Title Page

Allostatic Load and Depression Symptoms in Cancer Survivors: A NHANES Study

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Abstract

Background: Individuals with cancer often experience stress throughout the cancer trajectory and have a high risk of suffering from depression.

Objective: To examine the relationship between allostatic load (AL), a measure of cumulative stress-related physiologic dysregulation of different body systems, and symptoms of depression in cancer survivors.

Methods: Participants were 294 adult cancer survivors from the US National Health and Nutrition Examination Survey (NHANES 2007-2018). Allostatic load was measured using 14 indicators representing cardiometabolic risk, glucose metabolism, cardiopulmonary functioning, parasympathetic functioning, and inflammation. Depressive symptoms were measured with the Patient Health Questionnaire-9. The relationship between AL and depressive symptoms was investigated using multiple regression adjusted for diverse socio-demographic and diagnosis variables.

Results: Higher AL was associated with higher depressive symptom scores. The higher risk of depression was concentrated among those survivors in the highest AL quartile, with 21% (95% CI: 11% to 32%) of survivors presenting high risk of depression compared to 8%-11% of survivors in the lower quartiles. In exploratory analyses, the relationship between AL and depressive symptoms was only significant among survivors with lower income. In contrast, in survivors in the highest income group depressive symptoms were lower and unrelated to AL.

Conclusions: High AL is associated with more depressive symptoms among cancer survivors.

Implications for practice: Nurses have an important role in identifying psychological distress in cancer patients and survivors. Further research is needed to investigate the usefulness of AL as a marker in the context of cancer follow-up care and screening for psychological distress.

Depressive spectrum disorders are among the most frequent psychiatric disorders in oncology settings with an estimated prevalence of around 16% based on clinical interviews in adults with cancer in a hospital setting.[1] Actual prevalence of depression may be even higher because symptoms associated with depression often go unrecognized.[2] Previous studies have observed a somewhat higher prevalence of depression during the first year after diagnosis,[3] with rates becoming lower than or similar to those of cancer-free populations in the long term (e.g., in survivors > 5 years after diagnosis).[4]

Cancer diagnosis and treatment are significant stressful life events.[5] In response to stress, an adaptive and dynamic regulatory process known as *allostasis* is produced to maintain physiological stability.[6] However, long-term chronic activation of the body's stress response systems may result in *allostatic load* (AL). AL was first described in 1993 by McEwen and Stellar as a measure of chronic stress using biological indicators.[7] AL reflects the cumulative physiological burden experienced due to the repeated adaptation to stressors over time.[8] It is measured using a combination of autonomic, metabolic, and immune system biomarkers reflecting multi-systemic biological risk.[9]

The allostatic process begins with the activation of primary mediators of AL as a consequence of acute stress, such as stress hormones (epinephrine, norepinephrine, and cortisol) and their antagonists, in addition to proinflammatory and anti-inflammatory cytokines, which can produce mood swings, anxiety, and reduced sleep quality.[10,11] After a constant secretion of these primary mediators, a long-term stress response is produced, causing subclinical alterations at the cardiovascular, immune, and metabolic levels.[12] This produces an allostatic overload causing physiological deregulations that could increase the risk of cardiovascular disease, cognitive impairment, cancer, depression, cellular aging or fatigue.[10,12,13] Thus, allostatic

overload would ultimately result in multimorbidity, which in turn has been related to higher risk of depression in cancer survivors.[14]

Previous studies with diverse populations have shown that higher AL is associated with worse physical and mental well-being, and higher all-cause, cardiovascular, and cancer mortality.[15,16,9] With regard to depression, previous studies have shown mixed results, with several reports finding no relationship between AL and depressive symptoms in the general population. [17,18] However, research on the role of AL in cancer remains relatively scarce,[8] and to the best of our knowledge, the relationship between AL and depression in cancer survivors has not been studied before.

Cancer diagnosis and treatment open a "window of psychological vulnerability" that can increase the risk of depression.[14] In particular, the combination of the clinical, psychological, and social consequences of the disease could trigger several physiological and biological mechanisms that can result in increased allostatic load.[14] In accordance with this, individuals with cancer history have been found to have higher AL than controls.[8] In addition, inflammatory biomarkers (a component of AL) are more strongly related to depressive symptoms among people with chronic diseases such as cancer than among healthy individuals.[19]

In cancer survivors, depressive symptoms tend to co-occur with cognitive disturbance, fatigue, sleep disturbance, and pain to form a "psychoneurological symptom cluster."[20] Three biological pathways have been proposed to contribute to the emergence of these psychoneurological symptoms in cancer survivors, including activation of proinflammatory cytokines, dysregulation of the hypothalamic-pituitary-adrenal axis, and dysregulation of the monoamine neurotransmission system.[20] These mechanisms contribute to allostatic load[12] and

have been related to depressive symptoms,[20] suggesting that a relationship between allostatic load and depressive symptoms may be present in cancer survivors.

