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Original Contribution

Diet Quality Indices and Leukocyte Telomere Length Among Healthy US Adults: Data From the National Health and Nutrition Examination Survey, 1999–2002

Cindy W. Leung*, Teresa T. Fung, Claire T. McEvoy, Jue Lin, and Elissa S. Epel

* Correspondence to Dr. Cindy Leung, Department of Nutritional Sciences, School of Public Health, University of Michigan, 1415 Washington Heights, SPH I, Ann Arbor, MI 48104 (e-mail: cindyleung@post.harvard.edu).

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Aging is the biggest risk factor for the development of chronic diseases. Telomere length may represent one important mechanism by which dietary intake influences risk of age-related diseases; however, it is unknown which diet pattern is most strongly related to telomere length. We compared the relationships between 4 evidence-based diet quality indices and leukocyte telomere length in a nationally representative sample of healthy adults, and the extent to which these associations differed between men and women. Data on 4,758 adults aged 20–65 years with no prior diagnosis of major chronic disease were obtained from the 1999–2002 cycles of the National Health and Nutrition Examination Survey. Diet was assessed using one 24-hour dietary recall. After adjustment for sociodemographic and health characteristics, comparison of the top and bottom quintiles showed that higher Healthy Eating Index 2010 scores ($\beta = 0.065$, 95% confidence interval (CI): 0.018, 0.112; P-trend = 0.007), Alternate Healthy Eating Index 2010 scores ($\beta = 0.054$, 95% CI: 0.010, 0.097; P-trend = 0.007), Mediterranean Diet scores ($\beta = 0.058$, 95% CI: 0.017, 0.098; P-trend = 0.008), and Dietary Approaches to Stop Hypertension (DASH) scores ($\beta = 0.052$, 95% CI: 0.014, 0.090; P-trend = 0.007) were each associated with longer telomere length in women. These results may provide insight into the complex associations between optimal nutrition and longevity. Further investigation is needed to understand why associations were not observed in men.

Alternate Healthy Eating Index; cellular aging; diet patterns; Dietary Approaches to Stop Hypertension score; Healthy Eating Index; leukocyte telomere length; Mediterranean Diet score

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010; BMI, body mass index; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; LTL, leukocyte telomere length; MedDiet, Mediterranean Diet; NHANES, National Health and Nutrition Examination Survey; SD, standard deviation; T/S, telomere to single copy gene.

Telomeres are the DNA-protein caps at the end of eukaryotic chromosomes that promote chromosomal stability and protect the genomic DNA from damage (1). Telomere length naturally shortens with each cell cycle. When telomere length reaches a critical short length, the cell is no longer able to divide and reaches senescence, a mechanism that may underlie age-related disease processes (2, 3). While chronological age is among the strongest predictors of telomere length, studies have recently shown that telomere length is also sensitive to lifestyle behaviors like physical activity (4), smoking (5), and dietary intake (6). Telomere length has also been inversely related to risk of cardiovascular disease, type 2 diabetes, and some cancers (7–11).

Many studies have examined dietary intake in relation to telomere length, but across studies there is little agreement as to specific foods, food groups, or nutrients that are beneficial or harmful for telomere length (6). The lack of consistency in findings may be partly due to the fact that foods are consumed not in isolation but with complementary foods and nutrients that can have synergistic and larger effects on health outcomes (12). Diet pattern analysis captures the cumulative effects of foods and nutrients consumed in one's diet, viewing these dietary components as an integrated system rather than as individual factors. To date, there have been 7 studies examining the associations between diet quality indices and telomere length. Three of these studies used empirically derived diet patterns, often termed the "prudent pattern" and the "Western pattern," which organize foods commonly consumed together in the analytical population (13–15). A diet characterized by high intakes of fruits, vegetables, whole grains, fish, poultry, and legumes, labeled the "prudent" pattern, was positively associated with telomere length in a study of middle-aged and older South Koreans (14), marginally associated with telomere length in a study of healthy US women (13), and not associated with telomere length in a racially/ethnically diverse group of US adults (15). In contrast, the "Western" pattern, which is characterized by intakes of refined grains, white potatoes, red and processed meats, and high-fat dairy foods, was not associated with telomere length in any of these studies. Other studies of telomere length have examined diet quality indices using evidence-based dietary guidelines. Two studies have observed positive associations between high adherence to the Mediterranean diet and telomere length, including a small study of elderly adults in Italy (16) and a large study of female nurses in the United States (13).

To date, the Mediterranean diet and diet quality scores have been frequently studied in relation to risk of major chronic disease (17–20). However, to our knowledge, only 1 study has compared multiple diet quality indices with telomere length in the same study (13). Thus, our objective in this study was to examine the associations of diet quality scores with leukocyte telomere length (LTL) in a large and nationally representative sample of healthy men and women. Four evidence-based diet scores were examined: Healthy Eating Index 2010 (HEI-2010), Alternate Healthy Eating Index 2010 (AHEI-2010), the Mediterranean Diet (MedDiet) score, and the Dietary Approaches to Stop Hypertension (DASH) score. We hypothesized that healthful diet quality, as determined by each of these measures, would be positively associated with LTL.

METHODS

Study population

The National Health and Nutrition Examination Survey (NHANES) is an ongoing, multistage survey representative of the civilian, noninstitutionalized US population that is administered by the National Center for Health Statistics. The analytical population for the current study was comprised of 4,758 healthy adults aged 20–65 years who had complete dietary and LTL data measured in the 1999–2002 cycles of NHANES. The NHANES response rates for these years ranged from 69% to 81%. Adults with a prior diagnosis of coronary heart disease, angina, myocardial infarction, stroke, diabetes, congestive heart failure, and cancer were excluded ($n = 826$), as these conditions are known to influence both health behaviors and telomere length.

