




Organic food consumption is associated with inflammatory biomarkers among older adults

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Abstract

Objective: The association between organic food consumption and biomarkers of inflammation, C-reactive protein (CRP) and cystatin C (CysC) was explored in this cross-sectional analysis of older adults.

Design: Dietary data and organic food consumption was collected in 2013 from a FFQ. Alternative Mediterranean diet score (A-MedDiet) was calculated as a measure of healthy eating. Biomarkers CRP and CysC were collected in serum or plasma in 2016. We used linear regression models to assess the associations between organic food consumption and CRP and CysC.

Setting: This cross-sectional analysis uses data from the nationally representative, longitudinal panel study of Americans over 50, the Health and Retirement Study.

Participants: The mean age of the analytic sample (n 3815) was 64.3 (SE 0.3) years with 54.4% being female.

Results: Log CRP and log CysC were inversely associated with consuming organic food after adjusting for potential confounders (CRP: $\beta = -0.096$, 95% CI 0.159, -0.033 ; CysC: $\beta = -0.033$, 95% CI -0.051 , -0.015). Log CRP maintained statistical significance ($\beta = -0.080$; 95% CI -0.144 , -0.016) after additional adjustments for the A-MedDiet, while log CysC lost statistical significance ($\beta = -0.019$; 95% CI -0.039 , 0.000). The association between organic food consumption and log CRP was driven primarily by milk, fruit, vegetables and cereals, while log CysC was primarily driven by milk, eggs and meat after adjustments for A-MedDiet.

Conclusions: These findings support the hypothesis that organic food consumption is inversely associated with biomarkers of inflammation CRP and CysC, although residual confounding by healthy eating and socioeconomic status cannot be ruled out.

Keywords

Organic food consumption
Conventional food consumption
C-reactive protein
Cystatin C
Health and Retirement Study
Pesticides
Chronic disease

Since the coining of the term ‘organic farming’ in 1940 by Lord Northbourne, the agricultural movement has taken root around the world spreading to a total of 130 countries^(1,2). In the USA alone, the demand for organically grown products has grown 18.5% from 1997 to 2005 and by 2014 the market was valued at \$39.1 billion^(3,4). Consumer motivation for buying organic foods spans environmental concerns, human health and safety, nutritional value, taste and freshness of the products consumed⁽²⁾. There are known socio-demographic factors that contribute to higher consumption of organic foods: having a family with children, attaining a higher education level, being higher income, being female and, to a more modest degree, being younger⁽²⁾. Research shows that people who buy organic food are also more likely to eat a healthy diet^(5,6). Therefore, it is

challenging to disentangle the effect of consuming organic food from eating healthy.

The past 20 years have seen a marked increase in research aimed at understanding the differences in nutritional value for organic foods compared with conventional foods. Overall, the results show healthier trends for organic food but are still inconclusive. Most studies show higher concentrations of vitamin C, Fe, Mg and lower concentrations of nitrates in organic fruits and vegetables^(7–9). Organically grown grains have been found to contain less protein and amino acids, yet have a higher quantity of essential amino acids⁽¹⁰⁾. Organic dairy products and other organic animal products have been found to contain more beneficial fatty acids than their conventional counterparts^(7,9).

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Beyond just the examination of nutritional content in organic foods, there is considerable interest in evaluating the impact that organic food has on human health. Current research has begun to show a relationship between organic food consumption and reduced allergic diseases, atopy, CVD, metabolic syndrome, preeclampsia, non-Hodgkin lymphoma, hypospadias and higher sperm concentrations in men^(11–20).

As the health benefits of organic foods are still largely unexplored, this research aims to further understand the relationship between organic food consumption and chronic disease outcomes. C-reactive protein (CRP) and cystatin C (CysC) will be used as biomarkers of inflammation for chronic disease outcomes in the current analysis. CRP is a common biomarker associated with inflammation used to predict atherosclerosis, type 2 diabetes, CVD, cancer and chronic obstructive pulmonary disease^(21–26). CysC is a common biomarker used to detect renal dysfunction, CVD, heart failure and diabetes^(27,28). At present, there is no known research conducted in humans examining the relationship between organic food consumption and the outcomes of interest in CRP and CysC. In the current study of older adults in the USA, the association between organic food consumption, CRP and CysC will be explored.

Methods

Subjects

This cross-sectional analysis uses data from the longitudinal panel study of Americans over 50 and their spouses, the Health and Retirement Study, conducted by the University of Michigan and funded jointly by the National Institute of Aging (NIA U01AG009740) and the Social Security Administration⁽²⁹⁾.

Socio-demographic and health variables were drawn from the Health and Retirement Study 2012 core dataset and linked to the Tracker Cross-Wave Tracker File for variables on complex sampling design and combined with the RAND 1992–2014 Cross-Wave Income and Wealth data set along with two supplemental studies: 2013 Health Care and Nutrition Study and the Venous Blood Study 2016 (VBS)^(30,31). The Health Care and Nutrition Study was a mail survey delivered in 2013 to a subsample of Health and Retirement Study participants (*n* 8073) collecting data about food and nutrition including a FFQ and information on the consumption of organic foods in the past year.⁽³²⁾ The VBS was requested of all study participants who completed an interview during 2016 (*n* 9934) and included serum CRP and CysC sample collection managed by Hooper Holmes Health & Wellness⁽³³⁾. Once the data were combined, 4404 participants had completed both surveys with 4378 having complete data on organic food variables and CRP and 4379 having complete data on organic food variables and CysC. The participants from the VBS who were included in the current analysis are

comparable in socio-demographic characteristics to those from the VBS who were not included, thereby enabling generalisability of the study results to the participants of the VBS at large as well as to the general US population aged 50 and older.

Exclusion criteria

Age, total caloric intake and cancer were used as exclusion criteria. Participants < 50 years of age were not included in the analysis as they were not sampled following the complex sample design and were not representative for their age group. Participants with extreme or unlikely caloric intake were excluded including men who reported eating < 3347.2 kJ/d (800 kcal/d) or more than 16 736 kJ/d (4000 kcal/d) and women who reported eating < 2092 kJ/d (500 kcal/d) or more than 14 644 kJ/d (3500 kcal/d)⁽³⁴⁾. There were 575 previous cases of cancer, one of which had undergone chemotherapy. The participant who had chemotherapy was excluded from the sample size and a sensitivity analysis was conducted on the remaining cases of cancer. There was no significant difference observed upon removing the participants with previous cases of cancer; therefore, they were included in the analysis. After all exclusion criteria were implemented, 3719 people were included in the descriptive analysis. Furthermore, for the regression analysis participants with missing values for covariates were also excluded in order to ensure comparability between models (*n* 3653, see online supplementary material, Supplemental Figure 1 for a sample size flow diagram). Three hundred nineteen participants with CRP > 10 were excluded only from the CRP regression analysis in accordance with previous literature to eliminate participants with acute inflammation (*n* 3433)⁽³⁵⁾; however, regression analysis with all CRP values is also presented as a supplementary table since some authors suggest that a CRP cut-off of 10 is arbitrary and may exclude some participants who do not have acute inflammation⁽³⁶⁾.

