



Place-based Opportunities and Physiological Stress: Understanding Neighborhood-level Disparities in Allostatic Load

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ABSTRACT

Background: Allostatic load, representing cumulative physiological stress, is linked to various health outcomes. While neighborhood conditions influence health, the relationship between comprehensive neighborhood opportunity measures and allostatic load remains understudied.

Methods: Using data from 2118 participants in the Midlife in the United States study, we examined associations between neighborhood opportunity (measured by the Childhood Opportunity Index) and allostatic load (measured using standard clinical cut-offs of eight biomarkers: systolic and diastolic blood pressure, hemoglobin A1C, high-density lipoprotein cholesterol, body mass index, waist circumference, total cholesterol, and c-reactive protein). The index comprised three subdomains: Education, Health and Environment, and Social and Economic Resources. Negative binomial regression models quantified these associations, adjusting for sociodemographic characteristics, health behaviors, and prescribed medication use.

Results: Lower Overall Neighborhood Opportunity was significantly associated with higher allostatic load, even after full covariate adjustment (18 % increase in expected allostatic load count, 95 % CI: 8 %–29 %, $p < 0.001$). Social and Economic Resources emerged as the subdomain that consistently tracked with expected allostatic load count. Negative binomial regression models provided evidence of similar significant patterns across the Education and Health and Environment models when comparing low to high groups.

Conclusions: Low neighborhood opportunity is associated with increased physiological stress as measured by allostatic load. These findings further indicate that neighborhood-level interventions may be crucial for reducing health inequities and improving population health outcomes.

1. Introduction

Allostatic load, the cumulative physiological burden of repeated stress, is associated with increased risk of premature death and chronic diseases, including diabetes, coronary heart disease, and stroke (Parker et al., 2022; Beckie, 2012; Logan and Barksdale, 2008; Juster et al., 2010; McEWEN, 1998a). This biological phenomenon manifests as dysregulation of multiple physiological systems, including the immune and sympathetic nervous systems, cardiovascular and metabolic processes and the hypothalamic-pituitary-adrenal axis (Seeman et al., 2001).

The full range of factors influencing allostatic load remains incompletely understood, as researchers continue to uncover new physiological, psychological, and environmental variables that contribute to this complex measure of cumulative stress on the body (Beckie, 2012; Logan and Barksdale, 2008; Juster et al., 2010; McEWEN, 1998a; Miller et al., 2021). A recent review of highlights that interpersonal discrimination, manifesting as unfair treatment based on race, gender, or other social identities, is associated with higher allostatic load (Miller et al., 2021). Similarly, a systematic review demonstrated that adverse childhood experiences, such as maltreatment, abuse, and psychological neglect, are associated with elevated allostatic load, suggesting that early-life stress

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primes physiological systems for dysregulation over the lifespan (Finlay et al., 2022). While these factors of individual behavior and social characteristics are critical in activating physiological stress pathways, focusing exclusively on interpersonal experiences risks obscuring the broader context. Therefore, it is equally essential to examine structural determinants (i.e., macro-level mechanisms that create and maintain social inequities) that create and perpetuate environments conducive to chronic stress.

Neighborhood conditions play a crucial role in biological stress mechanisms such as physiological inflammation and allostatic load. A 2010 study found that neighborhood deprivation—measured by education, employment, crowding, and income—was associated with increased physiological inflammation, while neighborhood safety was linked to lower levels of inflammation (Nazmi et al., 2010). These findings align with previous research connecting neighborhood resources to allostatic load, a relationship particularly well-documented in studies of cognitive function (D'Amico et al., 2020; Park et al., 2024). In a systematic review, Wu et al. found significant associations between neighborhood deprivation and accelerated cognitive decline and increased risk of cognitive impairment (Wu et al., 2015). Corroborating these results, subsequent research has demonstrated that greater neighborhood resources are associated with slower rates of health decline over the lifespan (Clarke et al., 2015). The cumulative burden of neighborhood-level stressors during critical developmental periods triggers persistent physiological stress responses that not only endure but also intensify throughout adulthood (Nazmi et al., 2010). This chronic exposure to environmental adversity fundamentally alters biological regulatory systems, dramatically accelerating allostatic load through cascading inflammatory pathways and neuroendocrine dysregulation (McEwen, 2007). While research suggests an influence of neighborhood conditions on health trajectories, existing studies identify the most impactful intervention points for reducing health disparities (Nazmi et al., 2010; Clarke et al., 2015; Majoka and Schimming, 2021).

