The Dietary Inflammatory Index® and Alternative Healthy Eating Index 2010 in relation to leucocyte telomere length in postmenopausal women: a cross-sectional study

A. T. Mickle1,2, D. R. Brenner1,2,3,4,5, T. Beattie3,4,5,6, T. Williamson1,4,7, K. S. Courneya8 and C. M. Friedenreich1,2,3,4,5*

1Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
2Department of Cancer Epidemiology Prevention Research, CancerControl Alberta, Alberta Health Services, Alberta, Canada
3Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
4O’Brien Institute of Public Health, Calgary, Alberta, Canada
5A. R. Charbonneau Cancer Institute, University of Calgary, Calgary, Alberta, Canada
6Department of Biochemistry and Molecular Biology, University of Calgary, Calgary, Alberta, Canada
7Alberta Children’s Hospital Research Institute, Calgary, Alberta, Canada
8Faculty of Physical Education and Recreation, University of Alberta, Edmonton, Alberta, Canada

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Abstract
Telomeres are nucleoprotein complexes that form the ends of eukaryotic chromosomes where they protect DNA from genomic instability, prevent end-to-end fusion and limit cellular replicative capabilities. Increased telomere attrition rates, and relatively shorter telomere length, is associated with genomic instability and has been linked with several chronic diseases, malignancies and reduced longevity. Telomeric DNA is highly susceptible to oxidative damage and dietary habits may make an impact on telomere attrition rates through the mediation of oxidative stress and chronic inflammation. The aim of this study was to examine the association between leucocyte telomere length (LTL) with both the Dietary Inflammatory Index® 2014 (DII®) and the Alternative Healthy Eating Index 2010 (AHEI-2010). This is a cross-sectional analysis using baseline data from 263 postmenopausal women from the Alberta Physical Activity and Breast Cancer Prevention (ALPHA) Trial, in Calgary and Edmonton, Alberta, Canada. No statistically significant association was detected between LTL z-score and the AHEI-2010 (P = 0.20) or DII® (P = 0.91) in multivariable adjusted models. An exploratory analysis of AHEI-2010 and DII® parameters and LTL revealed anthocyanin intake was associated with LTL (P < 0.01); however, this association was non-significant after a Bonferroni correction was applied (P = 0.27). No effect modification by age, smoking history, or recreational physical activity was detected for either relationship. Increased dietary antioxidant and decreased oxidant intake were not associated with LTL in this analysis.

Key words: Telomeres: Alternative Healthy Eating Index: Dietary Inflammatory Index®: Chronic inflammation: Oxidative stress
to synthesise chromosomal ends completely. Telomeres therefore shorten naturally with each cell division or replication, eventually leading to cellular senescence. Leucocyte telomere length (LTL) may experience accelerated attrition directly through oxidative damage, and indirectly through increased cellular replication during chronic inflammation, both of which are hypothesised to mediate the association between lifestyle and LTL. Demographic and lifestyle variables, including dietary habits, physical activity levels and substance abuse, mediate levels of chronic inflammation and oxidative stress, and thus may be associated with LTL. LTL may serve as a marker of biological, rather than chronological, age, and may also provide insight into the risk of chronic diseases associated with oxidative stress and chronic inflammation, including CVD and several cancers.

Telomeric DNA is rich in guanine nucleotides, which are prone to be selectively oxidised to 8-oxo-2'-deoxyguanosine and 2,6-diamino-4-oxo-5-formamidopyrimidine by reactive oxygen species. Reactive oxygen species may also produce single-stranded DNA breaks directly, or single-stranded breaks may occur during the repair of oxidative base modifications. In addition to these mechanisms, single-strand breaks in telomeric DNA are less efficiently repaired by DNA repair machinery than in non-telomeric genomic DNA. It has been hypothesised that the susceptibility of telomeres to damage by reactive oxygen species is, in fact, an important mechanism whereby telomeres act as ‘sentinels’ of excessive oxidative damage, disallowing the continued proliferation of damaged and potentially oncogenic cells. Lymphocyte LTL is further affected by oxidative stress because of the increased proliferation (and coinciding telomere loss) of these cells during the inflammatory response triggered by oxidative stress.

Current research is aimed at understanding the relationship between advanced telomere attrition and anthropometric measures including increased BMI and intra-abdominal fat, as well as lifestyle factors including smoking, alcohol intake and suboptimal psychosocial health, contributing through the impact of oxidative stress and chronic inflammation. Diet is an important source of oxidants and antioxidants and may affect levels of oxidative stress and inflammation in the blood and intestinal environment. Diets rich in fruit and vegetables high in antioxidants are associated with lower intracellular concentrations of inflammatory biomarkers and reduced risk of chronic diseases, cancer and CVD. Thus, telomere length may be a biomarker of dietary oxidant/antioxidant status. Traditionally, nutritional epidemiology has focused on the association of specific nutrients or food groups with telomeric length and other health outcomes; however, the study of dietary patterns has recently emerged as a more holistic approach at assessing these relationships.

The Alternative Healthy Eating Index 2010 (AHEI-2010) is a score that provides an assessment of the diet’s capacity to prevent chronic disease. Designed as an alternative to the Healthy Eating Index (HEI) which quantified adherence to the US 1995 Dietary Guidelines, the AHEI-2010 was based on foods and nutrients predictive of chronic disease risk. Higher AHEI-2010 scores have been associated with less weight gain over time, lower risk of acute myocardial infarction, lower chronic obstructive pulmonary disease, lower long-term chronic inflammation, lower cancer risk, lower all-cause mortality and longer LTL.

The Dietary Inflammatory Index® (DII®) is a tool for assessing diet quality based on inflammatory potential. The inflammatory capacity of the diet is assessed by estimating the intake of forty-five micro- and macronutrients, multiplying each by an overall inflammatory effect score and then centring each value on global mean intake values. In this study, each inflammatory effect score was estimated based on the results of a rigorous literature review (about 2000 articles read and scored). Higher DII® scores have been associated with higher incidence of cancer, CVD and all-cause mortality and lower LTL.

