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RESEARCH ARTICLE

The Role of BMI in Allostatic Load and Risk of Cancer Death

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Introduction: Obesity and proinflammatory conditions are associated with increased risks of cancer. The associations of baseline allostatic load with cancer mortality and whether this association is modified by body mass index (BMI) were examined.

Methods: A retrospective analysis was performed in March−September 2022 using National Health and Nutrition Examination Survey years 1988 through 2010 linked with the National Death Index through December 31, 2019. Fine and Gray Cox proportional hazard models were stratified by BMI status to estimate subdistribution hazard ratios of cancer death between high and low allostatic load status (adjusted for age, sociodemographics, and health factors).

Results: In fully adjusted models, high allostatic load was associated with a 23% increased risk of cancer death (adjusted subdistribution hazard ratio=1.23; 95% CI=1.06, 1.43) among all participants, a 3% increased risk of cancer death (adjusted subdistribution hazard ratio=1.03; 95% CI=0.78, 1.34) among underweight/healthy weight adults, a 31% increased risk of cancer death (adjusted subdistribution hazard ratio=1.31; 95% CI=1.02, 1.67) among overweight adults, and a 39% increased risk of death (adjusted subdistribution hazard ratio=1.39; 95% CI=1.04, 1.88) among obese adults, when compared to those with low allostatic load.

Conclusions: The risk of cancer death is highest among those with high allostatic load and obese BMI, but this effect was attenuated among those with high allostatic load and underweight/healthy or overweight BMI.

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INTRODUCTION

Approximately 30.7% of United States (U.S.) citizens have an overweight body mass index (BMI), and 42.4% have an obese BMI.[1] By 2030, U.S. obesity rates are projected to increase to 51%.[2] In the U.S., non-Hispanic Black (NH-Black) adults have the highest prevalence of obesity (49.9%) compared to Hispanic (45.6%), non-Hispanic White (NH-White) (41.4%), and Asian (16.1%) adults.[3] Obesity has been associated with an increased risk of cancer mortality.[4−7] Moreover, obesity has been shown to increase the risk of developing up to 13 obesity-related cancers.[8−10] Adults with obese BMI and cancer have a

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poorer prognosis, in part owing to the difficulty in screening due to excess adipose tissue, inadequate dosage of chemotherapy, and financial burdens related to costly treatments.[11,12] Moreover, metabolic, immune, and inflammatory dysfunction are hallmarks associated with both excess adipose tissue, oncogenesis, and metastasis.[13]

Coined in the late 1990s, McEwen and Seeman theorized the concept of allostatic load (AL) as the physiological effects of life-course stress or the cumulative wear and tear on the body from repeated exogenous stressors.[14] They linked biomarkers from multiple organ systems to understand physiologic mechanisms of health disparities, and observed that the effects of chronic stress and the overactivation of several adaptive processes may subsequently contribute to progression of various diseases.[14–17] Prior to literature on AL, Geronimus proposed the weathering hypothesis, which postulated that Black individuals experienced earlier health deterioration as a result of cumulative repeated stressors with social, economic, and political marginalization.[18,19] In 2006, Geronimus noted that AL algorithm is conceptually suited for studying the weathering hypothesis; therefore, this study has elected to establish AL score as a measure for weathering, also known as early health deterioration.[20] Conventionally, AL includes BMI as a component within its cumulative score[20,21]; however, this study did not include BMI as a component of AL and instead explored the moderating effects of BMI to better understand the influence of obesity with chronic stress and subsequent cancer death. Previous studies suggest that excess adipose tissue promotes a proinflammatory physiologic state that in turn increases tumorigenesis.[22–25] This study aimed to determine the role of BMI status on the effect of high AL and the risk of dying from cancer.

Furthermore, increased BMI may aid in cancer etiology by promoting AL through a chronic inflammatory state and metabolic dysregulation.[6,26,27] To date, few studies have examined the moderating role of BMI on the relationship between AL and cancer mortality. One U.S. prospective study, the REasons for Geographic and Racial Differences in Stroke (REGARDS), observed a 17% increased risk of cancer death among healthy weight individuals and a 9% risk of cancer death among individuals with overweight and obese BMI[28] with every unit increase of AL. Another U.S. study using the National Health and Nutrition Examination Survey (NHANES) III data and Multi-Systemic Biological Risk (MSBR), a proxy for AL, observed that individuals with a BMI ≥25 kg/m^2 had an increased risk of cancer death with increasing MSBR scores (48% increased risk comparing second with first quartiles of MSBR).[29]

Increasing BMI, notably obesity, is associated with increased cancer risk and mortality. Fewer studies have identified associations between AL and cancer death. However, little is known regarding whether increasing BMI—overweight versus obesity—modifies the association between AL and cancer death. Therefore, this study examined the associations of baseline AL with cancer mortality in a nationally representative sample of U.S. adults and whether this association is modified by BMI category.

