Association of the dietary inflammatory index with phenotypic age

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Running title

Dietary inflammation and phenotypic age
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Abstract

Objectives One of the underlying mechanisms of aging is chronic inflammation, which has been closely associated with daily diet. Phenotypic age (PhenoAge) has been used as an index to track the aging process before diseases show clinical symptoms. The present study aimed to explore the association between the dietary inflammatory index (DII) and PhenoAge.

Methods In total, 9275 adults aged 20 years old and over in the National Health and Nutrition Examination Survey (NHANES) were involved in this study. Dietary patterns were classified as pro-inflammatory or anti-inflammatory according to the DII. PhenoAge was regarded as a continuous variable, and linear regression was used to explore its association with dietary inflammation. Stratified analyses by sex, age, race, physical exercise, smoking status, drinking status, and body mass index were used to test the sensitivity of these associations.

Results The median value of PhenoAge was 38.60 years and 39.76 years for the participants with anti-inflammatory and pro-inflammatory diets, respectively. A pro-inflammatory diet was positively associated with PhenoAge ($\beta=0.73; 95\% CI, 0.31–1.14$), compared with participants who had an anti-inflammatory diet. There was an interaction between dietary inflammation and age for PhenoAge ($p_{interaction}<0.001$). The strength of the association between a pro-inflammatory diet and PhenoAge was stronger as age increased.

Conclusion A pro-inflammatory diet was associated with a higher PhenoAge, and the association was strongest in the elderly. We recommended reducing dietary inflammation to delay phenotypic aging, especially for the elderly.

Key words: DII, Phenotypic Age, elderly, NHANES, inflammation, aging
Introduction

According to a 2019 report from the United Nations, 9% of people in the world are over 65 years of age, and by 2050 this number will rise to 16% [1]. The world will then experience an unsustainable burden of chronic diseases, which already extract a significant social and economic toll [2]. Aging involves changes in body composition, homeostatic mechanisms, energetics, and brain health over time. Therefore, aging could be reflected by a systematic analytical approach that integrates multiple biomarkers simultaneously, which could provide an opportunity to identify comprehensive biomarker signatures of aging [3, 4]. Noteworthily, phenotypic age (PhenoAge) was developed as a novel multi-system-based aging measure capable of capturing mortality and morbidity risk in healthy individuals [5, 6]. Previous studies have proven that PhenoAge could facilitate the identification of individuals at risk for various chronic diseases or causes of death [7].

Chronic inflammation is a significant risk factor for morbidity and mortality in the elderly and a common molecular pathway for most age-related diseases [8]. It has been reported that diet is closely associated with inflammation, and inflammation might be a bridge that links diet and chronic diseases [9, 10]. The dietary inflammatory index (DII) is a literature-derived score developed to evaluate the inflammatory potential of the diet and link diet to inflammation [11]. Meanwhile, the DII could serve as a quantitative measure for assessing the relationships between diet and health outcomes [12]. A cohort study indicated that a higher DII (indicating more significant pro-inflammatory diet potential) was associated with an increased risk of incident dementia [13], and a cross-sectional study indicated that the DII was positively associated with cognitive impairment in the elderly [14]. The DII was also associated with frailty and 8-year mortality risk in adults of all ages by another cohort study [15]. Moreover, an association was also found between DII and leukocyte telomere length (LTL) [16]. A previous study pointed out that nutritional issues play a vital role in age-associated diseases and substantially contribute to morbidity, disability, and mortality [17]; thus, it is necessary to form better nutritional habits to improve health outcomes.
However, no studies have explored the association between DII and PhenoAge, especially for different age groups. In this study, we aimed to explore the association between dietary inflammation and aging via DII and PhenoAge in adults based on the National Health and Nutrition Examination Survey (NHANES), and we attempted to quantify the effect of a pro-inflammatory diet on aging. Furthermore, our results might provide a reference for specifying measurements for aging prevention.

Methods

Study population and protocol approval

The NHANES is an ongoing cross-sectional survey that enrolls randomly selected participants for a comprehensive health screening every 2 years to generate a nationally representative sample [18]. The responsible committee of the Ethics Committee of the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB) has approved the research protocol (Ethics ID: #98-12, #2005-06). A total of 32,464 participants aged over 20 were enrolled in NHANES from 1999 to 2010. After excluding participants who had missing data on PhenoAge, diet, and covariables, and who had extreme diet data, 9,275 participants were finally involved in the study. A flowchart is shown in Figure 1. We also described the characteristics of non-participants in Table S1 (Supplementary Materials).

