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Research Article

The Role of Body Mass Index in Allostatic Load and Risk of Cancer Death

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ABSTRACT

INTRODUCTION: Obesity and pro-inflammatory conditions are associated with increased risks of cancer. The associations of baseline allostatic load (AL) with cancer mortality and whether this association is modified by body mass index (BMI) was 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 sub-distribution hazard ratios (SHRs) of cancer death between high and low AL status (adjusted for age, sociodemographics, and health factors).

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

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

Credit Author Statement

SA: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing- Original Draft. **JM:** Conceptualization, Methodology, Software, Data curation, Investigation, Resources, Writing- Original Draft, Visualization, Supervision, Funding acquisition. **MLT, LF, DN:** Visualization, Validation, Writing- Review and editing. **ML, YH, SK:** Methodology, Data curation, Validation, Writing review and editing. **MT:** Supervision, Writing- review and editing.

INTRODUCTION

Approximately 30.7% of United States (US) citizens have an overweight body mass index (BMI), and 42.4% have an obese BMI.[1] By 2030 US obesity rates are projected to increase to 51%.[2] In the US, 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 adults (16.1%).[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 thirteen obesity-related cancers.[8-10] Adults with obese BMI and cancer have a poorer prognosis, in part due to 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 physiological 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; for this reason, the present 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 subsequently cancer death. Previous studies suggest excess adipose tissue promotes a pro-inflammatory physiologic state which in turn increases tumorigenesis.[22-25] The present study aimed to determine the role of BMI status on the effect of high AL and 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 US 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 9% risk of cancer death among individuals with overweight and obese BMI[28] with every unit increase of AL. Another US 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 $\geq$ 25 kg/m^2 had an increasing risk of cancer death with increasing MSBR scores (48% increased risk comparing 2nd to 1st quartiles of MSBR).[29]

Increasing BMI, notably obesity, is associated with increased cancer risk and mortality. Fewer studies have identified associations with AL and cancer death. However, little is known regarding if increasing BMI—overweight vs. 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 US adults and whether this association is modified by BMI category.

METHODS

Study Sample or Population: A retrospective cohort analysis was preformed using data from the NHANES survey, a representative sample of non-institutionalized US residents linked with the National Center for Health Statistics (NCHS) 2019 National Death Index (NDI) file. The NHANES program oversamples those aged 60 and older, Latinx and NH-Blacks, and weighted analysis generates generalizable estimates,[30] considered to be representative of the US 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 less than 18 years of age (N = 42,791), were missing AL biomarkers or not linked via NDI (N= 33,584), or had a past medical history of cancer (N= 1,464). This resulted in a final analytic sample of NHANES participants aged 18 and older, corresponding to a total of 17,430 participants over a 22- year study period (**Figure 1**). The Institutional Review Boards considered this study exempt from review because of the use of secondary, publicly available, and de-identified data.

Measures: AL has been defined using varying configurations, although most incorporate biomarker measures from three different categories of physiologic functioning including cardiovascular, metabolic, and immune systems.[32] While there is no consensus definition, the present study elected to define AL using the *Geronimus et al.* (2006) and *Mays et al.* (2018) taxonomies.[20, 33] AL had eight components, including diastolic blood pressure (DBP), glycated hemoglobin (HbA1c), systolic blood pressure (SBP), total cholesterol, serum triglycerides, serum albumin, serum creatinine, and C-reactive protein (CRP). 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 CRP, DBP, HbA1c, SBP, 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) based on sex reported at survey cutoffs for each component (**Appendix Table 1)**. Total AL score was calculated by summing the eight components, and this total score ranged from 0 to 8. In the main analysis, participants were further categorized with total AL score ≥ 3 as having high AL and participants with total AL score < 3 as having 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 based on NDI-NHANES publicly available linkages. The primary determination of mortality for eligible NHANES participants is based upon 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, NCHS' follow- up surveys (e.g., NHEFS), 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 (LMF) Data Dictionary.[35] Mortality status or vital status for participants was determined through NHANES-NDI linked file. Causes of death were harmonized to International Statistical Classification of Diseases, Injuries, and Causes of Death (ICD-10) guidelines.