METHODS

Study Sample

A retrospective cohort analysis was performed using data from the NHANES survey, a representative sample of non-institutionalized U.S. residents linked with the National Center for Health Statistics 2019 National Death Index (NDI) file. The NHANES program oversamples those aged ≥60 years, Latinx and NH-Black people, and a weighted analysis generates generalizable estimates[30] considered representative of the U.S. civilian non-institutionalized population.[31] The association between AL and cancer mortality was examined using participants that completed NHANES surveys from 1988 through 2010, with NDI follow-up data through December 31, 2019. NHANES includes demographic, socioeconomic, dietary, health-related questionnaires, clinical measures of blood pressure, fasting blood glucose, triglycerides, total cholesterol, and self-reported medication use for health conditions. Analysis was performed among NHANES participants with data on biomarkers and within a fasting subsample (n=95,359). Patients were excluded if they reported current pregnancy or were aged <18 years (n=42,791), if they were missing AL biomarkers or not linked through NDI (n=33,584), or if they had a past medical history of cancer (n=1,464). This resulted in a final analytic sample of NHANES participants aged ≥18 years, corresponding to a total of 17,430 participants over a 22- year study period (Figure 1). The IRB considered this study exempt from review because of the use of secondary, publicly available, and deidentified data.

Measures

AL has been defined using varying configurations, although most incorporate biomarker measures from 3 different categories of physiologic functioning, including cardiovascular, metabolic, and immune systems.[32] Although there is no consensus definition, this study elected to define AL using the Geronimus et al. (2006) and Mays et al. (2018) taxonomies.[20,33] AL had 8 components, including diastolic blood pressure, glycated hemoglobin (HbA1c), systolic blood pressure, total cholesterol, serum triglycerides, serum albumin, serum creatinine, and C-reactive protein. To determine the high-risk thresholds for each AL component, the distribution of each AL component was examined among the entire study sample with complete biomarker data. High-risk thresholds were determined by either being above the 75th percentile for C-reactive protein, diastolic blood pressure, HbA1c, systolic blood pressure, total cholesterol, serum triglycerides, and serum creatinine[28,34] or below the 25th percentile for serum albumin. Therefore, each NHANES participant was scored as either 1 (high risk) or 0 (low risk) on the basis of sex reported at survey