Previous metrics have been employed to investigate the relationship between specific neighborhood-level opportunities and biological outcomes. The Opportunity Atlas represents one widely used approach, retrospectively examining long-term economic and social outcomes of individuals based on their childhood neighborhood environments (Chetty et al., 2018). Similarly, the Area Deprivation Index (ADI) also offers another valuable methodology, ranking neighborhoods by socioeconomic disadvantage across multiple domains, including income, education, employment, and housing quality, and has demonstrated robust associations with various biomarkers of physiological stress and inflammation (Kind and Buckingham, 2018). While these metrics have advanced our understanding of specific neighborhood-environment relationships, they often differ in their temporal scope, granularity of measurement, and attention to specific neighborhood attributes and dimensionality, highlighting the need for inclusive, integrative approaches that capture the complex pathways through which neighborhoods become biologically embedded (Ludwig et al., 2012).

Developed in 2014, the Childhood Opportunity Index (COI) is a comprehensive tool for evaluating environmental indicators for human development and represents a novel opportunity to investigate the complex interplay between neighborhood opportunities and biological mechanisms (Acevedo-Garcia et al., 2014; Noelke et al.). The Childhood Opportunity Index examines current neighborhood resources affecting children's growth, measuring present-day factors that immediately impact their environments and future development. Encompassing 44 distinct metrics across three primary domains—education, health and environment, and social and economic resources—and 14 subdomains, this comprehensive assessment has been applied at the census tract level across all 50 states and generates relative opportunity scores, providing researchers with robust tools to investigate geographical disparities in health outcomes and their biological underpinnings (Noelke et al.; Maroko et al., 2016). Although originally developed to study childhood outcomes, the Childhood Opportunity Index is a multidimensional tool

that has proven additionally valuable for understanding how neighborhood environments shape adult health outcomes (Acevedo-Garcia et al., 2014). For example, a recent study found significant associations between the Childhood Opportunity Index and child mortality risk and even stronger associations with the mortality risks for a child's adult caregivers (Slopen et al., 2023; Gianaros et al., 2023). The application of the COI to adult populations is further supported by evidence demonstrating that neighborhood characteristics continue to influence health trajectories throughout the lifespan (Gianaros et al., 2023). In a recent study of midlife adults, Gianaros and colleagues, found that specific neighborhood features derived from the Childhood Opportunity Index were significantly associated with cardiometabolic risk factors and brain morphology changes that may presage neurocognitive decline (Gianaros et al., 2023). Although research is still growing, these findings collectively demonstrate how the Childhood Opportunity Index can provide valuable insight into adult health outcomes.

While previous studies using the Opportunity Atlas or Area Deprivation Index have established important connections between neighborhood disadvantage and physiological stress responses, they have primarily relied on retrospective economic measures or socioeconomic disadvantage rankings, leaving gaps in our understanding of how comprehensive neighborhood opportunity measures influence allostatic load. The current study addresses this limitation and complements existing research by utilizing the Childhood Opportunity Index to investigate the relationship between neighborhood opportunity and allostatic load. Drawing on established evidence demonstrating connections between neighborhood deprivation and physiological stress responses (Diez et al., 2010a; Ross and Mirowsky, 2001; Christine et al., 2015) (Diez et al., 2010a; Ross and Mirowsky, 2001; Christine et al., 2015), we hypothesized that reduced neighborhood opportunities would be associated with elevated allostatic load, reflecting greater physiological weathering in response to neighborhood disadvantage.

