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Trajectories in allostatic load as predictors of sleep quality among urban adults: Healthy aging in neighborhoods of diversity across the life span study

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ABSTRACT

Objective: /Background: The allostatic framework is a theoretical perspective that identifies allostatic load (AL) as a meaningful measure of dysregulation and desynchrony across biological processes due to cumulative stress exposure, thereby increasing disease risk. Research exploring the relationships of AL with sleep quality have yielded inconsistent findings. We examined AL at three visits (2004–2009 [Visit 1], 2009–2013 [Visit 2] and 2013–2017 [Visit 3]) in relation to sleep quality [Visit 3] among urban adults by sex, race and age group.

Patients/methods: We analyzed data on 1489 Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) participants [59.6% female, baseline age: 48.2 years, 58.5% African Americans] with available data on cardiovascular, metabolic and inflammatory AL markers and Pittsburgh Sleep Quality Index (PSQI) scores. Least squares regression models were constructed to evaluate AL score at Visit 1 (AL_{v1}) and z-transformed probability of higher trajectory in AL score between Visit 1 and Visit 3 (AL_{traj}) as predictors of PSQI score at Visit 3, controlling for demographic, lifestyle and health characteristics at Visit 1. AL_{traj} was generated using group-based trajectory modeling.

Results: In fully adjusted models, AL_{v1} and PSQI score were positively related among men only ($\beta = 0.43$, $P = 0.001$), whereas higher AL_{traj} was associated with PSQI score among women ($\beta = 0.51$, $P = 0.001$), White ($\beta = 0.45$, $P = 0.011$) and African American ($\beta = 0.33$, $P = 0.014$) populations. There were no statistically significant interactions according to age group (<50 vs. $\geq$ 50).

Conclusions: Disparities exist whereby AL trajectory predicted sleep quality among women irrespective of race and baseline AL predicted sleep quality among men. Future studies should examine bi-directional AL-sleep relationships.

1. Introduction

Major life events as well as daily hassles over the life course can alter physiological systems potentially leading to chronic stress and its associated morbidity and mortality risks, whereby genetic, epigenetic and behavioral characteristics can modify the burden of chronic stress [1]. The allostatic framework is a theoretical perspective that identifies allostatic load (AL) as a meaningful measure of dysregulation and desynchrony across biological processes due to cumulative exposure to stress, thereby increasing disease risk [2]. Allostatic mediators represent an adaptive

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List of abbreviations:

AL	Allostatic Load
AL_{v1}	AL at Visit 1
AL_{traj}	Trajectory in AL between Visit 1 and Visit 3
BMI	Body mass index
DBP	Diastolic blood pressure
HANDLS	Healthy Aging in Neighborhoods of Diversity across the Life Span
HbA1c	Glycosylated hemoglobin
HDL-C	High Density Lipoprotein-Cholesterol
HEI	Healthy Eating Index
HPA	Hypothalamic-Pituitary-Adrenal
hsCRP	high-sensitivity C-reactive protein
IRP	Intramural Research Program
MRV	Medical Research Vehicle
NIA	National Institute on Aging
PSQI	Pittsburgh Sleep Quality Index
SBP	Systolic blood pressure
SEM	Standard error of the mean
WHR	Waist-to-hip ratio
ZIP	zero-inflated Poisson

mechanism against chronic stress burden that may be protective in the short run but can ultimately lead to a multisystem dysregulation otherwise known as AL [1,3]. When coupled with inadequate regulation, exposure to stressful stimuli over a prolonged period can affect levels of AL cardiovascular, metabolic and inflammatory markers [3]. These markers have in turn been associated with risks of cardiovascular disease, cognitive decline, chronic fatigue, pain and mortality [3].

Researchers have leveraged the allostatic framework to enhance the scientific understanding of how sleep concerns can impede health among aging populations [3–5]. Older adults frequently report sleep disturbances, such as difficulty initiating or maintaining sleep, nocturnal awakening, feeling unrested after a night of sleep and frequent daytime napping [6–13], which have been attributed to a wide range of biological (*e.g.* age-related shift in circadian rhythm, sleep disorders) [9] and psychosocial (*e.g.* sleep hygiene, polypharmacy, mental health, physical activity factors) [9,11,14,15] characteristics. Sleep disturbance in older adults has been associated with increasing hospitalization costs over time [8] and to several determinants of health in late adulthood (*e.g.* cardiometabolic events, cognitive impairment, malnutrition, physical functioning, and depressive symptoms) [9,11,16–18]. Few studies have attempted to understand mechanisms that underlie the connection between sleep disturbance and health outcomes among older adults [4]. The allostatic framework is relevant to this connection because activation of the hypothalamic-pituitary-adrenal (HPA) axis (a marker of AL) can disrupt sleep quality [4,19], increasing the risk of stress reactivity and further dysregulating HPA axis processes [4,19].

Research exploring the relationships of sleep quality with AL and its associated health outcomes have so far yielded inconsistent findings [2,3,5,20–23]. A recent literature review and meta-analysis supported an association between sleep disturbance and AL across several studies of young, middle-aged, and older adult populations [4]. However, it is important to recognize that the burden of psychosocial stressors may differ potentially explaining the heterogeneity in the association between sleep, AL and health among diverse groups of older populations. We performed secondary analyses of data from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study to examine AL measured at Visit 1 (2004–2009), Visit 2 (2009–2013) and Visit 3 (2013–2017) in relation to sleep quality measured at Visit 3, before and after stratifying by sex, race, and age group. We hypothesized that increasing trajectories in AL will be associated with lower sleep quality and that the magnitude of this association will differ according to sex, race and age group.