Dietary assessment

Dietary intake was assessed using a single 24-hour dietary recall in the NHANES Mobile Examination Center (21). Persons without dietary data ($n = 214$) or with implausible total energy intakes (<500 kcal/day or >5,000 kcal/day) ($n = 134$) were excluded from analysis. Data from the US Department of Agriculture MyPyramid Equivalents Database, version 1.0 (22), and the NHANES dietary interview files (21) were used to calculate all diet pattern scores. The validity of the 24-hour recall method has been previously discussed (23, 24).

For all diet quality indices, higher scores indicate a more healthful diet pattern. The HEI-2010 is a measure of diet quality that assesses adherence to the 2010 Dietary Guidelines for Americans (25), developed by the US Department of Agriculture's Center for Nutrition Policy and Promotion. It is scored out of 100 points and assesses consumption of the following dietary components: total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy foods, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, and empty calories (26). Higher scores for these components reflect higher intakes, with the exceptions of refined grains, sodium, and empty calories. The AHEI-2010 was developed at the Harvard School of Public Health as a measure of diet quality inversely related to chronic disease risk (17). It is scored out of 110 points. Maximum scores are awarded for high intakes of vegetables, fruits, whole grains, nuts and legumes, long-chain fats, and polyunsaturated fats; moderate alcohol intake; and minimal intakes of sugar-sweetened beverages and fruit juice, red/processed meats, *trans-* fat, and sodium. In the current analysis, the AHEI-2010 was modified by excluding *trans-* fat, for which data were unavailable in NHANES, and the overall score was rescaled to the original total. The MedDiet score measures adherence to the traditional Mediterranean diet and was adapted for the US diet (27). Out of 55 points, scores are awarded for high consumption of whole grains, fruits, vegetables, potatoes, legumes, fish, and monounsaturated fats; moderate consumption of alcohol; and low consumption of red meat, poultry, and full-fat dairy products. The MedDiet index was originally developed for a Greek population but has been previously used in studies of US adults (28–30). The DASH score is a diet pattern associated with improved blood pressure in healthy and hypertensive adults (31). It includes components for fruits, vegetables, nuts and legumes, whole grains, low-fat dairy foods, sodium, red and processed meats, and sugary beverages, and is scored out of 40 points. Higher intakes of all components, except for sodium, red and processed meats, and sugary beverages, are awarded higher scores. While scoring for HEI-2010, AHEI-2010, and the MedDiet index are based on concrete guidelines, scoring for the DASH score is based on relative distributions from the analytical sample. In this analysis, sex-specific cutpoints were derived from the study population to estimate each of the DASH components.

Leukocyte telomere length

LTL was assayed from DNA samples purified from whole blood, collected from adult NHANES participants in the 1999–2002 waves. LTL was assayed using the quantitative polymerase chain reaction method to measure telomere length relative to standard reference DNA (telomere to single copy gene (T/S) ratio) at the University of California, San Francisco (32). Procedures were implemented to exclude outliers (<2% of samples) and ensure the validity of the assays. The procedures have been described in detail elsewhere (33). The interassay coefficient of variation was 6.5%.

Covariate assessment

Sociodemographic characteristics included in multivariate models included participant's age (in 5-year increments), sex, self-reported race/ethnicity, highest educational attainment, poverty income ratio, and marital status. Health-related variables included alcohol consumption (nondrinker, moderate drinker (≤1 drink/day for women or ≤2 drinks/day for men), or heavy drinker (>1 drink/day for women or >2 drinks/day for men)), smoking status, pack-years of smoking, physical activity (any vigorous or moderate physical activity or muscle-strengthening activities in the past 30 days), self-reported change in physical activity over the past year, and total energy intake (kcal/day; log-transformed). Anthropometric measures of adiposity included body mass index (BMI; weight (kg)/height $(m)^2$) and waist circumference (cm). Height, weight, and waist circumference were measured by trained personnel in the NHANES Mobile Examination Center. BMI categories were defined as underweight (BMI <18.5), normal-weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), and obese (BMI ≥30.0). Elevated waist circumference was defined as ≥102 cm for men ≥88 cm for women.

Missing-data indicators were used to account for missing educational attainment ($n = 6$), family income ($n = 373$), marital status ($n = 239$), alcohol consumption ($n = 7$), physical activity ($n = 3$), smoking status ($n = 7$), BMI ($n = 56$), and waist circumference ($n = 82$). A complete-case analysis was also conducted as a sensitivity analysis.

Statistical analysis

NHANES complex survey weights were used to account for unequal selection probabilities and patterns of nonresponse and to obtain nationally representative estimates (34). All analyses incorporated the 4-year dietary survey weights for the 1999–2002 period. Because the 4 diet quality indices contained similar components, correlations between the indices were estimated using Pearson correlation coefficients. LTL data were skewed and log-transformed prior to analysis. The first set of analyses examined quintiles of diet pattern indices in relation to LTL, in order to allow for nonlinear associations. Tests for linear trend were conducted by including the midpoint of each quintile of diet quality index as a trend variable. The second set of analyses examined standardized diet quality indices in relation to LTL, to allow a more appropriate comparison across the 4 scores. Separate models were examined for men and women in the analyses. Heterogeneity by sex was determined using a Wald test of the cross-product term for interaction between sex and the diet quality indices. All models adjusted for sociodemographic and health characteristics. Further adjustment for BMI and waist circumference was conducted as a sensitivity analysis, since these anthropometric measures of adiposity could serve as mediators rather than confounders. Supplemental analyses were conducted by examining individual components of diet quality indices in relation to LTL.