2. Methods

2.1. Study design, setting, and sample

We analyzed data from the Midlife in the United States (MIDUS), a study tracking the health of a national probability-based sample (Radler, 2014a). The initial MIDUS cohort (MIDUS 1; $n = 7108$) was recruited nationally during 1995–1996. The second wave (MIDUS 2, 2004–2005) retained 4963 original participants and added 592 African American participants from Milwaukee, Wisconsin to improve racial minority representation, totaling 5555 individuals. From 2011 to 2014, the MIDUS Refresher Study (MIDUS Refresher 1) enrolled an additional 4085 adults to supplement the original cohort, including targeted recruitment of 508 African Americans from Milwaukee, Wisconsin. MIDUS Refresher 1 participants completed identical enrollment surveys as the main cohort.

Survey participants who remained in good health and were able to travel qualified for follow-up biomarker assessments (Dienberg et al., 2010a). The MIDUS 1 Biomarker Project initiated recruitment in 2004, enrolling 1255 participants who visited one of three clinical research centers: Georgetown University, the University of Wisconsin-Madison, or the University of California, Los Angeles. The MIDUS Refresher 1 Biomarker Study (2012–2016) comprised 863 adults from the MIDUS Refresher 1 cohort. A total of 2118 biomarker participants comprised the analytic sample.

Biomarker participants received comprehensive support including detailed protocol information, \$200 compensation for the two-day clinic assessment, complete travel expense coverage, and travel coordination assistance. Older adults could bring companions, and childcare costs were covered when necessary. Detailed study protocols have been published elsewhere (Brim et al., 2019; Radler, 2014b; Dienberg et al., 2010b). The University of Wisconsin Institutional Review Board approved these study protocols, and all study participants provided

informed consent. The present study was exempt from review by the New York University Institutional Review Board and followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (von Elm et al., 2007).

2.2. Allostatic load

During a two-day stay at one of the three study sites, participants completed biomarker assessments, including physical examinations and tissue sample collection. We derived allostatic load scores using eight biomarkers: systolic blood pressure, diastolic blood pressure, hemoglobin A1C, high-density lipoprotein cholesterol, body mass index (BMI), waist circumference, total cholesterol, and C-reactive protein. We applied standard clinical cut-offs to determine high-risk categories for each biomarker. Participants received a score of '1' for each biomarker meeting the following thresholds: systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, hemoglobin A1C ≥ 6.4 %, high-density lipoprotein cholesterol < 40 mg/dL, BMI ≥ 30 kg/m², waist circumference > 102 cm (males) or > 88 cm (females), total cholesterol ≥ 240 mg/dL, and C-reactive protein > 3 mg/L. Summed scores ranged from 0 to 8, with higher scores indicating greater allostatic load. We treated allostatic load as a count outcome in all analyses.

2.3. Neighborhood opportunity

Neighborhood opportunity was assessed using the Childhood Opportunity Index 3.0, which incorporates 44 standardized indicators arranged into an overall metric (Overall Neighborhood Opportunity) and three subdomains: Education, Health and Environment, and Social and Economic Resources (Table 1). (Noelke et al.) Census tract data corresponded to participants' addresses at survey completion, with data linkage performed by the MIDUS Geocode team under special privacy protections to maintain participant confidentiality. Following z-score transformation and weighting, indicators were combined into nationally standardized measures. Overall Childhood Opportunity Index scores and subdomain scores were categorized into quintiles: very low (≤ 20 th percentile), low (> 20 th to ≤ 40 th percentile), moderate (> 40 th to ≤ 60 th percentile), high (> 60 th to ≤ 80 th percentile), and very high (> 80 th percentile). For analysis, these were collapsed into three groups: low (≤ 40 th percentile), moderate (> 40 th to ≤ 60 th percentile), and high (> 60 th percentile).

2.4. Covariates

Covariates included age (measured continuously), sex (male vs. female), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other), educational attainment ($<$ high school, high school/GED, some college and above), annual household income ($<$ \$50,000, \$50,000-\$100,000, \$100,000+), marital status (married, divorced/separated/widowed, never married), smoking status (never, past, current), past month alcohol consumption (never, < 1 day a week, 1–2 days a week, 3–4 days a week, 5–6 days a week, every day), and prescription medication use (yes vs. no). The non-Hispanic Other group encompassed Native American, Alaskan Native, Native Hawaiian, Pacific Islander, and Asian identities. Hispanic participants identified as Hispanic/Latino regardless of race. Annual household income categories followed U.S. Census Bureau classifications. (Guzman and Kollar) We consolidated categories to prevent small group sizes that could compromise participant anonymity.