The aim of the present study was to assess the association between the intake of foods and nutrients predictive of chronic disease (AHEI-2010), and of the overall inflammatory potential of the diet (DII®) and LTL in postmenopausal, healthy Canadian women. While use of the DII® aligns more closely with the objectives of this study, but because relationships between AHEI-2010 scores and LTL have been extensively explored in the literature, we therefore chose to implement both. We hypothesised that AHEI-2010 scores would be positively associated with LTL and DII® scores inversely associated with LTL. The secondary objective was to assess intake of the individual components of both the AHEI-2010 and DII® for association with LTL, with the hypothesis that certain food groups or nutrients were driving any associations detected in the primary objective.

Methods

Subjects

We conducted a cross-sectional analysis using the baseline data from the Alberta Physical Activity and Breast Cancer Prevention (ALPHA) Trial. Women were recruited for the ALPHA Trial through mailings to participants in the Alberta Breast Screening Programme, media campaigns and brochures and posters distributed through the Alberta Family Physicians Research Network. The main inclusion criteria included: aged 50–74 years, English speaking, residents in the Calgary or Edmonton areas, postmenopausal, no previous cancer diagnosis except non-melanoma skin cancer, no major co-morbidities, acceptable heart and lung function, BMI 22.0 to 40.0 kg/m², breast tissue density ≥ 50%, able to undertake unrestricted physical activity as determined through completion of the Physical Activity Readiness-Medical Exam (PAR-MedX) Questionnaire, inactive lifestyle, not currently planning to undertake a weight control/loss programme, not currently, previously (<12 months) or planning to take drugs related to oestrogen metabolism or breast tissue growth, not currently planning on taking weight loss medications, not a current smoker or excessive drinker. Baseline assessments were performed from 2003 through 2007.

Ethics

Research ethics boards at the Alberta Cancer Board and Universities of Calgary and Alberta approved the protocol.
for this ancillary study of the ALPHA Trial. The Conjoint Health Research Ethics Board at the University of Calgary and the Health Research Ethics Board of Alberta Health Services approved the LTL analysis protocol. The ALPHA Trial was conducted according to the Declaration of Helsinki, and all participants provided written informed consent. The trial was registered at ClinicalTrials.gov (identifier: NCT00522262).

Health and lifestyle assessments

Participants completed four separate questionnaires focused on their baseline health, quality of life and psychosocial factors, physical activity in the past year and dietary intake. The Baseline Health Questionnaire measured health and sociodemographic variables including menstrual and reproductive history; medical and health history; past hormone replacement therapy; medication and vitamin/supplement use; previous benign breast disease; alcohol intake and smoking history. The General Health Questionnaire captured psychosocial fortification practices. It includes 124 items and generates estimates of food and supplemental macro- and micronutrient intake.

A sub-maximal modified Balke test was used to estimate maximum oxygen consumption from sub-maximal exercise intensities to measure cardiopulmonary fitness. Anthropometric measurements were taken by Certified Exercise Physiologists using standardised methods and equipment. These include height and weight (used to estimate BMI) and waist and hip circumferences (used to estimate waist:hip ratio). A dual-energy X-ray absorptiometry (DXA) scan was used to assess overall percentage body fat and fat distribution with a Hologic 4500 DXA Scanner (Calgary) or GE Lunar Prodigy High Speed Digital Fan Beam X-ray-based Bone Densitometer (Edmonton). A single-slice computed tomography (CT) scan was used to measure central adiposity (total abdominal fat, intra-abdominal fat and subcutaneous fat) using a Marconi PQ5000 Vision Master/Picker (Calgary) or Phillips/Marconi MX8000 multi-slice scanner (Edmonton).

Measurement of Alternative Healthy Eating Index 2010 and Dietary Inflammatory Index

DII® and AHEI-2010 scores were estimated for each participant using data derived from the 124-item C-DHQ-I using Diet*Calc software (version 1.4.3) downloaded from the United States National Cancer Institute’s Website, Division of Cancer Control and Population Sciences. The DII® was scored for all participants using methods previously described by Shivappa et al. Briefly, mean intake was standardised using the global mean and standard deviation, converted to represent a range between -1 (maximally anti-inflammatory) and +1 (maximally pro-inflammatory), multiplied by the overall inflammatory effect score, and summed to generate an overall dietary inflammatory effect score for each participant. A total of thirty-eight of the forty-five dietary parameters were available for the DII® estimation (Table 1) and included both dietary and supplemental intake. AHEI-2010 score was estimated using methods described by Chiave et al. Intake of eleven food groups/macronutrients was used to calculate the corresponding score out of 10 and summed to obtain a score between 0 (minimally ‘healthy’) and 110 (maximally ‘healthy’).

Measurement of telomere length

Blood samples were collected at study baseline using standardised blood collection, processing, storage and shipment protocols. Nucleic acid extraction was automated on the Hamilton STARlet (Hamilton Robotics Inc.) using the Macherey-Nagel NucleoMag Blood 200 µl kit. DNA was eluted in nuclease-free water and quantified using a Qubit dsDNA HS Assay Kit (ThermoFisher Scientific Inc.).

LTL (T) relative to a standard single-copy β-globin gene (S; 36B4) reference was quantified and expressed as a ratio (T:S). Three reference samples were run on each plate: wild-type BJ (human foreskin fibroblast primary cells), BJ + hTERT (human foreskin fibroblast primary cells transformed to express hTERT), and a pooled standard DNA to estimate inter-plate variation. Pooled standard DNA was prepared by pooling thirty buffy coats selected at random into one sample, and DNA extracted using a QIAMP DNA Mini Kit. All samples were measured in triplicate, and laboratory staff was blinded to the participant ID and time point. Final telomere length measurements were normalised to correct for between-run variation using methods described previously.