Assessment of diet

A self-administered FFQ, based on Willett and colleagues Harvard FFQ⁽³⁷⁾, was mailed to a subset of the Health and Retirement Study participants as a part of the Health Care and Nutrition Study in 2013. In addition to the FFQ, participants were asked if they had eaten any organic foods in the past year (yes/no), if so what type: milk, eggs, meat, fruit (fresh or frozen), vegetables (fresh or frozen), bread or cereals, frozen prepared meals (e.g., Amy's frozen entrees, Organic Bistro entrees) or other (specify)⁽³⁸⁾. Participants who answered 'no' or 'missing' to the initial organic food question but then said they ate any of the organic food types were recoded as 'yes' to the initial organic food question. A sensitivity analysis excluding recoded participants revealed no significant difference from their inclusion in the analysis (see online supplementary material, Supplemental Table 1).



For analytic purposes, the organic food type variables were transformed from a binary yes/no variable into categorical variables that distinguish between eating a particular organic food, eating other organic foods but not that particular organic food and not eating organic food of any kind. For example, organic milk became drinks organic milk, eats organic food but not organic milk and does not eat organic food. The Alternative Mediterranean diet score (A-MedDiet) was calculated by summing together one point given for nine categories derived from the FFQ on a scale of 0–9⁽³⁹⁾. The categories were servings of fruits, vegetables, whole grains, red/processed meats, alcohol, nuts, legumes, fish and ratio of MUFA to SFA. The gender-specific median values for each category were then computed and used as the cut point for each category. A score of 1 was given to all participants who were above the gender-specific median and a score of 0 to those participants who were below the cut point in every category except red/processed meats and alcohol. For red/processed meats, a score of 1 was given to participants who were below the gender-specific median and a score of 0 to those who were above. For alcohol, a score of 1 was given to those who drank moderately and a score of 0 to participants who did not drink at all or who drank heavily (see online supplementary material, Supplemental Table 2).

Assessment of biomarkers

Venous blood samples were collected in the home by trained phlebotomists with the goal of scheduling the blood draw in the morning. CRP was assessed via serum using a latex-particle enhanced immunoturbidimetric assay kit (Roche Diagnostics) and CysC was assessed using a CysC reagent (Gentian)⁽³³⁾. Both biomarkers were analyzed via Roche COBAS 6000 Chemistry analyzer (Roche Diagnostics)⁽³³⁾. Continuous CRP and CysC values were log-transformed to account for their non-normal distributions. Cut points for high risk, consistent with previous research and clinical practice, were instituted for CysC at > 1.55 mg/l and CRP \geq 3.00 mg/l in order to conduct logistic regression analyses^(40,41).

Covariate definitions

Age at the time of completing the Health Care and Nutrition Study (2013) was utilized for all analyses. Race is presented as a categorical variable: Black, Hispanic, White and Other. BMI was calculated during in-person interviews from measured height and weight using a rafter's square, tape measure and scale⁽⁴²⁾. It was then categorized into four groups for analysis: underweight (BMI below 18.5), normal or healthy weight (BMI 18.5–24.9), overweight (25.0–29.9) and obese (30 and above)⁽⁴³⁾. Years of education completed was divided into four categories: less than high school graduate (0–11 years), graduated from high school (12 years), some college or college graduate (13–16 years) and post-college (17+ years). Income was measured using total wealth of all assets excluding secondary residence⁽³¹⁾.

Participants current employment status was divided into currently working or not working which included: unemployed and looking for work, temporarily laid off, disabled, retired, homemaker, sick leave or other leave. All three cholesterol variables were measured in blood serum and presented continuously using different methods: total cholesterol with a cholesterol oxidase method (Roche Diagnostics) in mg/dl, HDL-cholesterol with Roche HDL-Cholesterol 3rd generation direct method (Roche Diagnostics) in mg/dl and LDL-cholesterol with the Friedewald LDL = $TC - HDL - TG / 5.0$ (Friedewald WT, Fredrickson DS) in mg/dl⁽³³⁾. TAG were measured in blood serum by enzymatic Triglyceride Reagent (Roche Diagnostics) and reported continuously as mg/dl⁽³³⁾. Diabetes was self-reported if the participant reporting having ever been told by a medical professional that they had diabetes or high blood sugar. High blood pressure was self-reported if the participant reported having ever been told by a medical professional that they had high blood pressure. Participants were asked how often they engaged in vigorous or moderate physical activity. These two variables were combined into one variable with three categories: hardly ever or never engage in vigorous/moderate physical activity, a few times per month engage in vigorous/moderate physical activity and once a week or more engage in vigorous/moderate physical activity. Self-reported current smoking status was reported as a binary variable yes/no. Alcohol consumption was calculated from the FFQ in g per d. Following a vegetarian diet was self-reported as yes or no.

Statistical analysis

Statistical significance was tested between organic food consumers and non-organic consumers by χ^2 for binary and categorical predictors (BMI, gender, race, diabetes status, smoking status, moderate or vigorous physical activity, education, job status and organic food consumption) and by *t* test for continuous predictors that were normally distributed and log-transformed if non-normally distributed (age, HDL-cholesterol, LDL-cholesterol, total cholesterol, TAG, alcohol consumption and income) taking into account the complex study sample design: strata, cluster and weight.

Linear regression models were constructed with the exposures of interest, consumption of organic foods (yes/no) and by each organic food type (milk, eggs, meat, fruit, vegetables, bread or cereals and frozen prepared meals) individually, with the outcomes of interest being log-transformed CRP and CysC. A crude model was constructed for each outcome along with multiple adjusted analyses: the first adjusting for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, education, income, job status and daily caloric intake, the second adding vegetarian status to the covariates and the third adding A-MedDiet to the covariates. A logistic regression model was also constructed using

previously established cut-points for high-risk CRP and CysC^(40,41). The unadjusted and adjusted models were tested taking into account the sample weights and complex design features of the study. Adjusted models were tested for multicollinearity using variance inflation factor.

Furthermore, interaction terms for vegetarian and organic food, education and organic food, along with A-MedDiet and organic food, were constructed and tested for statistical significance. The probability level at which differences were considered significant was ≤ 0.05 . Statistical analysis was carried out in SAS version 9.4.

Results

The descriptive characteristics, including potential confounders, are shown by organic food consumption in Table 1. People who ate organic foods had similar characteristics to those described previously in literature; they tended to be younger, White, more highly educated and more physically active⁽²⁾. They also had overall better health indicators and were more likely to still be working.