To address this possibility, the main aim of the present study was to investigate the relationship between AL and depressive symptoms in cancer survivors from the National Health and Nutrition Examination Survey (NHANES). As a secondary aim, we explored the relationship of diverse socio-demographic and diagnosis variables with allostatic load and depressive symptoms.

Methods

The study sample included cancer survivors who participated in NHANES. NHANES is a periodic cross-sectional survey representative of the noninstitutionalized United States civilian population residing in the 50 states and the District of Columbia.[21] A nationally representative sample of about 5000 people is collected each year based on complex multistage probability sampling. The sample design includes multi-year, stratified, clustered four-stage samples, with data release in 2-year cycles. Each sample is drawn in four stages: (a) primary sampling units (PSUs) (counties, groups of tracts within counties, or combinations of adjacent counties, sampled from all US counties), (b) segments within PSUs (census blocks or combinations of blocks), (c) dwelling units (households) within segments, and (d) individuals within households. Besides interview data, the survey collects physical examination and laboratory testing data in mobile examination centers. The survey is granted approval by the National Center for Health Statistics Institutional Review Board and all respondents provide informed consent.[21]

For the current study, we selected participants of the survey waves collected between 2007 and 2018 who: a) reported a cancer diagnosis within the 5 years preceding the survey (excluding individuals diagnosed with skin non-melanoma tumors, more than one cancer, or

unknown tumor site); b) were ≥ 18 years old at the time of diagnosis and < 80 years old at the time of the survey[1]; and c) had available data on the depression and allostatic load assessments. A total of 294 people met these criteria and formed the cancer survivors study population.

Measures

Socio-demographic characteristics. Data were obtained on self-reported age, sex, race (Non-Hispanic White, Mexican American, Other Hispanic, Non-Hispanic Black, and Other), education level (up to 11th grade, high school graduate/General Educational Development (GED), some college or associate's (AA) degree, and college graduate or above), and civil status (married/living with partner, single, divorced/separated, and widowed). The ratio of family income to poverty was used as a measure of socio-economic status. It is calculated by dividing family (or individual) income by the US Department of Health and Human Services poverty guidelines specific to the survey year and values <1.3 were considered as lowest income, 1.3 to 3.5 as medium income, and ≥3.5 as highest income.[22]

Cancer diagnosis. Survivors were grouped by tumor site in the following categories: prostate, female breast, colorectal, gynecological, skin melanoma, lung, or other cancer, which comprised all remaining cancer diagnoses. The time since diagnosis was calculated as the difference between the participant's current self-reported age and the age they reported when asked "How old were you when the cancer was first diagnosed?"

Depressive symptoms. The Patient Health Questionnaire-9 (PHQ-9) is a validated self-report instrument based on the DSM-IV criteria for diagnosis of depressive disorder,[23] and measures anhedonia, depressed mood, sleep, energy, appetite, guilt and worthlessness, concentration, feeling slowed down or restless, and suicidal thoughts over the past two weeks. It

[1] This final criterion had to be applied because the exact age of respondents who are older than 80 is censored at 80 due to privacy concerns, something which made it impossible to calculate the number of years elapsed since diagnosis.

contains nine items scored from 0 to 3, resulting in a total score between 0 and 27 reflecting the degree of depressive symptomatology. Because the distribution of the obtained scores was skewed, they were square-root transformed for analysis. In addition, individuals scoring ≥10 were considered at high risk of depression as this cut-off has demonstrated 78% sensitivity and 85% specificity for major depression.[24]

Allostatic load. Allostatic load was measured using 14 indicators (11 biomarkers and 3 types of medication), described in detail in Table 1, covering cardiometabolic risk, glucose metabolism, cardiopulmonary functioning, parasympathetic functioning, and inflammation. These indicators were based on previous studies using NHANES data.[17,25] Based on clinical criteria, a score of 0 (low risk), 0.5 (medium risk), or 1 (high risk) was assigned for each indicator. When no established clinical criteria existed, scoring was based on 75th and 90th percentile scores.[26] The sum of the scores for each indicator constitutes the allostatic load score (max. of 11), where higher values reflect higher cumulative physiological burden of stress.