2. Materials and Methods

2.1. Database

Initiated in 2004 b y the National Institute on Aging (NIA) Intramural Research Program (IRP), the HANDLS study is an ongoing prospective cohort study whereby middle-aged African American and White individuals of both sexes (baseline age: 30–64 years) with widely ranging household incomes were selected from thirteen Baltimore city neighborhoods using an area probability sampling strategy [24]. Novel research tools are applied and mobile medical research vehicles (MRVs) are used to improve participation and retention of non-traditional research subjects. The work described was carried out in accordance with the Declaration of Helsinki and the Institutional Review Board of the National Institutes of Health approved the HANDLS study with written informed consent obtained from all HANDLS participants [24–31].

Baseline (Visit 1) data collection occurred in two phases between 2004 and 2009. The first phase consisted of an in-home interview focused on health status, health service utilization, psychosocial factors, nutrition, neighborhood characteristics and demographics. The second phase covered medical history, physical examination, dietary recall, cognitive evaluation, psychophysiological assessments (*e.g.* arterial thickness, carotid ultrasonography, assessments of muscle strength, bone density), and laboratory measurements (*e.g.* blood chemistries, hematology, biomaterials for genetic studies) and was conducted in MRVs. Follow-up visits occurred every five years, with Visit 2 completed between 2009 and 2013, and Visit 3 completed between 2013 and 2017. HANDLS data elements available for analysis can be located at https://handls.nih.gov/06Coll-w00dataDocR.cgi. We analyzed cross-sectional and longitudinal data on cardiovascular, metabolic and inflammatory risk indicators to estimate AL at Visit 1 (AL_{v1}) and trajectories in AL between Visit 1 and Visit 3 (AL_{traj}) and their relationships with sleep quality at Visit 3, before and after controlling for demographic, lifestyle and health characteristics assessed at Visit 1. Researchers outside of the NIA IRP obtained access to restricted HANDLS data after approval and execution of a data sharing agreement. This project received exempt determination at Fort Belvoir Community Hospital.

2.2. Measures

2.2.1. Allostatic load

Nine risk indicators measured at Visits 1, 2 and 3 of the HANDLS study were used to calculate an AL score based on previously described methodologies [32] (Table A1). Cardiovascular, metabolic and inflammatory risk indicators were added together without weighting after being dichotomized and coded as 0/1 variables. Cardiovascular risk indicators included systolic blood pressure (≥140 mm Hg; <140 mm Hg), diastolic blood pressure (≥90 mm Hg; <90 mm Hg) and resting heart rate (≥90 beat/min; <90 beat/min). Metabolic risk indicators included total cholesterol (≥240 mg/dl; <240 mg/dl), High Density Lipoprotein-Cholesterol (<40 mg/dl; ≥40 mg/dl), glycosylated hemoglobin (≥6.4%; <6.4%) and sex-specific waist-to-hip ratio (>0.9 (men) and >0.85 (women); ≤0.9 (men) and ≤0.85 (women)). Inflammatory risk

Table 1
Summary statistics for demographic, lifestyle, and health characteristics at visit 1, allostatic load (at visit 1 and change between visit 1 and visit 3) and sleep quality at visit 3, overall, and according to tertiles of visit 1 allostatic load (n = 1489).

	% or Mean ± SEM	AL tertiles at Visit 1		
		1st	2nd	3rd
ALLOSTATIC LOAD:	P < 0.0001			
AL_{v1} (n = 1489)	1.88 ± 0.033	0.68 ± 0.02	–	3.49 ± 0.036
	P < 0.0001			
AL_{traj} (raw score) (n = 1489)	0.78 ± 0.0069	0.57 ± 0.01	0.88 ± 0.0062	0.97 ± 0.0020
DEMOGRAPHIC (n=1489):				
Sex:		P = 0.62		
Male	40.4	41.6	40.5	38.6
Female	59.6	58.4	59.5	61.3
Age (years):		P < 0.0001		
Continuous	48.16 ± 0.24	46.42 ± 0.35	48.53 ± 0.44	50.28 ± 0.42
Race:		P = 0.40		
White	41.5	41.6	39.1	43.6
African American	58.5	58.4	60.9	56.4
Poverty status:		P = 0.56		
<125% federal poverty line	35.9	37.3	34.1	35.7
≥ 125% federal poverty line	64.1	62.7	65.8	64.3
Education:		P = 0.0004		
Less than high school	5.9	4.6	4.8	8.6
High school	57.5	53.1	60.6	60.9
More than high school	36.6	42.2	34.6	30.5
LIFESTYLE (n=1489):				
Cigarette smoking:		P = 0.30		
Yes	44.4	46.3	44.6	41.4
No	55.6	53.6	55.4	58.6
Drug use:		P = 0.0001		
Yes	17.1	21.7	16.4	11.1
No	82.9	78.3	83.6	88.9
HEI-2010 score:		P = 0.14		
	43.01 ± 0.35	43.76 ± 0.49	42.47 ± 0.59	42.45 ± 0.63
HEALTH (n=1489):				
Body mass index (kg/m^2):		P < 0.0001		
	30.16 ± 0.19	26.58 ± 0.24	31.09 ± 0.34	34.36 ± 0.38
Self-rated health:		P < 0.0001		
Poor/Average	23.9	18.9	20.6	34.0
Good	40.9	37.6	43.6	43.2
Very good/Excellent	35.1	43.3	35.8	22.7
Hypertension:		P < 0.0001		
Yes	45.7	25.9	47.9	72.0
No	54.3	74.1	52.1	28.0
Diabetes:		P < 0.0001		
None	65.6	83.5	62.1	43.4
Pre-diabetes	18.3	11.4	24.7	22.0
Diabetes	16.1	5.1	13.1	34.5
Dyslipidemia:		P < 0.0001		
Yes	26.0	16.2	27.4	38.5
No	74.0	83.8	72.6	61.5
Cardiovascular disease:		P < 0.0001		
Yes	15.8	10.9	15.7	22.9
No	84.2	89.1	84.3	77.1
CES-D score:		P = 0.22		
SLEEP QUALITY:[a]	14.73 ± 0.29	14.25 ± 0.46	15.50 ± 0.56	14.69 ± 0.54
		P = 0.0001		
PSQI total score (n = 1489)	7.57 ± 0.11	7.02 ± 0.18	7.78 ± 0.21	8.15 ± 0.20

