[12.713]-[15.167]	12.5985***	[10.745]-[14.452]	12.5627***	[10.692]-[14.434]
R-sq	0.0271		0.0303		0.0249		0.0252	

** p<0.05, ** p<0.01, *** p<0.001* AL: Allostatic Load NH: Non-Hispanic

5. Discussion

This study was conducted to test race by sex differences in the relationship between allostatic load and depression in a nationally representative sample of US adults. While we found evidence supporting the link between allostatic load and depression, this association was stronger for Black women the White women. This Black-White difference in the link between allostatic load and depression observed in women was not because of socioeconomic factors.

We found stronger link between allostatic load and depression in Black women than White women. Some existing empirical evidence exists on Black-White differences in the association between depression and physiological changes. Using NHANES data, Jokela

and colleagues showed CRP and depression are linked [54] However Stewart has shown that this effect is stronger for Black than White people [35]. In a 6-year follow study by Stewart, showed a weak bidirectional relationship between depression and CRP in Black people [36]. Similarly, Bey and colleagues used NHANES 2005–2010 (n = 6431) and showed that high CRP was associated with depression among White women (adjusted odds ratio (aOR) = 1.7) and men (aOR = 1.8) but not Black women (aOR = 0.8) or men (aOR = 0.9) [37].

Multiple theories suggest that racial variation may exist in the link between AL and depression. The Environmental Affordance Model [15,16] posits that Black individuals may develop coping mechanisms in response to chronic stress, heightening their metabolic and physiological risks while concurrently safeguarding their mental health. This model implies that the coping strategies employed by Black individuals may differ from those of White individuals, thereby influencing the manifestation of physiological and mental health outcomes [17]. Conversely, the Flourishing Hypothesis [18] suggests that Black individuals may possess coping mechanisms effectively mitigating the impact of stress and physiological strain, preventing these factors from culminating in depression [19-22]. This perspective underscores the resilience and adaptability of Black individuals in the face of adversity, potentially shaping the connection between allostatic load and depression in this population [23,24]. Furthermore, the Minorities' Diminished Returns theory [25,26,55,56] proposes that the impact of resources and risk factors on outcomes is less pronounced for minority groups. This theory can also be extended to suggest that factors such as socioeconomic status or chronic diseases related to depression may exert a different influence on Black individuals compared to White individuals. Supporting this argument, the effects of chronic diseases on depression are shown to be weaker for Black than White individuals [27-29]. Consequently, this implies that the connection between allostatic load and depression may be less straightforward for Black individuals, as their health outcomes are shaped by an intricate interplay of various factors. The Black Mental Health Paradox [31,32] introduces another layer to this discourse, proposing that, despite facing numerous stressors, Black individuals exhibit a lower likelihood of experiencing depression, indicative of a unique form of resilience [33,34]. Taken collectively, these theoretical frameworks suggest that the link between allostatic load and depression may be less robust for Black individuals compared to their White counterparts. Nevertheless, comprehending these nuanced dynamics remains crucial for customizing interventions and addressing mental health disparities across diverse racial groups.

The examination of depression can better benefit from the measurement of allostatic load for Black woman than White woman. For Black women, utility of AL measurement as an indicator of depression is probably justified. This may suggest that researchers and investigators may consider that the contribution of stressors and physiological changes and coping for 'allostatic load model may differ across race by sex intersectional groups.

Race by sex variation in the utility of 'allostatic load model' suggests that different mechanisms may be relevant to physiological dysregulation in response to chronic stress exposure across intersectional population groups [54]. Although allostatic load embodies the cumulative toll of prolonged stressors [3], diverse intersectional populations may not show similar correlates of allostatic load.

Although an extensive body of research conducted by McEwen and others have documented lasting physiological changes in response to long term exposure to psychosocial stressors [6,57,58], these pathways may differ in race by sex groups. A study involved 239 adults from Black, White, or Mexican backgrounds who were residing in Detroit. The author's hypothesis, validated by the results, showed an interaction between poverty and racial-ethnic groups. Specifically, poor whites exhibited shorter telomere length compared to their nonpoor counterparts, while poor and nonpoor blacks showed equivalent telomere length. Surprisingly, poor Mexicans had longer telomere length than nonpoor Mexicans. These findings underscore the significance of unobserved

heterogeneity bias, emphasizing its potential to impact the validity of telomere length differences estimates across racial and ethnic groups. The results also emphasize the health impacts of social identity as contingent outcomes shaped by structurally rooted biopsychosocial processes [59].

