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### Authors

Zhang, Yurong  
Francis, Ellen C  
Xia, Tong  
[et al.](#)

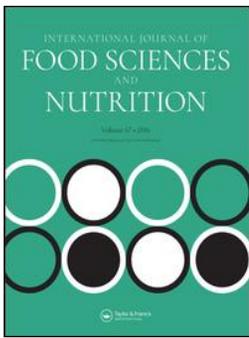
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RESEARCH ARTICLE



## Adherence to DASH dietary pattern is inversely associated with osteoarthritis in Americans

Yurong Zhang<sup>a</sup>, Ellen C. Francis<sup>b</sup>, Tong Xia<sup>c</sup>, Karen Kemper<sup>b</sup>, Joel Williams<sup>b</sup> and Liwei Chen<sup>c</sup>

<sup>a</sup>Department of Neurology, The First Affiliated Hospital of Xi'an Jiaotong University, Shaanxi, China; <sup>b</sup>Department of Public Health Sciences, Clemson University, Clemson, SC, USA; <sup>c</sup>Fielding School of Public Health, University of California, Los Angeles, CA, USA

### ABSTRACT

Osteoarthritis (OA) is one of the most common diseases that cause disability among older adults. The objective of this study was to assess the association between adherence to the Dietary Approaches to Stop Hypertension (DASH) and OA in American adults. This study included adults ( $\geq$  aged 20 years) who participated in the National Health and Examination Survey (NHANES) 2007–2016 in the United States. Adherence to the DASH score was calculated from 8 food groups. Higher scores indicate better adherence to the DASH dietary pattern. Among the 21,901 participants included in this study, 10.26% reported having OA. Results of our multivariable logistic regression indicated a statistically significant inverse association between DASH score tertiles and OA. The adjusted ORs (95% CI) were 1.00 (ref), 0.89 (0.72; 1.10), and 0.78 (0.60; 1.00) across increasing DASH score tertiles ( $P$  for trend = 0.045). In this representative sample of American adults, greater adherence to the DASH dietary pattern was associated with lower likelihood of having OA.

### ARTICLE HISTORY

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### KEYWORDS

DASH diet; osteoarthritis; adults; nutrition; degenerative joint disease

### Introduction

Osteoarthritis (OA) is the most prevalent degenerative joint disease and the fastest growing cause of disability and pain in the United State (US). Among US adults 20 years and older, the prevalence of OA increased from 6.6% in 1999 to 14.3% in 2014 (Park et al. 2018). The number of people with OA is expected to increase in the US due in part to the obesity epidemic and aging of the population. Globally, approximately 18% of women and 9.6% of men aged over 60 years have symptomatic OA, and by 2050, OA is projected to affect 130 million people (Conaghan et al. 2015).

OA is one of the most challenging joint diseases for clinicians. Besides symptom management and surgical approaches, there is no cure for OA (Zhang et al. 2016). Recently, dietary factors have received considerable interest due to their potential roles in OA prevention. Most previous studies on dietary intake and OA only focussed on an individual nutrient. For example, vitamin D (McAlindon et al. 1996; Lane et al. 1999) and vitamin K (Misra et al. 2013; Shea et al. 2015) play a physiological role in bone and cartilage mineralization, and have been associated with risk of OA in several prospective cohort studies.

However, randomised controlled trials on vitamin D, K, or E supplementation have failed to show success in improving the symptoms and progression of OA (Neogi et al. 2008; Arden et al. 2016; Jin et al. 2016; Diao et al. 2017). One explanation could be that individual nutrients only have a limited effect, and therefore the impact may be difficult to detect in single-nutrient supplementation trials. To gain a better understanding of dietary factors in relation to OA development or progression, studies investigating overall dietary quality/pattern are needed. However, such studies are sparse, and to our best knowledge, only two studies have examined the association between an individual's dietary pattern and OA risk (Veronese et al. 2017; Veronese et al. 2019).