Abbreviations: AL_{v1} = Allostatic Load at Visit 1; AL_{traj} = Probability of belonging to a group with higher allostatic load over time (Visit 1 – Visit 3) according to group-based trajectory modeling; HEI = Healthy Eating Index; n = Sample size; PSQI = Pittsburgh Sleep Quality Index; SEM = Standard error of the mean.
[a] Sleep quality total score was measured at Visit 3 using the PSQI scale.

indicators included albumin (<3.8 g/dl; ≥3.8 g/dl) and high-sensitivity C-reactive protein (≥0.3 mg/dl; <0.3 mg/dl). Group-based trajectory modeling was also performed for AL score at Visit 1, 2 and 3 using *traj* and *trajplot* commands in STATA [33,34]. This group-based approach utilizes a multinomial modeling strategy and maximum likelihood to estimate model parameters, with maximization achieved by the quasi-Newton procedure. We specified a zero-inflated Poisson (ZIP) distribution with intercept, linear or quadratic orders for each group trajectory, as appropriate, and displayed group-based trajectories over time with 95% confidence intervals (CI).

2.2.2. Sleep quality

Sleep quality was assessed by self-report at Visit 3 of the HANDLS study using the 19-item Pittsburgh Sleep Quality Index (PSQI) questionnaire [35]. A global sleep quality score and seven component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction) can be generating using the PSQI questionnaire. We calculated a PSQI total score using the sum of the seven component scores as the outcome variable of interest.

2.2.3. Covariates

Demographic (sex (male, female), age (years), race (White, African American), poverty status (<125% federal poverty line, ≥125% federal poverty line), education (less than high school, high school, more than high school), lifestyle (current cigarette smoking [Yes, No]), current drug use (Yes, No [using any of marijuana, opiates, and cocaine]), the 2010 Healthy Eating Index [HEI-2010]) and health (body mass index [BMI; weight/height^2 in kg.m^{-2}, continuous], depressive symptoms score) characteristics were examined as potential confounders of hypothesized relationships. Poverty status was operationalized using Department of Health and Human Services poverty thresholds according to household income and total household size [36]. A diet quality (HEI-2010) score [37] was calculated based on food and macronutrient-related guidelines for Americans and a depressive symptoms score was calculated using the 20-item Center for Epidemiological Studies Depression scale [38]. We also described the relationship of baseline AL with comorbidities and self-rated health. Comorbidities were defined as hypertension (no, yes), diabetes (non-diabetic, pre-diabetic, diabetic), dyslipidemia ([or statin use] no, yes), and self-reported history of any of several cardiovascular diseases [atrial fibrillation, angina, coronary artery disease, congestive heart failure, and myocardial infarction]. Finally, self-rated health was categorized as 'poor/average', 'good' and 'very good/excellent'.

2.3. Statistical methods

We used STATA version 16 (StataCorp, College Station, TX) to perform all statistical analyses. Bivariate associations were evaluated using Chi-square test, independent samples *t*-test, one-way ANOVA, Pearson's correlations or their non-parametric counterparts, as appropriate. Ordinary least squares [OLS] regression models were constructed whereby demographic, lifestyle and health characteristics at baseline were examined as potential confounders. Since each covariate had on average < 5% missing data, we ensured sample sizes were constant between distinct adjusted models by conducting multiple imputations (5 imputations, 10 iterations) with the chained equations methodology. All covariates were used simultaneously during this estimation process, and, similar to previous studies [39,40], continuous predictor variables were centered on their means. First, baseline demographic, lifestyle and health characteristics, sleep quality test score at Visit 3, AL_{v1} and the probability of having a higher AL trajectory (Visit 1-Visit 3) were described, before and after stratifying according to AL_{v1} tertiles, using the largest sample after excluding subjects with missing data on PSQI total score. Second, a series of OLS regression models were constructed separately for AL_{v1} as a predictor of PSQI test score at Visit 3 and AL_{traj} (z-transformed probability of having a higher AL trajectory [Visit 1-Visit 3]) as a predictor of PSQI test score at Visit 3, adjusting for distinct sets of covariates. *Models 1* were adjusted for age, sex, race, poverty status, and inverse mills ratio (IMR). *Models 2* were adjusted for age, sex, race, poverty status, education, smoking, drug use, HEI-2010, BMI, depressive symptoms score and IMR. As a sensitivity analysis, interaction effects of AL_{v1} or AL_{traj} with sex, race and age group were evaluated for *Models 1* and *2*, and stratified analyses were conducted separately for men, women, White and African American participants, as well as those <50 years and ≥50 years of age. As such, we applied *Models 1–2* to two exposures (AL_{v1} and AL_{traj}) and one PSQI total score with three stratifying variables (sex, race, age group). In all models, we adjusted for sample selectivity due to missing data using a two-stage Heckman selection strategy. After predicting an indicator of selection with sex, age at Visit 1, race and poverty status using a probit regression model, which yielded an IMR (a function of the probability of being selected given these characteristics), we estimated OLS regression models adjusted for the IMR in addition to aforementioned covariates [41]. Type I error rate was set *a priori* for main and interactive effects before correction for multiple testing to 0.05 and 0.10, respectively [42]. We accounted for exposure multiplicity (AL_{v1} and AL_{traj}) using the approach of familywise Bonferroni correction [43], specifically for *Model 1*. *Model 2* was considered as a sensitivity model in which potential confounders and/or mediators were included. Thus, adjusted significance levels for main effects to $p < 0.025$ (0.05/3 or 0.016) and for two-way interaction terms to (0.10/3 or 0.033) [44]. A sensitivity analysis was also performed whereby AL_{v1} and AL_{traj} were evaluated in relation to PSQI component scores in fully adjusted models.

