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Relationship Between Mean Leucocyte Telomere Length and Measures of Allostatic Load in US Reproductive-Aged Women, NHANES 1999–2002

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Abstract

Background: Reproductive health disparities may be partly explained by the cumulative effects of chronic stress experienced by socially disadvantaged groups. Although, telomere length (TL) and allostatic load score have each been used as biological markers of stress, the relationship between these two measures is unknown.

Methods: We investigated the association between leucocyte TL and allostatic load score in 1503 non-pregnant women (20–44 years) participating in the National Health and Nutrition Examination Survey, 1999–2002. We constructed six different allostatic load scores using either quartile- or clinical-based cut-points for 14 biomarkers based on previously published methods. We estimated associations between TL and allostatic load scores and component biomarkers using linear regression, also assessing interactions by race/ethnicity.

Results: After adjustment for age, longer TL was associated with higher HDL cholesterol and lower C-reactive protein and creatinine clearance; TL was not associated with the other component biomarkers. Shorter TL was associated with higher allostatic load scores for the two clinical cut-point-based scores after adjustment for age, but not the four scores based on quartile cut-points. Significant interactions by race/ethnicity were observed for TL and HbA1c and triglycerides, but not for other component biomarkers or allostatic load scores.

Conclusions: Although TL and allostatic load score are both considered measures of cumulative stress, most component biomarkers and scores using quartile-based cut-points were not associated with TL. In reproductive-aged women, allostatic load scores using clinical-based cut-points were more strongly associated with TL compared with quartile-based scores.

Keywords

telomere length; allostatic load; health disparity; perinatal epidemiology

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Disclosure and conflict of interest

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In the US, non-Hispanic black women experience higher rates of preterm birth and low birthweight deliveries compared with non-Hispanic white women.[1] Premature 'weathering' refers to the hypothesis that cumulative, chronic stress resulting from socio-economic adversity can adversely affect physical health[2]; this construct has been hypothesised to contribute to the long-standing racial disparities in reproductive outcomes observed in the US.[2,3] Telomere length[4–8] and allostatic load scores[9–13] have each been used to measure premature weathering, but the relationship between these two measures has not yet been examined.

Telomeres are the protective DNA-protein complexes capping the end of chromosomes and naturally shorten with each cellular division, leading to genetic instability and eventually resulting in cellular senescence. Shorter telomeres are associated with both chronological ageing and increased mortality and morbidity independent of chronological age.[14] To date, telomere length (TL) has been related to a variety of factors including race, education, socioeconomic status, smoking, physical activity, diet, and stress – supporting the hypothesis that telomeres shorten in response to cumulative, chronic stress.[4–6,14–17] Recently, TL has also been shown to be associated with reproductive outcomes.[18–20]

Allostasis refers to an organism's dynamic physiologic response to the demands of a changing environment. 'Allostatic load' represents 'the wear and tear the body experiences when repeated allostatic responses are activated during stressful situations;'[9,11] like TL, allostatic load is often considered a biological effect of cumulative, chronic stress and is related to subsequent adverse health outcomes.[9–13] Allostatic load has been operationalised using a variety of score-based approaches with no gold standard.[9] The association between allostatic load score and various demographic factors and clinical conditions has been evaluated using the National Health and Nutrition Examination Study (NHANES) data in over 25 publications (Table S1).[21–26]

We examined the association between leucocyte TL and allostatic load scores in a national sample of non-pregnant reproductive-aged women using data from NHANES. We selected reproductive-aged women to represent the source population from which pregnancies, and therefore disparities in pregnancy outcomes, arise. Allostatic load was operationalised according to several previously used methods. Published analyses of NHANES data have shown higher allostatic load scores,[27] but longer TL,[16] in non-Hispanic blacks compared with non-Hispanic whites, which is an unexpected finding given allostatic load score and TL purport to measure the same phenomenon. One possible explanation for this might be an inconsistent relationship between allostatic load score and TL by race/ethnicity, which we investigated as part of our analysis.

Methods

Study population

NHANES is a cross-sectional, complex, multistage probability sampling survey conducted by the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS) designed to assess the health and nutritional status of non-institutionalised civilians living in the US.[28] During 1999–2002, 3569 women aged 20–49 were eligible for

the survey, 2935 (82%) were interviewed and 2771 (78%) participated in the examination component.[29] The NCHS Ethics Review Board at the CDC approved the NHANES data collection and no specific additional review was required for this analysis, which used data from public-use files.