Data measurement

Definition of PhenoAge

The PhenoAge calculation was proposed by Liu et al. as a marker to track the aging process before diseases show clinical symptoms [5, 6]. PhenoAge was calculated using chronological age and 9 biomarkers (albumin, creatinine, glucose, log [C-reactive protein (CRP)], lymphocyte percent, mean cell volume, red blood cell distribution width, alkaline phosphatase, and white blood cell count). PhenoAge was selected through a Cox proportional hazards elastic net model for mortality based on 10-fold cross-validation [5, 6], and PhenoAge was found to represent a person’s expected age within the population, consistent with a person’s estimated mortality hazard as a
function of his/her profile of chemistry biomarkers [19]. The resulting final equation [20] to calculate PhenoAge is shown below:

\[
\text{PhenoAge} = 141.50 + \frac{\ln[-0.00553 \times \ln(1 - M)]}{0.09165}
\]

Where

\[
M = 1 - \exp\left(-\frac{1.51714 \times \exp(xb)}{0.0076927}\right)
\]

\[
xb = -19.907 - 0.0336 \times \text{albumin} + 0.0095 \times \text{creatinine} + 0.1953 \times \text{glucose} + 0.0954
\]

\[
\times \ln(CRP) - 0.0120 \times \text{lymphocyte percent} + 0.0268
\]

\[
\times \text{mean cell volume} + 0.3306 \times \text{red cell distribution width} + 0.0018
\]

\[
\times \text{alkaline phosphatase} + 0.0554 \times \text{white blood cell count} + 0.0804
\]

\[
\times \text{chronological Age}
\]

**Definition of the DII**

We used the revised version of the DII calculation developed by Shivappa et al., and the specific algorithm has been detailed in a previous study [11]. In this study, 26 nutrients were used to calculate the DII, including alcohol, vitamin B12/B6, β-carotene, caffeine, carbohydrate, cholesterol, total fat, fiber, folic acid, iron, magnesium, zinc, selenium, monounsaturated fatty acids, niacin, n-3 fatty acids, n-6 fatty acids, protein, polyunsaturated fatty acids, riboflavin, saturated fat, thiamin, and vitamins A/C/E. Importantly, even if fewer than 30 nutrients are applied, the DII can still be calculated [11]. Participants were divided into those with an anti-inflammatory diet (DII<0) and those with a pro-inflammatory diet (DII≥0) [21].

**Covariate assessment**

Body mass index (BMI) groups were defined into three categories: underweight and healthy weight (BMI < 25.0 kg/m²), overweight (25.0 kg/m² ≤ BMI < 30.0 kg/m²), and obese (BMI ≥ 30.0 kg/m²) [22]. The physical activity level was measured with the Global Physical Activity Questionnaire [23] and divided into 3 groups (“inactive,” “moderate,” and “vigorous”) based on self-reported questions. Smoking status was divided into 3 categories: Non-smokers were defined as those who never smoked or smoked fewer than 100 cigarettes in their lifetime; former smokers were defined as those who had smoked at least 100 cigarettes but did not smoke now; and current
smokers were defined as participants who had smoked least 100 cigarettes and
reported a non-zero number of cigarettes per day in the past 30 days [24]. The NHANES
defined 1 alcohol-based drink as 12 ounces of beer, 4 ounces of wine, or 1 ounce of
liquor. Drinking status was divided into 3 categories: non-drinkers were defined as
participants who had consumed fewer than 12 alcohol-based drinks in the past year or
lifetime; former drinkers were defined as participants who had consumed at least 12
drinks in their lifetime but not in the past year; and current drinkers were defined as
participants who had at least 12 drinks in the past year and reported a non-zero number
of drinks per week [24]. Moreover, the educational level was categorized into 3 groups:
under high school, high school, and college degree or above. Income was measured by
the ratio of family income to the poverty threshold.