CRP and CysC range from 0.21 to 211.80 mg/l and 0.51 to 9.12 mg/l, respectively. Characteristics of the study population by CRP and CysC high-risk cut points are shown in Table 2. Study participants with high CRP and high CysC consumed fewer organic foods and most socio-demographic, lifestyle and medical history characteristics were distributed in the expected directions.

Log CRP was inversely associated with consuming organic food (Table 3) in the crude model ($\beta = -0.152$, 95 % CI -0.216 , -0.089 ; online supplementary material, Supplemental Figure 2 illustrates this relationship through histograms). Once potential confounders were controlled for, the relationship was attenuated but remained significant ($\beta = -0.096$, 95 % CI -0.159 , -0.033). Controlling for vegetarian status ($\beta = -0.088$, 95 % CI -0.152 , -0.024) and the A-MedDiet ($\beta = -0.080$, 95 % CI -0.144 , -0.016) attenuated the results a bit further, but statistical significance was maintained. Log CysC was inversely associated with consuming organic food ($\beta = -0.0921$, 95 % CI -0.1160 , -0.0683 ; see online supplementary material, Supplemental Figure 2 for histograms). Controlling for potential confounders attenuated the results yet they remained statistically significant ($\beta = -0.033$, 95 % CI -0.051 , -0.015). Controlling for vegetarian status did not change the results ($\beta = -0.034$, 95 % CI -0.053 , -0.016) while controlling for the A-MedDiet further attenuated the results and statistical significance was lost ($\beta = -0.019$, 95 % CI -0.039 , 0.000). Interaction terms for vegetarian and organic food, education and organic food, along with A-MedDiet and organic food, were not statistically significant.

Using the clinically determined high-risk cut points for CRP and CysC, CRP was inversely associated with consuming organic food in the crude model (OR = 0.699, 95 % CI 0.590, 0.827). Once potential confounders were controlled

for the relationship was attenuated (OR = 0.781, 95 % CI 0.642, 0.950). The OR continued to attenuate with the addition of vegetarian status (OR = 0.799, 95 % CI 0.652, 0.979) and the A-MedDiet (OR = 0.814, 95 % CI 0.673, 0.984). CysC was inversely associated with consuming organic food in the crude model (OR = 0.664, 95 % CI 0.540, 0.817). However, once potential confounders were controlled for, the relationship was completely attenuated and lost statistical significance (OR = 0.982, 95 % CI 0.764, 1.262). Further controlling for vegetarian status or the A-MedDiet did not change the results (OR = 0.971, 95 % CI 0.748, 1.262) and (OR = 1.063, 95 % CI 0.816, 1.384), respectively. The logistic regression results are not presented in the current study but are available upon request.

Linear regression analysis including all CRP values showed that log CRP was inversely associated with consuming organic food (see online supplementary material, Supplemental Table 3) in the crude model ($\beta = -0.165$, 95 % CI -0.240 , -0.089). Once potential confounders were controlled for, the relationship was attenuated but remained significant ($\beta = -0.083$, 95 % CI -0.154 , -0.013). Controlling for vegetarian status did not change the results ($\beta = -0.076$, 95 % CI -0.147 , -0.006), whereas controlling for the A-MedDiet attenuated the results further and statistical significance was lost ($\beta = -0.062$, 95 % CI -0.133 , 0.009). Influential points were identified for each biomarker and an exclusion analysis showed improved point estimates and *P*-values. Therefore, a conservative approach was implemented that included the influential points in the analysis (see online supplementary material, Supplemental Table 4 for linear regression analysis without influential points). After the removal of the influential points, log CRP and log CysC were inversely associated with consuming organic food after controlling for the A-MedDiet ($\beta = -0.085$, 95 % CI -0.151 , -0.019) and ($\beta = -0.026$, 95 % CI -0.045 , -0.007), respectively. All four models for log CRP and log CysC were statistically significant and inversely associated with consuming organic food.

Organic milk ($\beta = -0.244$, 95 % CI -0.373 , -0.115), eggs ($\beta = -0.156$, 95 % CI -0.256 , -0.056), meat ($\beta = -0.164$, 95 % CI -0.263 , -0.065), fruit ($\beta = -0.162$, 95 % CI -0.232 , -0.092), vegetables ($\beta = -0.164$, 95 % CI -0.232 , -0.097) and cereals ($\beta = -0.206$, 95 % CI -0.303 , -0.109) were inversely associated with log CRP in the unadjusted analysis (Table 4). Organic milk, fruit, vegetables and cereals maintained statistical significance once all potential confounders along with the A-MedDiet were adjusted for ($\beta = -0.156$, 95 % CI -0.273 , -0.040); ($\beta = -0.075$, 95 % CI -0.140 , -0.010); ($\beta = -0.081$, 95 % CI -0.150 , -0.012); and ($\beta = -0.098$, 95 % CI -0.184 , -0.012), respectively, while the rest of the organic food types maintained an inverse association. Organic milk ($\beta = -0.137$, 95 % CI -0.171 , -0.103), eggs ($\beta = -0.123$, 95 % CI -0.154 , -0.092) and meat ($\beta = -0.128$, 95 % CI -0.158 , -0.097) were the primary drivers, greatest magnitude, of the inverse association with log CysC (Table 4). Controlling for potential confounders attenuated the results yet they remained statistically significant: organic milk ($\beta = -0.057$, 95 % CI -0.083 , -0.030),

**Table 1** Organic food consumption in the Health and Retirement Study population by covariates (*n* 3719)

| Characteristics | Organic food consumption (no) (<i>n</i> 1981)* | Organic food consumption (yes) (<i>n</i> 1738)* | <i>P</i> |
|--|--|---|-----------|
| Age (years) | | | < 0.0001† |
| Mean | 65.06 | 63.46 | |
| SE | 0.31 | 0.35 | |
| BMI | | | 0.0295† |
| Underweight | 0.39 | 0.98 | |
| Normal | 17.8 | 20.62 | |
| Overweight | 32.83 | 33.7 | |
| Obese | 48.99 | 44.69 | |
| Gender | | | 0.0099† |
| Female | 52.17 | 57.25 | |
| Race | | | 0.2019 |
| White | 80.05 | 81.33 | |
| Black | 9.05 | 6.82 | |
| Hispanic | 7.79 | 8.09 | |
| Other | 3.11 | 3.76 | |
| High blood pressure | 58.25 | 50.17 | < 0.0001† |
| Diabetes | 22.61 | 16.59 | 0.0003† |
| Current smoker | 25.02 | 19.81 | 0.0538 |
| Alcohol consumption (per d in g) | 6.64(0.49) | 8.36(0.56) | 0.0418† |
| Moderate or vigorous physical activity | | | < 0.0001† |
| Hardly ever or never | 16.91 | 8.94 | |
| A few times per month | 12.6 | 7.49 | |
| Once a week or more | 70.49 | 83.57 | |
| Years of education | | | < 0.0001† |
| Less than high school | 13.92 | 10.14 | |
| High school grad | 37.6 | 23.2 | |
| Some college/college grad | 39.29 | 44.78 | |
| Post-college | 9.19 | 21.87 | |
| Total net worth | | | 0.3347 |
| Mean | 479 481 | 612 838 | |
| SE | 127 638 | 57 136 | |
| Currently working | 43.59 | 52.47 | < 0.0001† |