Statistical analysis

Analyses were performed using the package "survey" (v.3.37) in R (v.3.6.2),[27,28] and followed the analytic guidelines provided by NHANES.[21] The provided sample weights (combined across the used waves) corresponding to the samples who participated in the mobile examination center data collection were applied in all analyses unless otherwise specified.

We first investigated what socio-demographic and cancer diagnosis characteristics were related to higher allostatic load. In a second step, we studied the relationship between allostatic load and the square-root transformed depressive symptom scores. We first conducted univariate linear regressions, followed by multiple regression adjusted for age, sex, civil status, race, education, income, cancer site, and years since diagnosis.

To test the significant contribution of variables to the multiple regression models, we used the Akaike Information Criterion (AIC),[29] comparing the difference (ΔAIC) between the full model and the model without the respective variable of interest, where a significantly smaller AIC for the full model (ΔAIC≤-2) signifies improved model fit due to the inclusion of the variable.

Results

The 294 survivors represented a population of 1.969.775 individuals. The mean age of the sample was 57 years (SE=1.29), and its main features are described in Table 2.

Allostatic load (AL)

The mean AL score was 2.67 (*SE*=0.10, *median*=2.5). In univariate models, older age, Non-Hispanic black race, and lower education were related to higher AL (see Table 3).

In the multiple regression model (see Table 4), age ($F(1,53^2)$=49.69, ΔAIC= -15), race ($F(4,45)$=13.02, ΔAIC= -5), and income-to-poverty ratio ($F(2,35)$=28.31, ΔAIC= -25) were significantly related to AL (all $P < .05$). In particular, AL was higher among older vs. younger survivors ($P = .010$) and in Non-Hispanic Black survivors compared to Non-Hispanic White survivors ($P = .011$). Allostatic load also increased as income level decreased (see Table 2), although the specific group comparisons were not significant in the model ($P > .05$). The rest of the socio-demographic variables, the type of cancer diagnosed, or the years elapsed since diagnosis had no significant effects.

Depressive symptoms

The mean PHQ-9 score was 3.71 (*SE*=0.44, *median*=1.35) and 13% (95% CI:7-19%) of the sample was at high risk of depression (PHQ-9≥10). In univariate models, being female, divorced

[2] The first value in parenthesis are the degrees of freedom and the second value the design degrees of freedom.

or separated, having lower education, lower income, and gynecological or lung cancer were related to higher depression scores (see Table 3).

In the multiple regression model (see Table 4), sex ($F(1, 52)=22.61$, $\Delta AIC= -2$), income-to-poverty ratio ($F(2, 35)=81.67$, $\Delta AIC= -89$), and allostatic load ($F(1, 27)=7.87$, $\Delta AIC= -6$) were significantly related to depressive symptoms (all $P < .05$). Females had higher PHQ-9 scores than males (see Table 2), although the regression coefficient was not significant ($P = .479$). Survivors in the lowest income group also had higher PHQ-9 scores compared to the highest income group ($B=1.13$, $SE=0.21$, $P < .001$).

Finally, higher allostatic load was associated with more depressive symptoms ($B=0.14$, $SE=0.07$, $P = .045$). To further illustrate the effect, mean PHQ-9 scores were 2.9 (95% CI: 1.7-4.12) for Q1 of AL scores compared to 4.5 (95% CI: 2.9-6.1) for Q4 (see Table 2). Regarding the proportion of survivors at increased risk of depression (PHQ-9≥10), this was between 8% and 11% for Q1 to Q3 but was 21% (95% CI: 11-32) for Q4 (see Table 2).

To test whether the relationship between allostatic load and depressive symptoms may be sensitive to the inclusion of cancer survivors who may currently be in treatment, we conducted the same analysis after excluding survivors with time since diagnosis ≤1 year. This did not change the direction or strength of the relationship ($B=.18$, $SE=0.07$, $P = .018$).

Additional exploratory analysis

Because both income-to-poverty ratio and AL were related to depressive symptoms, we explored whether the relationship between allostatic load and depressive symptoms varied among the different income groups. There was no significant interaction between allostatic load and income-to-poverty ratio on depressive symptoms ($F(2, 45)=3.74$, $P = .296$, $\Delta AIC= -3$). However, in stratified analysis, allostatic load was significantly related to depressive symptoms among the

two lower income groups (*B*=0.21, *SE*=0.08, *P* = .008) but not among the highest income group (*B*=0.07, *SE*=0.12, *P* = .551). The Figure illustrates this effect further, showing that depressive symptoms were increased among allostatic load Q2 to Q4 for the lowest and medium income groups.