Statistical analysis

Multivariable linear regression analysis was used to model the association between DII® and AHEI-2010 scores with relative LTL. Relative LTL was square root transformed to achieve a more Gaussian distribution and converted to z-scores to simplify interpretation and comparison between studies (Fig. 1 (a)), since the calculation of the T:S ratio results in the right skewed distribution inherent of relative data. The inter-plate CV from our quantitative PCR analysis were relatively large, with values for our standard pooled DNA and wild-type human foreskin fibroblast primary cells reference DNA of 39 and 27 %, respectively. After applying a previously described normalisation factor, inter-plate variation was reduced to 10 % for standard pooled DNA and 12 % for the wild-type BJ reference DNA. Finally, square root-transformed relative telomere lengths were normalised using z-scores for ease of interpretation and for comparison with existing literature. Relative, square root-transformed, normalised LTL is referred to simply as LTL from this point forth.
Age-only and multivariable-adjusted estimates were reported. Final models were adjusted for: age, years since menopause, smoking history (<100 lifetime cigarettes; former casual smoker; former smoker), recreational physical activity (metabolic equivalent (MET)-h/week per year), cardiopulmonary fitness (VO₂max), BMI, intra-abdominal fat area (cm²), self-perceived psychosocial health, current employment (dichotomous) and marital status. For the secondary analysis

![Histogram of baseline data from participants in the Alberta Physical Activity and Breast Cancer Prevention (ALPHA) Trial (n=275) in Alberta, Canada (2003–2006)](https://www.cambridge.org/core/journals/jns/article/association-between-alternative-healthy-eating-index-2010-score-and-dietary-inflammatory-index-score-with-leucocyte-telomere-length-ltl-z-score-for-continuous-and-categorised-dietary-indices-in-in-alberta-physical-activity-and-breast-cancer-prevention-alpha-trial-participants-alberta-canada-2003-2006/89f7c2d83ac32f02f705a0f2a1a67d68)

**Fig. 1.** Histogram of baseline data from participants in the Alberta Physical Activity and Breast Cancer Prevention (ALPHA) Trial (n=275) in Alberta, Canada (2003–2007) (a) Square root transformed relative leucocyte telomere length z-score, (b) Alternative Healthy Eating 2010 score, (c) Dietary Inflammatory Index® score and (d) anthocyanidin intake (mg/d).

### Table 1. Association between Alternative Healthy Eating Index 2010 score and Dietary Inflammatory Index® score with leucocyte telomere length (LTL) z-score for continuous and categorised dietary indices in in Alberta Physical Activity and Breast Cancer Prevention (ALPHA) Trial participants, Alberta, Canada (2003–2006)

| Dietary index                  | Age adjusted (n=275) | Multivariable adjusted* (n=261) |                  |                  |                  |
|-------------------------------|----------------------|-------------------------------|-----------------|-----------------|-----------------|
|                               | β (× 10⁻¹)           | 95% CI                        | P               | β (× 10⁻¹)      | 95% CI          | P               |
|--------------------------------|----------------------|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| Alternative Healthy Eating Index 2010 | -0.07                | -0.19, 0.06                   | 0.29            | -0.09           | -0.22, 0.04     | 0.20            |
| Dietary Inflammatory Index® | -0.09                | -0.39, 0.27                   | 0.71            | -0.02           | -0.34, 0.38     | 0.91            |

Pairwise comparisons of multivariable adjusted* LTL z-score by quarters

| Quartile of index score | Before adjustment (n) | After adjustment (n) | Index score median | LTL z-score median | β (× 10⁻¹) | 95% CI | P | P-trend |
|-------------------------|-----------------------|----------------------|--------------------|--------------------|------------|-------|---|--------|
| Alternative Healthy Eating Index 2010 | Q1 68 64 | 45.01 | Reference | 0.06 | -0.30, -0.32, -0.65, 0.06 |
|                         | Q2 69 65 | 52.48 | Reference | 0.63 | -0.09, -0.30, -0.64, 0.08 |
|                         | Q3 69 66 | 58.89 | Reference | 0.12 | -0.18, -0.30, -0.64, 0.03 |
|                         | Q4 69 68 | 68.06 | Reference | 0.75 | -0.17, -0.05, -0.39, 0.28 |

Dietary Inflammatory Index®

| Quartile of index score | Before adjustment (n) | After adjustment (n) | Index score median | LTL z-score median | β (× 10⁻¹) | 95% CI | P | P-trend |
|-------------------------|-----------------------|----------------------|--------------------|--------------------|------------|-------|---|--------|
| Q1 68 66               | -4.98                 | 0.04                | Reference | 0.57 | -0.28, -0.08, -0.41, 0.25 |
| Q2 69 67               | -2.69                 | -0.01               | -0.07, -0.12       |       | -0.60, 0.12 |
| Q3 69 65               | -0.35                 | -0.17               | -0.39, 0.75        |       | -0.28, 0.75 |
| Q4 69 65               | 3.55                  |                     |                    |       |               |

* Model adjusted for age, years since menopause, smoking history, physical activity from recreational activities, cardiopulmonary fitness (VO₂max), BMI, intra-abdominal fat area, self-perceived psychosocial health, current employment status and marital status.
of the eleven individual components of the AHEI-2010 and thirty-eight available components of the DII®, a Bonferroni correction (51) was applied to adjust for multiple comparisons. Based on an extensive review of the literature, age, smoking history and past-year recreational physical activity (metabolic equivalent (MET)-h/week per year) were assessed for potential effect modification by including an interaction term in the multivariable linear regression model for each potential modifier. A P value <0·05 for the interaction term was considered statistically significant evidence for effect modification that would have resulted in stratum-specific estimates being reported. Non-linear relationships for each index and LTL were assessed using restricted cubic spline analysis with five knots at the 5th, 27·5th, 50th, 72·5th and 95th percentiles of diet score.

Sensitivity analyses were conducted to explore the effect of the DII® estimated with food only (no supplements), age-adjusted models for those for whom smoking data were available only to match the multivariable-adjusted population, and AHEI-2010 models additionally adjusted for total energy intake. Statistical analyses were performed using STATA (Intercooled (IC) version 14.0 for Mac), P values were two-sided, with α-level = 0·05.

Results

Dietary, LTL and demographic data were available for 263 women. A full project flow chart can be visualised in Fig. 2. The mean age was 60·9 (sd 5·5) years (range 50–74 years) and BMI was 29·3 (sd 4·4) kg/m². Women were primarily Caucasian (91·6 %), non-smokers (69·2 % had smoked less than 100 lifetime cigarettes) and relatively well educated (67·6 % with college/trade diploma or university degree). Detailed population characteristics are summarised in Table 2.