2.5. Statistical analysis

Descriptive statistics included means and standard deviations for continuous variables and counts and percentages for categorical measures. We fit negative binomial regression models relating allostatic load scores to Overall Neighborhood Opportunity (primary analyses) (Alan

Table 1

The 44 components of the Childhood Opportunity Index 3.0 (Acevedo-Garcia et al., 2014).

Domain	Components
Education	<ul style="list-style-type: none"> private pre-K enrollment public pre-K enrollment reading and math test scores reading and math test score growth poverty-adjusted reading and math test scores advanced Placement course enrollment college enrollment in nearby institutions high school graduation rate adult educational attainment child enrichment-related non-profits teacher experience school poverty
Health and Environment	<ul style="list-style-type: none"> airborne microparticles ozone concentration industrial pollutants in air water or soil hazardous waste dump sites healthy food retailer density extreme heat exposure NatureScore walkability community safety-related non-profits vacant housing health-related non-profits health insurance coverage
Social and Economic Resources	<ul style="list-style-type: none"> employment rate high-skill employment rate full-time year-round earnings median household income poverty rate public assistance rate adults with advanced degrees very high-income households adults without high school degrees very low-income households broadband access crowded housing mobility-enhancing friendship networks single-parent families non-profit organizations homeownership rate aggregate home values aggregate capital income aggregate real estate taxes

Agresti, 2015). We first expressed allostatic load scores as a log-linear function of overall neighborhood opportunity (Model 1: unadjusted). To assess whether neighborhood associations persisted in the presence of sociodemographic factors, we controlled for age, sex, race/ethnicity, educational attainment, annual household income, and marital status in Model 2. Model 3 further controlled for health behaviors (smoking status and alcohol consumption) and prescription medication use. Secondary analyses followed a similar modeling approach to quantify the relationships between each neighborhood opportunity subdomain (Education, Health and Environment, and Social and Economic Resources) and allostatic load. Incident rate ratios (IRRs) with 95 % confidence intervals (CIs) are presented to compare expected allostatic load count across neighborhood opportunity levels. IRRs greater than one indicated higher expected allostatic load count in the comparison group and IRRs less than one indicated lower expected allostatic load count. Analyses used R version 4.4.2 (R Core Team, R Foundation for Statistical Computing), with statistical significance assessed as 2-sided $p < 0.05$.

Missing covariate data were handled through multivariate imputation by chained equations using the *mice* R package (van et al., 2011). Imputation methods varied by data type: predictive mean matching for continuous measures, multinomial logistic regression for nominal categorical variables, and ordinal logistic regression for ordered categorical measures. Regression estimates were pooled across ten imputed datasets

following Rubin's rules (Little et al., 2020).

3. Results

3.1. Summary statistics

Of the 2118 participants (mean age 53.0 years, SD = 12.6), 54.9 % were female, 72.9 % were non-Hispanic White, and 43.3 % resided in areas with low Overall Neighborhood Opportunity (Table 2). The mean allostatic load was 2.0 (SD = 1.6). However, this differed significantly across levels of Overall Neighborhood Opportunity (Table 3). Compared to those in high opportunity areas, individuals in areas with low Overall Neighborhood Opportunity had a higher allostatic load (low mean = 2.3 vs. high mean = 1.7, $p < 0.001$). We observed the following correlations of Overall Neighborhood Opportunity with race/ethnicity ($\rho = 0.30$), educational attainment ($\rho = -0.21$), and annual household income ($\rho = -0.27$).

3.2. Primary analyses

Table 4 shows the results from the negative binomial models relating allostatic load count to neighborhood opportunity. Across all three models, Overall Neighborhood Opportunity significantly correlated with allostatic load counts. In the primary analyses, Model 1 indicated that the expected allostatic load count among individuals in low Overall Neighborhood Opportunity areas was 1.36 times (95 % CI: 1.26–1.48, $p < 0.001$) that of those in high Overall Neighborhood Opportunity areas, without adjusting for confounders. The magnitude of this association attenuated when further controlling for sociodemographic factors in Model 2 (IRR: 1.22, 95 % CI: 1.12–1.33, $p < 0.001$). Introducing health behaviors and prescription medication use as covariates in Model 3 further attenuated this association's magnitude (IRR: 1.18, 95 % CI: 1.08–1.29, $p < 0.001$).