Participant characteristics included variables that were selected based on a priori inclusion from NHANES questionnaires and plausible confounding on the relationship between obesity, allostatic load, and cancer mortality.[36] Socio-demographic 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 socio-economic 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. Poverty income ratio (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 less than 1 are considered below the official poverty line, whereas PIR values greater than 1 are above the poverty level.[37] PIR was attained at baseline interview for NHANES participants and reflects the changes in PIR during the three decades of the study. BMI was categorized into three categories: 1) combined underweight and healthy weight, BMI <24.9 kg/m^2; 2) overweight, BMI 25-29.9 kg/m^2; 3) obese, BMI >30 kg/m^2. Health behaviors were evaluated as they may influence total AL score in analysis, including self-reported smoking status, self-reported response to a physician-diagnosed history of congestive heart failure and heart attack. Congestive heart failure

and heart attack were considered confounders based on being prior 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, while participants with at least 100 cigarettes smoked in lifetime but no current smoke use were categorized as past smokers.[38] Participants with at least 100 lifetime cigarettes used and current smoking use 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 non-response bias.

Categorical variables were presented as weighted row percentages and continuous variables as mean and associated standard errors (SEs). 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. Additionally, 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 sub-distribution hazard ratios (SHR) and associated 95% confidence intervals (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 based on 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**), 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 present 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, USA) and Stata (version 17, StataCorp, 4905 Lakeway Drive College Station, Texas 77845 USA).

RESULTS

Table 1 displays 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 are more likely to be female (51.4% vs. 48.6%), older (mean age: 55.7 years vs. 36.1 years), identify as NH-Black (11.8% vs. 8.6%), and have a lower level of education attainment (some college or associates degree: 21.8% vs. 27.6%; college graduate: 19.9% vs. 28%), be a current smoker (34.3% vs 28.3%), have ever been diagnosed

with congestive heart failure (3% vs. 0.4%) when compared to those with low AL. Among participants with overweight BMI (25-29.9 kg/m^2), those with high AL are more likely to be male (57.9% vs. 42.1%), older (mean age: 54 years vs. 40.4 years), identify as NH-Black (12.8% vs 8.4%), and have a lower level of educational attainment (some college or associates degree: 22.4% vs. 28.6%; college graduate: 18.2% vs. 25.5%), be a current smoker (25.7% vs. 21,4%) when compared to those with low AL. Among participants with obese BMI (>30 kg/m^2), those with high AL are more likely to be older (mean age: 50.1 years vs. 40.3 years), identify as NH-White (70.1% vs. 66.2%), have a lower level of educational attainment (some college or associates degree: 26.7% vs. 31%; college graduate: 16.1% vs. 20.9%), be a current smoker (22% vs. 20.3%), or have ever been diagnosed with congestive heart failure (3.6% vs. 1.0%) when compared to 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**, **Figure 2**). For instance, among all NHANES participants those with high AL were 34% more likely to have a death attributed to cancer when compared to those with low AL (Model 1 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 (adjusted sub-distribution ratio (aSHR): 1.31, 95% CI: 1.05-1.63) when compared to all adults with low AL. The present study examined whether BMI modified the effects of high AL on cancer mortality, but observed non-significant 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) when compared to those with low AL, though 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) when compared to 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 to those with low AL in fully adjusted models.