Telomere length

Persons aged 20 and over at the time of the interview were asked to provide whole blood for DNA analysis. At the Division of Health Statistics Laboratory, CDC, DNA was extracted from specimens and stored at −80°C; purified DNA samples were then coded and shipped to an outside laboratory (Dr. Elizabeth Blackburn at the University of California, San Francisco) for analysis as part of a surplus specimen project.[16] The leucocyte telomere/standard (T/S) ratio was measured for each sample three times (in duplicate) using the quantitative polymerase chain reaction (PCR) method, resulting in six measurements which were used to calculate the mean and standard deviation of the T/S ratio for each participant.[15] The T/S ratio (also referred to as 'relative telomere length') is directly proportional to mean TL and will be referred to as 'telomere length' throughout this manuscript for ease of understanding.[30] The mean T/S ratio can be converted to number of base pairs using the following formula: 3274 + 2413 * (T/S ratio).[16]

Allostatic load

In addition to whole blood collection, the NHANES examination component consisted of physical measurements and serum and urine collection. Laboratory methods for biospecimen analysis have previously been described.[31,32] Approximately half of the participants were instructed to fast overnight before their examination appointment in order to ascertain fasting blood glucose and lipid levels.

Allostatic load has been operationalised in many different ways. Following previously published algorithms that have been applied to NHANES 1999–2002 data among reproductive-aged adults, we operationalised allostatic load scores in six different ways to examine whether associations with TL might differ according to the method of defining allostatic load. These six different scoring methods used either quartile-based[22,24,26,27,33,34] or clinical-based[25,35] cutpoints to categorise individuals as low risk (score of 0) or high risk (score of 1) for each of the component biomarkers included its score. These component scores were then summed across the included biomarkers to generate a total allostatic load score. All six methods of defining allostatic load scores were therefore count-based, though each was constructed using a different set of biomarkers and/or cut-points (see Table S2 for biomarkers and cut-points used in each allostatic load score). The total number of biomarkers measured across all of the previously published scoring methods was 14, though each score summed over a subset of 9 or 10 biomarkers.

High-risk quartile cut-points were determined from the weighted distribution of each of the following biomarkers in our analytic sample: C-reactive protein (CRP), mg/dL; serum albumin, g/dL; body mass index (BMI), kg/m^2; glycohaemoglobin (HbA1c), %; systolic blood pressure, mm Hg; diastolic blood pressure, mmHg; high-density lipoprotein (HDL) cholesterol, mg/dL; total cholesterol, mg/dL; triglyceride, mg/dL; homocysteine, μmol/L;

pulse, beats/min; serum creatinine, mg/dL; urine creatinine, mg/dL and creatinine clearance, mL/min (estimated using the Cockcroft-Gault equation).[36] For the following biomarkers, high-risk groups were also determined based on clinically significant or empirically defined cut-points:[25,35] CRP, serum albumin, BMI, HbA1c, systolic blood pressure, diastolic blood pressure, HDL, total cholesterol, and pulse.

Participants reporting medication use for diabetes, hypertension, or high cholesterol, were assigned to the high-risk group for HbA1c; systolic and diastolic blood pressure; and total cholesterol, respectively. Ten-point allostatic load scores were calculated by summing membership in high-risk groups with each biomarker equally weighted (possible range 0–10); prior to summation, 9-point scores were rescaled to 10-point scores for comparison purposes.[25,26,35] Allostatic load scores were only calculated for women with non-missing values for all component biomarkers for each score.

Participant characteristics

Participant characteristics examined included age, Hispanic origin and race, marital status, smoking history, educational attainment, and household income as a percentage of poverty level. Pregnancy status was ascertained by combining information from the interview with results from a spot urine pregnancy test.

Statistical analysis

We limited our analysis to women 20–44 years old who provided DNA specimens for TL measurement and who completed the examination component of the survey. Pregnant women were excluded from our analysis because many allostatic load biomarkers are affected by pregnancy.[24] For the comparisons of TL and allostatic load component biomarkers, women missing individual biomarkers were excluded from that biomarker's analysis but retained in other bio-marker analyses if information was available. All analyses accounted for the multistage, complex sampling design and used either the mobile examination centre weights or the fasting morning subsample weights (for analyses concerning triglycerides).[37] No adjustment was made for fasting, as recent evidence suggests fasting time shows little association with total cholesterol and HDL levels.[38]

Telomere length was log-transformed. We used unadjusted linear regression to calculate mean TL by characteristics of study participants and for component biomarkers (low-risk quartile, 25th to 75th percentile, high-risk quartile). We performed significance testing of the difference in mean TL between the highest and lowest risk quartiles for each component bio-marker. In addition, differences in mean TL were estimated per 1 or 10 unit increase (depending on the range of biomarker values) in each allostatic load bio-marker using linear regression. Similarly, we estimated the difference in TL per 1 unit increase in allostatic load score. All regression models were further adjusted for age, which is positively associated with higher allostatic load scores and shorter TL, by including continuous age (in years) as a covariate. Linear regression coefficients were exponentiated to calculate the percent change in TL on the original scale for ease of interpretation. All *P*-values for general linear *F* tests were determined using the Satterth-waite adjusted *F*-test.[39]

To assess differences in the relationship between TL and allostatic load biomarkers and scores by race/ethnicity, interaction terms for race/ethnicity (Mexican American, non-Hispanic white, non-Hispanic black) and allostatic load were added to regression models adjusted for age and race/ethnicity. We used the general linear Satterthwaite adjusted *F*-test to determine the significance of adding the interaction term to the model. To evaluate the effect of assigning high-risk group status based on medication use, we reran the models of TL and allostatic load scores after excluding women who had been assigned to high-risk groups based solely on their medication use. We also used multiple imputation to assign values to individual missing biomarkers so that allostatic load scores could be constructed for all women in our analysis; imputations used chained equations and predictive mean matching with demographics and non-missing biomarkers as predictor variables. Results using allostatic load scores based on these imputations were compared with the main results in a sensitivity analysis.