Discussion

In this cross-sectional study of cancer survivors with diverse diagnoses, higher allostatic load was associated with higher depression scores. In particular, the higher risk of significant depression symptoms (PQH-9 score ≥ 10) was concentrated among those survivors with highest AL scores: about 1 in 5 survivors in the highest AL quartile (defined by AL score≥3.5) was at high risk of depression compared to about 1 in 10 among survivors with lower AL scores. This is the first study to our knowledge to investigate the relationship between AL and depression in cancer survivors. Previous studies in general population samples without specific somatic diagnoses found mixed results.[18] For instance, a recent study found that AL scores were higher in patients with major depression compared to controls in models adjusted for diverse socio-demographic factors.[30] However, another study using the NHANES database found no relationship between AL and depressive disorder in the general population.[17] Finally, yet another NHANES study found that associations between inflammatory markers (one of the components of AL) and depression symptoms were significantly stronger in participants with chronic somatic diseases than those without.[19] The current results might therefore shed some light on the mixed results in the literature suggesting that in individuals with chronic somatic diseases such as cancer, AL might be more tightly connected to depressive symptomology than in the general population.

Future studies should seek to confirm the relationship between AL and depression in larger samples of cancer survivors that would allow to investigate how it varies as a function of the specific cancer diagnosed. It would also be interesting to investigate whether there is a specific biological dysregulation profile that may increase depression risk in individuals with different types of cancer. Using the AL framework, a recent study found that individuals who met the criteria for depression were characterized by frequent metabolic, immune, and parasympathetic dysregulation but not sympatho-medullary (SAM) pathway or HPA axis dysregulation.[31] Research using metabolic syndrome biomarkers also found that depression was more common among individuals who qualified as having the metabolic syndrome.[32] The current study did not include any measures of SAM or HPA axis functioning (e.g., cortisol, epinephrine, norepinephrine, dopamine) that are otherwise key components of the AL conceptual framework.[7,33] Whereas this decreases the conceptual validity of the AL scores used in the current study against the construct's original formulation,[33] the previous results suggest that these missing components may not have a significant role in the relationship of AL with depression symptoms.

There are multiple previous studies showing that individuals with lower socio-economic status (e.g., indexed by education or income) have higher AL.[18,33] This was the case in our study for education, although the differences disappeared when we took other characteristics into account (e.g., age, sex, race, marital status). Importantly, in exploratory analysis the relationship between AL and depressive symptoms was only present among survivors with income closer to the poverty level. In contrast, in survivors in the highest income group depressive symptoms were lower and unrelated to allostatic load. It is possible that the adversity of the cancer

diagnosis and treatment is further exacerbated by the adversity of difficult socio-economic circumstances, thus contributing to higher allostatic load and higher depression symptoms.

Future studies should use longitudinal measurement to try to identify to what extent high AL contributes to the development of depression after cancer diagnosis and to what extent high AL is an expression of an already present psychiatric condition. Some AL components have been investigated both as precursors and consequences of depression (e.g., inflammation),[34] suggesting that the cause-and-effect relationship may not be one-sided. In addition, certain lifestyle coping behaviors (e.g., smoking, alcohol and substance use, physical inactivity) have also been associated with the development of both AL and depression.[35,36]

Study limitations

Limitations of the current study include survivor bias, its cross-sectional design which does not allow to investigate the trajectories of AL and depressive symptoms, the relatively small number of survivors with different diagnoses, and the long period of data collection that spanned more than 10 years and may not reflect the circumstances of current cancer survivors. We selected respondents who reported having a primary cancer diagnosed in the past five years, because elevated depression risk after a cancer diagnosis has been found primarily for this period.[3,4] However, depression risk may remain elevated for patients with certain types of cancer (e.g., gynecological) and it may be worth examining AL in survivors beyond the 5th year mark.[14]

The AL scoring was based on previous studies using the NHANES database to investigate similar research questions, however, some important biomarkers could not be included because of their inconsistent availability within NHANES waves or because they were never collected as part of the survey (e.g., C-reactive protein, interleukin-6, and tumor necrosis factor-alpha as measures of inflammation, or HPA axis function measures). No gold standard AL

measure exists and there is substantial variability in the choice of biomarkers and other analytic decisions even when using the same data source.[37] In fact, different systematic reviews conclude that the heterogeneity in AL operationalization across studies is a major drawback and that this aspect should be improved in future research.[8,18,33,38]

The findings regarding the role of socio-economic status in the AL-depression link were based on exploratory post-hoc analysis. Although the results in stratified analyses are consistent with a moderation effect of income-to-poverty ratio, there was no significant interaction. The sample size of the current study was relatively small and there is a possibility for Type I error. Future studies should try to replicate the current results to confirm the role of AL in depression during cancer survivorship.