Several demographic and anthropometric characteristics were statistically significantly associated with LTL including recreational physical activity (β = 0·01; P = 0·01) and intra-abdominal fat area (β < −0·01; P = 0·04) but no association was found with age (β = −0·02; P = 0·06; Table 2). The inflammatory biomarker IL-6 was inversely associated with LTL (β = −0·15; pg/ml;
Table 2. Baseline characteristics for participants (n 275) and univariate associations between baseline characteristics with Alternative Healthy Eating Index 2010 (AHEI-2010) score, Dietary Inflammatory Index® (DII®) score and leukocyte telomere length (LTL) in the Alberta Physical Activity and Breast Cancer Prevention (ALPHA) Trial, Alberta, Canada (2003–2006)

| Characteristic (continuous) | n  | Mean  | SD   | Median | Q1, Q3 | % With characteristic | Association with AHEI-2010 score | Association with DII® score | Association with LTL z-score |
|-----------------------------|----|-------|------|--------|--------|-----------------------|---------------------------------|-------------------------------|-------------------------------|
| Age at baseline (years)     | 275| 60.9  | 5.5  | 60.4   | 56.6   | 64.4                  | 0.06 (0.58)                     | −0.05 (0.17)                  | −0.02 (0.06)                  |
| Time since menopause (years)| 274| 12.7  | 8.3  | 10.6   | 6.0    | 17.7                  | 0.05 (0.51)                     | 0.04 (0.12)                   | −0.02 (0.03)                  |
| Self-perceived general health (/100) | 272 | 82.4  | 13.3 | 82.0   | 77.0   | 92.0                  | 0.04 (0.36)                     | 0.01 (0.59)                   | −0.01 (0.91)                  |
| Self-perceived psychosocial health (/100) | 275 | 83.6  | 11.8 | 88.0   | 80.0   | 92.0                  | 0.04 (0.44)                     | −0.01 (0.59)                  | −0.01 (0.67)                  |
| Fasting glucose (mmol/l)    | 275| 5.6   | 1.1  | 4.9    | 4.6    | 6.0                   | <0.01 (0.75)                    | <0.01 (0.37)                  | <0.01 (0.21)                  |
| mg/dl                       | 275| 100.3 | 20.7 | 97     | 89.0   | 108.0                 | 0.01 (0.75)                     | <0.01 (0.37)                  | <0.01 (0.21)                  |
| Insulin (µIU/ml)            | 275| 7.3   | 5.8  | 6.0    | 3.4    | 8.9                   | −0.09 (0.41)                    | 0.01 (0.81)                   | <0.01 (0.61)                  |
| IL-6 (pg/ml)                | 275| 1.8   | 1.2  | 1.4    | 1.1    | 2.0                   | −0.35 (0.49)                    | 0.04 (0.81)                   | <0.15 (<0.01)                 |
| TNF-α (pg/ml)               | 275| 1.6   | 0.6  | 1.4    | 1.2    | 1.8                   | −0.88 (0.39)                    | 0.65 (0.08)                   | −0.04 (0.72)                  |
| CRP (mg/l)                  | 275| 3.0   | 4.0  | 1.0    | 0.7    | 3.0                   | −9.40 (0.48)                    | 2.90 (0.56)                   | −1.80 (0.20)                  |
| Total energy intake (kcal/d)| 275| 6527.5| 2282.8| 6266.8| 4945.5| 7729.1                | −0.01 (0.22)                    | <0.01 (<0.01)                 | <0.01 (0.83)                  |
| Alcohol intake (g/d)        | 275| 1560.1| 545.6| 1497.8| 1182.0| 1847.3                | −0.01 (0.22)                    | <0.01 (<0.01)                 | <0.01 (0.83)                  |
| Total physical activity (MET-h/week) | 375 | 123.2 | 71.2 | 108.3 | 76.0 | 150.0                 | 0.14 (0.62)                     | <0.01 (0.41)                  | <0.01 (0.17)                  |
| Employment physical activity (MET-h/week) | 275 | 52.8 | 55.3 | 45.0 | 24.0 | 86.4                  | −0.01 (0.28)                    | <0.01 (0.04)                  | <0.01 (0.90)                  |
| Household physical activity (MET-h/week) | 275 | 58.8 | 44.9 | 50.3 | 35.0 | 69.4                  | 0.0004 (0.98)                   | <0.02 (0.01)                  | <0.01 (0.10)                  |
| Recreational physical activity (MET-h/week) | 275 | 10.9 | 12.7 | 6.6 | 2.0 | 15.3                  | 0.10 (0.04)                     | <0.03 (0.03)                  | 0.01 (0.01)                   |
| Cardiopulmonary fitness (VO₂max) | 274 | 26.9 | 6.0 | 27.5 | 23.8 | 30.7                  | 0.26 (0.01)                     | <0.04 (0.30)                  | 0.01 (0.38)                   |
| BMI (kg/m²)                 | 275| 29.3  | 4.4  | 28.7   | 25.9   | 32.0                  | −0.30 (0.03)                    | 0.11 (0.02)                   | −0.02 (0.23)                  |
| Total body fat (%)          | 275| 42.3  | 5.4  | 42.5   | 38.5   | 45.7                  | −0.22 (0.05)                    | 0.08 (0.06)                   | −0.01 (0.38)                  |
| Intra-abdominal fat area (cm²) | 275 | 101.9 | 56.9 | 94.9   | 55.0   | 14.05                 | −0.02 (0.04)                    | <0.01 (0.16)                  | <0.01 (0.04)                  |
| Characteristic (categorical) |     |       |      |        |        |                       |                                 |                               |                               |
| Ever pregnant (% yes)       | 274| –     | –    | –      | –      | –                     | 92.7                             | −0.30 (0.90)                  | −0.44 (0.60)                  | 0.04 (0.87)                   |
| Family history of breast cancer (% yes) | 274 | –     | –    | –      | –      | –                     | 21.2                             | 1.67 (0.25)                  | 0.14 (0.80)                  | 0.23 (0.12)                   |
| Smoking history (% former smoker) | 263 | –     | –    | –      | –      | –                     | 20.9                             | −1.93 (0.20)                 | 0.39 (0.48)                  | 0.12 (0.44)                   |
| Ethnicity (% Caucasian)     | 274| –     | –    | –      | –      | –                     | 91.6                             | 2.02 (0.34)                  | −0.11 (0.98)                 | 0.02 (0.91)                   |
| Education (% with college or university degree) | 273 | –     | –    | –      | –      | –                     | 67.8                             | 3.16 (0.01)                  | −0.91 (0.05)                 | 0.17 (0.18)                   |
| Employment status (% employed) | 263 | –     | –    | –      | –      | –                     | 52.9                             | −0.35 (0.77)                 | 0.96 (0.03)                  | 0.02 (0.88)                   |
| Marital status (% married/common law) | 274 | –     | –    | –      | –      | –                     | 74.1                             | −0.084 (0.95)                | 0.28 (0.57)                  | −0.06 (0.65)                  |
| Past hormone medication use (% ever) | 275 | –     | –    | –      | –      | –                     | 45.0                             | −0.32 (0.79)                 | −0.07 (0.88)                 | 0.03 (0.79)                   |
| Past hormone replacement therapy use (% ever) | 274 | –     | –    | –      | –      | –                     | 44.2                             | −0.57 (0.62)                 | −0.11 (0.80)                 | 0.02 (0.88)                   |
| High cholesterol or TAG (% ever) | 274 | –     | –    | –      | –      | –                     | 32.5                             | 0.58 (0.64)                  | 0.08 (0.98)                  | −0.17 (0.18)                  |