3.3. Secondary analyses

Social and Economic Resources emerged as the subdomain that consistently tracked with the expected allostatic load count (Table 4). Model 1 indicated that middle-aged adults living in areas with moderate (IRR: 1.24, 95 % CI: 1.12–1.36, $p < 0.001$) or low (IRR: 1.41, 95 % CI: 1.30–1.53, $p < 0.001$) Social and Economic Resources had significantly higher allostatic load counts than those in areas with high Social and Economic Resources. Like the primary analyses, the magnitude of these associations slightly weakened with further covariate adjustment: Model 2 (moderate IRR: 1.17, 95 % CI: 1.06–1.29, $p = 0.001$; low IRR: 1.25, 95 % CI: 1.14–1.37, $p < 0.001$) and Model 3 (moderate IRR: 1.14, 95 % CI: 1.03–1.25, $p = 0.009$; low IRR: 1.20, 95 % CI: 1.10–1.31, $p < 0.001$). Negative binomial regression models provided evidence of similar significant patterns across the Education and Health and Environment models when comparing low to high groups (Table 4; all $p < 0.05$).

4. Discussion

This study demonstrated robust associations between neighborhood opportunity and allostatic load, suggesting that neighborhood context plays a crucial role in physiological stress responses. Our findings reveal that individuals living in low-opportunity neighborhoods exhibit higher allostatic load compared to those in high-opportunity areas, with Educational Opportunities, Health and Environment, and Social and Economic Resources remaining significant, even after accounting for individual-level factors.

The association between low Educational Opportunity and increased allostatic load implies that neighborhood educational resources may have effects on physiological stress beyond individual circumstance. Areas with low educational opportunity, including access to educational

resources and post-secondary education, are frequently characterized by broader patterns of neighborhood disruption that amplify stress exposure (Evans and English, 2002; Nieuwenhuis and Hooimeijer, 2015; Sampson et al., 1979; National Academies of Sciences E and MH et al., 2019). Specifically, previous literature suggests that limited educational resources often cluster with other indicators of neighborhood disadvantage, including economic disinvestment, residential instability, social disorganization, and reduced collective efficacy (Henneberger et al., 2023; Wilson, 2012; Timberlake, 2013). These stress experiences are frequently intensified by a cycle in which neighborhoods with inadequate educational resources experience high turnover as economically mobile families leave for better districts, while less advantaged families remain behind (Jeffrey and Brennan, 2007; Annette, 2011). This residential instability weakens social networks and community cohesion, reducing the availability of social support systems that normally buffer against stress (Rios et al., 2012; Shaw and McKay, 1969). The resulting social fragmentation creates an environment where chronic vigilance and stress become normalized responses to daily life. This suggests that childhood educational opportunities influence adult allostatic load through complex pathways, including direct stress exposure from neighborhood disruption (McEWEN, 1998b). Understanding these mechanisms highlights the importance of educational investment not just for academic outcomes, but as a fundamental public health intervention that can reduce physiological stress and improve long-term health outcomes across entire communities (Vale et al., 2020; National Academies of Sciences E and MH and MD et al., 2019).