3. Results

As shown in Fig. 1, of 3720 HANDLS participants enrolled at Visit 1, 2930 (78.8%) had complete AL data at Visit 1, Visit 2 and/or Visit 3. The final analytic sample for cross-sectional and longitudinal analyses consisted of 1489 (50.8%) [59.6% female, mean (± standard error [SEM]) baseline age: 48.16 (±0.24) years, 58.5% African Americans] of those 2930 HANDLS participants that also had complete data on PSQI total score at Visit 3.

Table 1 presents summary statistics for demographic, lifestyle, and health characteristics at Visit 1, AL_{v1}, probability of having a higher AL trajectory (Visit 1-Visit 3), as well as PSQI total score at Visit 3, overall, and according to tertiles of AL_{v1}, and the distribution of AL_{v1} is presented in Figure A1. Overall, mean (±SEM) scores on AL_{v1} and AL_{traj} were 1.88 (±0.033) and 0.78 (±0.0069), respectively. Higher AL tertile at Visit 1 (AL_{v1}) was associated with older age at Visit 1, lower education, less drug use, higher BMI, worse self-rated health, more frequent comorbid conditions at Visit 1 and higher Visit 3 PSQI total score suggesting worse sleep quality. By contrast, distributions by sex, race, poverty, and cigarette smoking status as well as depressive symptoms scores did not differ significantly across tertiles of AL at Visit 1 (AL_{v1}).

Table 2 displays the results of OLS regression models for AL_{v1} as a predictor of PSQI total score at Visit 3, in *Models 1* and *2*, before and after stratifying by sex, race and age group. Overall, AL_{v1} was positively related to PSQI total score at Visit 3 in *Model 1* ($\beta = 0.37$, $P < 0.0001$), but not in *Model 2* ($\beta = 0.19$, $P = 0.039$). Although interactions between AL_{v1} and sex were not statistically significant in *Models 1* or *2* (Table A2), AL_{v1} was positively associated with PSQI total score at Visit 3 in *Models 1* ($\beta = 0.44$, $P = 0.001$) and *2* ($\beta = 0.43$, $P = 0.001$) among men, but only in *Model 1* among women ($\beta = 0.34$, $P = 0.004$). By contrast, *Models 1* and *2* suggested interactions between AL_{v1} and race that were statistically significant (Table A2), and AL_{v1} was positively associated with PSQI total score only in *Model 1* ($\beta = 0.69$, $P < 0.0001$) among White

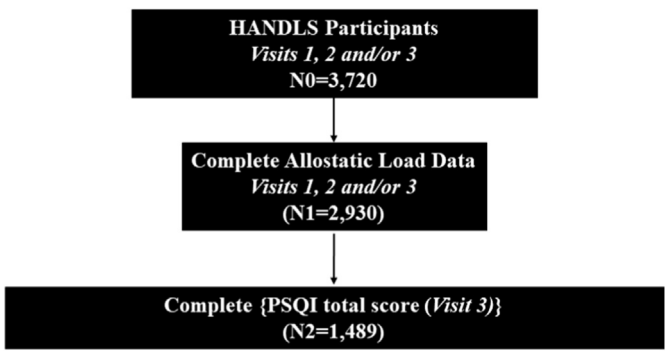


Fig. 1. Study flowchart. *Notes:* HANDLS=Healthy aging in neighborhoods of diversity across the life span; PSQI = Pittsburgh sleep quality index.

Table 2
Relationship of allostatic load at visit 1 with sleep quality total score at visit 3, overall, and by stratifying variables (n = 1489).