All analyses were conducted with SAS 9.3 (SAS Institute, Cary, NC, USA) and SAS-callable SUDAAN 11.0 (RTI International, Research Triangle Park, NC, USA).

Results

Study population

There were 2386 women between the ages of 20 and 44 years at the time of the interview who participated in NHANES 1999–2002 and took part in the examination component. Of those, 1954 (82%) had leucocyte TL measured, 451 of whom were excluded from our analysis (444 were pregnant and 7 were 45 years old at time of the exam), leaving 1503 in our analytical sample. Among those eligible for TL measurement, non-Hispanic white women were more likely than non-Hispanic black women to provide specimens (Table S3). No significant differences in provision of specimens for TL measurement were observed by age, marital status, smoking, education, and poverty level.

Telomere length

Geometric mean TL (reported as T/S ratio), was 1.12 (95% confidence interval (CI): 1.08, 1.16), which was equivalent to 6045 base pairs (95% CI 5951, 6139). After adjustment for age, mean TL varied by race/ethnicity and marital status (Table 1). Non-Hispanic black women had longer telomeres compared with non-Hispanic white and Mexican American women. Never married women had longer telomeres compared with married, living with partner, or no longer married (separated, divorced or widowed) women.

Allostatic load biomarkers

There were 37, 72, and 13 participants (not mutually exclusive) reporting medication use for diabetes, hypertension, or high cholesterol, respectively, who were subsequently assigned to the high-risk group for the corresponding biomarkers. In most of these instances (75/122), the women were already categorised in the high-risk group for the respective biomarker.

Telomere length and allostatic load biomarkers

Mean TL was shorter in the high-risk quartile compared with the low-risk quartile for CRP, BMI, and diastolic blood pressure (Table 2). After adjustment for age, mean TL was shorter in the high-risk quartiles for CRP and HDL. For the remaining biomarkers, there was no significant difference in TL between the high- and low-risk quartiles.

In models with component biomarkers as continuous linear variables, increases in BMI, HbA1c, systolic blood pressure, diastolic blood pressure, and total cholesterol were associated with shorter TL and an increase in HDL cholesterol was associated with longer TL (Table 3). However, all associations were null after adjustment for age except for HDL cholesterol, which showed a 1.2% longer TL ($\hat{\beta}$ (95% CI: 0.004, 0.020)) per 10 mg/dL increase and creatinine clearance, which gained significance showing a 0.4% shorter telomere length ($\hat{\beta}$ (95% CI: −0.008, 0.000)) per 10 mL/min increase. Interactions with race/ethnicity were significant for two biomarkers (Figure 1): HbA1c, which showed a negative relationship with TL for non-Hispanic whites compared with a flat slope for Mexican Americans and non-Hispanic blacks; and triglycerides, which showed a negative relationship with TL for non-Hispanic blacks compared with nearly flat slopes for non-Hispanic whites and Mexican Americans. For the remaining 12 biomarkers, differences in the relationship between TL and biomarker level were not observed among race/ethnicity groups.

Allostatic load scores

Clinical cut-points were generally more stringent than quartile-based cut-points, which resulted in lower average allostatic load scores for clinical-based scoring methods (scoring method 2: mean = 1.34 (95% CI:1.25, 1.43); scoring method 4: 1.74 (95% CI: 1.64, 1.85)) compared with quartile-based scores (scoring method 1: 2.52 (95% CI: 2.34, 2.70); scoring method 3: 2.55 (95% CI: 2.41, 2.68); scoring method 5: 2.54 (95% CI:2.42, 2.65); scoring method 6: 2.31 (95% CI: 2.20, 2.42)). The standard error was largest for scoring method 1, in part because this allostatic load score included triglycerides which were only available from the fasting morning subsample and reduced the number of observations by approximately half. The allostatic load scores based on clinical cut-points shared the same nine biomarkers (but not the same cut-points), which differed from the quartile-based cut-point scores by not including measures of creatinine, triglycerides, or homocysteine (Table S2). Mean allostatic load scores were higher for non-Hispanic black compared with white women for all scoring methods (range of difference: 0.58–0.89); and Mexican Americans had a lower mean allostatic load score compared to non-Hispanic white women for scoring method 5 (difference = −0.40 (95% CI: −0.63, −0.16)); no other differences in allostatic load score by race/ethnicity were observed.