Clinical implications for nursing

Nurses have an important role in identifying psychological distress and mental disorders in cancer patients and survivors and routinely collected biomarkers could help identify such individuals. A systematic review concluded that AL could be used as an index of physiological burden among individuals with cancer.[8] However, research on the role of AL in depression following cancer diagnosis and treatment is still in its infancy. Whereas the current findings may contribute to understanding the potential mechanisms behind depression in the cancer survivorship setting, they are too preliminary to have direct clinical implications. Should the current results be confirmed by further studies, AL could be tested for use in screening and assessment of survivors at high risk of depression, specifically those with lower socio-economic status. Most, if not all, of the AL biomarkers used in the current study are routinely collected in follow-up care and as part of routine medical testing, and could potentially be used to enhance the screening process for distress in cancer survivors.[39]

Conclusions

High AL is associated with more depressive symptoms among cancer survivors with lower socio-economic status. Further studies should explore the utility of the AL construct in the context of cancer follow-up care in general and screening for psychological distress in particular.

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Figure legend

Figure. PHQ-9 Scores as a Function of Allostatic Load Quartile and Income-To-Poverty Ratio Group. *Note:* The segment that divides each box into two parts is the median, while the dimensions of the box are the interquartile range. The low- and medium-income groups were joined to represent 45% of the study population, whereas the high-income group represented 55% of the study population.

Table(s)

Table 1. Description of the Calculation of Allostatic Load Scores

Physiological & anthropometric measurements & biomarkers		Low risk (0 points)	Medium risk (0.5 points)	High risk (1 point)
Blood pressure	**Systolic blood pressure**	< 120 mmHg	120 to < 150 mmHg	≥ 150 mmHg
	Diastolic blood pressure	< 80 mmHg	80 to < 90 mmHg	≥ 90 mmHg
	Medication for hypertension	0.5 points if low risk on both blood pressure measures but reported currently taking medication.		
60-second pulse rate		<82 bpm (<75th percentile)	82 to 89 bpm (>75th percentile but lower than 90th percentile)	≥ 90 bpm (>90th percentile)
Body-mass index (BMI)		< 25 kg/m^3	25 to < 30 kg/m^3	≥ 30 kg/m^3
Glucose metabolism	**Glycohemoglobin**	< 5.7%	5.7% to < 6.5%	≥ 6.5%
	Medication for diabetes	0.5 points if low risk on glycohemogobin but reported currently taking medication.		
Creatinine clearance[a]		≥ 60 mL/min/1.73 m2	30 to < 60 mL/min/1.73 m2	< 30 mL/min/1.73 m2
Cholesterol	**High-density lipoprotein (HDL)**	≥ 60 mg/dL	40 to < 60 mg/dL	< 40 mg/dL
	Total cholesterol/HDL ratio	< 5	5 to 5.99	≥ 6
	Total cholesterol	< 200 mg/dL	200 to < 240 mg/dL	≥ 240 mg/dL
	Medication for cholesterol	0.5 points if low risk on total cholesterol but reported currently taking medication.		
Albumin		≥ 3.8 µg/mL	3.0 to < 3.8 µg/mL	< 3.0 µg/mL
White blood cell count		< 8.4 x 10^3 cells/uL (<75th percentile)	8.4 to 10 x 10^3 cells/uL (>75th percentile but lower than 90th percentile)	> 10 x 10^3 cells/uL (>90th percentile)

[a]Based on a formula taking weight and age into account (Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16(1):31–41).

Table 2. Distribution of Study Variables, Allostatic Load and PHQ-9 Scores in n=294 Survivors (weighted n=1,969,775).