	Allostatic Load			
	Model 1 [a]		Model 2 [b]	
	β (SE)	P value	β (SE)	P value
OVERALL:[c]				
PSQI total score:	N = 1489		N = 1489	
AL_{v1}	0.37 (0.089)	<0.0001	0.19 (0.095)	0.039
MEN:				
PSQI total score:	N = 602		N = 602	
AL_{v1}	0.44 (0.14)	0.001	0.43 (0.13)	0.001
WOMEN:				
PSQI total score:	N = 887		N = 887	
AL_{v1}	0.34 (0.11)	0.004	0.094 (0.13)	0.46
WHITE:				
PSQI total score:	N = 618		N = 618	
AL_{v1}	0.69 (0.15)	<0.0001	0.29 (0.16)	0.07
AFRICAN AMERICAN:				
PSQI total score:	N = 871		N = 871	
AL_{v1}	0.16 (0.11)	0.16	0.11 (0.12)	0.35
AGE < 50 YEARS:				
PSQI total score:	N = 838		N = 838	
AL_{v1}	0.41 (0.12)	0.001	0.25 (0.13)	0.059
AGE ≥ 50 YEARS:				
PSQI total score:	N = 651		N = 651	
AL_{v1}	0.35 (0.13)	0.008	0.15 (0.13)	0.26

Abbreviations: AL_{v1} = Allostatic Load at Visit 1; n = Sample size; PSQI = Pittsburgh Sleep Quality Index; SE = Standard error.
[a] Model 1 is adjusted for age, sex, race, poverty status and inverse mills ratio.
[b] Model 2 is adjusted for age, sex, race, poverty status, education, smoking, drug use, 2010 healthy eating index, body mass index, depressive symptoms score and inverse mills ratio.
[c] Sleep quality total score was measured at Visit 3 using the PSQI scale.

participants. Finally, AL_{v1} was significantly related to PSQI total score at Visit 3 in *Models 1* only among individuals <50 years and ≥50 years, with no statistically significant interaction effects as shown in Table 2 and A.2.

Fig. 2 displays the results of group-based trajectory modeling for AL (Visit 1-Visit 3), whereby the table displays intercept, linear and quadratic terms for two groups identified using this modeling strategy. Group 1 had a lower y-intercept than Group 2, and both groups had significant and positive linear terms. A graphical display of these two groups is presented, whereby the y-axis represents the AL total score and the x-axis represents age as a time variable. Visit 1 AL score *[w1allostatic_load]*, Visit 2 AL score *[w3allostatic_load]* and Visit 3 AL score *[w4allostatic_load]* are also displayed to estimate the distributions of probabilities of belonging to Group 1 and Group 2.

Table 3 presents results of OLS regression models for the relationship of the z-transformed probability of having a higher AL trajectory (AL_{traj}) with PSQI total score at Visit 3 before and after stratifying by sex and race. Overall, AL_{traj} was positively associated with PSQI total score in *Models 1* (β = 0.68, P < 0.0001) and *2* (β = 0.41, P < 0.0001). As shown in Table A3, there were no significant interactions between AL_{traj} and sex in *Model 1* or *Model 2*, with a significant interaction between AL_{traj} and race in *Model 1* only. Among men, AL_{traj} was positively associated with PSQI total score in *Model 1* (β = 0.52, P < 0.0001), but not in *Model 2* (β = 0.28, P = 0.062). Among women, AL_{traj} was positively associated with PSQI total score in *Model 1* (β = 0.84, P < 0.0001) and *Model 2* (β = 0.51, P = 0.001). In fully adjusted models, there were no statistically significant interaction effects between AL_{v1} and AL_{traj} in relation to PSQI total score, either among men (P = 0.033) or women (P = 0.75). AL_{traj} was positively associated with PSQI total score in both *Models 1* and *2* in stratified analyses by race, that is, among White (*Model 1:* β = 1.01, P < 0.0001; *Model 2:* β = 0.45, P = 0.011) and African American (*Model 1:* β = 0.44, P = 0.001; *Model 2:* β = 0.33, P = 0.014) participants. Finally, AL_{traj} was significantly related to PSQI total score at Visit 3 in *Models 1* and *2* among individuals <50 years and ≥50 years, with no significant interaction effects as shown in Table 3 and A.3.

Different PSQI component scores were related to AL_{v1} and AL_{traj} in fully adjusted models as shown in Table A.4. Specifically, AL_{v1} was directly related to sleep dysfunction and efficiency scores, whereas AL_{traj} were directly related to sleep latency, efficiency and medication scores.