Telomere length and allostatic load scores

With the exception of scoring method 1, higher allostatic load scores were significantly associated with shorter TL in the unadjusted analysis (Figure S1). After adjustment for age, only allostatic load scores based on clinical-based cut-points remained associated with TL (−1.3% for scoring method 2 and −1.2%, for scoring method 4) (Figure 2). Differences by

race/ethnicity for the relationships between TL and allostatic load score were not significant (all interaction term *P*-values >0.26).

After the exclusion of women with at least one high-risk grouping determined solely by medication use, the associations between TL and allostatic load became stronger for all allostatic load scores (all $\hat{\beta}$ were farther from zero). This exclusion resulted in three of the four quartile-based allostatic load scores (scoring methods 3, 5, 6) becoming significantly associated with shorter TL after adjustment for age. The estimated relationships between TL and allostatic load scores using imputed biomarkers were 0.1–0.2 percentage points stronger and estimated with greater precision compared to the main analysis (Figure S2).

Comment

Among a nationally representative sample of non-pregnant reproductive-aged women aged 20–44, leucocyte TL was not consistently associated with allostatic load scores that used quartile-based cut-points. However, allostatic load scores based on clinical-cut points, which often were more stringent than quartile-based cut-points, were inversely associated with TL after adjusting for age. For these allostatic load scores, we found that every 1 point increase was associated with an approximately 1.5% shorter TL. In terms of component biomarkers, longer TL was associated with higher levels of HDL cholesterol, lower CRP, and, unexpectedly, lower creatinine clearance. For the most part, the associations between TL and allostatic biomarker components and scores did not differ by race/ethnicity. Our findings suggest that epidemiologic analyses concerning mechanisms of reproductive health disparities should consider how allostatic load scores are operationalised and that scores using clinical cut-points were more strongly associated with TL in our study population of reproductive-aged women.

While no previous study has assessed the relationship between TL and allostatic load score, studies have described associations between TL and total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, and systolic and diastolic blood pressure.[14] Our study's finding of longer TL associated with higher HDL cholesterol after adjustment for age is in general agreement with one previous study,[40] although other studies have found null or negative associations.[14] Our finding of shorter TL associated with higher CRP is in-line with at least one previous study;[41] another study found no association in women.[42]

Several mechanisms have been proposed to explain how allostatic load and telomere shortening may be related. Epel suggested higher allostatic load leads to shorter telomeres via increased abdominal adiposity, inflammation, and oxidative stress.[8] Geronimus proposed that responses to repeated or prolonged stressors can increase allostatic load which, in turn, shortens TL via accelerated biological ageing.[43] Telomere length has also been recommended as bio-marker for inclusion in allostatic load score.[3] Our findings of inconsistent relationships between allo-static load biomarkers and scores and TL suggests further investigation of the relationship between these measures may be necessary.

Consistent with previous studies that have found allostatic load to be higher in black compared with white women[24,27,44], but shorter telomeres in whites as compared to blacks,

[14] we observed longer mean TL and higher mean allostatic load scores in black compared with white women. However, we found no statistically significant interactions by race/ethnicity. These patterns were therefore seemingly not the result of differing relationships between TL and allostatic load scores across race groups, but instead show differences by race in the distributions of these measures of cumulative, chronic stress. While differential rates of age-related telomere shortening by race could also contribute to these patterns, especially as new evidence suggests TL might be longer in blacks compared to whites at birth,[45] this cannot be explored using cross-sectional data.

This analysis has a few limitations. We compared TL with a limited set of previously used allostatic load-scoring methods which were originally constructed based on the biomarkers available in NHANES and included markers of secondary effects of primary stress mediators.[27] Primary mediators include cortisol, epinephrine, and other substances the body releases when stressed, but were not available in NHANES. Future research may consider whether an allostatic load score comprised of primary mediators of stress might have a stronger association with TL. Telomere length was measured using PCR, which is a method that is amenable to epidemiologic studies because it is faster and uses a smaller quantity of blood compared with Southern Blot. However, PCR methods may be inferior to Southern Blot because of high within person heterogeneity and no agreed-upon reference gene standard.[14] Non-Hispanic white women were more likely to provide DNA samples compared with non-Hispanic black women, which, although ostensibly corrected using non-response reweighting techniques, may have resulted in residual selection bias. However, we have no reason to believe that the relationship between telomeres and allostatic load was different for women who did and did not provide DNA samples. Finally, we evaluated the relationship between TL and allostatic load in non-pregnant reproductive-aged women; future research could explore the relationship between these measures of cumulative stress and adverse pregnancy outcomes. Studies could also consider the relationship between these two measures in other age groups and in men.