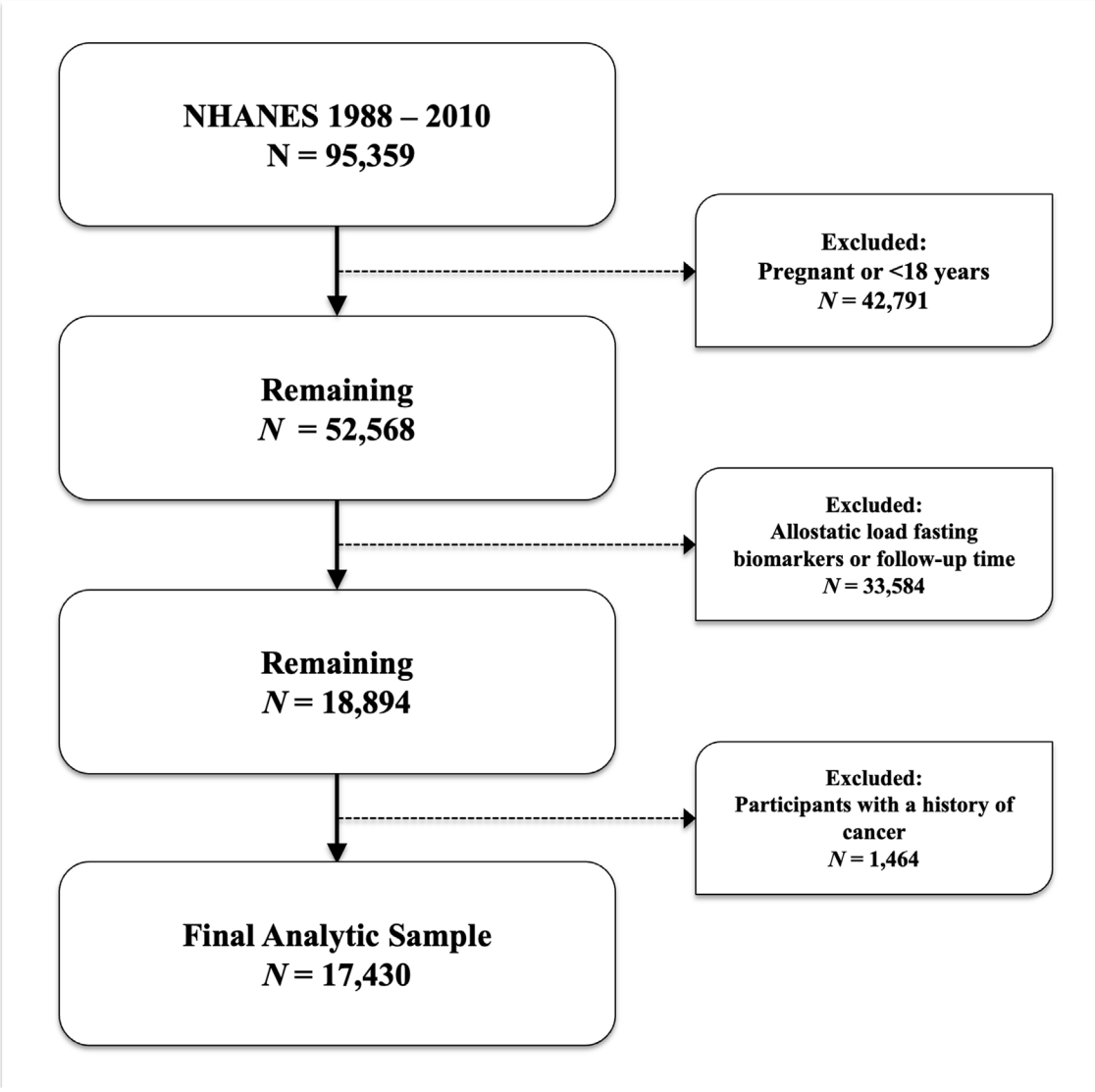

Figure 1. Flowchart of exclusion criteria and final study population of NHANES participants.
NHANES, National Health and Nutrition Examination Survey.

cutoffs for each component (Appendix Table 1, available online). The total AL score was calculated by summing the 8 components, and this total score ranged from 0 to 8. In the main analysis, participants were further categorized such that those with a total AL score ≥3 were said to have high AL and participants with a total AL score <3 were said to have low AL.[32,33]

The primary outcome of interest was time to cancer-related death. Follow-up data for this analysis was available through December 31, 2019 on the basis of NDI–NHANES publicly available linkages. The primary determination of mortality for eligible NHANES participants is based on matching survey records to the NDI, although additional sources are also incorporated. These sources include the Social Security Administration, the Centers for Medicare and Medicaid Services, data collection, the National Center for Health Statistics' follow-up surveys, and ascertainment of death certificates. Variables indicating which source or sources were used to determine vital status are included in the 2019 Linked Mortality Files Data Dictionary.[35] Mortality status or vital status for participants was determined through NHANES–NDI linked file. Causes of death were harmonized with ICD-10 guidelines.

Participant characteristics included variables that were selected on the basis of a priori inclusion from NHANES questionnaires and plausible confounding on the relationship between obesity, AL, and cancer mortality.[36] Sociodemographic characteristics included in this study are sex at birth (male/female), age (continuous), race/ethnicity (NH-White, NH-Black, Latinx, and other mixed race), education, and poverty-to-income ratio (PIR) to estimate socioeconomic status (adjusted for inflation). The NHANES education variable was categorized into (1)