DISCUSSION

In a diverse, nationally representative sample of US adults, the highest risk of cancer mortality was among adults with obese BMI (> 30 kg/m^2). The present study observed a 23% increased risk of cancer death among all NHANES adults with high AL compared to 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) with high AL compared to 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 on cancer risk for individuals experiencing high levels of cumulative stress and have 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 a 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%). The present study's population consisted of a large nationally representative sample of healthy community-dwelling participants aged 18+, while the REGARDS study was limited to those aged 45+ with oversampling for African Americans in the Southeastern US. In addition, this study provides a more detailed understanding on the moderating role of BMI as the statistical models accounted for BMI categorization at three levels (underweight and healthy weight, overweight, and obese) while *Akinyemiju* and colleagues dichotomized BMI at <25 kg/m^2. When comparing findings from *Acheampong et al.* to the findings of the present 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 Multi-Systemic Biological Risk (MBSR) score, a proxy to AL, were dependent on tertial distribution, while components of allostatic load 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 to the measure of body fat in clinical and public health settings. However, BMI is a measurement of access weight not body fat, and factors like 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 measurement of body fat. Additionally, the current analysis was unable to discern cancer incidence, as the NHANES data were linked with National Death Index data. Due to dataset limitations, risks for cancer-specific (i.e., breast, colorectal, lung) mortality was unable to be

determined. Lastly, 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 was 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 US population, allowing for the analytic sample to be representative of the US civilian population. The study at present 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), with 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 causal mechanism between cumulative stress and obesity related cancers.

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CONFLICTS OF INTEREST

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Table 1: Sociodemographic characteristics by allostatic load status, among 17,430 NHANES participants.

	Underweight and Healthy Weight BMI < 24.9 kg/m^2 N=6144	Underweight and Healthy Weight BMI < 24.9 kg/m^2 N=6144	Overweight BMI 25-29.9 kg/m^2 N=6101	Overweight BMI 25-29.9 kg/m^2 N=6101	Obese BMI > 30 kg/m^2 N=5185	Obese BMI > 30 kg/m^2 N=5185
Sociodemographics	**Low AL [a] (N= 4566)**	**High AL [a, b] (N= 1578)**	**Low AL [a] (N= 3415)**	**High AL [a, b] (N= 2686)**	**Low AL [a] (N= 2090)**	**High AL [a, b] (N= 3095)**
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	2392 (56.0)	759 (51.4)	1483 (40.3)	1152 (42.1)	1188 (52.9)	1718 (52.3)
Male	2174 (44.0)	819 (48.6)	1932 (59.7)	1534 (57.9)	902 (47.1)	1377 (47.7)
Mean Age 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	2139 (40.7)	124 (7.3)	1013 (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	2115 (74.2)	763 (73.1)	1430 (70.7)	1153 (71.6)	811 (66.2)	1236 (70.1)
Non-Hispanic Black	947 (8.6)	417 (11.8)	580 (8.4)	669 (12.8)	484 (13.7)	916 (15.7)
Latinx	1234 (8.7)	301 (5.4)	1284 (15.4)	777 (9.8)	732 (15.2)	860 (9.5)
Other & Mixed Race	270 (8.5)	97 (9.7)	121 (5.5)	87 (5.8)	63 (4.9)	83 (4.6)
Education						
< High school	1290 (16.5)	653 (26.9)	1074 (17.8)	1136 (27.3)	646 (21.1)	1207 (24.9)
High school/GED	1373 (27.7)	447 (31.1)	954 (28.0)	742 (32.0)	567 (26.9)	875 (32.3)
Some college or Associates degree	1040 (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 Federal Poverty Line						
1st quartile (0 – 1.11)	1067 (14.0)	371 (14.7)	737 (13.4)	599 (14.6)	502 (15.6)	737 (15.0)
2nd quartile (1.11 – 2.08)	982 (19.9)	388 (20.0)	756 (17.6)	649 (19.0)	468 (19.9)	729 (20.2)
3rd quartile (2.08 – 3.77)	1074 (27.2)	351 (25.1)	787 (25.2)	608 (25.6)	514 (28.4)	712 (26.0)
4th quartile (3.77 – 11.89)	1053 (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	1155 (28.3)	505 (34.3)	668 (21.4)	616 (25.7)	387 (20.3)	627 (22.0)
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 (standard error) or mean (standard error) for continuous variables. Estimated using sampling weights from National Health and Nutrition Examination Survey (NHANES).

[b] High Allostatic load is defined as total Allostatic load score greater than or equal to 3.

[c] Allostatic load total score was calculated as sum of components based on high-risk thresholds: albumin, C-reactive protein, creatinine clearance, diastolic blood pressure, glycated hemoglobin, systolic blood pressure, total cholesterol, triglycerides. Score range from 0 to 8.