One strength of our study was that TL and biomarkers were from a large, nationally representative sample of US women. Most prior studies examining TL were based on smaller, less diverse samples. Additionally, our analysis was able to replicate the construction of allostatic load scores using several different scoring methods with the same data source; however, our analyses were not identical to the previous studies due to differences in the age of our study population and global analytic decisions about exclusion criteria and how missing biomarker data were handled. We also performed separate sensitivity analyses excluding women assigned to a high-risk biomarker group-based solely on medication use and multiply imputing missing biomarker values, which each resulted in slightly stronger associations between TL and allostatic load score. Though our original approach regarding medication use is generally preferred because medication use reflects previous exposure to high-risk levels of biomarkers, at least one study explicitly ignored medication use when determining high-risk status.[22] The results of our multiple imputation sensitivity analysis suggest that if all biomarker data were available our estimates of association would be 0.1–0.2 percentage points stronger per 1 unit increase in allostatic load score.

In conclusion, although TL and allostatic load score are both considered measures of cumulative, chronic stress, associations between these two measures were inconsistent in our study population of reproductive-aged women. While TL was not associated with most individual component biomarkers of the allostatic load scores we examined, some combination of biomarkers with clinically defined high-risk cut-points might be. Telomere length and allostatic load scores might also be measurements of different aspects of cumulative stress exposure. Epidemiologic analyses concerning mechanisms of reproductive health disparities should consider how best to opera-tionalised premature weathering given the variety of biological data available.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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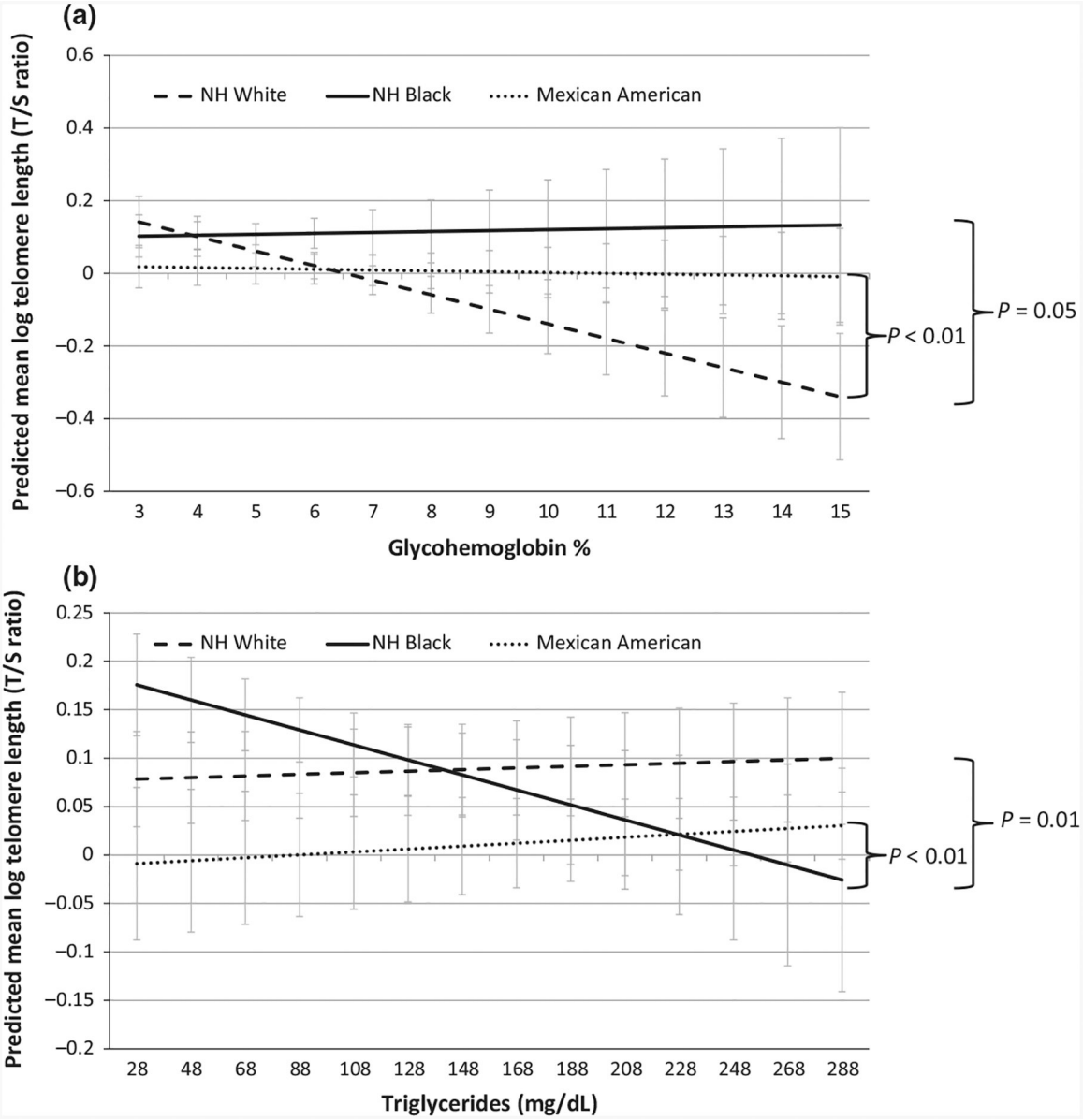

Figure 1.