Statistical analysis

The mean and standard error (SE) were used to describe continuous variables, and
the unweighted frequency and weighted percentage were used to describe categorical
variables. Multivariate linear regression was used to evaluate the associations between
dietary inflammation and PhenoAge with adjustments. Sensitivity analyses were
conducted via stratified analyses, and p-values for interaction between dietary
inflammation and each stratified variable were also tested. All statistical analyses were
conducted using SPSS version 24.0 (IBM Corp., Armonk, NY, USA) and R version
4.1.0, and the packages “forestplot”[25] and “survey”[26] were used. A 2-sided p-value
<0.05 was considered significant. All the analyses were performed using the complex
sampling weight of NHANES.

Results

Table 1 shows the basic characteristics of the 9,275 participants, of whom 4,496 had
an anti-inflammatory diet and 4,779 had a pro-inflammatory diet. The median
PhenoAge was 39.04 years, 38.60 years, and 39.76 years for the total participants, the
participants with an anti-inflammatory diet, and the participants with a pro-
inflammatory diet, respectively.
We conducted univariate linear regression to test the relationships of variables with PhenoAge in adults, as shown in Table 2. The variables showed statistically significant associations with PhenoAge except for sex and income. Table 3 shows the association between dietary inflammation and PhenoAge in adults according to multivariate linear regression. Compared to participants with an anti-inflammatory diet, those with a pro-inflammatory diet had a PhenoAge in model 1 (pro-inflammatory diet: $\beta=1.78; 95\% \text{ CI}, 1.43–2.14$). Similar results were observed in model 2 (pro-inflammatory diet: $\beta=1.38; 95\% \text{ CI}, 1.05–1.71$) and model 3 (pro-inflammatory diet: $\beta=0.73; 95\% \text{ CI}, 0.31–1.14$). A larger coefficient indicated a greater risk of the pro-inflammatory diet for higher PhenoAge.

As shown in the forest plot in Figure 2, the positive association between a pro-inflammatory diet and PhenoAge was robust after a stratified analysis. Noteworthily, there was an interaction between dietary inflammation and age on PhenoAge ($p_{\text{interaction}}<0.001$). The association between a pro-inflammatory diet and PhenoAge was stronger as age increased. Moreover, we did not observe statistically significant interactions of dietary inflammation with sex, race, physical exercise, smoking status, drinking status, or BMI group on PhenoAge.

**Discussion**

In this study, we investigated the association between dietary inflammation and PhenoAge, and we found that a pro-inflammatory diet was significantly associated with a higher PhenoAge. Additionally, an interaction was found between a pro-inflammatory diet and age, with the strongest association between a pro-inflammatory diet and PhenoAge found in the elderly.

No previous cohort or cross-sectional study has examined the relationship between the DII and PhenoAge. Our study was the first to do so, to the best of our knowledge. PhenoAge has been proven to be more than a measure of disease or morbidity; instead, it may be a marker that tracks the effect of aging before diseases become clinically evident [6]. Meanwhile, PhenoAge could capture pre-clinical aging and future...
morbidity/mortality risk, facilitate the evaluation of intervention efficacy, and avoid the
need for decades of follow-up [27]. Based on the positive association observed between
a pro-inflammatory diet and PhenoAge, we recommend following an anti-inflammatory
diet to lower PhenoAge in the elderly, thereby preventing the adverse consequences of
aging.

Aging is a ubiquitous and complex phenomenon, and epidemiological evidence has
indicated that elevated inflammatory biomarkers, including CRP and interleukin (IL)-
6 could reflect a mild inflammatory state associated with many aging phenotypes
[8]. “Inflamma-aging” is a common finding in aging and age-related disease that
involves dysregulation of the cytokine network and its homeostasis [28]. The major pro-
inflammatory cytokines, such as IL-6, tumor necrosis factor-alpha, and IL-1α,
contribute significantly to inflammatory aging in healthy elderly individuals [29].
Moreover, based on the direct effect of pro-inflammatory cytokines on the muscle
catabolic and anabolic signaling pathways, inflammation may contribute to the
development of sarcopenia [30].