Table 2: Fine & Gray proportional hazard models; association between allostatic load and cancer death.

Variable	No. Cancer Deaths (%) [a]	No. All-cause Deaths (%) [a]	Mean Survival Months (Standard Error)	Sub-Distribution Hazard Ratio and 95% Confidence Interval	Sub-Distribution Hazard Ratio and 95% Confidence Interval	Sub-Distribution Hazard Ratio and 95% Confidence Interval
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 (Referent)	1.00 (Referent)	1.00 (Referent)
High Allostatic Load	650 (7.6%)	2528 (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 (Referent)	1.00 (Referent)	1.00 (Referent)
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 Overweight Adults (BMI 25-29.9 kg/m^2)						
Low Allostatic Load	113 (2.8%)	321 (6.9%)	336.97 (0.85)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
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 Obese Adults (BMI > 30 kg/m^2)						
Low Allostatic Load	57 (2.4%)	189 (7.0%)	325.25 (1.05)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
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 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.

FIGURE TITLE AND FOOTNOTE

Figure 1

Title:
Figure 1: Flowchart of exclusion criteria and final study population of NHANES participants.

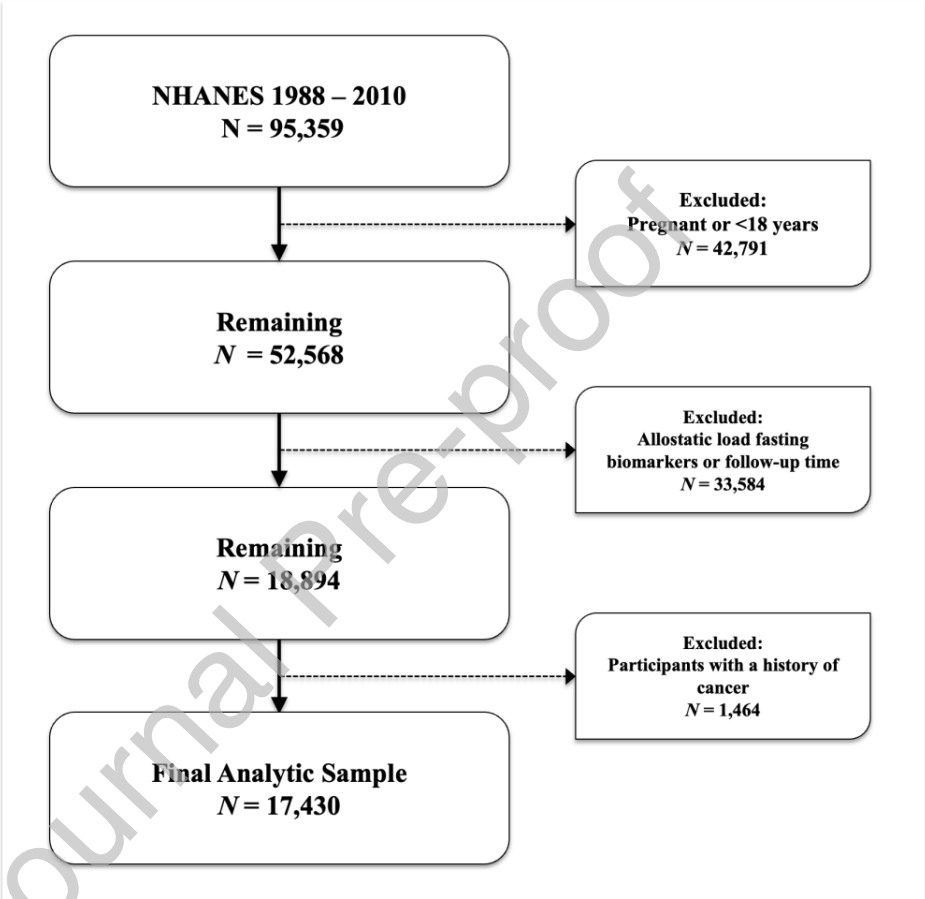
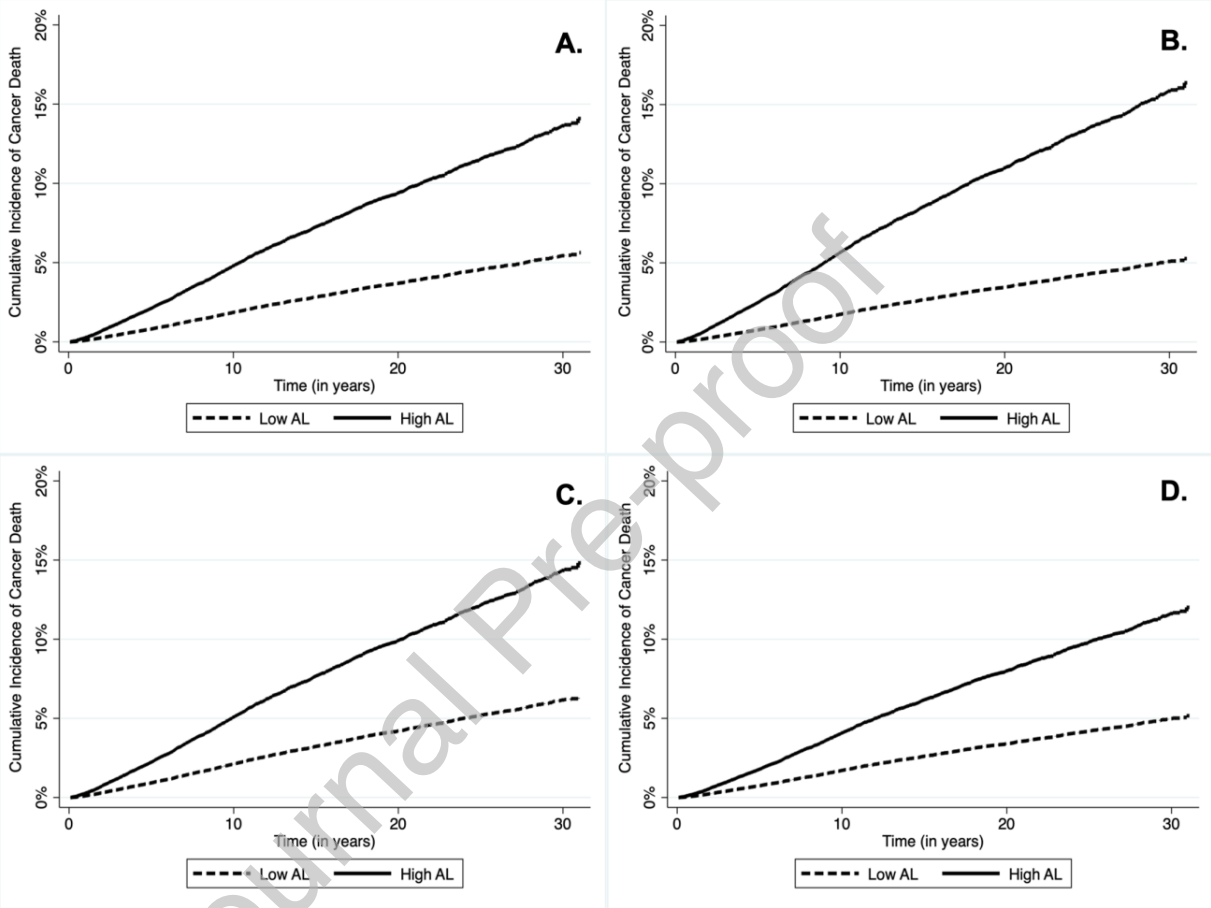


Figure 2

Title:

Figure 2: Cumulative incidence function plots for time to cancer death, comparing high versus low allostatic load groups.



Footnote:

A. Among all NHANES adults.

B. Among Underweight and Healthy weight adults (BMI < 24.9 kg/m2).

C. Among Overweight adults (BMI 25-29.9 kg/m2).

D. Among Obese adults (BMI >30 kg/m2).