The Dietary Approaches to Stop Hypertension (DASH) dietary pattern, which was originally developed to reduce blood pressure, is low in red meat, sweets and oils; and rich in fruits, vegetables, low-fat dairy products, whole grains, fish, and nuts (Appel et al. 1997). In the recent Dietary Guidelines for Americans (2015–2020), the United States Department of Agriculture recommended the DASH dietary pattern as a healthy eating plan for Americans based on

growing evidence that adherence to the DASH dietary pattern had beneficial effects on preventing type II diabetes, cardiovascular diseases (CVD), metabolic syndrome, and Alzheimer's disease, in addition to hypertension (Asemi et al. 2013; Nilsson et al. 2019; Pickworth et al. 2019; Samadi et al. 2019). A recent randomised cross-over study among children showed that the DASH diet significantly reduced the circulating levels of serum high-sensitivity C-reactive protein (hs-CRP: a biomarker of chronic inflammation), independent of changes in body weight and lipid profile (Saneei et al. 2014). Therefore, we hypothesised that adherence to the DASH dietary pattern would be associated with lower risk of OA. The objective of this study was to examine the association of adherence to the DASH dietary pattern with OA in American adults.

## Methods

### Study population

The study population included participants from the National Health and Nutrition Examination Survey (NHANES) 2007–2016. The NHANES is a nationally representative cross-sectional survey of the non-institutionalized US population aged 2 years or older with data collected in 2-year cycles. During each cycle, the NHANES was conducted based on a stratified multi-stage probability sampling design and included two components: a household interview and a health examination. The health examination component consisted of medical, dental, and physiological measurements, as well as laboratory tests administered by trained medical personnel in a fully equipped mobile examination centre (MEC). Additional information on the design and procedures of the NHANES are available at the Centre for Disease Control and Prevention (CDC) website. For this study, we included individuals who were aged 20 years or older and participated in the NHANES 2007–2016 survey cycles, which includes the most recent dietary data released for public use. We excluded participants who declined or had missing data on arthritis information, those who had no or invalidated data on dietary intake, had total energy intake  $<500$  or  $>8000$  kcal/day, or who reported being on a special diet for medical reasons or to lose weight. The final sample size included in this analysis was 21,901. The NHANES survey was approved by the Research Ethics Review Board of the National Centre for Health Statistics (NCHS) and conducted following the rules of the Declaration of Helsinki.

### Assessment of osteoarthritis (OA)

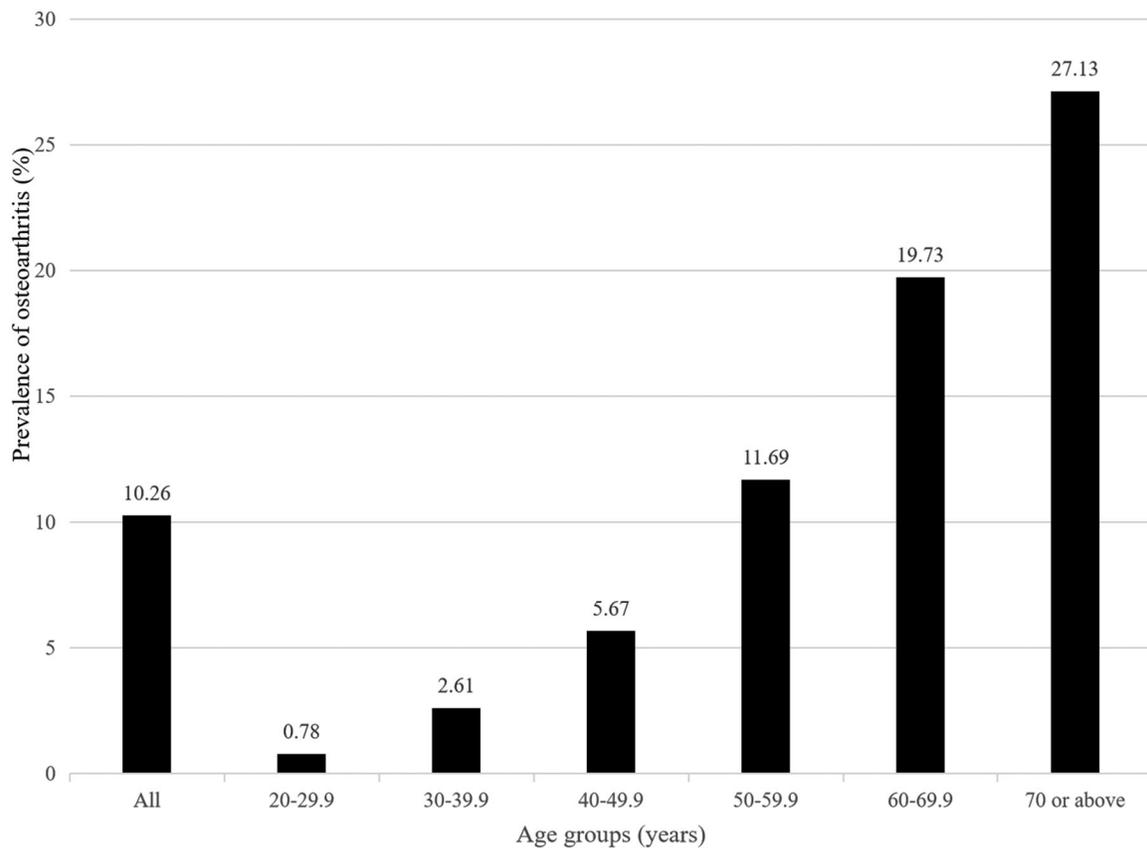
OA was assessed using the data from the medical conditions questionnaire which was collected during the NHANES household interview. Participants were classified as having OA if they reported ever being told they had arthritis by a health care provider and indicated that it was osteoarthritis.