The Health and Environment domain demonstrated significant associations with allostatic load when comparing low to high opportunity areas, providing important insights into how environmental conditions influence physiological stress responses. The observed association between low Health and Environment opportunity and elevated allostatic load aligns with established research demonstrating that environmental stressors can influence multiple physiological systems captured in allostatic load indices (Geronimus et al., 2006; Thomson, 2019). Poor air quality, for instance, has been linked to chronic inflammation, with pollutants such as particulate matter further exacerbating conditions such as weight gain, an important indicator of allostatic load (Sierra-Vargas et al., 2023; Brook et al., 2010; Shi et al., 2022). Furthermore, regions with inadequate health insurance coverage can restrict residents' ability to manage health conditions or obtain preventive care, potentially leading to the buildup of physiological stress indicators measured by allostatic load (Ward and Martinez, 2014; Kawachi and Berkman, 2001). For instance, diminished health and environmental opportunities create obstacles to quality healthcare access, heightening the likelihood that manageable conditions like pre-diabetes will advance to diabetes, a key biomarker in allostatic load assessment (Carvalho-Azevedo et al., 2025). Other built environment components captured in this domain, including walkability, and access to healthy food retailers, likely influence allostatic load through limited access to healthy food options which may constrain residents' ability to engage in health-promoting behaviors, leading to increased physiological stress over time (Powell et al., 2007; Roe et al., 2020; Cortes et al., 2021). These components may also interact synergistically, where multiple environmental disadvantages compound each other's effects on physiological stress. For example, areas with poor air quality may also lack green spaces for physical activity, creating environments where multiple stressors operate simultaneously with few protective factors available (Diez et al., 2010b; Evans, 2003). This pattern demonstrates that environmental disadvantage creates a particularly toxic breeding ground for physiological stress that extends far beyond individual risk factors.

Lastly, the Social and Economic Resources domain demonstrated robust and consistent associations with allostatic load. The components measured within this domain, including employment rates, household income, poverty levels, educational attainment, housing quality, and social capital indicators, represent fundamental determinants of

Table 2

Descriptive statistics on 2118 participants from the Midlife in the United States study.

Characteristic	N = 2118
Age, Mean (SD)	53.0 (12.6)
Sex, No. (%)	
Male	955 (45.1 %)
Female	1163 (54.9 %)
Race/ethnicity, No. (%)	
non-Hispanic White	1544 (72.9 %)
non-Hispanic Black	393 (18.6 %)
Hispanic	76 (3.6 %)
non-Hispanic Other	93 (4.4 %)
Missing	12 (0.6 %)
Educational attainment, No. (%)	
<High school	107 (5.1 %)
High school/GED	392 (18.5 %)
Some college and above	1615 (76.3 %)
Missing	4 (0.2 %)
Annual household income, No. (%)	
<\$50,000	1040 (49.1 %)
\$50,000 to \$100,000	558 (26.3 %)
\$100,000+	417 (19.7 %)
Missing	103 (4.9 %)
Marital status, No. (%)	
Married	1314 (62.0 %)
Divorced/Separated/Widowed	478 (22.6 %)
Never married	321 (15.2 %)
Missing	5 (0.2 %)
Smoking status, No. (%)	
Never	1205 (56.9 %)
Past	645 (30.5 %)
Current	268 (12.7 %)
Past month alcohol consumption, No. (%)	
Never	734 (34.7 %)
<1 day a week	588 (27.8 %)
1–2 days a week	338 (16.0 %)
3–4 days a week	211 (10.0 %)
5–6 days a week	112 (5.3 %)
Every day	135 (6.4 %)
Prescription medication use, No. (%)	
No	595 (28.1 %)
Yes	1523 (71.9 %)
Overall Neighborhood Opportunity, No. (%)	
High	787 (37.2 %)
Moderate	413 (19.5 %)
Low	918 (43.3 %)
Education domain, No. (%)	
High	904 (42.7 %)
Moderate	356 (16.8 %)
Low	858 (40.5 %)
Health and Environment domain, No. (%)	
High	475 (22.4 %)
Moderate	529 (25.0 %)
Low	1114 (52.6 %)
Social and Economic Resources domain, No. (%)	
High	781 (36.9 %)
Moderate	446 (21.1 %)
Low	891 (42.1 %)
Characteristic	N = 2118
Systolic blood pressure, Mean (SD)	130.0 (17.9)
Missing, No. (%)	1 (<1 %)
Diastolic blood pressure, Mean (SD)	76.5 (10.6)
Missing, No. (%)	1 (<1 %)
Hemoglobin A1C (%), Mean (SD)	5.9 (1.1)
Missing, No. (%)	36 (1.7 %)
High-density lipoprotein cholesterol (mg/dL), Mean (SD)	56.9 (18.7)
Missing, No. (%)	25 (1.2 %)
Body mass index (kg/m²), Mean (SD)	30.0 (7.0)
Missing, No. (%)	1 (<1 %)
Waist circumference (centimeters), Mean (SD)	98.1 (18.0)
Missing, No. (%)	3 (0.1 %)
Total cholesterol (mg/dL), Mean (SD)	184.7 (40.1)
Missing, No. (%)	22 (1.0 %)
C-reactive protein (mg/L), Mean (SD)	3.0 (4.9)
Missing, No. (%)	34 (1.6 %)
Allostatic load, Mean (SD)	2.0 (1.6)
Missing, No. (%)	47 (2.2 %)