less than high school education, (2) high school graduate/GED/or equivalent, (3) some college, (4) college graduate or above, and (5) unknown/refused to answer. PIR was calculated as the ratio of total family income to poverty threshold values (in dollars). Persons who reported having had no income were assigned a zero value for PIR. PIR values <1 are considered below the official poverty line, whereas PIR values >1 are above the poverty level.[37] PIR was attained at baseline interview for NHANES participants and reflects the changes in PIR during the 3 decades of the study. BMI was categorized into 3 categories: (1) combined underweight and healthy weight, BMI <24.9 kg/m^2; (2) overweight, BMI of 25−29.9 kg/m^2; and (3) obese, BMI >30 kg/m^2. Health behaviors were evaluated because they may influence total AL score in analysis, including self-reported smoking status and self-reported response to a physician-diagnosed history of congestive heart failure and heart attack. Congestive heart failure and heart attack were considered confounders on the basis of being previous medical conditions and chronic diseases that are related to obese BMI and cancer. Participants that had not smoked 100 cigarettes in their lifetime were categorized as never smokers, whereas participants with at least 100 cigarettes smoked in their lifetime but not currently smoking were categorized as past smokers.[38] Participants with at least 100 lifetime cigarettes used and currently smoking were categorized as current smokers.[38]

Statistical Analysis

Analyses were performed using the NHANES-generated sampling statistical strata, clusters, and weights as designated and described in detail within the NHANES methodology handbook.[30] The NHANES only measures biomarkers among a random sample of participants each survey period and, in turn, created subsample weights to account for the probability of being selected into the subsample component and additional nonresponse bias.

Categorical variables were presented as weighted row percentages, and continuous variables were presented as mean and associated Standard errors. Characteristics were compared (i.e., descriptive statistics) between high and low AL stratified by BMI categories using Rao-Scott chi-square tests for categorical variables and weighted Wald *F*-tests for continuous variables.

Comparisons of relative cumulative incidence functions for risks of cancer death by AL groups, overall and stratified by BMI status, were done using Fine & Gray competing risks analysis, accounting for all-cause death. After confirming the proportionality of hazards assumption, relative rates of cancer death between high and low AL participants were estimated. In addition, an unweighted (did not account for NHANES-specific statistical weights) Fine & Gray model[39] was performed to examine all-cause mortality as a potential competing risk for cancer deaths. Results presented from competing risks analysis as subdistribution hazard ratios and associated 95% CIs. Participants were censored at the time of their cancer death or end of follow-up (December 31, 2019). Models were sequentially adjusted for potential confounders on the basis of known risk factors and those varied between levels of AL in bivariate analyses, including (1) continuous age, (2) sociodemographics (sex, race, PIR, and education), and (3) health factors (smoking status, ever diagnosed congestive heart failure, and ever diagnosed heart attack). A priori, the study examined BMI as a potential effect modifier (Appendix Figure 1, available online), and thus analysis was stratified to examine the association between cancer deaths by BMI. Multiplicative interactions of AL and BMI were examined by introducing an interaction term within the model and presenting the corresponding *p*-value for this association; *p*-values ≤0.05 were considered statistically significant. All statistical analyses were performed using SAS in March−September 2022 (Version 9.4, SAS Institute, Inc., Cary, North Carolina) and Stata (Version 17, StataCorp, College Station, Texas).

RESULTS

Table 1 displays the demographics of NHANES participants (*n*=17, 430) (Figure 1) at baseline interview by BMI category and AL status. Among participants with underweight and healthy weight (BMI<24.9 kg/m^2), those with high AL were more likely to be female (51.4% vs 48.6%), to be older (mean age=55.7 years vs 36.1 years), to identify as NH-Black (11.8% vs 8.6%), and to have a lower level of education attainment (some college or associates degree: 21.8% vs 27.6%; college graduate: 19.9% vs 28%); to be a current smoker (34.3% vs 28.3%); and to have ever been diagnosed with congestive heart failure (3% vs 0.4%) than those with low AL. Among participants with overweight BMI (25−29.9 kg/m^2), those with high AL were more likely to be male (57.9% vs 42.1%), to be older (mean age=54 years vs 40.4 years), to identify as NH-Black (12.8% vs 8.4%), to have a lower level of educational attainment (some college or associates degree: 22.4% vs 28.6%; college graduate: 18.2% vs 25.5%) and be a current smoker (25.7% vs 21.4%) than those with low AL. Among participants with obese BMI (>30 kg/m^2), those with high AL were more likely to be older (mean age=50.1 years vs 40.3 years), to identify as NH-White (70.1% vs 66.2%), to have a lower level of educational attainment (some college or associates degree: 26.7% vs 31%; college graduate: 16.1% vs 20.9%), to be a current smoker (22% vs 20.3%), or to have ever been diagnosed with congestive heart failure (3.6% vs 1.0%) than those with low AL.