Interactions in the linear relationship with mean log telomere length by race for glycohaemoglobin (a) and triglycerides (b). *P*-value for slopes from Wald test using linear regression model adjusted for age.

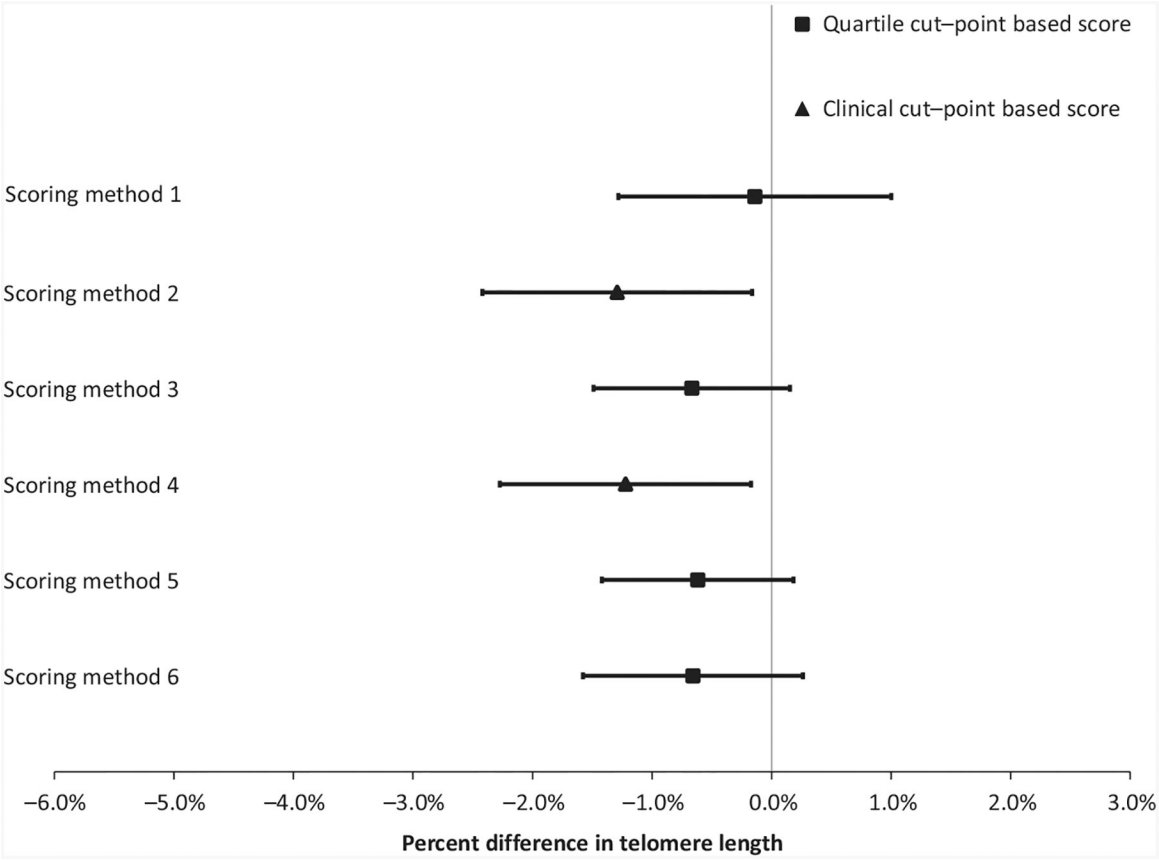

Figure 2.

Percent difference in mean telomere length per 1 unit increase in allostatic load score adjusted for age among non-pregnant reproductive-aged women (20–44 years old) in NHANES, 1999–2002. NHANES, National Health and Nutrition Examination Survey. Allostatic load scores were constructed using biomarkers and cut-point methods previously implemented. See text, Table S2 and reference list for details. *P*-value for slopes from Wald test using linear regression model adjusted for age. Of the 1503 observations with telomere data, the following biomarkers and number of observations were used for allostatic load score construction for each method: scoring method 1 – SBP, DBP, BMI, A1C, ALB, CRU, TRI, CRP, HOM, TC (n = 627); scoring method 2 – SBP, DBP, BMI, A1C, ALB, CRP, TC, HDL, PLS (n = 1417); scoring method 3 – SBP, DBP, BMI, A1C, ALB, CRP, HOM, TC, HDL, PLS (n = 1416); scoring method 4 – SBP, DBP, BMI, A1C, ALB, CRP, TC, HDL, PLS (n = 1417); scoring method 5 – SBP, DBP, A1C, ALB, CRS, CRP, HOM, TC, HDL, PLS (n = 1428); and scoring method 6 – SBP, DBP, BMI, A1C, ALB, CRC, CRP, TC, HDL (n = 1422). SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; A1C, glycosylated haemoglobin; ALB, serum albumin; TRI, triglycerides; CRP, C-reactive protein; HOM, homocysteine; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; PLS, pulse; CRU, urine creatinine; CRS, serum creatinine; CRC, creatinine clearance.