*With the exception of missing values for high blood pressure (9), diabetes (11), current smoker (1720), moderate or vigorous physical activity (11) and currently working (1).
†Significant *P*-values below 0.05.

eggs ($\beta = -0.046$, 95% CI -0.071 , -0.022) and meat ($\beta = -0.053$, 95% CI 0.076 , -0.030). Controlling for vegetarian status did not change the results: organic milk ($\beta = -0.058$, 95% CI -0.085 , -0.031), eggs ($\beta = -0.048$, 95% CI -0.072 , -0.024) and meat ($\beta = -0.054$, 95% CI -0.076 , -0.031), while controlling for the A-MedDiet further attenuated the results yet the association remained statistically significant: organic milk ($\beta = -0.041$, 95% CI -0.069 , -0.014), eggs ($\beta = -0.031$, 95% CI -0.056 , -0.005) and meat ($\beta = -0.038$, 95% CI -0.063 , -0.013).

Discussion

In this cross-sectional analysis, consumption of organic food was inversely associated with CysC and CRP. CRP and CysC remained inversely associated with consumption of organic food even after controlling for all potential confounders and vegetarian status. CRP also maintained statistical significance after controlling for the A-MedDiet and showed an inverse association. While CysC still demonstrated an inverse association, it lost statistical significance once the A-MedDiet was adjusted for; however, once influential points were removed CysC maintained statistical significance as well. As demonstrated above, the linear

regression analysis for organic food consumption was inversely associated with CRP and CysC. Once categorized by their high-risk cut points and analyzed in logistic regressions, CRP maintained its inverse association and statistical significance. However, the association with CysC lost statistical significance after adjustment for potential confounders which most likely occurred due to the loss of statistical power from creating dichotomous variables out of continuous outcomes⁽⁴⁴⁾.

Overall, the results of the current study reveal a potential connection between eating organic food and preventing chronic disease. In past studies, eating organic food has been linked to reduced risk factors for CVD and reduced risk of cancer^(18,19). In a large prospective study of women in the United Kingdom, a decrease in the incidence of non-Hodgkin's lymphoma was found in those who consumed organic food⁽¹⁸⁾. In a second study of Italian men, consumption of a Mediterranean organic diet showed the ability to lower the risk of CVD by reducing hyperphosphataemia, microalbuminuria, inflammation and adiposity in comparison with a Mediterranean conventional diet alone⁽¹⁹⁾. Our findings may help to explain the biological mechanism behind those associations, through altered concentrations of inflammatory biomarkers. Previous research establishes

Table 2 Characteristics of the Health and Retirement Study population by CRP and CysC high-risk cut points (*n* 3719)

| Characteristics | Normal CRP (<i>n</i> 2230)* | High CRP (<i>n</i> 1489)* | <i>P</i> | Normal cystatin C (<i>n</i> 3233)* | High cystatin C (<i>n</i> 486)* | <i>P</i> |
|--|---------------------------------|-------------------------------|-----------|--|-------------------------------------|-----------|
| Age (years) | | | 0.2412 | | | < 0.0001† |
| Mean | 64.45 | 63.98 | | 63.38 | 71.81 | |
| SE | 0.35 | 0.37 | | 0.29 | 0.62 | |
| BMI | | | < 0.0001† | | | < 0.0001† |
| Underweight | 0.98 | 0.2 | | 0.71 | 0.45 | |
| Normal | 24 | 11.28 | | 20.2 | 10.64 | |
| Overweight | 37.64 | 26.06 | | 33.79 | 28.8 | |
| Obese | 37.38 | 62.46 | | 45.31 | 60.11 | |
| Gender | | | 0.0002† | | | 0.0693 |
| Female | 51.44 | 59.95 | | 53.75 | 59.42 | |
| Race | | | < 0.0001† | | | 0.199 |
| White | 83.19 | 76.56 | | 80.64 | 80.99 | |
| Black | 6.11 | 11 | | 7.68 | 10.28 | |
| Hispanic | 7.37 | 8.86 | | 8.17 | 5.95 | |
| Other | 3.33 | 3.59 | | 3.5 | 2.78 | |
| HDL-cholesterol (mg/dl) | | | < 0.0001† | | | < 0.0001† |
| Mean | 60.72 | 54.67 | | 59.30 | 51.13 | |
| SE | 0.51 | 0.63 | | 0.45 | 0.74 | |
| LDL-cholesterol (mg/dl) | | | 0.0007† | | | < 0.0001† |
| Mean | 100.23 | 105.76 | | 103.84 | 89.23 | |
| SE | 1.01 | 1.07 | | 0.76 | 1.71 | |
| Total cholesterol (mg/dl) | | | 0.0219† | | | < 0.0001† |
| Mean | 187.71 | 191.60 | | 191.12 | 172.88 | |
| SE | 1.02 | 1.34 | | 0.85 | 2.33 | |
| TAG (mg/dl) | | | < 0.0001† | | | 0.0042† |
| Mean | 136.32 | 157.84 | | 142.77 | 158.75 | |
| SE | 2.06 | 3.58 | | 2.12 | 5.02 | |
| High blood pressure | 48.86 | 63.2 | < 0.0001† | 50.77 | 83.92 | < 0.0001† |
| Diabetes | 17.5 | 23.19 | < 0.0001† | 17.61 | 36.94 | < 0.0001† |
| Current smoker | 20.09 | 26.11 | 0.0044 | 21.77 | 28.76 | 0.0763 |
| Alcohol consumption (per d in g) | | | 0.0038† | | | < 0.0001† |
| Mean | 8.32 | 6.11 | | 7.99 | 3.23 | |
| SE | 0.45 | 0.53 | | 0.37 | 0.50 | |
| Moderate or vigorous physical activity | | | < 0.0001† | | | < 0.0001† |
| Hardly ever or never | 10.39 | 17.28 | | 11.33 | 27.07 | |
| A few times per month | 7.8 | 13.86 | | 9.85 | 12.14 | |
| Once a week or more | 81.81 | 68.87 | | 78.82 | 60.79 | |
| Years of education | | | < 0.0001† | | | < 0.0001† |
| Less than high school | 10.04 | 15.39 | | 11.03 | 20.78 | |
| High school grad | 29.06 | 32.94 | | 29.46 | 39.54 | |
| Some college/college grad | 42.62 | 40.96 | | 43.26 | 31.29 | |
| Post-college | 18.28 | 10.71 | | 16.25 | 8.39 | |
| Total net worth | | | 0.0203† | | | 0.0220† |
| Mean | 648 029 | 375 695 | | 568 470 | 346 561 | |
| SE | 110 752 | 41 348 | | 80 634 | 48 277 | |
| Currently working | 49.68 | 45.11 | 0.0368 | 51.28 | 19.88 | < 0.0001† |
| Organic foods consumption | 52.32 | 43.81 | < 0.0001† | 50.18 | 39.94 | < 0.0001† |

*With the exception of missing values for LDL-cholesterol (63), high blood pressure (9), diabetes (11), current smoker (1720), moderate or vigorous physical activity (11) and currently working (1).