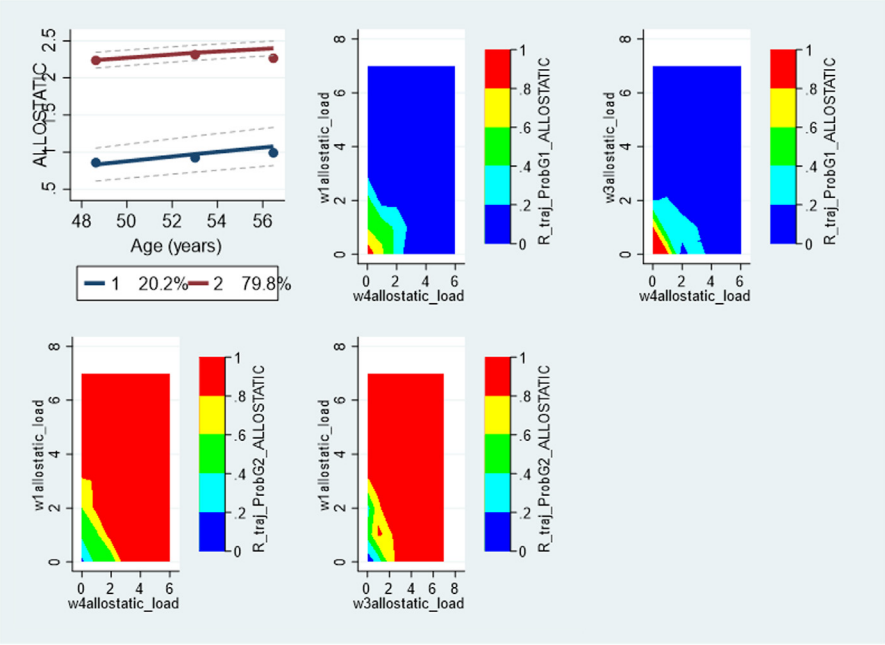
4. Discussion

In this study, data from 1489 HANDLS participants were analyzed to examine AL score at Visit 1 (AL_{v1}) and z-transformed probability of higher trajectory in AL score between Visits 1 and 3 (AL_{traj}) as predictors of PSQI total score at Visit 3. Results suggested that AL_{v1} was positively related to PSQI score among men whereas AL_{traj} was positively related to PSQI total score among women, White and African American populations, controlling for age, sex, race, poverty status, education, smoking, drug use, healthy eating index, body mass index and depressive symptoms.

Besides its connection with job insecurity [22,45], racial discrimination [46], and health disparities [47,48], AL reflects multisystem, cumulative, biological risk that correlates more strongly with detrimental outcomes than either of its individual components [2]. The relationship between AL markers and sleep disturbance is likely bi-directional, whereby sleep problems can mediate the relationship between chronic stress and AL or contribute to AL through neurophysiological impairments that increase pro-inflammatory cytokines, oxidative stress, evening cortisol and insulin concentrations, which in turn can contribute to sleep problems in a vicious cycle [3]. Recently conducted epidemiologic studies suggest that inadequate sleep, sleep disturbance and sleep disorders are detrimental to quality of life and may contribute to risks of obesity, hypertension, diabetes, cardiovascular disease and death, through repeated disruptions to cardiovascular, metabolic and immune regulatory systems [2,3]. Specifically, fragmented and non-restorative sleep may have an adverse impact on the circadian rhythm, which regulates various biological systems, and on markers of cardiometabolic health such as blood pressure, lipids, glucose and inflammation [2].

To our knowledge, this study is among few to examine AL in relation to sleep quality in the context of a population-based cohort [2,3,5,21,23]. In a cross-sectional study, Chen et al. examined AL in relation to sleep apnea, insomnia, short sleep duration and other sleep disturbances by analyzing data on 3330 adults from the 2005–2008 National Health and Nutrition Examination Surveys [3]. Their results suggested that AL score≥3 was associated with nearly twice the odds of sleep apnea, snoring, snorting and diagnosed sleep disorder, and with nearly 50% increased odds of prolonged sleep latency and short sleep duration (<6 h) [3]. Similarly, Hux et al. examined the cross-sectional relationship between early-pregnancy AL—measured using nine physiologic components that reflect cardiovascular, metabolic, and inflammatory functions— and sleep quality —measured using the PSQI scale— among 103 low-risk, community-dwelling pregnant women, suggesting a positive correlation between these two measurements (r = 0.23, p = 0.018) [5]. Other studies identified a central role for sleep as a mediator for the relationship between psychosocial stress and AL [45], and as a key health behavior associated with the cardiometabolic dysregulation that characterizes AL [23].

Nevertheless, interpretation of findings should take into consideration several limitations. First, the link between AL and sleep quality was examined using a sub-sample of the original



Group	β	SE	P
Group 1			
Intercept	-4.03	1.32	0.002
Linear	0.12	0.048	0.01
Quadratic			
Group 2			
Intercept	-0.52	0.27	0.06
Linear	0.043	0.010	<0.0001
Quadratic	-0.00033	0.00010	0.0008

Fig. 2. Group-based trajectory modeling for allostatic load between Visit 1 and Visit 3. *Notes:* HANDLS=Healthy Aging in Neighborhoods of Diversity across the Life Span.

Table 3
Relationship of allostatic load trajectory with sleep quality total score at visit 3, overall, and by stratifying variables (n = 1489).

	Allostatic Load			
	Model 1 [a]		Model 2 [b]	
	β (SE)	P value	β (SE)	P value
OVERALL:[c]				
PSQI total score:	N = 1489		N = 1489	
AL_{traj}	0.68 (0.10)	<0.0001	0.41 (0.11)	<0.0001
MEN:				
PSQI total score:	N = 602		N = 602	
AL_{traj}	0.52 (0.15)	<0.0001	0.28 (0.15)	0.062
WOMEN:				
PSQI total score:	N = 887		N = 887	
AL_{traj}	0.84 (0.14)	<0.0001	0.51 (0.15)	0.001
WHITE:				
PSQI total score:	N = 618		N = 618	
AL_{traj}	1.01 (0.17)	<0.0001	0.45 (0.17)	0.011
AFRICAN AMERICAN:				
PSQI total score:	N = 871		N = 871	
AL_{traj}	0.44 (0.13)	0.001	0.33 (0.14)	0.014
AGE < 50 YEARS:				
PSQI total score:	N = 838		N = 838	
AL_{traj}	0.65 (0.13)	<0.0001	0.41 (0.13)	0.002
AGE ≥ 50 YEARS:				
PSQI total score:	N = 651		N = 651	
AL_{traj}	0.75 (0.17)	<0.0001	0.45 (0.17)	0.010

Abbreviations: AL_{traj} = z-transformed probability of belonging to a group with higher allostatic load over time according to group-based trajectory modeling between Visit 1 and Visit 3; n = Sample size; PSQI = Pittsburgh Sleep Quality Index; SE = Standard error.