The conversion from the T/S ratio to base pairs was calculated based on comparison of telomeric restriction fragment length from Southern blot analysis and T/S ratios using DNA samples from the human diploid fibroblast cell line IMR90 at different population doublings. The formula used to convert the T/S ratio to base pairs was $3{,}274 + 2{,}413 \times (T/S)$.

All statistical tests were 2-sided, and statistical significance was considered to be present at $P < 0.05$. Statistical analyses were performed using SAS 9.3 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

In the analytical sample, the mean HEI-2010 score was 46.3 (out of 100); the mean AHEI-2010 score was 37.0 (out of 110); the mean MedDiet score was 21.0 (out of 55); and the mean DASH score was 23.9 (out of 40). Pearson correlation coefficients for correlations between the 4 dietary patterns ranged from 0.56 to 0.73, with the lowest correlation being that between HEI-2010 and MedDiet and the highest being that between AHEI-2010 and DASH. Sociodemographic and health characteristics of the study participants are shown in Table 1. In bivariate analyses, being of Hispanic ethnicity, having higher educational attainment, being married or living with a partner, having a higher household income, moderate alcohol intake, and being a former smoker were positively associated with higher mean scores on all 4 diet indices.

Associations between quintiles of diet quality scores and log-transformed LTL are shown in Table 2. Among women, a comparison of the top and bottom quintiles showed that higher HEI-2010 scores ($\beta = 0.065$, 95% confidence interval (CI): 0.018, 0.112; P-trend $= 0.007$), AHEI-2010 scores ($\beta = 0.054$, 95% CI: 0.010, 0.097; P-trend $= 0.007$), MedDiet scores ($\beta = 0.058$, 95% CI: 0.017, 0.098; P-trend $= 0.008$), and DASH scores ($\beta = 0.052$, 95% CI: 0.014, 0.090; P-trend $= 0.007$) were each significantly associated with longer LTL, after adjustment for sociodemographic and health characteristics (Table 2, Figure 1). Among men, there were no significant associations when comparing the top and bottom quintiles of any diet quality scores with LTL, though there was marginal evidence of a linear trend with DASH scores and longer LTL (P-trend $= 0.06$).

We further examined diet quality z scores in relation to log-transformed LTL in Table 3. Among women, 1–standard-deviation (1-SD) increases in HEI-2010 scores ($\beta = 0.024$, 95% CI: 0.008, 0.039), AHEI-2010 scores ($\beta = 0.019$, 95% CI: 0.007, 0.031), MedDiet scores ($\beta = 0.020$, 95% CI: 0.008, 0.033), and DASH scores ($\beta = 0.019$, 95% CI: 0.003, 0.035) were each associated with longer LTL. Further inclusion of BMI and waist circumference in the models did not change these effect estimates, and results obtained via the missingness indicator method for missing data were identical to those from the complete-case analysis (data not shown). When pairs of HEI-2010, AHEI-2010, MedDiet, and DASH z scores were included in the models together, estimates were attenuated (data not shown). No diet quality z scores were associated with LTL among men. Using the age-associated rate of telomere shortening of 14.6 base pairs per year in this sample, a 1-SD increase in the HEI-2010 score corresponded to 3.9 additional years of aging, a 1-SD increase in the AHEI-2010 score to 3.2 additional years of aging, a 1-SD increase in the MedDiet score to 3.3 additional years of aging, and a 1-SD increase in the DASH score to 3.2 additional years of aging.

Individual components of the HEI-2010 and MedDiet scores were examined in relation to log-transformed LTL (see Web Tables 1 and 2, available at https://academic.oup.com/aje). The HEI-2010 and MedDiet indices were selected for these analyses because their associations with LTL were largest in magnitude

Table 1. Mean Leukocyte Telomere Length and Diet Quality Index Scores According to Characteristics of Study Participants, National Health and Nutrition Examination Survey, 1999–2002