†Significant *P*-values below 0.05 using the Rao-Scott χ^2 test for categorical variables and a *t* test for continuous variables.

elevated CysC and CRP as markers of CVD, cancer and other chronic diseases^(21–28). Consumption of conventional foods may increase the concentration of inflammatory biomarkers in the body. Two potential differences in conventional and organic food stand out to explain this association: pesticide contamination and *n*-3/*n*-6 ratio. In the current study when organic food was broken into its individual food components, the association between organic food consumption and CRP appeared to be driven by milk, fruit, vegetables and cereal, whereas CysC was driven largely by animal-sourced foods: milk, meat and eggs.

The first notable difference between organic and conventional foods is the difference in *n*-3/*n*-6 ratio found in animal-sourced foods^(7,9). Organic animal products have been shown to contain higher levels of *n*-3 fatty acids than their conventional counterparts^(7,9). Chronic inflammation is ameliorated by higher consumption of *n*-3s and speculated to increase with *n*-6^(7,9,45). This is a plausible explanation for the notable contributions of milk, meat and eggs in the protective association between organic food and biomarkers of inflammation, particularly CysC in the current analysis.

Table 3 Linear regression analysis for the association between organic food consumption and log CRP (n 3334)/ log CysC (n 3653)

| Predictor | Organic foods consumption | 95 % CI | Vegetarian | 95 % CI | Alternative Mediterranean diet score | 95 % CI |
|-----------|---------------------------|---------|------------|------------------|--------------------------------------|----------------|
| CRP | Model 1* | -0.152 | - | -0.216, -0.089 | - | - |
| | Model 2† | -0.096 | - | -0.159, -0.033 | - | - |
| | Model 3‡ | -0.088 | -0.132 | -0.152, -0.024 | -0.289, 0.026 | - |
| | Model 4§ | -0.080 | - | -0.144, -0.016 | - | -0.037, -0.005 |
| CysC | Model 1* | -0.092 | - | -0.1160, -0.0683 | - | - |
| | Model 2† | -0.033 | - | -0.051, -0.015 | - | - |
| | Model 3‡ | -0.034 | 0.025 | -0.053, -0.016 | -0.031, 0.081 | - |
| | Model 4§ | -0.019 | - | -0.039, 0.000 | -0.019 | -0.024, -0.013 |

*Model 1: unadjusted.

†Model 2: Adjusted for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, job status, total net worth, education and daily caloric intake.

‡Model 3: Adjusted for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, job status, total net worth, education, daily caloric intake and vegetarian status.

§Model 4: Adjusted for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, job status, total net worth, education, daily caloric intake and A-MedDiet.

The second plausible explanation for the protective association between organic food and biomarkers of inflammation points to one of the fundamental differences in the production methods of organic and conventional agriculture, pesticide/herbicide use. It has been proven that organic food is far less contaminated with pesticides and toxicants than conventionally grown food⁽⁴⁶⁾. Therefore, we speculate that residual pesticides and herbicides remaining in food after production could be responsible for differences in inflammatory biomarkers, particularly with animal-sourced foods that have an increased exposure to pesticides and herbicides as they are consuming foods treated with them throughout the course of their life.

Over 1 billion pounds of pesticides are used each year in the USA for agricultural production⁽⁴⁷⁾. The amount that remains on food and is consumed by humans may have adverse health effects even when consumption is below the non-observable adverse effect level. A recent study showed that the combination of pesticides consumed, all individually below the non-observable adverse effect level, may together have harmful health impacts⁽⁴⁸⁾. Some view the quantity of pesticides on conventional food as negligible; however, a recent study conducted by Hyland *et al.* showed that urinary pesticide levels were significantly reduced in children and adults across America when an organic diet was followed⁽⁴⁹⁾. Pengcheng *et al.* reported recently that alterations in the gut microbiome occurred after consumption of herbicides⁽⁵⁰⁾. Their research highlights the gut microbiota as a potential biological pathway for understanding the differential inflammatory response to consumption of conventional and organic foods. Concentrations of pesticides and herbicides consumed along with their impact on the human gut microbiome provide an encouraging direction for researchers to explore the protective effect of organic food consumption on biomarkers of inflammation.

A secondary finding in our study population is that eating healthy, defined by the A-MedDiet, is also associated with decreased biomarkers of inflammation CRP and CysC. This finding is in agreement with previous research that found an inverse association of fruits and vegetable intake with CRP in a cross-sectional study of female teachers in Tehran⁽⁵¹⁾. Two other studies directly drew the connection between the Mediterranean diet and biomarkers CRP and CysC. Lahoz *et al.* showed that compliance with a Mediterranean diet was inversely associated with CRP concentrations in Madrid⁽⁵²⁾ and Vallianou *et al.*⁽⁵³⁾ found that compliance with a Mediterranean diet was inversely associated with CysC concentrations. In our study, point estimates for organic food consumption are -0.080 and -0.019, whereas the point estimates for the A-MedDiet score are -0.021 and -0.019 for log CRP and log CysC, respectively. It is important to recognize the considerable attenuation of the organic food point estimates once the A-MedDiet was controlled for especially in regard to

Table 4 Adjusted linear regression analysis for log CRP (*n* 3334)/log CysC (*n* 3653) by organic food type