			Allostatic		PHQ-9		High depression risk		
		% of sample	Mean	SE	Mean	SE	%	LLCI	ULCI
Survey wave	2007-2008	15	2.59	0.32	4.12	0.93	22	8	37
	2009-2010	16	2.67	0.31	2.89	0.91	11	0	24
	2011-2012	18	2.63	0.29	2.74	0.64	6	0	13
	2013-2014	20	2.51	0.18	3.76	0.89	10	1	20
	2015-2016	13	2.85	0.23	3.23	0.84	8	0	19
	2017-2018	18	2.80	0.11	5.23	1.55	22	0	43
Age group (in years)	20-39	51	1.39	0.21	3.83	0.89	19	6	32
	40-59	35	2.79	0.20	4.00	0.81	15	3	27
	60-79	14	2.93	0.11	3.47	0.49	10	4	17
Sex	Male	45	2.82	0.12	2.91	0.61	8	2	15
	Female	55	2.54	0.15	4.35	0.58	17	9	26
Civil status	Married/partnered	69	2.72	0.12	3.06	0.45	10	4	16
	Single	10	1.90	0.31	4.68	1.21	18	1	34
	Divorced/separated	16	2.77	0.22	5.90	1.36	24	4	45
	Widowed	5	3.10	0.29	3.34	0.88	13	0	27
Race/origin	Non-Hispanic White	80	2.58	0.12	3.54	0.53	13	6	20
	Mexican American	4	2.90	0.23	6.00	1.36	29	8	51
	Other Hispanic	4	2.55	0.21	3.15	0.84	1	0	3
	Non-Hispanic Black	8	3.26	0.19	3.81	0.65	12	3	21
	Other	4	3.13	0.32	5.32	1.46	26	4	48
Education	College graduate or	35	2.53	0.16	2.56	0.95	7	0	15
	Some college or AA	36	2.73	0.18	4.16	0.82	18	5	30
	High school	18	2.58	0.17	4.21	0.79	11	0	22
	9-11th grade	7	2.99	0.18	4.74	1.01	15	4	25
	Less than 9th grade	4	3.17	0.27	5.88	1.11	36	14	57
Income-to-poverty ratio	Highest income	55	2.60	0.15	2.47	0.57	8	1	15
	Medium income	29	2.68	0.19	3.74	0.54	11	4	17
	Lowest income	16	2.72	0.18	6.28	0.73	23	10	37
Cancer type diagnosed	Prostate	18	2.71	0.13	2.32	0.61	5	0	11
	Breast	18	2.90	0.23	5.12	1.29	24	4	44
	Colorectal	7	3.19	0.27	4.75	1.11	9	0	20
	Gynecological	14	2.31	0.34	5.19	0.92	22	5	40
	Melanoma	14	2.38	0.32	2.38	1.32	11	0	26
	Lung	3	2.66	0.49	5.91	1.35	7	0	20
	Other	26	2.67	0.17	3.06	0.67	10	0	18
Years since diagnosis	0	14	2.45	0.34	3.84	1.55	17	0	40
	1	23	2.93	0.20	4.38	0.97	17	5	28
	2	16	2.41	0.24	4.32	0.88	15	2	27
	3	18	3.00	0.21	3.69	0.86	13	0	25
	4	13	2.34	0.23	3.21	0.92	11	0	22
	5	16	2.61	0.24	2.44	0.61	6	0	15
Allostatic load	Q1 (<2)	24	-	-	2.93	0.61	11	2	21
	Q2 (≥2 and <2.5)	12	-	-	3.58	0.82	8	0	15
	Q3 (≥2.5 and <3.5)	32	-	-	3.53	0.79	8	0	19
	Q4 (≥3.5)	32	-	-	4.51	0.79	21	11	32

Note: SE=standard error of the mean. LLCI/ULCI=lower/upper level 95% confidence interval.

Table 3. Detailed Results from Univariate Linear Regression Analyses on Allostatic Load and PHQ-9 Scores.