CRP, C-reactive protein; MET, metabolic equivalent.
P < 0.01), yet not with the AHEI-2010 (β = −0.35; P = 0.49) or the DII® (β = 0.04; P = 0.81). C-reactive protein was not associated with LTL (β = −1.80; P = 0.20), the AHEI-2010 (β = −0.94; P = 0.48) or DII® (β = 0.29; P = 0.56). A complete summary of univariate associations between AHEI-2010, DII® score and LTL with baseline demographic and anthropometric characteristics are shown in Table 2.

AHEI-2010 score was approximately normally distributed, with a mean score of 56.3 (SD 9.75) (Fig. 1(b)). Results from the age-adjusted model estimated that for a one-unit increase in AHEI-2010 score, LTL decreased by approximately 0.07 (95% CI −0.019, 0.06) standard deviations (P = 0.29).

Similarly, no significant association was detected between LTL and AHEI-2010 in the fully adjusted model, where a one-unit increase in AHEI-2010 score corresponded to an estimated decrease of 0.09 (95% CI −0.22, 0.04) standard deviations of LTL (P = 0.20). There was no statistical evidence of effect modification for age, smoking history or recreational physical activity. Primary results are summarised in Table 1. Restricted cubic spline regression analysis provided no evidence of a non-linear relationship between AHEI-2010 and LTL (P = 0.37). Results of the multivariable adjusted pairwise comparisons of AHEI-2010 quartiles with LTL (Table 1) indicated no statistically significant relationship between the first and second quartiles (β = −0.32; P = 0.06), third quartile (β = −0.30; P = 0.08) or fourth quartile (β = −0.30; P = 0.08). The test for linear trend across quartiles was also non-statistically significant (P-trend = 0.07). An exploratory analysis which assessed the eleven individual parameters that comprise the index as individual exposures also found no significant association between dietary intake from any parameter and LTL in age-adjusted or multivariable adjusted models (Table 3). AHEI-2010 scores correlated inversely (r = −0.44; P < 0.01) with DII® scores (Fig. 3). DII® score was approximately normally distributed as illustrated in Fig. 1(c), with a mean score of −1.01 (SD 3.58). As indicated in Table 1, the age-adjusted model estimated that for a one-unit increase in DII® score, the LTL decreased by approximately 0.06 (95% CI −0.39, 0.27) standard deviations (P = 0.71). Similarly, no statistically significant association was detected between LTL and the DII® in the multivariable adjusted model where a one-unit increase in DII® score corresponded to an estimated increase of 0.02 (95% CI −0.34, 0.38) standard deviations of the LTL (P = 0.91). There was no statistical evidence of effect modification by age, smoking history or recreational physical activity. Restricted cubic spline regression analysis provided no evidence of a non-linear relationship between the DII® and LTL (P = 0.56). Multivariable adjusted pairwise comparisons of DII® quartiles with LTL (Table 3) indicated no statistically significant relationships for any of the quartiles of DII® and there was no statistically significant linear trend.

An exploratory analysis that assessed each of the thirty-eight available parameters of the DII® (Table 3) as individual potential predictors of LTL found that anthocyanidin intake was significantly associated with LTL (β-score in both age-adjusted (β = 0.01; P = 0.01) and multivariable adjusted (β = 0.09; P < 0.01) models, but not in Bonferroni corrected (P = 0.23) models. All sensitivity analyses conducted had a trivial effect on the interpretation of the results and conclusions of the study (data not shown).

Discussion

This study found neither DII® nor AHEI-2010 scores to be associated with LTL in this population of healthy, postmenopausal women. Additionally, none of the eleven components of the AHEI-2010 were associated with LTL. LTL was not statistically significantly correlated with age, and neither DII® nor AHEI scores were associated with the inflammatory biomarkers C-reactive protein or IL-6 as expected.