In the unweighted Fine and Gray competing risks analysis, there were 967 deaths attributed to cancer among the cohort. NHANES participants with high AL were more likely to die from cancer and have a shorter mean survival time than participants with low AL (Table 2 and Figure 2). For instance, among all NHANES participants, those with high AL were 34% more likely to have a death attributed to cancer than those with low AL (Model 1 adjusted subdistribution hazard ratio [aSHR]=1.34; 95% CI=1.15, 1.55) (Table 2). In fully adjusted models, all adults with high AL had a 23% increased risk of cancer death (aSHR=1.31; 95% CI=1.05, 1.63) compared with all adults with low AL. This study examined whether BMI

Table 1. Sociodemographic Characteristics by Allostatic Load Status, Among 17,430 NHANES Participants

Sociodemographics	Underweight and healthy weight BMI<24.9 kg/m^2 *n*=6,144 Low AL[a] (*n*=4,566)	Underweight and healthy weight BMI<24.9 kg/m^2 *n*=6,144 High AL[a,b] (*n*=1,578)	Overweight BMI 25–29.9 kg/m^2 *n*=6,101 Low AL[a] (*n*=3,415)	Overweight BMI=25–29.9 kg/m^2 *n*=6,101 High AL[a,b] (*n*=2,686)	Obese BMI>30 kg/m^2 *n*=5,185 Low AL[a] (*n*=2,090)	Obese BMI>30 kg/m^2 *n*=5,185 High AL[a,b] (*n*=3,095)
Allostatic load total score[c]	0.83 (0.02)	3.7 (0.03)	1.1 (0.02)	3.9 (0.03)	1.3 (0.02)	4.0 (0.02)
Sex						
Female	2,392 (56.0)	759 (51.4)	1,483 (40.3)	1,152 (42.1)	1,188 (52.9)	1,718 (52.3)
Male	2,174 (44.0)	819 (48.6)	1,932 (59.7)	1,534 (57.9)	902 (47.1)	1,377 (47.7)
Mean ge in years	36.1 (0.29)	55.7 (0.64)	40.4 (0.34)	54.0 (0.54)	40.3 (0.47)	50.1 (0.37)
Age group in years						
18–29	2,139 (40.7)	124 (7.3)	1,013 (27.2)	147 (6.0)	623 (26.5)	245 (7.1)
30–39	923 (24.6)	119 (11.1)	767 (25.1)	293 (13.3)	488 (26.6)	510 (18.1)
40–49	624 (17.4)	214 (18.0)	680 (23.1)	437 (21.5)	379 (21.2)	618 (24.4)
50–59	352 (9.4)	244 (21.0)	379 (13.1)	463 (22.2)	234 (13.3)	571 (22.9)
60–69	246 (4.4)	332 (18.5)	313 (6.9)	636 (18.6)	228 (8.3)	689 (17.5)
70+	282 (3.4)	545 (24.0)	263 (4.7)	710 (18.5)	138 (4.1)	462 (10.0)
Race/ethnicity						
Non-Hispanic White	2,115 (74.2)	763 (73.1)	1,430 (70.7)	1,153 (71.6)	811 (66.2)	1,236 (70.1)
Non-Hispanic Black	947 (8.6)	417 (11.8)	580 (8.4)	669 (12.8)	484 (13.7)	916 (15.7)
Latinx	1,234 (8.7)	301 (5.4)	1,284 (15.4)	777 (9.8)	732 (15.2)	860 (9.5)
Other and mixed race	270 (8.5)	97 (9.7)	121 (5.5)	87 (5.8)	63 (4.9)	83 (4.6)
Education						
Less than high school	1,290 (16.5)	653 (26.9)	1,074 (17.8)	1,136 (27.3)	646 (21.1)	1,207 (24.9)
High school/GED	1,373 (27.7)	447 (31.1)	954 (28.0)	742 (32.0)	567 (26.9)	875 (32.3)
Some college or Associates degree	1,040 (27.6)	267 (21.8)	786 (28.6)	484 (22.4)	547 (31.0)	659 (26.7)
College graduate	850 (28.0)	202 (19.9)	595 (25.5)	316 (18.2)	326 (20.9)	345 (16.1)
Missing	13 (0.1)	9 (0.3)	6 (0.1)	8 (0.1)	4 (0.1)	9 (0.1)
Income relative to the federal poverty line						
First quartile (0–1.11)	1,067 (14.0)	371 (14.7)	737 (13.4)	599 (14.6)	502 (15.6)	737 (15.0)
First quartile (1.11–2.08)	982 (19.9)	388 (20.0)	756 (17.6)	649 (19.0)	468 (19.9)	729 (20.2)
Third quartile (2.08–3.77)	1,074 (27.2)	351 (25.1)	787 (25.2)	608 (25.6)	514 (28.4)	712 (26.0)
Fourth quartile (3.77–11.89)	1,053 (34.3)	317 (32.3)	859 (37.4)	570 (33.7)	464 (31.2)	634 (32.5)
Missing	390 (6.9)	151 (8.0)	276 (6.4)	260 (7.1)	142 (4.8)	283 (6.3)
Current smoker status	1,155 (28.3)	505 (34.3)	668 (21.4)	616 (25.7)	387 (20.3)	627 (22.0)