Table 1.

Characteristics of non-pregnant reproductive-aged women (20–44 years old) by mean telomere length in NHANES, 1999–2002

	n	Telomere length Mean[a] (95% CI)	Telomere length adjusted for age Mean[a] (95% CI)
All	1503		
Age			
20–24	286	1.20 (1.16,1.25)	NA
25–29	260	1.15 (1.10,1.21)	
30–34	290	1.11 (1.06,1.16)	
35–39	323	1.09 (1.04,1.13)	NA
40–44	344	1.08 (1.04,1.11)	NA
Hispanic origin and race			
Mexican American	416	1.07 (1.03,1.11)	1.06 (1.03,1.10)
Non-Hispanic white	643	1.11 (1.07,1.15)	1.11 (1.07,1.15)
Non-Hispanic black	308	1.17 (1.13,1.20)	1.17 (1.14,1.21)
Other[b]	136	1.17 (1.09,1.26)	1.16 (1.09,1.25)
Marital status[c]			
Married	728	1.10 (1.06,1.13)	1.11 (1.07,1.15)
Living with partner	125	1.09 (1.04,1.14)	1.08 (1.03,1.12)
Separated, divorced or widowed	212	1.07 (1.02,1.12)	1.08 (1.04,1.13)
Never married	379	1.19 (1.14,1.24)	1.16 (1.13,1.20)
Smoking[c,d]			
Current	369	1.10 (1.05,1.14)	1.10 (1.05,1.14)
Former	182	1.09 (1.05,1.13)	1.10 (1.07,1.14)
Never	950	1.14 (1.10,1.18)	1.14 (1.10,1.18)
Education[c]			
No high school diploma or GED	405	1.08 (1.03,1.13)	1.08 (1.03,1.13)
High school diploma or GED	352	1.11 (1.06,1.16)	1.11 (1.06,1.16)
Some college, no bachelor's degree	469	1.13 (1.09,1.18)	1.13 (1.10,1.17)
Bachelor's degree or higher	275	1.14 (1.10,1.18)	1.15 (1.11,1.19)

	n	Telomere length Mean[a] (95% CI)	Telomere length adjusted for age Mean[a] (95% CI)
Percentage of poverty level[c]			
Less than 100%	329	1.15 (1.08,1.22)	1.14 (1.07,1.20)
100–199%	340	1.10 (1.06,1.15)	1.09 (1.05,1.14)
200–399%	397	1.10 (1.06,1.14)	1.11 (1.07,1.15)
400% or more	324	1.12 (1.08,1.15)	1.13 (1.09,1.16)

NHANES, National Health and Nutrition Examination Survey; CI, confidence interval; GED, general educational development.

[a]Geometric mean of non-transformed telomere length (expressed as T/S ratio).

[b]Includes Hispanic or Latina women other than Mexican American and non-Hispanic women of races other than black or white, including multiracial women.

[c]Information on characteristics was missing for marital status ($n = 19$), smoking ($n = 2$), educational attainment ($n = 2$), and percentage of poverty level ($n = 113$).

[d]Current smoking includes any reported cigarette smoking at the time of interview. Former smoking includes no current cigarette smoking, but reported smoking at least 100 cigarettes over her lifetime.

Table 2.

Mean telomere length by quartile of allostatic load biomarkers among non-pregnant reproductive-aged women (20–44 years old) in NHANES, 1999–2002

Allostatic load biomarker	*n*	Range	Telomere length		
			Low-risk quartile Mean[b] (95% CI)	25th to 75th percentile Mean[b] (95% CI)	High-risk quartile[a] Mean[b] (95% CI)
Inflammatory markers					
C-reactive protein (mg/dL)	1503	0.01–16.3	1.16 (1.11,1.21)	1.12 (1.09,1.15)	1.09 (1.05,1.14)
Serum albumin (g/dL)	1502	3.0–5.3	1.10 (1.05,1.14)	1.13 (1.09,1.17)	1.11 (1.06,1.17)
Metabolic factors					
Body mass index (kg/m^2)	1480	15.2–66.4	1.14 (1.09,1.19)	1.12 (1.09,1.16)	1.09 (1.03,1.15)
Glycohaemoglobin: (%)	1501	3.8–14.3	1.13 (1.08,1.18)	1.12 (1.08,1.17)	1.10 (1.07,1.14)
Cardiovascular markers					
Systolic blood pressure (mmHg)	1431	73–198	1.13 (1.09,1.16)	1.12 (1.08,1.17)	1.09 (1.05,1.13)
Diastolic blood pressure (mmHg)	1431	10–110	1.15 (1.11,1.19)	1.11 (1.08,1.15)	1.09 (1.05,1.13)
High-density lipoprotein (mg/dL)	1503	8–160	1.13 (1.09,1.16)	1.13 (1.09,1.17)	1.10 (1.05,1.14)
Total cholesterol (mg/dL)	1503	97–337	1.15 (1.10,1.21)	1.11 (1.07,1.14)	1.11 (1.07,1.15)
Triglyceride (mg/dL)[c]	656	28–852	1.15 (1.10,1.20)	1.12 (1.07,1.19)	1.12 (1.06,1.18)
Homocysteine (μmol/L)[d]	1502	2.99–43.71	1.11 (1.07,1.15)	1.13 (1.10,1.17)	1.10 (1.06,1.15)
Pulse (beats/min)	1437	38–130	1.11 (1.07,1.15)	1.13 (1.08,1.17)	1.11 (1.07,1.15)
Other marker					
Serum creatinine (mg/dL)	1502	0.40–10.8	1.10 (1.06,1.15)	1.13 (1.09,1.18)	1.11 (1.08,1.15)
Urine creatinine (mg/dL)	1485	7–774	1.14 (1.10,1.18)	1.10 (1.07,1.14)	1.13 (1.06,1.22)
Creatinine clearance (mL/min)	1483	7.8–345.2	1.09 (1.04,1.14)	1.14 (1.10,1.18)	1.11 (1.06,1.15)