		Allostatic load				Depression symptoms (sqrt PHQ-9)			
Variable	**Coefficient interpretation**	**B**	**LLCI**	**ULCI**	**p**	**B**	**LLCI**	**ULCI**	**p**
Age	1-year increase	**0.03**	**0.02**	**0.04**	<.001	-0.00	-0.01	0.01	.918
Sex	Female vs. Male	-0.28	-0.67	0.11	.159	**0.54**	**0.12**	**0.96**	.013
Civil status	Single vs. Married	-0.82	-1.42	-0.21	.009	0.37	-0.41	1.17	.343
	Divorced/separated vs. Married	0.05	-0.47	0.58	.839	**0.66**	**0.01**	**1.31**	.047
	Widowed vs. Married	0.38	-0.29	1.06	.265	0.11	-0.54	0.74	.714
Race/origin	Mexican American vs. Non-Hispanic White	0.32	-0.18	0.81	.205	0.61	-0.10	1.33	.092
	Other Hispanic vs. Non-Hispanic White	-0.03	-0.51	0.45	.896	-0.05	-0.71	0.61	.877
	Non-Hispanic Black vs. Non-Hispanic White	**0.68**	**0.25**	**1.11**	.002	0.12	-0.33	0.59	.583
	Other vs. Non-Hispanic White	0.54	-0.21	1.29	.150	0.34	-0.42	1.09	.372
Education	Some college or AA degree vs. College graduate or above	0.20	-0.24	0.65	.368	0.47	-0.05	0.99	.076
	High school graduate/GED vs. College graduate or above	0.06	-0.42	0.53	.819	0.47	-0.03	0.97	.062
	9-11th grade vs. College graduate or above	0.46	-0.10	0.94	.055	0.57	-0.02	1.17	.060
	Less than 9th grade vs. College graduate or above	**0.64**	**0.02**	**1.25**	.042	**0.96**	**0.24**	**1.68**	.009
Income-to-poverty ratio	Medium vs. Highest	0.07	-0.34	0.51	.710	**0.42**	**0.01**	**0.84**	.045
	Lowest vs. Highest	0.11	-0.33	0.56	.613	**1.14**	**0.69**	**1.60**	<.001
Cancer site	Prostate vs. Other	0.04	-0.40	0.48	.868	-0.29	-0.80	0.21	.254
	Breast vs. Other	0.22	-0.31	0.75	.403	0.61	-0.09	1.32	.089
	Colorectal vs. Other	0.51	-0.16	1.18	.132	0.51	-0.23	1.27	.175
	Gynecological vs. Other	-0.36	-1.13	0.40	.345	**0.71**	**0.08**	**1.34**	.028
	Melanoma vs. Other	-0.29	-1.04	0.46	.442	-0.42	-1.12	0.26	.223
	Lung vs. Other	-0.01	-1.04	1.01	.982	**0.81**	**0.02**	**1.60**	.044
Years since diagnosis	1-year increase	-0.02	-0.14	0.09	.748	-0.06	-0.19	0.06	.296
Allostatic load score	1-point increase	-	-	-	-	0.14	0.00	0.28	.055

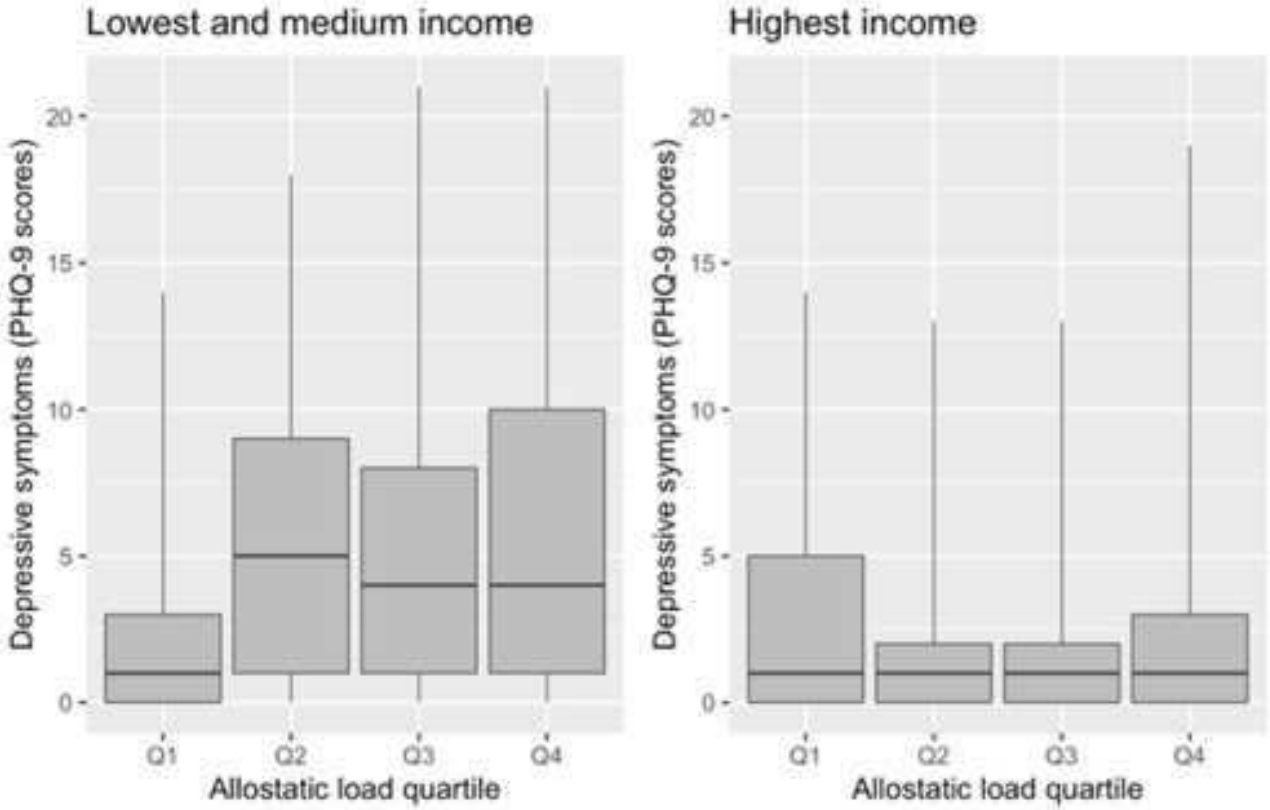
Note: LLCI/ULCI=Lower and upper level 95% confidence intervals.