(*continued on next page*)

Table 1. Sociodemographic Characteristics by Allostatic Load Status, Among 17,430 NHANES Participants (*continued*)

Sociodemographics	Underweight and healthy weight BMI<24.9 kg/m^2 *n*=6,144 Low AL[a] (*n*=4,566)	Underweight and healthy weight BMI<24.9 kg/m^2 *n*=6,144 High AL[a,b] (*n*=1,578)	Overweight BMI 25−29.9 kg/m^2 *n*=6,101 Low AL[a] (*n*=3,415)	Overweight BMI=25−29.9 kg/m^2 *n*=6,101 High AL[a,b] (*n*=2,686)	Obese BMI>30 kg/m^2 *n*=5,185 Low AL[a] (*n*=2,090)	Obese BMI>30 kg/m^2 *n*=5,185 High AL[a,b] (*n*=3,095)
Ever congestive heart failure	37 (0.4)	73 (3.0)	39 (1.1)	122 (3.4)	26 (1.0)	170 (3.6)
Ever heart attack	59 (0.1)	94 (4.5)	63 (1.5)	159 (5.1)	51 (2.4)	200 (5.9)

[a]Presented as column proportion (SE) or mean (SE) for continuous variables. Estimated using sampling weights from NHANES.
[b]*High allostatic load* is defined as a total allostatic load score ≥3.
[c]Allostatic load total score was calculated as the sum of components on the basis of high-risk thresholds: albumin, C-reactive protein, creatinine clearance, diastolic blood pressure, HbA1c, systolic blood pressure, total cholesterol, and triglycerides. Score range from 0 to 8.
NHANES, National Health and Nutrition Examination Survey.

modified the effects of high AL on cancer mortality but observed nonsignificant multiplicative interactions (Model 3 *p*-value for interaction=0.23). When limited to participants with underweight and healthy weight BMI (BMI<24.9 kg/m^2) and in fully adjusted models, those with high AL had a 3% increased risk of cancer death (aSHR=1.03; 95% CI=0.78, 1.34) compared with those with low AL, although this was not statistically significant. Among participants with overweight BMI (BMI=25−29.9 kg/m^2) in fully adjusted models, those with high AL had a 31% increased risk of cancer death (aSHR=1.31; 95% CI=1.02, 1.67) compared with those with low AL. Among participants with obese BMI (BMI>30 kg/m^2), those with high AL had a 39% increased risk of cancer death (aSHR=1.39; 95% CI=1.04, 1.88) compared with those with low AL in fully adjusted models.

DISCUSSION

In a diverse, nationally representative sample of U.S. adults, the highest risk of cancer mortality was among adults with obese BMI (>30 kg/m^2). This study observed a 23% increased risk of cancer death among all NHANES adults with high AL compared to adults with low AL. However, there was some suggestion that the effect seemed to be modified by BMI category. A 3%, 31%, and 39% increased risk of cancer mortality was observed among participants who were underweight and healthy weight (BMI<24.9 kg/m^2), overweight (BMI=25−29.9 kg/m^2), and obese (BMI>30.0 kg/m^2), respectively, with high AL compared with those with low AL. This study is novel in its findings on the moderating effects of increasing BMI on associations between AL and cancer mortality. Findings from this study provide insights into cancer risk for individuals experiencing high levels of cumulative stress and having overweight or obese BMI.