Characteristic	No. (Weighted %)	Mean (SE) LTL, T/S ratio[a]	Mean (SE) Diet Quality Index Score			
			HEI-2010	AHEI-2010	MedDiet	DASH
Age, years[b]	39.5 (0.3)	1.10 (0.02)	46.3 (0.5)	37.0 (0.3)	21.0 (0.1)	23.9 (0.2)
Sex						
Male	2,208 (49.0)	1.09 (0.02)	46.0 (0.5)	35.1 (0.4)[c]	20.4 (0.1)[c]	24.4 (0.2)[c]
Female	2,550 (51.0)	1.10 (0.02)	46.6 (0.7)	38.8 (0.4)	21.5 (0.2)	23.4 (0.2)
Race/ethnicity						
Non-Hispanic white	2,239 (71.2)	1.09 (0.02)	46.3 (0.7)[c]	37.1 (0.4)[c]	21.0 (0.2)[c]	24.1 (0.2)[c]
Non-Hispanic black	814 (9.6)	1.15 (0.02)	43.9 (0.8)	34.8 (0.5)	19.9 (0.2)	22.4 (0.2)
Hispanic	1,544 (15.1)	1.09 (0.02)	48.1 (0.7)	37.7 (0.6)	21.5 (0.2)	24.0 (0.2)
Other	161 (4.1)	1.07 (0.03)	46.2 (1.5)	36.2 (1.6)	21.0 (0.5)	23.5 (0.4)
Education						
Less than high school graduate	1,378 (17.5)	1.07 (0.02)	43.0 (0.6)[c]	35.2 (0.6)[c]	20.2 (0.2)[c]	22.8 (0.2)[c]
High school or equivalent	1,088 (24.8)	1.09 (0.02)	43.5 (0.6)	34.3 (0.7)	20.0 (0.2)	22.7 (0.2)
Some college	1,293 (30.5)	1.11 (0.02)	45.7 (0.6)	36.1 (0.4)	20.8 (0.2)	23.6 (0.2)
College graduate	993 (27.0)	1.12 (0.02)	51.7 (0.7)	41.6 (0.7)	22.6 (0.3)	26.0 (0.2)
Marital status						
Single	911 (19.6)	1.18 (0.02)	43.5 (0.8)[c]	33.9 (0.7)[c]	19.9 (0.3)[c]	23.1 (0.2)[c]
Married or living with partner	2,979 (61.2)	1.08 (0.02)	47.4 (0.6)	38.0 (0.4)	21.4 (0.2)	24.3 (0.2)
Separated, widowed, or divorced	629 (13.1)	1.04 (0.02)	45.3 (1.0)	37.0 (0.7)	20.7 (0.3)	23.4 (0.3)
Poverty income ratio[d]						
≤100.0	777 (12.6)	1.14 (0.02)	43.2 (1.0)[c]	35.2 (1.0)[c]	20.4 (0.3)[c]	22.9 (0.3)[c]
100.1–200.0	994 (16.7)	1.08 (0.02)	42.4 (0.8)	33.8 (0.7)	19.6 (0.2)	22.4 (0.3)
200.1–300.0	694 (14.0)	1.10 (0.02)	46.0 (0.9)	35.2 (0.8)	20.6 (0.3)	23.3 (0.2)
300.1–400.0	556 (13.2)	1.11 (0.03)	46.4 (0.7)	36.7 (0.6)	20.9 (0.3)	23.9 (0.3)
>400.0	1,364 (36.7)	1.08 (0.02)	49.0 (0.7)	39.9 (0.5)	22.0 (0.2)	25.2 (0.2)

Table continues

for women. For the HEI-2010 score, a higher "empty calories" score (reflecting lower consumption of empty calories) was associated with longer LTL in women. For the MedDiet index, whole-fat dairy food and alcohol scores (reflecting lower consumption of whole-fat dairy foods and moderate alcohol consumption) were associated with longer LTL in women.

DISCUSSION

In this national sample of 4,758 healthy, nonelderly adults, we examined 4 evidence-based diet quality indices in relation to LTL. Our results showed that HEI-2010, AHEI-2010, MedDiet, and DASH scores were each positively associated with LTL in women, roughly equivalent to 3.2–3.9 additional years of aging for every 1-SD score increase on these diet quality indices. The magnitudes of these associations are comparable to those in other studies of dietary intake and cellular aging: 4.5 additional years for a 33% increase in the Alternate Mediterranean Diet score (13), 4 fewer years for each additional serving of processed meat consumed (35), and 4.6 fewer years of aging for each additional 20-ounce (0.6-L) bottle of sugared soda consumed (36). These magnitudes are also similar to analyses of other lifestyle behaviors and cellular aging, such as smoking (4.6 fewer years) (5). and physical activity (4.4 additional years) (4). When pairs of indices were examined together in the same model, the effect sizes were attenuated, indicating that their associations were not different from each other. These results corroborate those of a prior study that found positive associations between Mediterranean diet adherence and (to a lesser extent) AHEI-2010 scores and longer telomere length in US women (13).

When individual components of the diet quality indices were examined, only 1 component of the HEI-2010 score—empty calories—was associated with LTL in women. This suggests that there may be synergistic effects of the other dietary components driving the positive association between HEI-2010 scores and LTL. For the MedDiet score, lower intake of whole-fat dairy foods and moderate alcohol consumption were both associated with LTL, which suggests that these components may be driving the positive association between MedDiet score and LTL. However, we caution against placing too much focus on 1 individual dietary component in this analysis, as examining foods in isolation could potentially ignore the synergistic effects of foods commonly consumed together. Overall, our findings