[a] Model 1 is adjusted for age, sex, race, poverty status and inverse mills ratio.

[b] Model 2 is adjusted for age, sex, race, poverty status, education, smoking, drug use, 2010 healthy eating index, body mass index, depressive symptoms score and inverse mills ratio.

[c] Sleep quality total score was measured at Visit 3 using the PSQI scale.

HANDLS study with the potential for selection bias. Second, self-reported data pertaining to sleep quality, demographic, lifestyle and health characteristics may have resulted in measurement error as well as residual confounding. In particular, the PSQI total score reflects a subjective and non-specific measure of sleep quality. Third, the AL score was calculated at three visits while the PSQI total score was calculated at one follow-up time (Visit 3) only, making it difficult to ascertain the temporal sequence of events or assess the influence of change in AL on change in sleep quality over time. The HANDLS study collected some but not all of the PSQI sub-scales during a visit prior to Visit 3. Accordingly, the PSQI total score could only be calculated at Visit 3, and we could not evaluate the change in PSQI total score between visits in order to distinguish new onset sleep problems from chronic sleep disruption. Finally, results are generalizable to urban adults in similar settings to HANDLS participants.

5. Conclusions

Among urban adults, sex and race disparities exist whereby AL trajectories may predict sleep quality among women irrespective of race, whereas baseline AL may predict sleep quality at a later time point among men only. These findings imply that the dynamic nature of AL is more relevant to women and confirm the importance of screening for sleep disturbance in clinical settings to identify patients with potentially high chronic stress burden, which can lead to adverse cardiometabolic outcomes. Future studies should examine bi-directional AL-sleep relationships.

Disclaimer

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CRediT authorship contribution statement

Hind A. Beydoun: Conceptualization, Methodology, Project administration, Validation, Writing – original draft. **May A.**

Beydoun: Data curation, Formal analysis, Software, Visualization, Writing – review & editing. **Alyssa Gamaldo:** Conceptualization, Investigation, Writing – review & editing. **Edward Kwon:** Investigation, Writing – review & editing. **Jordan Weiss:** Investigation, Writing – review & editing. **Sharmin Hossain:** Investigation, Writing – review & editing. **Michele K. Evans:** Funding acquisition, Investigation, Resources, Supervision. **Alan B. Zonderman:** Funding acquisition, Investigation, Resources, Supervision, Writing – review & editing.

Declaration of competing interest

Authors declare no conflict of interest.

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Appendix A. Supplementary data

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Appendix A

Table A.1. Allostatic load criteria [1]

	High-risk clinical
Waist-to-Hip Ratio	>0.9 for men; > 0.85 for women [2]
Albumin (g/dL)	< 3.8 [3]
C-reactive protein (mg/dL)	≥ 0.3 [4]
Total cholesterol (mg/dL)	≥240 [5]
HDL (mg/dL)	<40 [5]
Glycated hemoglobin (%)	≥6.4 [6, 7]
Resting heart rate (beat/min)	≥90 [8]
Systolic BP	≥140 [9]
Diastolic BP	≥90 [9]

Abbreviations: HDL = High Density Lipoprotein; BP = Blood pressure.

Table A.2. Interaction effects by sex, race and age group for the effects of allostatic load at visit 1 on PSQI total score at visit 3 (n=1,489)

	Model 1 [1]		Model 2 [2]	
	β (SE)	P value	β (SE)	P value
SEX				
PSQI total [AL_{v1}]	0.14 (0.18)	0.40	0.25 (0.17)	0.14
RACE				
PSQI total [AL_{v1}]	-0.51 (0.18)	0.005	-0.35 (0.17)	0.038
AGE GROUP				
PSQI total [AL_{v1}]	-0.13 (0.18)	0.44	-0.049 (0.17)	0.77

Abbreviations: AL_{v1} = Allostatic load at Visit 1; PSQI = Pittsburgh Sleep Quality Index; SE = Standard error; [1] Model 1 is adjusted for age, sex, race, poverty status and inverse mills ratio. [2] Model 2 is adjusted for age, sex, race, poverty status, education, smoking, drug use, 2010 healthy eating index, body mass index, depressive symptoms score and inverse mills ratio.

Table A.3. Interaction effects by sex, race and age group for the effects of allostatic load trajectory (visit 1 – visit 3) on PSQI total score at visit 3 (n=1,489)

	Model 1 [1]		**Model 2** [2]	
	β (SE)	P value	β (SE)	P value
SEX				
PSQI total [AL_{traj}]	-0.32 (0.21)	0.13	-0.16 (0.19)	0.42
RACE				
PSQI total [AL_{traj}]	-0.59 (0.21)	0.005	-0.38 (0.19)	0.057
AGE GROUP				
PSQI total [AL_{traj}]	0.0068 (0.21)	0.97	0.072 (0.19)	0.72