### Adherence to dietary approaches to stop hypertension (DASH)

Dietary intake was assessed by two 24-h dietary recalls administered by trained interviewers. We constructed the DASH score based on intakes of 8 DASH targeted food groups/items (i.e. whole grains, vegetables, fruits, dairy products, red meats, nuts/seeds/legumes, sweets, and sodium) using the method developed by Fung et al. (Fung et al. 2008). Briefly, we ranked study participants according to their intake of each individual food group/item and classified them into quintiles. We assigned a score of 1 for individuals in the 1st quintile and 5 for individuals in the 5<sup>th</sup> quintile for whole grains, vegetables, fruits, dairy products, nuts/seeds/legumes because high intake is desired for these foods. For red meats, sweets, and sodium, we inverted scores assigning 5 for the 1st quintile and 1 for the 5th quintile because low intake is desired for these food groups/items. We then summed the score of each food group/item to generate an overall DASH adherence score ranging from 8 (lowest adherence) to 40 (best adherence).

### Covariates

We considered the following variables as potential confounders in examining the association between adherence to the DASH dietary pattern and OA. Age, sex, race/ethnicity, annual household income, education, and smoking, which were self-reported during the household interviews. Alcohol intake was assessed by 24-h dietary recalls. Physical activity (PA) was measured using a structured questionnaire and calculated as the sum of the minutes spent being physically active for commuting, recreation, and work on average for each day. Adequate PA was defined as time of all PA  $\geq 150$  minutes per week. Height, weight, and waist circumference were directly measured by trained personnel in the MEC. Body mass index (BMI) was calculated by weight (kg) divided height squared ( $m^2$ ).



**Figure 1.** Prevalence (%) of osteoarthritis in NHANES 2007–2016 by age group.

### Statistical analysis

Descriptive data on study participants' characteristics were expressed as weighted means (standard error) for continuous variables or weighted percent for categorical variables if not mentioned otherwise. Student's *t*-test and  $\chi^2$  test were applied to compare continuous variables and categorical variables, respectively. The prevalence of OA was estimated in all participants and by age groups (20–29.9, 30–39.9, 40–49.9, 50–59.9, 60–69.9,  $\geq 70$  years). Logistic regressions were performed to estimate the association of DASH score with OA. The DASH score was analysed both as a categorical variable (tertiles) and a continuous variable. Because age is a strong risk factor for OA, all models were adjusted for age. Other covariates controlled for in the multivariable regression models included sex (female versus male), race/ethnicity (non-Hispanic White, non-Hispanic Black, or Mexican American/other Hispanics), annual household income (<\$20,000, \$20,000–49,999, \$45,000–\$74,999,  $\geq$ \$75,000), education (less than high school, high school, some college, college graduate or above), smoking (current, former, or never), alcohol intake (g/day), PA (adequate vs. non-adequate), and BMI (normal weight: BMI <25; overweight: BMI 25–29.9;

obese: BMI  $\geq 30$  kg/m<sup>2</sup>). Additionally, we performed stratified analyses by gender (males and females), BMI (normal weight, overweight and obese), and smoking status (smokers and never smokers). All analyses considered the complex survey design including stratification, clustering, and weighting to account for the oversampling of subgroups, unit non-response and non-coverage in the NHANES. All the statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

### Results

Among the 21,901 participants included in this study, the weighted prevalence of OA was 10.26% (0.35). The prevalence of OA increased substantially with age: 0.78% in age group 20–29.9 years, 2.61% in 30–39.9 years, 5.67% in 40–49.9 years, 11.69% in 50–59.9 years, 19.73% in 60–69.9 years, and 27.13% in  $\geq 70$  years, respectively (Figure 1).