Table 1. Continued

Characteristic	No. (Weighted %)	Mean (SE) LTL, T/S ratio[a]	Mean (SE) Diet Quality Index Score			
			HEI-2010	AHEI-2010	MedDiet	DASH
Alcohol intake[e]						
Never drinker	277 (4.8)	1.11 (0.03)	44.5 (1.4)[c]	35.3 (1.2)[c]	20.8 (0.6)[c]	23.0 (0.3)[c]
Moderate drinker	2,656 (55.5)	1.09 (0.02)	47.8 (0.6)	38.8 (0.4)	21.5 (0.2)	24.6 (0.2)
Heavy drinker	1,818 (39.6)	1.11 (0.02)	44.5 (0.7)	34.7 (0.5)	20.3 (0.2)	23.0 (0.2)
Smoking status						
Never smoker	2,582 (52.4)	1.11 (0.02)	47.7 (0.6[c]	38.4 (0.4)[c]	21.6 (0.2)[c]	24.3 (0.2)[c]
Former smoker	987 (21.3)	1.06 (0.02)	49.4 (0.7	39.5 (0.6)	21.7 (0.3)	25.0 (0.2)
Current smoker	1,182 (26.2)	1.10 (0.02)	41.0 (0.6	32.2 (0.4)	19.1 (0.2)	22.1 (0.2)
Physical activity						
No activity	1,730 (27.8)	1.11 (0.02)	43.6 (0.6)[c]	35.6 (0.6)[c]	20.2 (0.2)[c]	22.9 (0.2)[c]
Any activity[f]	3,025 (72.1)	1.07 (0.01)	47.3 (0.6)	37.5 (0.3)	21.3 (0.2)	24.2 (0.2)
Body mass index[g] category						
Underweight (<18.5)	70 (1.9)	1.14 (0.04)	44.1 (2.1)[c]	33.1 (1.7)	20.1 (0.8)	23.2 (0.7)[c]
Normal-weight (18.5–24.9)	1,487 (34.6)	1.13 (0.02)	48.0 (0.8)	37.7 (0.6)	21.2 (0.3)	24.0 (0.3)
Overweight (≥25.0)	1,685 (34.0)	1.08 (0.02)	46.7 (0.6)	36.9 (0.4)	20.9 (0.2)	24.2 (0.2)
Obese (≥30.0)	1,460 (28.3)	1.07 (0.02)	44.1 (0.6)	36.5 (0.5)	20.8 (0.2)	23.3 (0.2)
Waist circumference						
Normal	2,414 (55.0)	1.12 (0.02)	47.2 (0.6)[c]	36.9 (0.4)	21.0 (0.2)[c]	24.1 (0.2)
Elevated[h]	2,262 (43.5)	1.06 (0.02)	45.3 (0.7)	37.1 (0.5)	20.9 (0.2)	23.5 (0.2)

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; LTL, leukocyte telomere length; MedDiet, Mediterranean Diet; SE, standard error.

[a] Telomere to single copy gene (T/S) ratio.

[b] Values are presented as mean (SE).

[c] Significant difference in diet quality within category levels ($P < 0.05$).

[d] Household income as a percentage of the federal poverty level.

[e] Moderate alcohol consumption was defined as ≤1 drink/day for women or ≤2 drinks/day for men. Heavy alcohol consumption was defined as >1 drink/day for women or >2 drinks/day for men.

[f] Any vigorous or moderate physical activity or muscle-strengthening activities in the past 30 days.

[g] Weight (kg)/height (m)^2.

[h] Elevated waist circumference was defined as ≥102 cm for men ≥88 cm for women.

suggest that the protective associations with LTL extend to a general healthful diet pattern high in fruits, vegetables, whole grains, dairy products, and plant-based proteins and low in red and processed meats, sodium, and added sugars, and that consuming these foods in combination is related to healthy cellular aging among women.

High scores on the HEI-2010, AHEI-2010, MedDiet, and DASH indices have been consistently shown to reduce the risk of major chronic disease, including risk of type 2 diabetes (17, 19, 37), cardiovascular disease (17), cancer (17), and all-cause, cardiovascular disease, and cancer mortality (18). The fact that these 4 evidence-based diet quality indices are all predictive of lower chronic disease risk may be expected given their shared components; however, the correlations between scores in the present study ranged from 0.56 to 0.73. Other qualitative differences between the 4 indices include the fact that the HEI-2010 awards points for consuming any type of protein, including red and processed meats, whereas the others prioritize plant-based protein sources (e.g., nuts, legumes) and fish. The HEI-2010 also awards points for consuming any dairy product, but full-fat dairy food is penalized in the MedDiet index and only low-fat dairy food is awarded points in the DASH index. In contrast, the AHEI-2010 and MedDiet are the only indices to award points for moderate alcohol consumption. Regardless of these differences, high scores on all diet quality indices were associated with longer LTL in women, suggesting that LTL maintenance may represent an additional mechanism by which high diet quality is protective against major chronic disease and mortality in women (20).

The relationships between multiple healthful diet quality indices and LTL were significantly different between men and women. Although the mechanisms underlying the associations between diet and LTL are unknown, the differential sex-specific associations we observed agree with findings from other studies. For example, in the Prevención con Dieta Mediterránea (PREDIMED)-Navarra trial, García-Calzón et al. (38) observed a positive association between baseline Mediterranean diet adherence and basal telomere length in women, but not in men.

Table 2. Log-Transformed Leukocyte Telomere Length According to Quintiles of 4 Diet Quality Indices, National Health and Nutrition Examination Survey, 1999–2002