NHANES, National Health and Nutrition Examination Survey; CI, confidence interval.

[a]High-risk quartile was defined as >75th percentile based on the weighted distribution for women aged 20–44 years with both telomere and individual biomarker measurements for all biomarkers except serum albumin, high-density lipoprotein cholesterol, urine creatinine, and creatinine clearance where the highest risk quartile was defined as <25th percentile. For total cholesterol, systolic and diastolic blood pressure, and glycohaemoglobin, reports of medication use for controlling cholesterol, hypertension, and diabetes, respectively, were also used to determine the high-risk quartile.

[b]Geometric mean of original telomere length (expressed as T/S ratio).

[c]Triglycerides were measured in morning fasting subsample. Separate subsample weights were available to reweight this subsample to reflect national data.

[d] Homocysteine values from 1999–2000 were converted to 2001–2002 assay values using the following equation: new homocysteine = 10 * (0.983 * log10 (old homocysteine) + 0.0418). Reference: http://wwwn.cdc.gov/nchs/nhanes/2003-2004/L06MH_C.htm

Table 3.

Difference in mean log telomere length per 1 or 10 unit increase in allostatic load biomarker

Allostatic load biomarker	Unadjusted $\hat{\beta}$ (95% CI)	Adjusted for age $\hat{\beta}$ (95% CI)
Inflammatory markers		
C-reactive protein (mg/dL)	−0.012 (−0.040, 0.015)	−0.009 (−0.037, 0.019)
Serum albumin (g/dL)	−0.003 (−0.072, 0.065)	−0.012 (−0.082, 0.057)
Metabolic factors		
Body mass index (kg/m^2)	−0.003 (−0.005, 0.000)	−0.002 (−0.005, 0.000)
Glycohaemoglobin (%)	−0.021 (−0.037, −0.005)	−0.014 (−0.031, 0.002)
Cardiovascular markers		
Systolic blood pressure (mmHg)[a]	−0.011 (−0.020, −0.002)	−0.005 (−0.014, 0.004)
Diastolic blood pressure (mmHg)[a]	−0.019 (−0.032, −0.007)	−0.010 (−0.023, 0.003)
High-density lipoprotein (mg/dL)[a]	0.008 (0.000, 0.016)	0.012 (0.004, 0.020)
Total cholesterol (mg/dL)[a]	−0.004 (−0.008, −0.001)	−0.002 (−0.005, 0.002)
Triglyceride (mg/dL)[ab]	−0.001 (−0.003, 0.001)	0.000 (−0.002, 0.002)
Homocysteine (μmol/L)[ac]	−0.003 (−0.060, 0.054)	0.016 (−0.039, 0.071)
Pulse (beats/min)[a]	−0.005 (−0.019, 0.010)	−0.008 (−0.022, 0.006)
Other marker		
Serum creatinine (mg/dL)	0.014 (−0.027, 0.055)	0.020 (−0.022, 0.062)
Urine creatinine (mg/dL)[a]	0.000 (−0.003, 0.003)	−0.001 (−0.004, 0.003)
Creatinine clearance (mL/min)[a]	−0.003 (−0.007, 0.001)	−0.004 (−0.008, 0.000)

Beta coefficients and 95% confidence interval from simple or multiple (included continuous age as covariate) linear regression with log-transformed telomere length as the dependent variable.

CI, confidence interval.

[a]Per 10 unit increase in biomarker.

[b]Triglycerides were measured in morning fasting subsample. Separate subsample weights were available to reweight this subsample to reflect national data.

[c]Homocysteine values from 1999–2000 were converted to 2001–2002 assay values using the following equation: new homocysteine = 10 * (0.983 * $\log_{10}$ (old homocysteine) + 0.0418). Reference: http://wwwn.cdc.gov/nchs/nhanes/2003-2004/L06MH_C.htm.