Only one study has examined the relationship between the AHEI-2010 and LTL in 4676 disease-free women from the Nurses’ Health Study (NHS), in which the authors found higher AHEI-2010 scores to be associated with longer LTL.59 Results from two other studies that had previously examined the association between DII® score and LTL indicated a statistically significant inverse association between baseline DII® and LTL.43,46 Shivappa et al.41 found that higher DII® scores were associated both with shorter LTL, and with C-reactive protein (serving as a construct validation of the DII®) in a cross-sectional analysis of 7215 National Health and Nutrition Examination Survey (NHANES) participants. Garcia-Calzon et al.43 found that an increase in DII® score was associated with a two-fold increased LTL attrition over a 5-year follow-up in 520 Spanish men and women from the PREvenció con DIeta MEDITerránea (Prevention with Mediterranean Diet Study; PREDIMED-NAVARRA) study. Conversely, in 2018, De Meyer et al.50 published cross-sectional results indicating no association between DII® scores and LTL in 2509 healthy men and women, concluding an at most limited association between dietary patterns and LTL in the general population. Similarly, Meinilä et al.53 recently reported no association between DII® scores in either cross-sectional analyses or longitudinal assessments over 10 years in their cohort of 1046 elderly men and women who participated in the Helsinki Birth Cohort Study. Our study differs in sample size (n = 263 n. 4676 in the NHS) and design (cross-sectional v. prospective with change in LTL measured) to studies that reported relationships between the DII® and LTL, we could conclude that our analyses limited our ability to detect differences in LTL. Our study findings do, however, align with the findings of Meinilä et al.53 and De Meyer et al.52 and therefore we must consider that the inflammatory potential of the diet does not directly or indirectly influence LTL, as hypothesised.

While the statistically significant association between anthocyanidin intake and LTL was no longer statistically significant after correction for multiple testing, some discussion of this finding is warranted. Anthocyanidins are common plant pigments that reflect light in in the red to blue range and are responsible for the pigmentation in foods such as blueberries, raspberries, red onions and purple yams54,55 (list not exhaustive). Anthocyanidins are considered the most important subcategory of flavonoids because of their strong in vitro and in vivo antioxidant activity56-58,54,55. While this finding may be a result of type I error from multiple testing, further investigation into this highly biologically plausible association is justified.
This study had several strengths of note. First, we were able to evaluate several well-measured potential confounders. For example, direct measurements of body size and composition were taken including a DXA scan for overall percentage body fat and fat distribution and a computed tomography (CT) scan for central adiposity (total abdominal fat, intra-abdominal

| Overall inflammation effect score | Mean | SD | β (× 10⁻¹) | P | β (× 10⁻¹) | P |
|----------------------------------|------|----|------------|---|------------|---|
| **Alternative Healthy Eating Index 2010 component** | | | | | | |
| Vegetables† (servings/d) | – | 4.28 | 2.67 | –0.10 | 0.65 | –0.09 | 0.70 |
| Fruits† (servings/d) | – | 2.68 | 2.04 | –0.21 | 0.45 | –0.17 | 0.53 |
| Whole grains (servings/d) | – | 1.01 | 0.73 | 0.24 | 0.77 | 0.41 | 0.66 |
| Sugar-sweetened beverages and fruit juices (servings/d) | – | 0.69 | 0.96 | –0.32 | 0.61 | –0.10 | 0.91 |
| Nuts and legumes (servings/d) | – | 1.10 | 1.35 | –2.21 | 0.09 | –2.31 | 0.08 |
| Red/processed meats (servings/d) | – | 0.50 | 0.44 | –0.12 | 0.93 | 1.59 | 0.35 |
| Trans-fats (% of energy) | – | 3.22 | 1.89 | –0.07 | 0.93 | 0.13 | 0.89 |
| Long-chain (n-3) fats|| (mg/d) | – | 93.67 | 84.85 | <0.01 | 0.48 | <0.01 | 0.38 |
| PUFA (% of energy) | – | 13.30 | 7.22 | –0.33 | 0.19 | –0.33 | 0.23 |
| Na (mg/d) | – | 2421.75 | 1035.07 | <0.01 | 0.97 | <0.01 | 0.93 |
| Alcohol (drinks/d) | – | 4.66 | 6.70 | 0.14 | 0.11 | 0.07 | 0.50 |
| **Dietary Inflammatory Index® Component** | | | | | | |
| Energy intake | | | | | | |
| kcal/d | 0.180 | 6527.54 | 2286.97 | <0.01 | 0.95 | <0.01 | 0.67 |
| Total fat (g/d) | 0.298 | 57.07 | 27.55 | <0.01 | 0.76 | <0.01 | 0.85 |
| Total carbohydrate (g/d) | 0.097 | 202.06 | 74.51 | <0.01 | 0.89 | <0.01 | 0.62 |
| Total protein (g/d) | 0.021 | 63.17 | 24.94 | <0.01 | 0.97 | <0.01 | 0.96 |
| Alcohol (g/d) | –0.278 | 4.66 | 6.70 | 0.14 | 0.10 | 0.07 | 0.50 |
| Cholesterol (mg/d) | –0.110 | 194.27 | 116.93 | <0.01 | 0.52 | <0.01 | 0.44 |
| Saturated fat (g/d) | –0.373 | 17.53 | 8.89 | 0.03 | 0.63 | 0.07 | 0.31 |
| Monounsaturated fat (g/d) | –0.009 | 21.74 | 10.96 | –0.03 | 0.61 | <0.01 | 0.92 |
| Polyunsaturated fat (g/d) | –0.337 | 13.30 | 7.22 | –0.08 | 0.35 | –0.04 | 0.67 |
| Trans-fatty acids (g/d) | 0.229 | 3.21 | 1.89 | 0.06 | 0.84 | 0.21 | 0.55 |
| n-3 Fatty acids (g/d) | –0.436 | 1.33 | 0.69 | –0.15 | 0.86 | 0.34 | 0.73 |
| n-6 Fatty acids (g/d) | –0.159 | 11.87 | 6.56 | –0.09 | 0.33 | –0.05 | 0.62 |
| Total dietary fibre (g/d) | –0.663 | 19.40 | 9.58 | –0.02 | 0.72 | –0.01 | 0.80 |
| Vitamin A (retinol equivalents/d) | –0.401 | 1990.62 | 1197.34 | <0.01 | 0.20 | <0.01 | 0.07 |
| β-Carotene (µg/d) | –0.584 | 4755.50 | 4215.64 | <0.01 | 0.23 | <0.01 | 0.23 |
| Vitamin D (µg/d) | –0.446 | 10.34 | 6.08 | 0.05 | 0.61 | –0.04 | 0.74 |
| Vitamin E (mg/d) | –0.419 | 12.57 | 7.75 | <0.01 | 0.48 | <0.01 | 0.99 |
| Vitamin C (mg/d) | –0.424 | 316.92 | 303.11 | <0.01 | 0.15 | <0.01 | 0.43 |
| Thiamine (mg/d) | –0.098 | 2.89 | 2.45 | 0.13 | 0.61 | 0.09 | 0.74 |
| Riboflavin (mg/d) | –0.068 | 2.95 | 1.83 | 0.18 | 0.57 | 0.06 | 0.87 |
| Niacin (mg/d) | –0.246 | 29.97 | 15.40 | –0.01 | 0.84 | –0.02 | 0.62 |
| Vitamin B6 (mg/d) | –0.365 | 7.43 | 12.27 | 0.06 | 0.20 | 0.06 | 0.30 |
| Total folate (µg/d) | –0.190 | 616.00 | 270.40 | <0.01 | 0.40 | <0.01 | 0.19 |
| Vitamin B12 (µg/d) | 0.106 | 6.61 | 3.52 | –0.02 | 0.91 | –0.13 | 0.49 |
| Mg (mg/d) | –0.484 | 364.04 | 126.41 | <0.01 | 0.55 | <0.01 | 0.39 |
| Fe (mg/d) | 0.032 | 19.57 | 9.84 | –0.08 | 0.21 | –0.09 | 0.16 |
| Zn (mg/d) | –0.313 | 16.31 | 9.40 | <0.01 | 0.97 | –0.03 | 0.67 |
| Se (µg/d) | –0.191 | 82.78 | 34.11 | <0.01 | 0.98 | <0.01 | 0.75 |
| Caffeine (g/d) | –0.110 | 3.90 | 3.46 | 0.21 | 0.22 | <0.01 | 0.16 |
| Flavonols (mg/d) | –0.467 | 27.94 | 20.46 | 0.02 | 0.44 | 0.01 | 0.63 |
| Flavones (mg/d) | –0.616 | 2.11 | 1.72 | 0.13 | 0.71 | <0.03 | 0.93 |
| Isoflavonoids (mg/d) | –0.093 | 6.95 | 36.61 | –0.02 | 0.37 | –0.03 | 0.22 |
| Anthocyanins (mg/d) | –0.131 | 21.40 | 17.98 | 0.09 | 0.01 | 0.09 | <0.01 |
| Flavanones (mg/d) | –0.250 | 31.98 | 27.82 | <0.01 | 0.80 | –0.02 | 0.50 |
| Flavan-3-ol (mg/d) | –0.415 | 345.38 | 488.57 | <0.01 | 0.41 | <0.01 | 0.52 |
| Onion (g/d) | –0.301 | 11.05 | 16.38 | –0.02 | 0.51 | –0.03 | 0.50 |
| Pepper (g/d) | –0.131 | 7.32 | 12.17 | –0.05 | 0.28 | –0.07 | 0.21 |
| Green/black tea (g/d) | –0.536 | 0.92 | 1.11 | 0.49 | 0.37 | 0.35 | 0.54 |