Diet Quality Index and Quintile	Log Leukocyte Telomere Length, T/S ratio[a]								
	All Adults			Men[b]			Women[b]		
	Mean (SE)	β	95% CI	Mean (SE)	β	95% CI	Mean (SE)	β	95% CI
HEI-2010 score									
Age-adjusted									
Q1	0.027 (0.022)	0	Referent	0.026 (0.018)	0	Referent	0.027 (0.029)	0	Referent
Q2	0.032 (0.019)	0.006	−0.024, 0.036	0.033 (0.023)	0.007	−0.033, 0.046	0.032 (0.022)	0.006	−0.041, 0.052
Q3	0.042 (0.018)	0.015	−0.022, 0.053	0.028 (0.021)	0.003	−0.042, 0.047	0.053 (0.019)	0.026	−0.026, 0.079
Q4	0.050 (0.016)	0.023	−0.010, 0.057	0.046 (0.018)	0.020	−0.015, 0.055	0.052 (0.017)	0.025	−0.022, 0.073
Q5	0.076 (0.018)	0.050	0.006, 0.095	0.059 (0.021)	0.033	−0.016, 0.082	0.094 (0.018)	0.067	0.015, 0.120
P-trend			0.02			0.12			0.01
Multivariate-adjusted[c]									
Q1	0.113 (0.031)	0	Referent	0.134 (0.039)	0	Referent	0.004 (0.063)	0	Referent
Q2	0.119 (0.030)	0.006	−0.024, 0.036	0.137 (0.043)	0.003	−0.039, 0.046	0.010 (0.064)	0.007	−0.037, 0.051
Q3	0.126 (0.030)	0.014	−0.021, 0.049	0.139 (0.042)	0.005	−0.039, 0.049	0.024 (0.064)	0.020	−0.026, 0.067
Q4	0.128 (0.031)	0.015	−0.016, 0.047	0.139 (0.046)	0.006	−0.031, 0.042	0.027 (0.061)	0.024	−0.020, 0.067
Q5	0.152 (0.031)	0.039	−0.001, 0.079	0.149 (0.045)	0.015	−0.033, 0.064	0.069 (0.064)	0.065	0.018, 0.112
P-trend			0.04			0.50			0.007
AHEI-2010 score									
Age-adjusted									
Q1	0.048 (0.019)	0	Referent	0.052 (0.020)	0	Referent	0.044 (0.021)	0	Referent
Q2	0.029 (0.017)	−0.019	−0.050, 0.011	0.014 (0.019)	−0.038	−0.077, 0.000	0.045 (0.021)	0.001	−0.038, 0.040
Q3	0.030 (0.020)	−0.018	−0.041, 0.006	0.039 (0.020)	−0.013	−0.051, 0.024	0.023 (0.023)	−0.021	−0.058, 0.016
Q4	0.049 (0.017)	0.001	−0.025, 0.027	0.038 (0.021)	−0.015	−0.045, 0.016	0.058 (0.019)	0.014	−0.030, 0.058
Q5	0.074 (0.017)	0.026	−0.008, 0.060	0.050 (0.020)	−0.002	−0.047, 0.044	0.095 (0.019)	0.051	0.007, 0.094
P-trend			0.04			0.73			0.01
Multivariate-adjusted									
Q1	0.136 (0.032)	0	Referent	0.159 (0.036)	0	Referent	0.021 (0.057)	0	Referent
Q2	0.113 (0.032)	−0.023	−0.053, 0.007	0.113 (0.040)	−0.045	−0.081, −0.010	0.016 (0.060)	−0.005	−0.045, 0.036
Q3	0.118 (0.033)	−0.018	−0.041, 0.005	0.142 (0.043)	−0.017	−0.049, 0.016	0.005 (0.067)	−0.016	−0.057, 0.025
Q4	0.132 (0.032)	−0.004	−0.030, 0.022	0.131 (0.040)	−0.028	−0.057, 0.002	0.039 (0.063)	0.018	−0.029, 0.064
Q5	0.155 (0.030)	0.019	−0.010, 0.049	0.140 (0.044)	−0.019	−0.064, 0.026	0.075 (0.058)	0.054	0.010, 0.097
P-trend			0.08			0.63			0.007

Table continues

Table 2. Continued

Diet Quality Index and Quintile	Log Leukocyte Telomere Length, T/S ratio[a]								
	All Adults			Men[b]			Women[b]		
	Mean (SE)	β	95% CI	Mean (SE)	β	95% CI	Mean (SE)	β	95% CI
MedDiet score									
Age-adjusted									
Q1	0.027 (0.022)	0	Referent	0.027 (0.022)	0	Referent	0.027 (0.024)	0	Referent
Q2	0.039 (0.018)	0.012	−0.021, 0.046	0.025 (0.020)	−0.003	−0.048, 0.043	0.051 (0.021)	0.024	−0.014, 0.061
Q3	0.055 (0.017)	0.028	−0.007, 0.063	0.046 (0.020)	0.019	−0.028, 0.065	0.065 (0.017)	0.038	0.002, 0.073
Q4	0.045 (0.017)	0.018	−0.010, 0.046	0.047 (0.020)	0.019	−0.017, 0.055	0.043 (0.021)	0.016	−0.026, 0.058
Q5	0.066 (0.019)	0.039	0.004, 0.073	0.045 (0.020)	0.018	−0.029, 0.065	0.087 (0.023)	0.059	0.013, 0.105
P-trend		0.02			0.31			0.02	
Multivariate-adjusted									
Q1	0.117 (0.032)	0	Referent	0.140 (0.039)	0	Referent	0.006 (0.063)	0	Referent
Q2	0.126 (0.035)	0.009	−0.025, 0.043	0.129 (0.047)	−0.010	−0.059, 0.038	0.028 (0.061)	0.021	−0.014, 0.057
Q3	0.140 (0.031)	0.023	−0.008, 0.053	0.152 (0.041)	0.012	−0.030, 0.054	0.040 (0.058)	0.034	0.001, 0.067
Q4	0.130 (0.034)	0.013	−0.011, 0.037	0.152 (0.044)	0.012	−0.022, 0.046	0.020 (0.064)	0.013	−0.025, 0.052
Q5	0.149 (0.032)	0.032	0.003, 0.061	0.146 (0.049)	0.007	−0.038, 0.051	0.064 (0.061)	0.058	0.017, 0.098
P-trend		0.03			0.56			0.008	
DASH score									
Age-adjusted									
Q1	0.032 (0.023)	0	Referent	0.024 (0.021)	0	Referent	0.040 (0.027)	0	Referent
Q2	0.035 (0.017)	0.003	−0.026, 0.032	0.026 (0.016)	0.002	−0.035, 0.039	0.044 (0.021)	0.004	−0.035, 0.044
Q3	0.026 (0.021)	−0.006	−0.044, 0.032	0.020 (0.025)	−0.005	−0.050, 0.040	0.030 (0.023)	−0.009	−0.053, 0.035
Q4	0.044 (0.019)	0.012	−0.032, 0.056	0.031 (0.020)	0.006	−0.035, 0.047	0.057 (0.024)	0.018	−0.048, 0.083
Q5	0.088 (0.017)	0.056	0.012, 0.100	0.089 (0.021)	0.064	0.014, 0.115	0.087 (0.016)	0.047	−0.003, 0.097
P-trend		0.002			0.01			0.006	
Multivariate-adjusted									
Q1	0.116 (0.033)	0	Referent	0.134 (0.041)	0	Referent	0.008 (0.067)	0	Referent
Q2	0.119 (0.033)	0.004	−0.024, 0.032	0.135 (0.039)	0.001	−0.039, 0.041	0.016 (0.067)	0.007	−0.025, 0.040
Q3	0.112 (0.038)	−0.003	−0.040, 0.033	0.124 (0.050)	−0.009	−0.057, 0.038	0.009 (0.067)	0.001	−0.041, 0.043
Q4	0.130 (0.038)	0.014	−0.029, 0.057	0.130 (0.048)	−0.004	−0.049, 0.042	0.042 (0.064)	0.034	−0.028, 0.096
Q5	0.166 (0.033)	0.05	0.015, 0.085	0.177 (0.045)	0.043	−0.004, 0.091	0.060 (0.063)	0.052	0.014, 0.090
P-trend		0.002			0.06			0.007	