The median DASH score was 24.0 with a range from 9.0 to 39. The median (min, max) DASH score in each tertile was 19 (9, 21), 24 (22, 25) and 28 (26, 39), respectively. Characteristics of the study participants in total and by DASH score tertiles are presented in Table 1. Compared to individuals in the

**Table 1.** Characteristics of study participants, NHANES 2007–2016.

| Characteristics                                   | DASH score               |                              |                              |                              | <i>p</i> Values |
|---|--------------------------|------------------------------|------------------------------|------------------------------|-----------------|
|   | All ( <i>N</i> = 21,901) | Tertile 1 ( <i>N</i> = 6957) | Tertile 2 ( <i>N</i> = 6917) | Tertile 3 ( <i>N</i> = 8027) |                 |
| DASH score, median (range)                        | 24 (9, 39)               | 19 (9, 21)                   | 24 (22, 25)                  | 28 (26, 39)                  |                 |
| Age (years) <sup>a</sup>                          | 46.80 (0.25)             | 42.11 (0.32)                 | 47.16 (0.33)                 | 51.42 (0.37)                 | <0.0001         |
| Female, %   | 49.94 (0.38)             | 61.27 (0.69)                 | 47.81 (1.02)                 | 39.99 (0.65)                 | <0.0001         |
| Race, %   |                          |                              |                              |                              | <0.0001         |
| Non-Hispanic White                                | 67.16 (1.62)             | 70.96 (1.76)                 | 66.23 (1.74)                 | 64.05 (1.69)                 |                 |
| Non-Hispanic Black                                | 11.29 (0.83)             | 12.75 (1.12)                 | 12.03 (0.94)                 | 9.04 (0.63)                  |                 |
| Hispanic  | 14.33 (1.12)             | 11.28 (1.06)                 | 14.78 (1.21)                 | 17.13 (1.27)                 |                 |
| Multiracial or other                              | 7.21 (0.45)              | 5.01 (0.37)                  | 6.96 (0.55)                  | 9.78 (0.26)                  |                 |
| Education Status, %                               |                          |                              |                              |                              | <0.0001         |
| Less than high school                             | 17.03 (0.71)             | 18.00 (0.92)                 | 16.82 (0.84)                 | 16.20 (0.78)                 |                 |
| High school                                       | 23.04 (0.58)             | 27.47 (0.82)                 | 23.71 (0.81)                 | 17.69 (0.55)                 |                 |
| Some college                                      | 31.05 (0.55)             | 33.89 (0.82)                 | 31.69 (0.80)                 | 27.42 (0.89)                 |                 |
| College graduate or above                         | 28.89 (1.01)             | 20.64 (1.23)                 | 27.77 (1.16)                 | 38.69 (1.17)                 |                 |
| Income, %   |                          |                              |                              |                              | <0.0001         |
| <20,000   | 15.11 (0.63)             | 16.15 (0.87)                 | 14.93 (0.68)                 | 14.16 (0.68)                 |                 |
| 20,000–49,999                                     | 26.53 (0.68)             | 27.31 (0.92)                 | 25.70 (0.85)                 | 26.50 (0.80)                 |                 |
| 45,000–74,999                                     | 21.83 (0.66)             | 23.30 (0.86)                 | 21.61 (0.91)                 | 20.44 (0.94)                 |                 |
| 75,000+   | 36.53 (1.17)             | 33.23 (1.33)                 | 37.75 (1.22)                 | 38.90 (1.42)                 |                 |
| Smoking status, %                                 |                          |                              |                              |                              | <0.0001         |
| Current   | 21.38 (0.56)             | 33.88 (0.94)                 | 9.44 (0.46)                  | 9.44 (0.46)                  |                 |
| Former  | 23.62 (0.50)             | 21.46 (0.78)                 | 24.89 (0.79)                 | 24.89 (0.79)                 |                 |
| Never   | 55.0 (0.69)              | 44.67 (1.01)                 | 65.67 (0.90)                 | 65.67 (0.90)                 | <0.0001         |
| Body Mass Index (kg/m <sup>2</sup> ) <sup>a</sup> | 28.51 (0.09)             | 29.46 (0.12)                 | 28.70 (0.13)                 | 27.32 (0.12)                 | <0.0001         |
| Waist circumference (cm) <sup>a</sup>             | 98.10 (0.23)             | 100.55 (0.31)                | 98.44 (0.36)                 | 95.11 (0.29)                 | <0.0001         |
| Dietary intake <sup>a</sup>                       |                          |                              |                              |                              |                 |
| Alcohol drinking, g/day                           | 172.58 (6.13)            | 289.78 (13.92)               | 136.32 (6.61)                | 83.04 (4.02)                 | <0.0001         |
| Sodium, mg/day                                    | 3540 (15.60)             | 3973 (29.45)                 | 3503 (29.22)                 | 3156 (19.64)                 | <0.0001         |
| Potassium, mg/day                                 | 2694.33 (14.50)          | 2511.25 (20.65)              | 2644.15 (21.39)              | 2936.37 (17.07)              | <0.0001         |
| Magnesium, mg/day                                 | 302.05 (1.92)            | 278.01 (2.38)                | 294.48 (2.46)                | 334.58 (2.47)                | <0.0001         |
| Saturated fat, g/day                              | 26.52 (0.19)             | 29.64 (0.28)                 | 26.79 (0.28)                 | 23.41 (0.24)                 | <0.0001         |
| Fibre, g/day                                      | 17.09 (0.14)             | 13.91 (0.13)                 | 16.63 (0.18)                 | 20.91 (0.19)                 | <0.0001         |
| Vitamin D, mcg/day                                | 4.68 (0.04)              | 3.74 (0.07)                  | 4.73 (0.09)                  | 5.63 (0.06)                  | <0.0001         |
| Vitamin K, mcg/day                                | 112.4 (3.04)             | 96.7 (7.44)                  | 108.2 (2.38)                 | 134.1 (2.66)                 | <0.0001         |
| Vitamin E, mg/day                                 | 8.48 (0.08)              | 7.94 (0.09)                  | 8.27 (0.10)                  | 9.26 (0.13)                  | <0.0001         |
| Vitamin C, mg/g                                   | 82.18 (1.16)             | 57.79 (1.47)                 | 79.5 (1.35)                  | 110.5 (1.40)                 | <0.0001         |