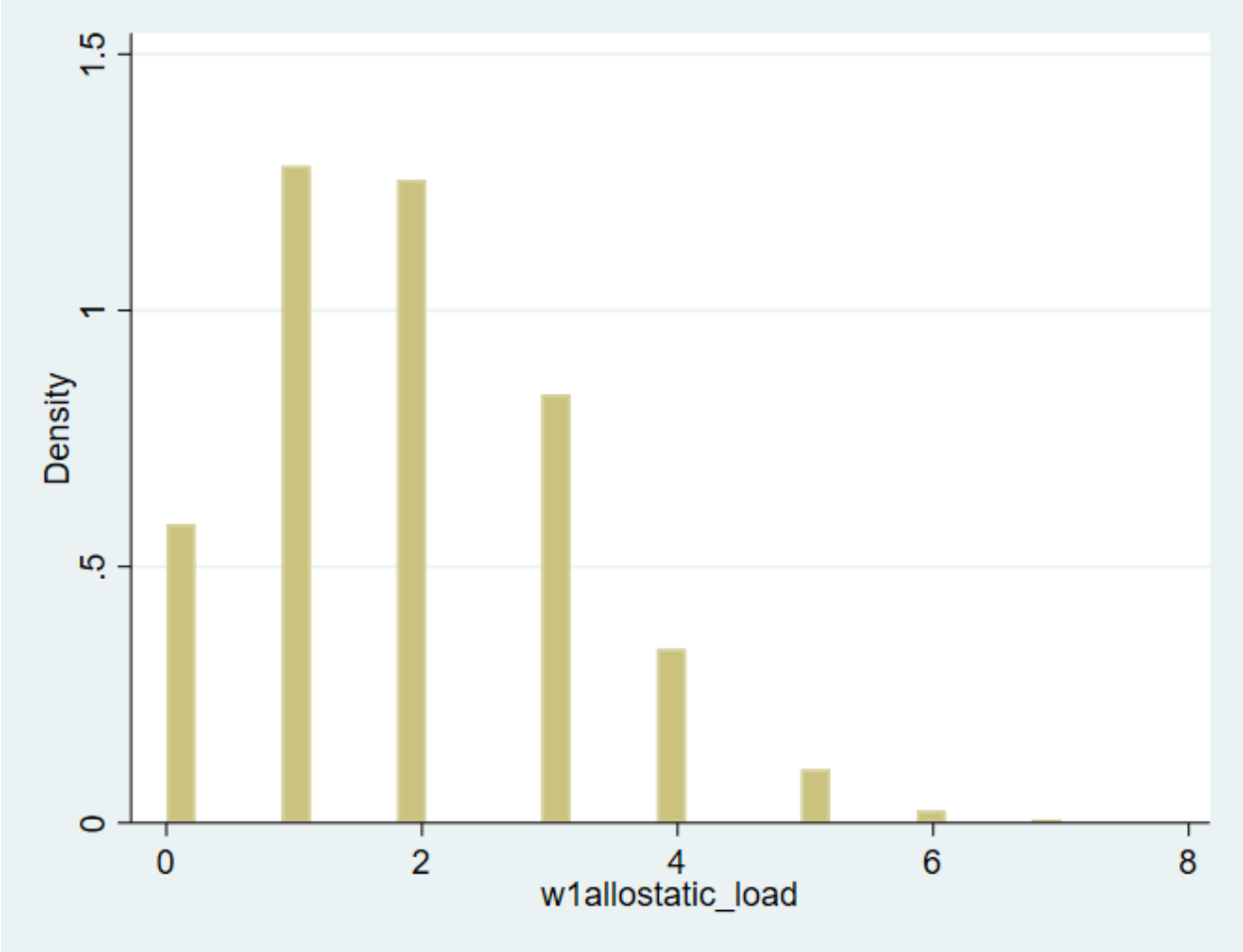
Abbreviations: AL_{traj} = z-transformed probability of belonging to a group with higher allostatic load over time according to group-based trajectory modeling between visit 1 and visit 3; PSQI = Pittsburgh Sleep Quality Index; SE = Standard error; [1] Model 1 is adjusted for age, sex, race, poverty status and inverse mills ratio. [2] Model 2 is adjusted for age, sex, race, poverty status, education, smoking, drug use, 2010 healthy eating index, body mass index, depressive symptoms score and inverse mills ratio.

Table A.4. Effects of allostatic load at visit 1 and allostatic load trajectory (visit 1 – visit 3) on PSQI component scores at visit 3 in fully adjusted models (n=1,489) [1]

	AL_{v1}		AL_{traj}	
	β (SE)	P value	β (SE)	P value
PSQI – Sleep duration	0.032 (.020)	0.11	0.034 (0.024)	0.16
PSQI – Sleep disorder	0.012 (0.020)	0.54	0.046 (0.024)	0.059
PSQI – Sleep latency	0.015 (0.021)	0.48	0.073 (0.024)	0.003
PSQI – Sleep dysfunction	0.060 (0.027)	0.028	0.041 (0.033)	0.22
PSQI – Sleep efficiency	0.044 (.022)	0.044	0.11 (0.028)	<0.0001
PSQI – Sleep quality	0.022 (0.021)	0.29	0.043 (0.025)	0.084
PSQI – Sleep medications	0.023 (0.031)	0.45	0.13 (0.038)	<0.0001

Abbreviations: AL_{v1} = Allostatic load at Visit 1; AL_{traj} = z-transformed probability of belonging to a group with higher allostatic load over time according to group-based trajectory modeling between visit 1 and visit 3; PSQI = Pittsburgh Sleep Quality Index; SE = Standard error; [1] Adjusted for age, sex, race, poverty status, education, smoking, drug use, 2010 healthy eating index, body mass index, depressive symptoms score and inverse mills ratio.

Figure A.1. Histogram for the distribution of allostatic load at visit 1



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