Table 4. Detailed Results from Multiple Linear Regression Analyses on Allostatic Load and PHQ-9 Scores, Adjusted for Age, Sex, Civil Status, Race, Education, Income-To-Poverty Ratio, Cancer Site, and Years Since Diagnosis.

		Allostatic load				**Depression symptoms (sqrt PHQ-9)**			
Variable	**Coefficient interpretation**	**B**	**LLCI**	**ULCI**	**p**	**B**	**LLCI**	**ULCI**	**p**
Intercept		1.64	0.57	2.70	.004	0.04	-1.19	1.28	.942
Age	1-year increase	**0.02**	**0.01**	**0.04**	.010	0.01	0.00	0.03	.139
Sex	Female vs. Male	-0.56	-1.16	0.05	.071	0.17	-0.32	0.66	.480
Civil status	Single vs. Married	-0.66	-1.34	0.01	.053	0.55	-0.28	1.38	.182
	Divorced/separated vs. Married	-0.06	-0.63	0.50	.825	-0.10	-0.60	0.40	.678
	Widowed vs. Married	0.02	-0.69	0.73	.964	-0.70	-1.47	0.07	.073
Race/origin	Mexican American vs. Non-Hispanic White	0.22	-0.57	1.02	.569	-0.06	-0.73	0.61	.854
	Other Hispanic vs. Non-Hispanic White	0.41	-0.15	0.97	.144	-0.38	-0.93	0.16	.161
	Non-Hispanic Black vs. Non-Hispanic White	**0.67**	**0.16**	**1.18**	.011	-0.08	-0.50	0.35	.716
	Other vs. Non-Hispanic White	0.07	-0.32	0.45	.725	0.13	-0.46	0.71	.662
Education	Some college or AA degree vs. College graduate or above	0.14	-0.37	0.66	.572	-0.05	-0.47	0.36	.795
	High school graduate/GED vs. College graduate or above	0.05	-0.50	0.60	.857	-0.23	-0.78	0.31	.388
	9-11th grade vs. College graduate or above	0.04	-0.69	0.76	.920	-0.51	-1.21	0.19	.148
	Less than 9th grade vs. College graduate or above	0.21	-0.74	1.16	.653	0.15	-0.70	1.01	.719
Income-to-poverty ratio	Medium vs. Highest	0.10	-0.33	0.52	.649	0.29	-0.18	0.77	.217
	Lowest vs. Highest	0.10	-0.46	0.66	.717	**1.13**	**0.69**	**1.57**	<.001
Cancer site	Prostate vs. Other	-0.50	-1.15	0.15	.128	-0.45	-1.04	0.15	.133
	Breast vs. Other	0.46	-0.18	1.09	.150	0.11	-0.52	0.74	.723
	Colorectal vs. Other	0.53	-0.28	1.33	.193	0.14	-0.55	0.84	.676
	Gynecological vs. Other	0.00	-0.87	0.86	.994	0.48	-0.16	1.13	.133
	Melanoma vs. Other	-0.18	-0.82	0.46	.562	-0.37	-1.10	0.36	.310
	Lung vs. Other	0.29	-0.50	1.08	.464	0.19	-0.61	0.99	.629
Years since diagnosis	1-year increase	-0.02	-0.12	0.09	.769	-0.02	-0.14	0.10	.723
Allostatic load score	1-point increase	-	-	-	-	**0.15**	**0.00**	**0.29**	.045

Note: LLCI/ULCI=Lower and upper level 95% confidence intervals.

Figure


Lowest and medium income
Highest income
Depressive symptoms (PHQ-9 scores)
0
5
10
15
20
Q1
Q2
Q3
Q4
Allostatic load quartile