These findings provide more granular evidence than previous studies examining the association between AL and cancer mortality by BMI status. A study using data from the REGARDS cohort observed the highest risk of cancer mortality among normal weight participants (17%),[28] whereas this analysis observed the highest risk of cancer mortality among adults with obese BMI (39%). This study's population consisted of a large nationally representative sample of healthy community-dwelling participants aged 18+ years, whereas the REGARDS study was limited to those aged 45+ years with oversampling for African Americans in the Southeastern U.S. In addition, this study provides a more detailed understanding of the moderating role of BMI because the statistical models

Table 2. Fine & Gray Proportional Hazard Models: Association Between Allostatic Load and Cancer Death

Variable	Number Cancer deaths (%)[a]	Number All-cause deaths (%)[a]	Mean survival Months (SE)	Subdistribution hazard ratio and 95% CI	Subdistribution hazard ratio and 95% CI	Subdistribution hazard ratio and 95% CI
Risk among all adults				Model 1[a,b]	Model 2[a,c]	Model 3[a,d]
Low allostatic load	317 (2.5%)	920 (6.6%)	341.34 (0.49)	1.00 (ref)	1.00 (ref)	1.00 (ref)
High allostatic load	650 (7.6%)	2,528 (27.3%)	337.31 (1.07)	1.34 (1.15, 1.55)	1.29 (1.11, 1.50)	1.23 (1.06, 1.43)
Risk among underweight and healthy-weight adults (BMI<24.9 kg/m^2)						
Low allostatic load	147 (2.3%)	410 (6.3%)	341.76 (0.69)	1.00 (ref)	1.00 (ref)	1.00 (ref)
High allostatic load	163 (8.7%)	679 (35.1%)	305.82 (2.19)	1.23 (0.94, 1.62)	1.14 (0.87, 1.50)	1.03 (0.78, 1.34)
Risk among adults with overweight (BMI=25–29.9 kg/m^2)						
Low allostatic load	113 (2.8%)	321 (6.9%)	336.97 (0.85)	1.00 (ref)	1.00 (ref)	1.00 (ref)
High allostatic load	265 (9.1%)	972 (27.5%)	331.12 (1.75)	1.38 (1.08, 1.77)	1.36 (1.06, 1.74)	1.31 (1.02, 1.67)
Risk among adults with obesity (BMI>30 kg/m^2)						
Low allostatic load	57 (2.4%)	189 (7.0%)	325.25 (1.05)	1.00 (ref)	1.00 (ref)	1.00 (ref)
High allostatic load	222 (6.0%)	877 (23.4%)	342.50 (1.52)	1.48 (1.10, 2.00)	1.44 (1.07, 1.94)	1.39 (1.04, 1.88)
p-value for interaction[e]				0.34	0.39	0.23

[a]Percentages and models are weighted.
[b]Model 1 is adjusted for age (continuous).
[c]Model 2 is adjusted for age and sociodemographic factors, including sex, race, PIR, and education.
[d]Model 3 is adjusted for age; sociodemographic factors; and health factors, including current smoker status, having ever been diagnosed with congestive heart failure, or ever diagnosed with heart attack.
[e]Interaction term between BMI category and allostatic load on association with cancer death determined by Wald chi-square.
PIR, poverty-to-income ratio.