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; MedDiet, Mediterranean Diet; Q, quintile; SE, standard error.

[a] Telomere to single copy gene (T/S) ratio.

[b] *P* values from Wald tests for heterogeneity of odds ratios by sex were 0.22 for HEI-2010 score, 0.01 for AHEI-2010 score, 0.50 for MedDiet score, and 0.94 for DASH score.

[c] The multivariate-adjusted model included age, sex (except for sex-specific models), race/ethnicity, educational attainment, marital status, poverty income ratio, alcohol consumption, smoking status, pack-years of smoking, physical activity, change in physical activity over the past year, and log total energy intake.

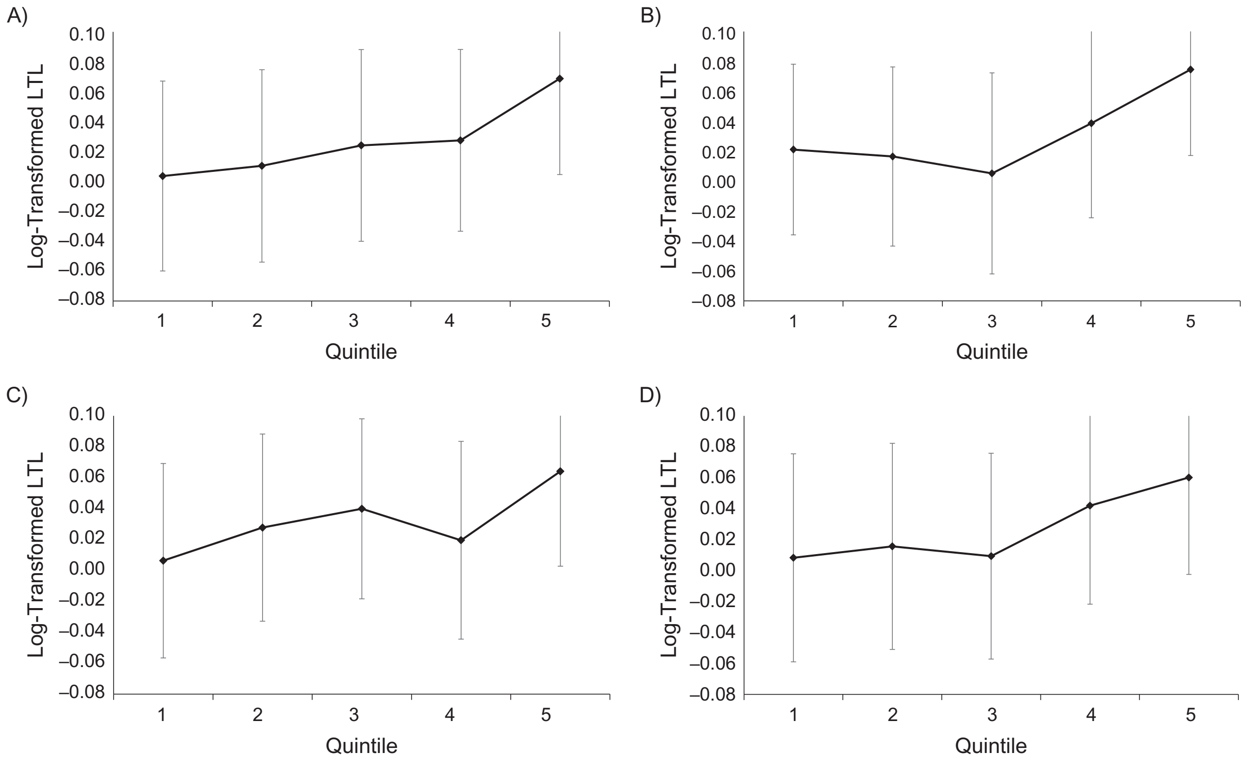

Figure 1. Multivariate-adjusted least-square mean values (and standard errors (bars)) for log-transformed leukocyte telomere length (LTL) among women, according to quintiles of diet quality indices, National Health and Nutrition Examination Survey, 1999–2002. A) Healthy Eating Index 2010 (HEI-2010); B) Alternate Healthy Eating Index 2010 (AHEI-2010); C) Mediterranean Diet (MedDiet) index; D) Dietary Approaches to Stop Hypertension (DASH) index. *P*-trend values for diet quality indices and log-transformed LTL were 0.007 for HEI-2010, 0.007 for AHEI-2010, 0.008 for MedDiet, and 0.007 for DASH.