Allostatic load may differently be useful to quantify the physiological costs incurred from repeated exposure to chronic stressful demands or insufficient responses to these demands [60]. While prolonged or inadequate physiological adaptation to social and environmental stress can lead to dysregulation of glucocorticoids like cortisol via the hypothalamic–pituitary–adrenal (HPA) axis [61] and catecholamines via the sympathetic nervous system (SNS) [62], these effects may vary by race. These dysregulations that result in dysfunction within the cardiovascular, immune, and metabolic systems [13,63], may not be identical for diverse racial and ethnic groups. As shown here, dysregulation of cortisol and downstream physiologic systems, as outlined by the allostatic load model, may have different implication for depression [64,65] across racial groups.

Most of past work on the link between allostatic load and depression has reported overall associations, without breaking the results by race or sex [64,65]. While we know that physiological components of allostatic load that are linked to depression [66-72], we are unaware of any past work on race by sex variation in the link between allostatic load and depression. While this link is established [73,74], culture and coping may change such link. In other terms, it is possible that physiological dysfunction differently correlate with dimensions of depression [75] across race by sex intersections of the US populations.

5.1. Implications

The findings concerning the divergent association between allostatic load and depression have far-reaching implications for health disparities research, practice, and policy, particularly with a pronounced emphasis on racial variations. The racial variability in this linkage underscores the importance of considering race in the utility of allostatic load in treatment, care, and diagnosis. From a policy standpoint, recognizing a stronger association between elevated allostatic load and increased depression in Black than White women highlights the race by sex variation in the critical integration of mental and physical health. Interventions designed for the general population, primarily informed by research in overall samples, may not be equally effective for Black or White men and women. Policymakers, relying on literature predominantly focused on overall and average effects, need to reevaluate, and tailor mental health programs, incorporating strategies addressing chronic stress and allostatic load that are sensitive to race by sex nuances. The race by sex variation implies the necessity for nuanced and culturally sensitive approaches in these programs. Initiatives promoting stress reduction, resilience-building, and community-based interventions should be tailored to the specific needs and experiences of diverse populations, recognizing potential racial disparities in the effectiveness of such interventions.

On a clinical level, healthcare providers should consider incorporating tailored and group-specific assessments of allostatic load into routine screenings for individuals at risk of depression. However, it is crucial to recognize that the same allostatic load may not have the same mental health correlates across all races by sex groups, and universal interventions may unintentionally widen race by sex disparities. Integrating allostatic load measures alongside traditional risk assessments can enhance the precision of identifying those who may benefit from such programs, and it is likely that one group benefits more than other individuals. Hence, rather than universally applied programs, there is a need for targeted, tailored interventions that consider racial differences. Moreover, the racial variation in the link between allostatic load and depression emphasizes the importance of culturally informed interventions. Healthcare professionals can utilize the study's insights to tailor interventions that specifically address the physiological toll of chronic stress, recognizing the potential racial differences in these

impacts. This might involve a combination of psychoeducation, stress management techniques, and lifestyle modifications aimed at reducing allostatic load and preventing or alleviating depression, with an emphasis on tailoring these interventions to diverse race by sex backgrounds. Furthermore, the study underscores the importance of a holistic approach to mental health care that considers both physiological and psychosocial factors within the context of racial disparities. Clinicians should collaborate across disciplines with a heightened awareness of the racial variation in the interplay between physiological stress and mental health, developing integrated care models that acknowledge and address the unique needs of different race by sex intersectional groups. These results may indicate that an integrated approach to mental health may not have similar suitability for subpopulations. Recognizing and addressing racial disparities in the impact of chronic stress on physiological functioning is crucial. By incorporating allostatic load assessments into policy initiatives and clinical practice, specifically tailored to racial variations, there is an opportunity to enhance mental health outcomes on a population level and provide more targeted and effective interventions for individuals at risk of depression, with a commitment to addressing race by sex disparities in mental health.