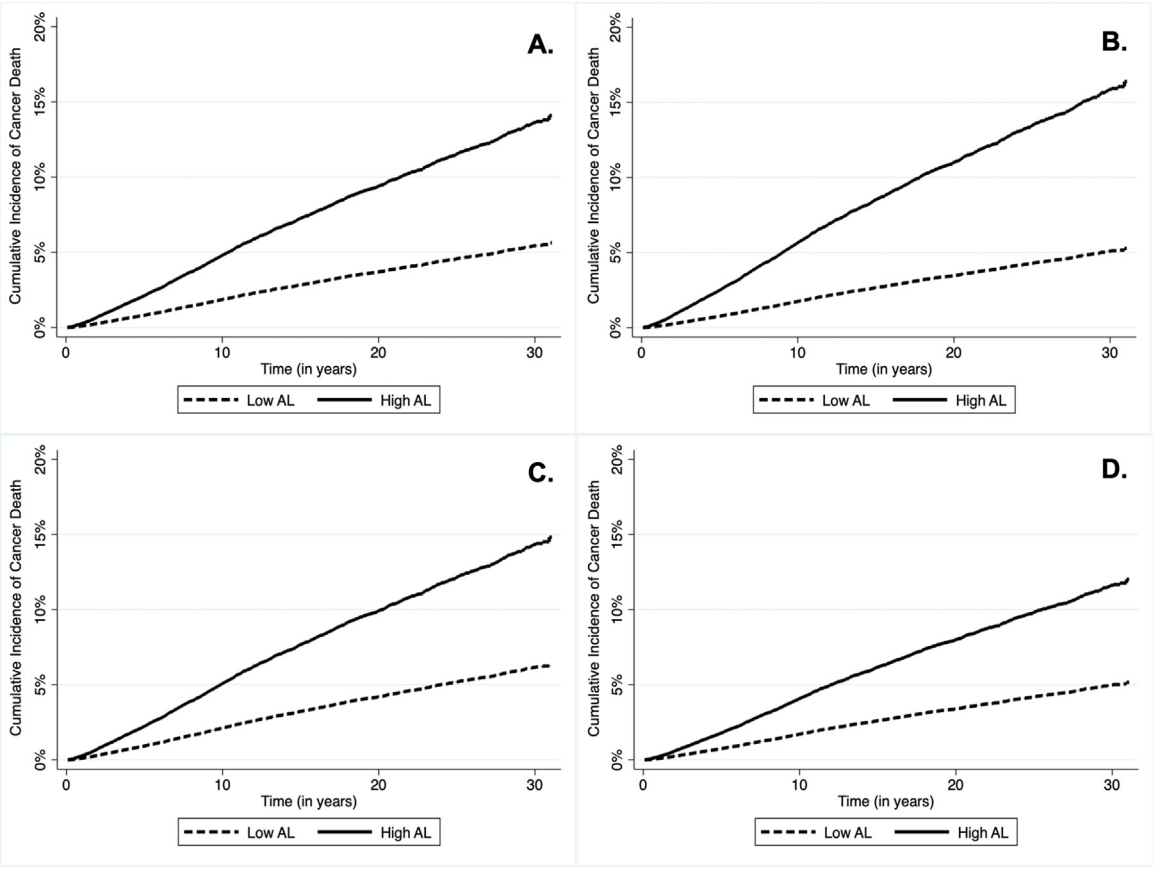

Figure 2. Cumulative incidence function plots for time to cancer death, comparing high with low allostatic load groups. **(A)** Among all NHANES adults. **(B)** Among underweight and healthy weight adults (BMI<24.9 kg/m^2). **(C)** Among adults with overweight (BMI=25–29.9 kg/m^2). **(D)** Among adults with obesity (BMI>30 kg/m^2).
NHANES, National Health and Nutrition Examination Survey.

accounted for BMI categorization at 3 levels (underweight and healthy weight, overweight, and obese), whereas Akinyemiju and colleagues dichotomized BMI at <25 kg/m^2. When comparing findings from Acheampong et al. with the findings of this study and other studies that investigate the effects of cumulative stress on cancer mortality, differences may be explained by information bias (i.e., classification error). For example, in the Acheampong et al. study, components of multisystemic Biological Risk score, a proxy to AL, were dependent on tertial distribution, whereas components of AL were based on high-risk quartile distribution.[29] This in turn may explain variation in parameter estimation.

Limitations

This study has a few limitations. Often, the measurement of BMI is considered a surrogate for the measure of body fat in clinical and public health settings. However, BMI is a measurement of access weight, not body fat, and factors such as race and ethnicity, muscle mass, and age can influence BMI. For example, BMI does not provide any information on the distribution of adipose tissue, nor does it differentiate excess fat, muscle, or bone mass among individuals.[40] Therefore, the measurement of BMI has inherent limitations when using it as a representation for the measurement of body fat. In addition, the current analysis was unable to discern cancer incidence because the NHANES data was linked with NDI data. Owing to data set limitations, risks for cancer-specific (i.e., breast, colorectal, lung) mortality was unable to be determined. Finally, this study utilized cross-sectional representative survey data linked with mortality data, and thus several of the study's variables, including AL and BMI status, were measured at one time and are static. Thus, temporality was unable to be established between BMI and AL. However, NHANES surveys a large sample of the general U.S. population, allowing for the analytic sample to be representative of the U.S. civilian population. This study was able to follow surveyed participants for a maximum of 31 years.

CONCLUSIONS

Overall, when stratified by BMI status, the risk of cancer death was highest among adults with obese BMI (BMI>30 kg/m^2) and high AL, closely followed by adults with overweight BMI (BMI=25–29.9 kg/m^2) and high AL. Future studies should characterize the association between obesity, AL, and cancer-specific–related mortality to better understand the causal mechanism between cumulative stress and obesity-related cancers.

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SUPPLEMENTAL MATERIAL

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