| Predictor (reference group is no organic food consumption) | Organic food consumption log CRP | 95 % CI | Organic food consumption log CysC | 95 % CI |
|--|-------------------------------------|----------------|--------------------------------------|----------------|
| Organic milk | | | | |
| Unadjusted* | | | | |
| Organic milk | -0.244 | -0.373, -0.115 | -0.137 | -0.171, -0.103 |
| Organic but not milk | -0.12 | -0.184, -0.056 | -0.077 | -0.102, -0.052 |
| Adjusted† | | | | |
| Organic milk | -0.173 | -0.291, -0.055 | -0.057 | -0.083, -0.030 |
| Organic but not milk | -0.07 | -0.134, -0.006 | -0.025 | -0.045, -0.006 |
| Vegetarian adjusted‡ | | | | |
| Organic milk | -0.164 | -0.278, -0.050 | -0.058 | -0.085, -0.031 |
| Organic but not milk | -0.064 | -0.131, 0.004 | -0.027 | -0.047, -0.007 |
| A-MedDiet adjusted§ | | | | |
| Organic milk | -0.156 | -0.273, -0.040 | -0.041 | -0.069, -0.014 |
| Organic but not milk | -0.056 | -0.123, 0.010 | -0.012 | -0.033, 0.008 |
| Eggs | | | | |
| Unadjusted* | | | | |
| Organic eggs | -0.156 | -0.256, -0.056 | -0.123 | -0.154, -0.092 |
| Organic but not eggs | -0.15 | -0.214, -0.086 | -0.066 | -0.096, -0.037 |
| Adjusted† | | | | |
| Organic eggs | -0.091 | -0.181, -0.001 | -0.046 | -0.071, -0.022 |
| Organic but not eggs | -0.099 | -0.165, -0.037 | -0.022 | -0.046, 0.002 |
| Vegetarian adjusted‡ | | | | |
| Organic eggs | -0.083 | -0.173, 0.007 | -0.048 | -0.072, -0.024 |
| Organic but not eggs | -0.092 | -0.159, -0.025 | -0.024 | -0.049, 0.001 |
| A-MedDiet adjusted§ | | | | |
| Organic eggs | -0.073 | -0.164, 0.018 | -0.031 | -0.056, -0.005 |
| Organic but not eggs | -0.086 | -0.152, -0.020 | -0.011 | -0.035, 0.014 |
| Meat | | | | |
| Unadjusted* | | | | |
| Organic meat | -0.164 | -0.263, -0.065 | -0.128 | -0.158, -0.097 |
| Organic but not meat | -0.147 | -0.220, -0.074 | -0.074 | -0.100, -0.048 |
| Adjusted† | | | | |
| Organic meat | -0.108 | -0.207, -0.009 | -0.053 | -0.076, -0.030 |
| Organic but not meat | -0.089 | -0.160, -0.018 | -0.023 | -0.044, -0.003 |
| Vegetarian adjusted‡ | | | | |
| Organic meat | -0.106 | -0.205, -0.007 | -0.054 | -0.076, -0.031 |
| Organic but not meat | -0.079 | -0.151, -0.007 | -0.025 | -0.046, -0.003 |
| A-MedDiet adjusted§ | | | | |
| Organic meat | -0.09 | -0.189, 0.008 | -0.038 | -0.063, -0.013 |
| Organic but not meat | -0.075 | -0.148, -0.003 | -0.01 | -0.032, 0.011 |
| Fruit | | | | |
| Unadjusted* | | | | |
| Organic fruit | -0.162 | -0.232, -0.092 | -0.1 | -0.125, -0.074 |
| Organic but not fruit | -0.133 | -0.242, -0.024 | -0.077 | -0.110, -0.044 |
| Adjusted† | | | | |
| Organic fruit | -0.092 | -0.159, -0.025 | -0.031 | -0.052, -0.010 |
| Organic but not fruit | -0.102 | -0.206, 0.001 | -0.037 | -0.062, -0.011 |
| Vegetarian adjusted‡ | | | | |
| Organic fruit | -0.083 | -0.150, -0.016 | -0.033 | -0.054, -0.011 |
| Organic but not fruit | -0.098 | -0.202, 0.006 | -0.038 | -0.063, -0.012 |
| A-MedDiet adjusted§ | | | | |
| Organic fruit | -0.075 | -0.140, -0.010 | -0.016 | -0.038, 0.006 |
| Organic but not fruit | -0.09 | -0.197, 0.016 | -0.026 | -0.052, 0.000 |
| Vegetables | | | | |
| Unadjusted* | | | | |
| Organic vegetables | -0.164 | -0.232, -0.097 | -0.094 | -0.120, -0.069 |
| Organic but not vegetables | -0.108 | -0.221, 0.006 | -0.084 | -0.119, -0.048 |
| Adjusted† | | | | |
| Organic vegetables | -0.098 | -0.166, -0.030 | -0.032 | -0.051, -0.013 |
| Organic but not vegetables | -0.088 | -0.191, 0.016 | -0.037 | -0.068, -0.006 |
| Vegetarian adjusted‡ | | | | |
| Organic vegetables | -0.089 | -0.159, -0.020 | -0.034 | -0.054, -0.013 |
| Organic but not vegetables | -0.084 | -0.187, 0.019 | -0.038 | -0.068, -0.007 |
| A-MedDiet adjusted§ | | | | |
| Organic vegetables | -0.081 | -0.150, -0.012 | -0.017 | -0.038, 0.004 |
| Organic but not vegetables | -0.077 | -0.182, 0.027 | -0.027 | -0.058, 0.004 |
| Cereals | | | | |
| Unadjusted* | | | | |
| Organic cereals | -0.206 | -0.303, -0.109 | -0.113 | -0.154, -0.072 |
| Organic but not cereals | -0.135 | -0.202, -0.068 | -0.085 | -0.111, -0.059 |



Table 4 Continued

| Predictor (reference group is no organic food consumption) | Organic food consumption log CRP | 95 % CI | Organic food consumption log CysC | 95 % CI |
|--|-------------------------------------|----------------|--------------------------------------|----------------|
| Adjusted† | | | | |
| Organic cereals | -0.121 | -0.205, -0.038 | -0.035 | -0.070, -0.001 |
| Organic but not cereals | -0.087 | -0.158, -0.017 | -0.032 | -0.051, -0.013 |
| Vegetarian adjusted‡ | | | | |
| Organic cereals | -0.108 | -0.193, -0.022 | -0.038 | -0.074, -0.002 |
| Organic but not cereals | -0.082 | -0.153, -0.011 | -0.033 | -0.053, -0.014 |
| A-MedDiet adjusted§ | | | | |
| Organic cereals | -0.098 | -0.184, -0.012 | -0.014 | -0.050, 0.021 |
| Organic but not cereals | -0.075 | -0.145, -0.005 | -0.021 | -0.041, -0.001 |
| Frozen | | | | |
| Unadjusted* | | | | |
| Organic frozen | -0.181 | -0.329, -0.322 | -0.09 | -0.141, -0.038 |
| Organic but not frozen | -0.148 | -0.213, -0.084 | -0.093 | -0.117, -0.068 |
| Adjusted† | | | | |
| Organic frozen | -0.111 | -0.253, 0.030 | -0.008 | -0.054, 0.037 |
| Organic but not frozen | -0.093 | -0.157, -0.030 | -0.036 | -0.056, -0.017 |
| Vegetarian adjusted‡ | | | | |
| Organic frozen | -0.092 | -0.228, 0.0433 | -0.011 | -0.060, 0.037 |
| Organic but not frozen | -0.088 | -0.153, -0.022 | -0.037 | -0.057, -0.018 |
| A-MedDiet adjusted§ | | | | |
| Organic frozen | -0.095 | -0.234, 0.045 | 0.006 | -0.040, 0.052 |
| Organic but not frozen | -0.078 | -0.143, -0.013 | -0.023 | -0.043, -0.003 |

*Model 1: unadjusted.