* Data unavailable for garlic, ginger, rosemary, saffron, thyme/oregano, turmeric and eugenol intake while calculating Dietary Inflammatory Index® score.
† Model adjusted for age, years since menopause, smoking history, physical activity from recreational activities, cardiopulmonary fitness (VO2max), BMI, intra-abdominal fat area, self-perceived psychosocial health, current employment status and marital status.
‡ Not including potatoes/French fries.
¶ Including fruit juices.
‖ EPA and DHA.
fat and subcutaneous fat). Self-reported physical activity was assessed using the reliable and validated Past Year Total Physical Activity Questionnaire (47). Moreover, the stringent exclusion criteria of the underlying ALPHA Trial reduced potential confounding by those restricted variables (e.g. alcohol consumption, current smoking, etc.). In addition, we had thirty-eight of the forty-five DII® parameters available to calculate the DII® score, where examples from the literature often include as few as twenty parameters (56). Extensive dietary data were also available for potentially important vitamins, minerals and flavonoids.

These results are limited by using self-reported dietary measurements which may be biased to over-reporting of healthy foods and under-reporting of unhealthy foods (social desirability bias) (57). There was some underreporting of total energy intake, which is common for FFQ such as the C-DHQ-I. In addition, neither dietary index was associated with the key inflammatory biomarkers C-reactive protein or IL-6, thus the DII® and AHEI-2010 are not validated by the present study. Measurement error is a common limitation when measuring telomere length, regardless of the assay chosen (58) and LTL did not correlate significantly with age, compromising the results of the present study. The cross-sectional study design prohibits temporality from being established, and generalisability is limited since this study was conducted on a relatively small sample of primarily Caucasian, healthy, postmenopausal women of relatively high education and socio-economic status. The inclusion of postmenopausal women only may have also limited our ability to detect associations, since the association between LTL and socio-demographic factors may take several years to occur (60). Variations or SNP in genes involved in the inflammatory response should be considered for future studies. Finally, our findings corroborate recent research which suggest that the diet’s inflammatory potential may have limited impact on telomere length and telomere attrition rates (59).

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References

1. Blackburn EH (2005) Telomeres and telomerase: their mechanisms of action and the effects of altering their functions. FEBS Lett 579, 859–862.

2. Podlevsky JD & Chen JJ (2012) It all comes together at the ends: telomerase structure, function, and biogenesis. Mutat Res 730, 3–11.

3. Baird DM & Kipling D (2004) The extent and significance of telomere loss with age. Ann N Y Acad Sci 1019, 265–268.

4. Sfeir AJ, Chai W, Shyu JW, et al. (2005) Telomere-end processing the terminal nucleotides of human chromosomes. Mol Cell 18, 131–138.

5. Hodes RJ (1999) Telomere length, aging, and somatic cell turnover. J Exp Med 190, 153–156.

6. Olovnikov AM (1973) A theory of marginotomy. The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon. J Theor Biol 41, 181–190.

7. von Zglinicki T (2002) Oxidative stress shortens telomeres. Trends Biochem Sci 27, 339–344.

8. Campisi J & d’Adda di Fagagna F (2007) Cellular senescence: when bad things happen to good cells. Nat Rev Mol Cell Biol 8, 729–740.