<sup>a</sup>Mean (SE).

highest DASH score tertile (tertile 3), those in the lowest DASH score tertile (tertile 1) were younger, had a greater BMI and waist circumference, were more likely to be female, non-Hispanic white (70.96% versus 64.05%), to be a current smoker, have an annual household income <\$20,000, and were less likely to have a college degree or above. Individuals in the lowest DASH score tertile had lower intakes of dietary fibre, potassium, magnesium, vitamin D, K, E, and C, but higher intakes of alcohol, sodium, and saturated fat than individuals in the highest tertile.

The DASH score was inversely associated with OA. The age-adjusted ORs (95% CIs) of OA across the DASH score tertiles were 1.00 (reference), 0.86 (0.72; 1.05), and 0.76 (0.63; 0.92), respectively (*P* for trend: 0.0005) (Table 2). The ORs of OA were similar following additional adjustment for gender, race/ethnicity, education, household income, smoking, alcohol drinking, and PA ((1.00 (reference), 0.85 (0.69; 1.04), and 0.74 (0.59; 0.93) across the DASH tertiles) (*P* for trend: 0.0003)). Further adjustment for BMI did not substantially change the results ((1.00 (reference); 0.89 (0.72; 1.10), and 0.78 (0.60; 1.00) across the DASH

tertiles)), however, the statistical significance of the linear trend across tertiles became borderline (*p* = 0.045). When modelling the DASH score continuously, a similar inverse association was observed in fully adjusted models (Model 3 in Table 2). A one unit increase in the DASH score was associated with a 3% lower odds (95% CI: 1–6%; *p* = 0.007) of having OA.

In the stratified analyses, the DASH-OA association was slightly stronger among obese individuals or smokers (combined current smokers and former smokers since there was no difference between these two groups regarding the ORs), but the tests for interactions were all statistically insignificant (Table 3).