†Model 2: Adjusted for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, job status, total net worth, education and daily caloric intake.

‡Model 3: Adjusted for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, job status, total net worth, education, daily caloric intake and vegetarian status.

§Model 4: Adjusted for age, BMI, gender, race, blood pressure, diabetes, alcohol consumption, physical activity, job status, total net worth, education, daily caloric intake and A-MedDiet.

CysC. It not only emphasizes the importance of a healthy diet on inflammatory biomarkers but also shows how challenging is to disentangle these two associations. Previous research has demonstrated that organic consumers adhere to healthier diets in comparison with conventional food consumers^(5,6) which is in accordance with the attenuation seen in our study. Therefore, although our research provides preliminary results showing that eating organic foods may help to reduce biomarkers of inflammation even beyond eating a healthy diet alone, residual confounding cannot be excluded.

One of the major strengths of the current study is that it is a large cross-sectional analysis conducted in a longitudinal study representative of the US population, aged 50 and older allowing for generalisability of the results. The lag between the FFQ (2013) and the VBS (2016) was brief, but allows for the establishment of temporality and avoids reverse causation, regardless of the cross-sectional analysis. There were several limitations to the current study. First, organic food was self-reported on a FFQ. The quantity of organic foods eaten in the past year is unknown; therefore, a dose-response could exist that we are not able to analyze with the given information. More research is needed to study the relationship between organic food consumption and biomarkers of inflammation particularly with organic food as a continuous rather than a binary predictor so that a dose-response may be examined. Second, our outcome measurements were only collected once which limited our ability to assess changes

over time. Finally, our observational study design is a limitation, we adjusted for the A-MedDiet and vegetarian status as proxies of healthy eating along with all indicators of socioeconomic status to mitigate confounding, but as in all observational studies we cannot rule out residual confounding by healthy eating as stated above. It is also important to note that the association between organic food consumption and inflammatory biomarkers may be due to residual confounding from socioeconomic status as organic foods are usually expensive commodities.

In conclusion, this is the first study to show that organic food consumption is inversely associated with biomarkers of inflammation CysC and CRP. These results are consistent with previous findings that show organic food consumption as a protective factor in CVD and some cancers. It is important to keep in mind the impact of eating a healthy diet on human health. The beneficial features of the A-MedDiet are in part due to the focus on consuming foods with minimal processing and high nutritional content such as fresh fruits, vegetables, legumes and fish rather than focusing on low consumption of foods with poor nutritional content. Organic food products are mostly available for these key beneficial components of the A-MedDiet which could potentially increase the benefits of consuming a healthy diet. Further research should be conducted in other populations to replicate these results and add to the depth of knowledge around health implications of organic food consumption. Future studies

could further quantify organic food consumption, focus on the duration of the exposure, as well as the impact across the lifespan.

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Supplementary material

For supplementary material accompanying this paper visit <https://doi.org/10.1017/S1368980020005236>

References

- Paull J (1983) Lord Northbourne, the man who invented organic farming, a biography. *J Org Syst* **9**, 31–53.
- Krystallis A & Chrysosoidis G (2005) Consumers' willingness to pay for organic food: factors that affect it and variation per organic product type. *Br Food J* **107**, 320–343.
- Monier S, Hassan D, Nichle V *et al.* (2009) Organic food consumption patterns. *J Agric Food Ind Organ* **7**, 1542–0485.
- Schrank Z & Running K (2018) Individualist and collectivist consumer motivations in local organic food markets. *J Consum Cult* **18**, 184–201.
- Kesse-Guyot E, Péneau S, Méjean C *et al.* (2013) Profiles of organic food consumers in a large sample of French Adults: results from the Nutrinet-Santé Cohort Study. *PLoS One* **8**, e76998.
- Baudry J, Touvier M, Allès B *et al.* (2016) Typology of eaters based on conventional and organic food consumption: results from the NutriNet-Santé cohort study. *Br J Nutr* **116**, 700–709.
- Galgano F, Tolve R, Colangelo MA *et al.* (2016) Conventional and organic foods: a comparison focused on animal products. *Cogent Food Agric* **96**, 1142818.
- Lairon D (2010) Nutritional quality and safety of organic food. A review to cite this version : HAL Id : hal-00886513 nutritional quality and safety of organic food. *Review* **30**, 33–41.
- Brantsæter AL, Ydersbond TA, Hoppin JA *et al.* (2017) Organic food in the diet: exposure and health implications. *Ann Rev Public Health* **20**, 295–313.
- Huber M, Rembiałkowska E, Średnicka D *et al.* (2011) Organic food and impact on human health: assessing the status quo and prospects of research. *NJAS-Wageningen J Life Sci* **58**, 103–109.
- Stenius F, Swartz J, Lilja G *et al.* (2011) Lifestyle factors and sensitization in children – the ALADDIN birth cohort. *Allergy Eur J Allergy Clin Immunol* **66**, 1330–1338.
- Alfvén T, Braun-Fahrlander C, Brunekreef B *et al.* (2006) Allergic diseases and atopic sensitization in children related to farming and anthroposophic lifestyle-the PARSIFAL study. *Allergy Eur J Allergy Clin Immunol* **61**, 414–421.
- Alm JS, Swartz J, Lilja G *et al.* (1999) Atopy in children of families with an anthroposophic lifestyle. *Lancet* **353**, 1485–1488.
- Christensen JS, Asklund C, Skakkebaek NE *et al.* (2013) Association between organic dietary choice during pregnancy and hypospadias in offspring: a study of mothers of 306 boys operated on for hypospadias. *J Urol* **189**, 1077–1082.
- Brantsæter AL, Torjusen H, Meltzer HM *et al.* (2016) Organic food consumption during pregnancy and hypospadias and cryptorchidism at birth: the Norwegian mother and child cohort study (MoBa). *Environ Health Perspect* **124**, 357–364.
- Torjusen H, Brantsæter AL, Haugen M *et al.* (2014) Reduced risk of pre-eclampsia with organic vegetable consumption: results from the prospective Norwegian mother and child cohort study. *BMJ Open* **4**, 1–11.
- Jensen TK, Giwercman A, Carlsen E *et al.* (1996) Semen quality among members of organic food associations in Zealand, Denmark. *Lancet* **347**, 1844.
- Bradbury KE, Balkwill A, Spencer EA *et al.* (2014) Organic food consumption and the incidence of cancer in a large prospective study of women in the United Kingdom. *Br J Cancer* **110**, 2321–2326.
- De Lorenzo A, Noce A, Bigioni M *et al.* (2010) The effects of Italian Mediterranean Organic Diet (IMOD) on health status. *Curr Pharm Des* **16**, 814–824.
- Baudry J, Lelong H, Adriouch S *et al.* (2018) Association between organic food consumption and metabolic syndrome : cross-sectional results from the NutriNet-Santé study. *Eur J Nutr* **57**, 2477–2488.
- Sonawane MD & Nimse SB (2017) C-Reactive protein: a major inflammatory biomarker. *Anal Methods* **9**, 3400–3413.
- Dadvand P, Nieuwenhuijsen MJ, Agustí À *et al.* (2014) Air pollution and biomarkers of systemic inflammation and tissue repair in COPD patients. *Eur Respir J* **44**, 603–613.
- Barbaresko J, Koch M, Schulze MB *et al.* (2013) Dietary pattern analysis and biomarkers of low-grade inflammation: a systematic literature review. *Nutr Rev* **71**, 511–527.
- Thorand B, Kolb H, Baumert J *et al.* (2005) Elevated levels of interleukin-18 predict the development of type 2 diabetes: results from the MONICA/KORA Augsburg Study, 1984–2002. *Diabetes* **54**, 2932–2938.
- Pradhan AD, Manson JE, Rifai N *et al.* (2001) C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* **286**, 327–334.
- Pearson TA, Mensah GA, Alexander RW *et al.* (2003) Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the centers for disease control and prevention and the American Heart Association. *Circulation* **107**, 499–511.
- Bashier AM, Fadlallah AAS, Alhashemi N *et al.* (2015) Cystatin C and its role in patients with Type 1 and Type 2 Diabetes Mellitus. *Adv Endocrinol* **2015**, 1–8.
- Sarnak MJ, Katz R, Stehman-Breen CO *et al.* (2005) Cystatin C concentration as a risk factor for heart failure in older adults. *Ann Intern Med* **142**, 497–505.
- Health and Retirement Study Survey Research Center (2017) The Health and Retirement Study: Aging in the