5.2. Limitations and Strengths

While providing valuable insights into the relationship between allostatic load and depression using National Health and Nutrition Examination Survey (NHANES) data, it is important to acknowledge several limitations. The cross-sectional nature of the analysis prevents the establishment of causal relationships between allostatic load and depression, necessitating longitudinal investigations to elucidate the temporal dynamics of this association, particularly with an emphasis on racial differences. Additionally, reliance on self-reported data for depression through the Patient Health Questionnaire introduces subjectivity and potential recall bias, with considerations for how these biases may differ across racial groups. Despite efforts to control for socioeconomic status and health-related behaviors, the complex and multifaceted nature of these variables may not have been fully captured, potentially confounding the observed associations, especially within racially diverse populations. The use of physiological markers as indicators of allostatic load may oversimplify the intricate physiological processes underlying chronic stress, particularly considering potential racial variations in these processes. Despite these limitations, this study contributes valuable evidence to the understanding of the relationship between allostatic load and depression at a national level, laying the groundwork for future research and interventions in mental health, with an increased awareness of racial nuances.

5.3. Future Research

To advance our understanding of the differential relationship between allostatic load and depression across race by sex intersectional groups, future research should explore several key avenues that have increased this connection in Black women in particular. Longitudinal studies are essential to establish a temporal sequence and causality, allowing for a more nuanced exploration of how changes in allostatic load relate to the onset and trajectory of depression over time, with explicit attention emergence of race by sex variations. Such designs would enable the identification of critical periods of vulnerability and resilience of Black women, shedding light on the dynamic nature of this association across diverse race by sex intersectional groups. In addition to refining the temporal aspect, future investigations could benefit from employing a more diverse array of measurement tools for both allostatic load and depression, considering the potential race by sex variations in the manifestation of these measures. Integrating objective physiological measures, such as biomarkers and neuroimaging, alongside self-reported assessments, would offer a comprehensive understanding of the biological underpinnings of the observed relationship, with acknowledgment of potential race by sex differences in

these biological processes. This multi-method approach would help address potential biases associated with self-reporting and provide a more robust foundation for drawing conclusions about the physiological impact of chronic stress across diverse race by sex intersectional groups. Furthermore, a more nuanced exploration of the role of socioeconomic status and health-related behaviors is warranted, with a specific focus on how these factors may differently influence race by sex intersectional groups. Future studies could employ more detailed and comprehensive assessments of socioeconomic status, considering factors such as education, occupation, and income separately, to better capture the intricate socioeconomic landscape within diverse race by sex intersectional groups. Moreover, investigating specific health-related behaviors, such as sleep patterns, physical activity, and dietary habits, may offer insights into the mechanisms through which allostatic load influences mental health, with considerations for potential racial variations in these behaviors. Lastly, interventions targeting allostatic loads could be explored, emphasizing their effectiveness in preventing or mitigating depression, with an explicit focus on racial disparities. Investigating whether interventions, such as stress management programs or lifestyle modifications, can modulate allostatic load and subsequently impact mental health outcomes would have practical implications for public health, with an awareness of potential racial variations in the effectiveness of these interventions. By addressing these considerations, future research can build upon the current findings, providing a more nuanced understanding of the complex interplay between allostatic load and depression and offering valuable insights for the development of targeted interventions to improve mental health on a broader scale, with a commitment to addressing racial disparities.

6. Conclusion

In conclusion, our study elucidates race by sex variation in the relationship between allostatic load and depression within the general population of US adults. The results affirm the strongest association between allostatic load and depression among Black women, even after adjusting for socioeconomic factors. This research significantly advances our comprehension of race by sex variations in the intricate interplay between physiological stress and mental health on a national scale. The outcomes underscore the imperative for a nuanced and tailored integrated approach to mental health, one that acknowledges the varying impact of chronic stress on physiological and psychological functioning across racial groups. Recognizing that the association between allostatic load and depression is stronger for Black women than to their White women or Black men and women, the integration of allostatic load assessments into the clinical management of depression would disproportionately benefit Black women. Implementation of such practices should be sensitive to racial variations, presenting an opportunity to optimize mental health outcomes at the population level and deliver targeted and effective interventions for those at risk of depression. A commitment to addressing race by sex differences in mental health is essential for fostering equitable mental health outcomes across diverse communities.

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