Table 3
Allostatic load by overall neighborhood opportunity.

Characteristic	Overall Neighborhood Opportunity			p-value
	High	Moderate	Low	
	N = 787	N = 413	N = 918	
Allostatic load, Mean (SD)	1.7 (1.6)	1.9 (1.6)	2.3 (1.6)	<0.001
Missing, No. (%)	13	6	28	

p-value by the Kruskal-Wallis rank sum test.

community stability and resident well-being (Aidoo, 2023; Fontefrancesco et al., 2025). For example, neighborhoods with limited economic resources may expose residents to chronic financial stressors that can activate stress response systems repeatedly over time (Fontefrancesco et al., 2025; Dowd et al., 2009). Additionally, areas characterized by high unemployment, low median incomes, and elevated poverty rates create environments where residents face persistent economic uncertainty. This chronic uncertainty can cause activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system which can lead to the physiological dysregulation captured by allostatic load measures (McDermott et al., 2024). The social components of this domain, including mobility-enhancing friendship networks and non-profit organizations, also represent critical stress-buffering resources (Wiley et al., 2017). Neighborhoods with strong social infrastructure, for instance, provide residents with access to social support, information networks, and collective efficacy, all of which can mitigate the physiological impact of stressors (Prior, 2021; Theall et al., 2012). Conversely, areas with weakened social capital may leave residents more vulnerable to the biological consequences of stress exposure, as they lack the community-level resources that typically help individuals cope with adversity.

The study findings have important implications for public health interventions and policy. First, they demonstrate that neighborhood-level interventions may be necessary to reduce health inequities, as individual-level interventions alone may be insufficient to address the physiological impact of living in low-opportunity areas. Second, the significant associations across all three opportunity domains suggest that comprehensive, multi-sector approaches may be most effective for reducing allostatic load. Specifically, the association between Educational Opportunity and Health and Environment indicates that investing in neighborhood educational resources, such as high-quality schools,

libraries, and post-secondary programs, alongside environmental improvements like access to healthy food retailers, walkability, and healthcare facilities could aid in reducing physiological stress at the population level. Similarly, the particularly robust associations with Social and Economic Resources indicate that investing in neighborhood economic development, employment opportunities, housing stability, and social infrastructure could have substantial health benefits.

The following limitations should be considered in the interpretation of our findings. One, despite its comprehensive nature, the Childhood Opportunity Index cannot fully capture the complex historical forces that have shaped neighborhood conditions (Diez et al., 2010a; Bailey et al., 2017). Therefore, residual confounding from impacts of discriminatory policies and institutionalized inequities may still exist. Combining innovative metrics, in addition to this index could provide deeper insights into how neighborhood contexts influence allostatic load. Two, the cross-sectional nature of our analysis precludes causal inference. Moreover, neighborhoods are not static environments - people relocate, communities undergo demographic changes, and residents may adapt to their surroundings over time. These dynamic processes could significantly influence the development of allostatic load. Future longitudinal studies are needed to better understand the ever-changing relationship between neighborhood opportunity and physiological stress factors. A further limitation involved the inability to account for clustering within census tracts. Due to privacy protection protocols requiring the MIDUS Geocode team to conduct data linkage, we were unable to implement hierarchical modeling approaches that would account for participant nesting within geographic units. Four, limited data regarding neuroendocrine biomarkers (e.g., Aldosterone), known mediators in the allostatic load cascade, limits our ability to fully understand the biological pathways through which neighborhood factors influence allostatic load. Lastly, while the Childhood Opportunity Index provides valuable insights into structural and environmental factors, it may not capture residents' lived experiences of their communities, resulting in possible misclassification. For example, some individuals in areas classified as "low opportunity" may benefit from protective neighborhood features not measured by the index, such as social connectedness or cultural resources that could buffer against physiological stress. Future research should employ mixed method approaches that integrate both subjective and objective measures of neighborhood context, to better understand how neighborhood opportunity influences allostatic load (Bather et al., 2024).