9. Finkel T & Holbrook NJ (2000) Oxidants, oxidative stress and the biology of ageing. Nature 408, 223–238.

10. Lin J, Epe B & Blackburn E (2012) Telomeres and lifestyle factors: roles in cellular aging. Mutat Res 730, 85–89.

11. Babishvay MA & Yegorov YE (2011) Smoking and health: association between telomere length and factors impacting on human disease, quality of life and life span in a large population-based cohort under the effect of smoking duration. Fundam Clin Pharmacol 25, 425–442.

12. Boesten DM, de Vos-Houwen JM, Timmermans I, et al. (2013) Accelerated aging during chronic oxidative stress: a role for PARP-1. Oxid Med Cell Longev 2013, 680414.

13. Sanders JL & Newman AB (2013) Telomere length in epidemiology: a biomarker of aging, age-related disease, both, or neither? Epidemiol Rev 35, 112–131.

14. Aviv A, Chen W, Gardiner JP, et al. (2009) Leukocyte telomere dynamics: longitudinal findings among young adults in the Bogalusa Heart Study. Am J Epidemiol 169, 323–329.

15. Houwen JM, Moonen HJ, van Schooten FJ, et al. (2008) Telomere length assessment: biomarker of chronic oxidative stress? Free Radiol Biol Med 44, 235–248.

16. Samoylenko A, Hossain JA, Mennerich D, et al. (2017) Nutritional and lifestyle factors associated with leukocyte telomere length in middle-aged men. J Nutr 147, 889–897.

17. Freitas-Simoes TM, Ros E & Sala-Vila A (2016) Nutrients, foods, and dietary patterns: interconnections and implications for dietary guidelines. Adv Nutr 7, 445–454.

18. Chiuve SE, Fung TT, Rimm EB, et al. (2012) Alternative dietary indices both strongly predict risk of chronic disease. J Natl Acad Sci USA 109, 1009–1018.

19. Tobias DK, Zhang C, Chavarro J, et al. (2016) Healthy dietary patterns and long-term weight change among women with a history of gestational diabetes mellitus. Int J Obes 40, 1748–1753.

20. Jacobs Jr DR Jr, Gross MD & Tapsell LC (2009) Food synergy: an operational concept for understanding nutrition. Am J Clin Nutr 89, 1543S–1548S.

21. Tapsell LC, Neale EP, Satija A, et al. (2016) Foods, nutrients, and dietary patterns: interconnections and implications for dietary guidelines. Adv Nutr 7, 434–444.

22. Reedy J, Krebs-Smith SM, Miller PE, et al. (2014) Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. J Natl Acad Sci USA 114, 1827–1837.

23. Sinha R, Pan R, Liu S, et al. (2012) Mediterranean diet and telomere length: a systematic review of cross-sectional and longitudinal analyses over 5 y. Am J Clin Nutr 95, 1112–1118.

24. Shivappa N, Steck SE, Hurley TG, et al. (2017) Association between the Dietary Inflammatory Index (DII) and telomere length and C-reactive protein from the National Health and Nutrition Examination Survey-1999–2002. Nutr J 16, e100241.10.
45. Friedenreich CM, Woolcott CG, McTiernan A, et al. (2010) Alberta Physical Activity and Breast Cancer Prevention Trial: sex hormone changes in a year-long exercise intervention among postmenopausal women. J Clin Oncol 28, 1458–1466.

46. Hays RD, Sherbourne CD & Mazel RM (1993) The RAND 36-Item Health Survey 1.0. Health Econ 2, 217–227.

47. Friedenreich CM, Courneya KS, Neilson HK, et al. (2006) Reliability and validity of the Past Year Total Physical Activity Questionnaire. Am J Epidemiol 163, 959–970.

48. Csizmadi I, Kahle L, Ullman R, et al. (2007) Adaptation and evaluation of the National Cancer Institute’s Diet History Questionnaire and nutrient database for Canadian populations. Public Health Nutr 10, 88–96.

49. Balke B & Ware RW (1959) An experimental study of physical fitness of Air Force personnel. U S Armed Forces Med J 10, 675–688.

50. Ruijter JM, Ruiz Villalba A, Hellemans J, et al. (2015) Removal of between-run variation in a multi-plate qPCR experiment. Biomed Detect Quantif 5, 10–14.

51. Ranstam J (2016) Multiple P-values and Bonferroni correction. Osteoarthritis Cartilage 24, 763–764.

52. De Meyer T, Bekaei S, De Buyzere ML, et al. (2018) Leukocyte telomere length and diet in the apparently healthy, middle-aged Asclepios population. Sci Rep 8, 6540.

53. Meimáł J, Perálá MM, Kaustianen H, et al. (2019) Healthy diets and telomere length and attrition during a 10-year follow-up. Eur J Clin Nutr 73, 1352–1360.

54. Juroszek P, Lumpkin HM, Yang RY, et al. (2009) Fruit quality and bioactive compounds with antioxidant activity of tomatoes grown on-farm: comparison of organic and conventional management systems. J Agric Food Chem 57, 1188–1194.

55. Li H, Deng Z, Zhu H, et al. (2012) Highly pigmented vegetables: anthocyanin compositions and their role in antioxidant activities. Food Res Int 46, 250–259.

56. Ren Z, Zhao A, Wang Y, et al. (2018) Association between Dietary Inflammatory Index, C-reactive protein and metabolic syndrome: a cross-sectional study. Nutrients 10, E831.

57. Mossavar-Rahmani Y, Tinker LF, Huang Y, et al. (2013) Factors relating to eating style, social desirability, body image and eating meals at home increase the precision of calibration equations correcting self-report measures of diet using recovery biomarkers: findings from the Women’s Health Initiative. Nutr J 12, 63.

58. Aubert G, Hills M & Lansdorp PM (2012) Telomere length measurement-caveats and a critical assessment of the available technologies and tools. Mutat Res 730, 59–67.

59. Aviv A, Valdes A, Gardner JP, et al. (2006) Menopause modifies the association of leukocyte telomere length with insulin resistance and inflammation. J Clin Endocrinol Metab 91, 635–640.

60. García-Calzon S, Gea A, Razzquin C, et al. (2014) Longitudinal association of telomere length and obesity indices in an intervention study with a Mediterranean diet: the PREDIMED-NAVARRA trial. Int J Obes 38, 177–182.