Diet is an important and potentially easily modifiable risk factor for chronic disease
[31]. There has been extensive interest in how dietary strategies can improve immunity
in the elderly, and the nutritional approach is particularly suitable for the aging
population [32]. Several previous studies have explored the associations between diet
and aging, including caloric restriction diets [33, 34], different dietary patterns such as
the plant-based Mediterranean diet [17, 35], and specific nutrients such as long-chain
omega-3 fatty acids (docosahexaenoic acid and eicosapentaenoic acid) [36]. The lower
CVD risk found in populations with high adherence to the Mediterranean diet may be
partly explained by the consumption of the Mediterranean diet reducing the
postprandial inflammatory response in mononuclear cells compared with saturated fatty
acid-rich and carbohydrate/polyunsaturated fatty acid-rich diets in older adults [37].
Another study proved that plant-based dietary patterns were associated with lower
oxidative stress and inflammation levels, which may provide a reasonable approach for
chronic disease prevention [38]. Although previous studies have focused on dietary
patterns and different age-related diseases, they all support the association between a healthy diet and longevity.

Moreover, dietary inflammation has been found to be positively associated with cognitive impairment, frailty, cardiometabolic risk, and other age-related diseases in previous studies [14, 15, 39]. Interestingly, some anti-aging nutrients are anti-inflammatory, such as vitamins A, D, E, and K and omega-3 fatty acids [40]. A previous study indicated that pro-inflammatory diets, which are typically high in refined grains, whole-fat dairy, red meat, total fat, and saturated fat, are positively associated with higher levels of inflammatory biomarkers [41]. It was reported that a higher DII was associated with a shorter LTL, an important aging biomarker [16]. The inflammatory potential of the diet was also related to incident frailty, slow walking, lower muscle mass, and poorer muscle function in older adults [42, 43].

There are some strengths and weaknesses of current research. As for the advantages, firstly, it was the first study focused on the DII and PhenoAge, which are combined indicators of dietary inflammation and aging, respectively. Secondly, our study could provide evidence to support preventing aging from a dietary perspective. Thirdly, our study was based on the NHANES, a nationally representative survey. As for the weaknesses, firstly, this was a cross-sectional study and might not enable robust causal inferences. Secondly, the study population was from the U.S., and the conclusions may not be generalized to other populations. Thirdly, the 24-hour recall diet data may have been subject to recall bias. Furthermore, we need to expand the cohort study’s sample size to explore in-depth associations between dietary inflammation and PhenoAge and how dietary inflammation affects aging in the general population. Finally, the age of participants was slightly lower than the age of non-participants, which may have caused selection bias; thus, the PhenoAge may have been underestimated. However, we performed a sensitivity analysis to reanalyze the imputed data, and consistent findings were obtained.
Conclusion

The participants with a pro-inflammatory diet had a higher PhenoAge, and this positive association was evident in almost all subgroups considered. There was an interaction between a pro-inflammatory diet and age, with the strongest association between a pro-inflammatory diet and PhenoAge found in the elderly. Based on this study, we recommended reducing dietary inflammation to delay phenotypic aging, especially for the elderly. Further research is warranted to confirm the association between the inflammatory potential of the diet and aging, as well as to verify these findings in other population groups.

Declarations

Ethics approval and consent to participate

The institutional review board approved the protocols of the NHANES of the National Center for Health Statistics, CDC. Written informed consent was obtained from each participant before participation in this study.

Availability of data and materials

The data that support the findings of this study are openly available at https://www.cdc.gov/nchs/nhanes/. Information from NHANES is made available through an extensive series of publications and articles in scientific and technical journals. For data users and researchers throughout the world, survey data are available on the internet and on easy-to-use CD-ROMs.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Author contributions

Mengzi Sun and Jiaxin Fang conducted the statistical analysis, supervised by Lina
Jin and Yanan Ma. Mengzi Sun and Jiaxin Fang wrote the paper, supervised by Lina Jin and Yanan Ma. All authors contributed to the data interpretation, revised each draft for important intellectual content, and read and approved the final manuscript. Lina Jin and Yanan Ma contributed equally as corresponding co-authors.

**Funding**

The funders had no role in the design of the study, the collection, analysis, and interpretation of data, or writing the manuscript.
REFERENCES


About the national health and nutrition examination survey [https://www.cdc.gov/nchs/nhanes/about_nhanes.htm]


Schaap LA, Pluijm SM, Deeg DJ, Visser M: Inflammatory markers and loss of


Figure 1. The flowchart of participants in this study.