Table 4
Associations between neighborhood opportunity and allostatic load in the Midlife in the United States study.

Characteristic	Model 1			Model 2			Model 3		
	IRR	95 % CI	p-value	IRR	95 % CI	p-value	IRR	95 % CI	p-value
Overall Neighborhood Opportunity									
High	–	–	–	–	–	–	–	–	–
Moderate	1.13	(1.02, 1.25)	0.018	1.10	(0.99, 1.21)	0.065	1.07	(0.97, 1.18)	0.19
Low	1.36	(1.26, 1.48)	<0.001	1.22	(1.12, 1.33)	<0.001	1.18	(1.08, 1.29)	<0.001
Education domain									
High	–	–	–	–	–	–	–	–	–
Moderate	1.10	(0.99, 1.22)	0.071	1.08	(0.97, 1.19)	0.16	1.05	(0.95, 1.16)	0.33
Low	1.29	(1.20, 1.40)	<0.001	1.14	(1.04, 1.24)	0.003	1.11	(1.02, 1.21)	0.014
Health and Environment domain									
High	–	–	–	–	–	–	–	–	–
Moderate	1.12	(1.01, 1.25)	0.029	1.07	(0.96, 1.18)	0.21	1.06	(0.96, 1.17)	0.26
Low	1.18	(1.07, 1.29)	0.001	1.13	(1.03, 1.23)	0.010	1.10	(1.01, 1.20)	0.036
Social and Economic Resources domain									
High	–	–	–	–	–	–	–	–	–
Moderate	1.24	(1.12, 1.36)	<0.001	1.17	(1.06, 1.29)	0.001	1.14	(1.03, 1.25)	0.009
Low	1.41	(1.30, 1.53)	<0.001	1.25	(1.14, 1.37)	<0.001	1.20	(1.10, 1.31)	<0.001

Boldface indicates $p < 0.05$; IRR = Incident rate ratio; CI = Confidence interval. Results were pooled across ten multiple imputed datasets. Model 1 was unadjusted.

Model 2 adjusted for sociodemographic characteristics (age, sex, race/ethnicity, educational attainment, annual household income, and marital status). Model 3 adjusted for sociodemographic characteristics, health behaviors (smoking status, alcohol consumption), and prescription medication use.

Despite these limitations, our study has several notable strengths, including the use of a nationally representative sample from the Midlife in the United States study, a comprehensive measurement of allostatic load using eight established biomarkers, and the application of the Childhood Opportunity Index, which provides a theoretically grounded, multidimensional assessment of neighborhood context across three distinct domains. Using this approach, we were able to identify domain-specific associations with physiological stress that may inform targeted interventions. Future research is needed to identify alternative explanations and contradictory patterns that may provide different perspectives on the relationship between neighborhood opportunity and allostatic load as this field continues to evolve.

5. Conclusion

The findings of the current study provide evidence that neighborhood opportunity is associated with allostatic load, with significant associations for Educational Opportunity, Health and Environment and Social and Economic Resources. Evidence of this study complements existing literature on neighborhood opportunity measures and allostatic load, a known physiological stress biomarker. The foundation of these findings lay the groundwork for future research to investigate the complex pathways and multifaceted nature of neighborhood opportunity and allostatic load.

CRediT authorship contribution statement

Alisha A. Crump: Writing – review & editing, Writing – original draft, Project administration, Methodology, Conceptualization. **Jemar R. Bather:** Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Ester Villalonga-Olives:** Writing – original draft, Supervision. **Emiko O. Kranz:** Writing – original draft. **Adolfo G. Cuevas:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization.

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Data availability

Data will be made available on request.

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