In a cohort of older Finnish adults, Tiainen et al. (39) found that vegetable intake was positively associated with LTL in women, while fruit intake was inversely associated with LTL in men. Lastly, in a sample of Chinese women, Gong et al. (40) found that an empirically derived high-vegetable dietary pattern was associated with longer LTL in women but not in men, and this relationship was partly mediated by C-reactive protein (inflammation). Telomere length is impacted by inflammation, insulin resistance, and oxidative stress (41–43), all of which can be affected by specific dietary behaviors. In fact, in another study using the same data set, Shivappa et al. (44) found that a pro-inflammatory diet was significantly associated with shorter LTL. In the present study, men consumed higher levels of red and processed meats and sugar-sweetened beverages across quartiles of LTL (data not shown); these are all foods known to induce inflammation, insulin resistance, and oxidative stress. The more prevalent consumption of these specific foods may largely negate the effect of beneficial properties of an otherwise healthful diet on LTL in men.

Our study was strengthened by the use of a large, nationally representative sample of adults; the availability of information on a large number of sociodemographic and health characteristics, which allowed for careful adjustments for potential confounding; and high response rates—all of which improve the generalizability of our findings. However, this study also had limitations. The primary limitation was the cross-sectional nature of the data, which prevented us from making causal inferences about our findings. To date, the majority of epidemiologic studies examining diet and telomere length have relied on cross-sectional data, even those embedded in prospective cohort studies. This highlights the need for longitudinal studies, with repeated concurrent measures of dietary intake and telomere length over time, to better understand how dietary changes influence telomere length. Furthermore, dietary intake was assessed using one 24-hour dietary recall. A single 24-hour dietary recall may not approximate usual dietary intake due to day-to-day variation, and future studies with more robust methods of dietary assessment are needed to confirm these findings.

In conclusion, the results of this large and nationally representative study suggest that a diet high in fruits, vegetables, whole grains, dairy products, and plant-based proteins and low in red and processed meats, sodium, and added sugars is related to healthy cellular aging, particularly among women. Although further research is still needed to understand how dietary intake and diet patterns relate to cellular aging among men, efforts to promote longevity and reduce chronic disease risk through optimal nutrition should focus on improving overall diet quality rather than emphasizing individual foods or nutrients.

Table 3. Log-Transformed Leukocyte Telomere Length According to Standardized Diet Quality Scores, National Health and Nutrition Examination Survey, 1999–2002

Diet Quality Index	Log Leukocyte Telomere Length, T/S ratio[a]					
	All Adults		Men[b]		Women[b]	
	β	95% CI	β	95% CI	β	95% CI
HEI-2010 score						
Age-adjusted	0.020	0.006, 0.034	0.015	0.000, 0.030	0.025	0.008, 0.041
Multivariate-adjusted[c]	0.015	0.003, 0.028	0.007	−0.007, 0.021	0.024	0.008, 0.039
AHEI-2010 score						
Age-adjusted	0.011	0.001, 0.022	0.004	−0.009, 0.018	0.017	0.004, 0.030
Multivariate-adjusted	0.009	−0.000, 0.018	−0.002	−0.015, 0.012	0.019	0.007, 0.031
MedDiet score						
Age-adjusted	0.014	0.003, 0.025	0.006	−0.008, 0.021	0.021	0.007, 0.035
Multivariate-adjusted	0.011	0.002, 0.020	0.003	−0.010, 0.016	0.020	0.008, 0.033
DASH score						
Age-adjusted	0.018	0.003, 0.033	0.020	0.005, 0.034	0.015	−0.003, 0.034
Multivariate-adjusted	0.016	0.003, 0.029	0.012	−0.002, 0.027	0.019	0.003, 0.035

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; HEI-2010, Healthy Eating Index 2010; MedDiet, Mediterranean Diet.

[a] Telomere to single copy gene (T/S) ratio.

[b] *P* values from Wald tests for heterogeneity of odds ratios by sex were 0.06 for HEI-2010 score, 0.02 for AHEI-2010 score, 0.04 for MedDiet score, and 0.89 for DASH score.

[c] The multivariate-adjusted model included age, sex (except for sex-specific models), race/ethnicity, educational attainment, marital status, poverty income ratio, alcohol consumption, smoking status, pack-years of smoking, physical activity, change in physical activity over the past year, and log total energy intake.

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Author affiliations: Center for Health and Community, University of California, San Francisco, San Francisco, California (Cindy W. Leung); Department of Nutritional Sciences, School of Public Health, University of Michigan, Ann Arbor, Michigan (Cindy W. Leung); Department of Nutrition, School of Nursing and Health Sciences, Simmons College, Boston, Massachusetts (Teresa T. Fung); Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, Massachusetts (Teresa T. Fung); Institute of Global Food Security (Center for Public Health), Queen's University Belfast, Belfast, Northern Ireland (Claire T. McEvoy); Department of Biochemistry and Biophysics, School of Medicine, University of California, San Francisco, San Francisco, California (Jue Lin); and Department of Psychiatry, School of Medicine, University of California, San Francisco, San Francisco, California (Elissa S. Epel).

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