Initial sample of the NHANES 1999-2010, ≥20 years old, N=32464

Remaining sample size N=15528

Exclusion of participants with missing phenotypic age data. n=16936

Remaining sample size N=15528

Exclusion of participants with missing or extreme diet data. n=4472

Remaining sample size N=15528

Exclusion of participants with missing data for covariables. n=1781
Figure 2. Forest plot of stratified analyses of the associations between a pro-inflammatory diet and phenotypic age in adults.

CI, confidence interval; BMI, body mass index.

Adjusted for age (years), sex (male, female), race (non-Hispanic White, other), BMI (kg/m²), energy intake (kcal), smoking status (non-smoker, current smoker, former smoker), drinking status (non-drinker, current drinker, former drinker), and physical exercise (inactive, moderate, vigorous). Educational level (under high school, high school, college or above), and ratio of family income to the poverty threshold.
Table 1. Baseline characteristics of participants in elderly in NHANES 1999-2010 by inflammatory diet (M(P25, P75)/N(%))

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total N=9275</th>
<th>Anti-inflammatory diet N=4496</th>
<th>Pro-inflammatory diet N=4779</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4584(49.4)</td>
<td>2638(59.4)</td>
<td>1946(38.0)</td>
</tr>
<tr>
<td>Female</td>
<td>4691(50.6)</td>
<td>1858(40.6)</td>
<td>2833(62.0)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>4736(73.3)</td>
<td>2546(77.8)</td>
<td>2190(68.3)</td>
</tr>
<tr>
<td>Other race</td>
<td>4539(26.7)</td>
<td>1950(22.2)</td>
<td>2589(31.7)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–39</td>
<td>3237(38.9)</td>
<td>1610(37.7)</td>
<td>1627(40.2)</td>
</tr>
<tr>
<td>40–64</td>
<td>3774(44.3)</td>
<td>1896(46.9)</td>
<td>1878(41.4)</td>
</tr>
<tr>
<td>≥65</td>
<td>2264(16.8)</td>
<td>990(15.4)</td>
<td>1274(18.4)</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under high school</td>
<td>2633(18.3)</td>
<td>971(13.3)</td>
<td>1662(24.0)</td>
</tr>
<tr>
<td>High school</td>
<td>2219(25.0)</td>
<td>989(21.7)</td>
<td>1230(28.7)</td>
</tr>
<tr>
<td>College degree or above</td>
<td>4423(56.7)</td>
<td>2536(65.1)</td>
<td>1887(47.3)</td>
</tr>
<tr>
<td>Ratio of family income to poverty</td>
<td>3.11(1.58, 5.00)</td>
<td>3.65(2.04, 5.00)</td>
<td>2.40(1.27, 4.20)</td>
</tr>
<tr>
<td>Physical exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactive</td>
<td>4465(42.0)</td>
<td>1934(38.3)</td>
<td>2531(46.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2486(28.6)</td>
<td>1266(28.9)</td>
<td>1220(28.2)</td>
</tr>
<tr>
<td>Vigorous</td>
<td>2324(29.4)</td>
<td>1296(32.8)</td>
<td>1028(25.4)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>4810(50.7)</td>
<td>2401(52.8)</td>
<td>2409(48.4)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>2493(26.2)</td>
<td>1311(29.1)</td>
<td>1182(22.9)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1972(23.1)</td>
<td>784(18.1)</td>
<td>1188(28.8)</td>
</tr>
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<td>Drinking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-drinker</td>
<td>1230(10.4)</td>
<td>454(7.7)</td>
<td>776(13.6)</td>
</tr>
<tr>
<td>Former drinker</td>
<td>3596(41.3)</td>
<td>1814(43.0)</td>
<td>1782(39.3)</td>
</tr>
<tr>
<td>Current drinker</td>
<td>4449(48.3)</td>
<td>2228(49.4)</td>
<td>2221(47.1)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.35(23.91, 31.77)</td>
<td>26.94(23.75, 31.04)</td>
<td>27.80(24.05, 32.55)</td>
</tr>
<tr>
<td>BMI group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight and healthy weight</td>
<td>2767(33.2)</td>
<td>1423(35.0)</td>
<td>1344(31.1)</td>
</tr>
<tr>
<td>Overweight</td>
<td>3237(33.2)</td>
<td>1618(34.3)</td>
<td>1619(32.1)</td>
</tr>
<tr>
<td>Obese</td>
<td>3271(33.6)</td>
<td>1455(30.7)</td>
<td>1816(36.8)</td>
</tr>
<tr>
<td>Energy intake (kcal)</td>
<td>2034.0(1551.5, 2644.5)</td>
<td>2449.0(1983.0, 3075.0)</td>
<td>1608.5(1289.2, 2030.0)</td>
</tr>
<tr>
<td>PhenoAge (years)</td>
<td>39.04(25.92, 53.49)</td>
<td>38.60(26.28, 51.65)</td>
<td>39.76(25.67, 55.61)</td>
</tr>
</tbody>
</table>