- 21st Century: Challenges and Opportunities for Americans. <http://hrsonline.isr.umich.edu/sites/docs/databook/inc/pdf/HRS-Aging-in-the-21st-Century.pdf> (accessed January 2017).
30. Health and Retirement Study 2012 (2017) Core Final, Version 2.0 December 2017 Data. 2017. https://hrsdata.isr.umich.edu/data-products/2012-hrs-core?_ga=2.198547884.2036214529.1609947055-214052492.1584638109 (accessed January 2018).
 31. Pantoja P, Bugliari D, Campbell N *et al.* (2014) *RAND HRS Detailed Imputations File 2014 (V3) Documentation*. Boston, MA: RAND HRS.
 32. Health Care and Nutrition Study (HCNS) 2013 Version 5: Data Description. https://hrsdata.isr.umich.edu/sites/default/files/documentation/data-descriptions/2013HCNS_data_description_nt.pdf (accessed January 2018).
 33. Crimmins E, Faul J, Thyagarajan B *et al.* (2016) Venous blood collection and assay protocol in the 2016 Health and Retirement Study 2016. 2017.
 34. Pimenta AM, Toledo E, Rodriguez-Diez MC *et al.* (2015) Dietary indexes, food patterns and incidence of metabolic syndrome in a Mediterranean cohort: the SUN project. *Clin Nutr* **34**, 508–514.
 35. Osman R, L'Allier PL, Elgharib N *et al.* (2006) Critical appraisal of C-reactive protein throughout the spectrum of cardiovascular disease. *Vasc Health Risk Manag* **2**, 221–237.
 36. Mac Giollabhui N, Ellman LM, Coe CL *et al.* (2020) To exclude or not to exclude: considerations and recommendations for C-Reactive Protein values higher than 10 mg/l. *Brain Behav Immun* **25**, 289–313.
 37. Harvard T. H. Chan School of Public Health. Department of Nutrition (2015) Harvard University Dietary Assessment FFQ. <https://regepi.bwh.harvard.edu/health/nutrition.html> (accessed January 2018).
 38. HRS (2013) Mail Survey Health Care and Nutrition Study. https://hrsdata.isr.umich.edu/data-products/2013-health-care-and-nutrition-study-hcns?_ga=2.195065391.2036214529.1609947055-214052492.1584638109 (accessed January 2018).
 39. Fung TT, McCullough ML, Newby PK *et al.* (2005) Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr* **82**, 163–173.
 40. Brown LL, Zhang YS, Mitchell C *et al.* (2018) Does telomere length indicate biological, physical, and cognitive health among older adults? Evidence from the health and retirement study. *J Gerontol A Biol Sci Med Sci* **73**, 1626–1632.
 41. Stephan Y, Sutin AR & Terracciano A (2015) Younger subjective age is associated with lower C-reactive protein among older adults. *Brain Behav Immun* [Internet] **43**, 33–36.
 42. HRS (2012) Health and Retirement Study Physical Measures ID. <https://hrs.isr.umich.edu/sites/default/files/meta/2012/core/qnaire/online/2012PhysicalMeasuresBiomarkers.pdf> (accessed January 2018).
 43. National Institutes of Health (1998) Clinical guide of the identification, evaluation and treatment of overweight and obesity in adult. *Obes Res* **6**, 51S–209S.
 44. Naggara O, Raymond J, Guilbert F *et al.* (2011) Analysis by categorizing or dichotomizing continuous variables is inadvisable: an example from the natural history of unruptured aneurysms. *Am J Neuroradiol* **32**, 437–440.
 45. Dinicolantonio JJ & O'Keefe JH (2018) Importance of maintaining a low $n-6/n-3$ ratio for reducing inflammation. *Open Heart* **5**, 3–6.
 46. Gomiero T (2018) Food quality assessment in organic vs. conventional agricultural produce: findings and issues. *Appl Soil Ecol* **123**, 714–728.
 47. Michael CR & Alavanja PH (2010) Pesticides use and exposure extensive worldwide. *Rev Env Heal* **24**, 303–309.
 48. Merhi M, Demur C, Racaud-Sultan C *et al.* (2010) Gender-linked haematopoietic and metabolic disturbances induced by a pesticide mixture administered at low dose to mice. *Toxicology* **267**, 80–90.
 49. Hyland C, Bradman A, Gerona R *et al.* (2019) Organic diet intervention significantly reduces urinary pesticide levels in US children and adults. *Environ Res* **171**, 568–575.
 50. Pengcheng T, Bei G, Liang C *et al.* (2019) Subchronic low-dose 2,4-D exposure changed plasma acylcarnitine levels and induced gut microbiome perturbations in mice. *Sci Rep* **9**, 1–11.
 51. Mehrabi Y, Hu FB, Willett WC *et al.* (2018) Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome. *Am J Clin Nutr* **84**, 1489–1497.
 52. Lahoz C, Castillo E, Mostaza JM *et al.* (2018) Relationship of the adherence to a Mediterranean diet and its main components with CRP levels in the Spanish population. *Nutrients* **10**, 1–10.
 53. Vallianou NG, Georgousopoulou E, Evangelopoulos AA *et al.* (2017) Inverse relationship between adherence to the Mediterranean diet and serum cystatin c levels. *Cent Eur J Public Health* **25**, 240–244.