BMI, body mass index; PhenoAge, phenotypic age.
Table 2. Univariate linear regression of variables on the PhenoAge in adults in NHANES 1999-2010

<table>
<thead>
<tr>
<th>Variables</th>
<th>β</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td>Dietary inflammation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-inflammation</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pro-inflammation</td>
<td>1.372</td>
<td>(0.29, 2.46)</td>
<td>0.014</td>
</tr>
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<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>-0.82</td>
<td>(-1.83, 0.18)</td>
<td>0.107</td>
</tr>
<tr>
<td>Race</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other race</td>
<td>-5.37</td>
<td>(-4.14, -6.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.06</td>
<td>(1.05, 1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age group</td>
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</tr>
<tr>
<td>20–39</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–64</td>
<td>22.29</td>
<td>(21.60, 22.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥65</td>
<td>46.55</td>
<td>(45.84, 47.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Educational level</td>
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<td></td>
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</tr>
<tr>
<td>Under high school</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>-1.62</td>
<td>(-3.68, 0.44)</td>
<td>0.121</td>
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<tr>
<td>College or above</td>
<td>-5.37</td>
<td>(-7.09, -3.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ratio of family income to poverty</td>
<td>0.06</td>
<td>(-0.34, 0.45)</td>
<td>0.765</td>
</tr>
<tr>
<td>Physical exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactive</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>-1.83</td>
<td>(-3.04, -0.62)</td>
<td>0.004</td>
</tr>
<tr>
<td>Vigorous</td>
<td>-10.22</td>
<td>(-11.46, -8.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>10.52</td>
<td>(9.20, 11.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>-0.65</td>
<td>(-2.06, 0.76)</td>
<td>0.363</td>
</tr>
<tr>
<td>Drinking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-drinker</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former drinker</td>
<td>-3.83</td>
<td>(-6.04, -1.63)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current drinker</td>
<td>-4.85</td>
<td>(-7.15, -2.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.51</td>
<td>(0.43, 0.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight and healthy weight</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>6.38</td>
<td>(5.19, 7.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obese</td>
<td>8.30</td>
<td>(7.11, 9.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Energy intake</td>
<td>-0.005</td>
<td>(-0.006, -0.004)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI, confidence interval; BMI, body mass index.
Table 3. Multivariate linear regression of dietary inflammation on the PhenoAge in the elderly in NHANES 1999-2010 in different models

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of events</th>
<th>$\beta$ (95% CI)</th>
<th>Model I$^a$</th>
<th>Model II$^b$</th>
<th>Model III$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary inflammation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-inflammation</td>
<td>4496</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pro-inflammation</td>
<td>4779</td>
<td>1.78(1.43, 2.14)</td>
<td>1.38(1.05, 1.71)</td>
<td>0.73(0.31, 1.14)</td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval.

$^a$ Adjusted for age (years) and sex (male, female).

$^b$ Adjusted for age (years), sex (male, female), race (non-Hispanic White, other), and BMI (kg/m$^2$).

$^c$ Adjusted for age (years), sex (male, female), race (non-Hispanic White, other), BMI, energy intake (kcal), smoking status (non-smoker, current smoker, former smoker), drinking status (non-drinker, current drinker, former drinker), physical exercise (inactive, moderate, vigorous), educational level (under high school, high school, college or above), and ratio of family income to the poverty threshold.