## Discussion

In this large study among a US representative sample, we found that adherence to the DASH dietary pattern was inversely associated with OA. Individuals with better adherence to the DASH dietary pattern had lower odds of having OA: individuals in the highest DASH adherence group (tertile 3) had a median

**Table 2.** Unadjusted and adjusted associations between DASH score and osteoarthritis, NHANES 2007–2016.

| DASH Score  | Sample Size (n) | Age-adjusted Model OR (95% CI) | p Value (trend) | Model 2 OR (95% CI) | p Value (trend) | Model 3 (fully adjusted) OR (95% CI) | p Value (trend) |
|-------------|-----------------|--------------------------------|-----------------|---------------------|-----------------|--------------------------------------|-----------------|
| Categorical |                 |                                |                 |                     |                 |                                      |                 |
| Tertile 1   | 6957            | Reference                      |                 | Reference           |                 | Reference                            |                 |
| Tertile 2   | 6917            | 0.86 (0.72, 1.05)              |                 | 0.85 (0.69, 1.04)   |                 | 0.89 (0.72, 1.10)                    |                 |
| Tertile 3   | 8027            | 0.76 (0.63, 0.92)              | 0.0005          | 0.74 (0.59, 0.93)   | 0.0003          | 0.78 (0.60, 1.00)                    | 0.045           |
| Continuous  |                 |                                |                 |                     |                 |                                      |                 |
| DASH score  | 21,901          | 0.97 (0.96, 0.99)              | 0.0004          | 0.96 (0.94, 0.98)   | 0.0003          | 0.97 (0.94, 0.99)                    | 0.007           |

Model 1: Age.

Model 2: Model 1+ gender, race/ethnicity, education, household income, smoking, alcohol drinking, and physical activity.

Model 3: Model 2+ body mass index.

**Table 3.** Adjusted associations between DASH score and osteoarthritis by gender, smoking status and BMI, NHANES 2007–2016.

|           | DASH score (continuous) | Sample size (n) | Multivariable-adjusted Model OR (95% CI) | p Value | p Value (interaction) |
|-----------|-------------------------|-----------------|--|---------|-----------------------|
| All       |                         | 21,901          | 0.97 (0.94, 0.99)                        | 0.007   |                       |
| By Gender | Males                   | 13,670          | 0.97 (0.93, 1.00)                        | 0.51    | 0.78                  |
|           | Females                 | 10,945          | 0.97 (0.94, 1.00)                        | 0.50    |                       |
| By BMI    | Normal weight           | 6777            | 0.98 (0.95, 1.02)                        | 0.30    | 0.39                  |
|           | Overweight              | 7306            | 0.98 (0.94, 1.02)                        | 0.39    |                       |
|           | Obese                   | 7663            | 0.94 (0.91, 0.98)                        | 0.006   |                       |
| Smoking   | Current and former      | 9903            | 0.98 (0.96, 1.02)                        | 0.16    | 0.11                  |
|           | Never                   | 12,038          | 0.95 (0.92, 0.99)                        | 0.009   |                       |

Model adjusted for age, gender, race/ethnicity, education, household income, smoking, alcohol drinking, physical activity, and body mass index

DASH score of 28 and a 22% lower likelihood of having OA compared to individuals in the lowest DASH adherence group (tertile 1) who had a median DASH score of 19. A one unit increase in the DASH score was associated with a 3% lower of odds of having OA, independent of sociodemographic and lifestyle factors such as age, education, race/ethnicity, household income, smoking, alcohol consumption, PA and BMI. To our knowledge, this is the first study to investigate the association between adherence to the DASH dietary pattern and OA in American adults. Our results are in line with the previous two studies that investigated the association of OA with adherence to a Mediterranean diet (Veronese et al. 2017) or the Dietary Inflammatory Index (Veronese et al. 2019). Our findings in conjunction with previous studies provide support that overall dietary quality/pattern may play an important role in OA development and should be considered in future interventions.

OA may be amenable to early prevention and treatment, and therefore modifiable factors should be identified. Diet is one of the modifiable risk factors of OA (Georgiev and Angelov 2019). Although the DASH diet was initially designed for lowering the blood pressure among individuals with hypertension, numerous studies have shown that this diet also has other metabolic benefits in different populations (Asghari et al. 2016; Razavi Zade et al. 2016; Kang et al. 2018; Tiong et al. 2018; Akhlaghi 2019). Our findings of an inverse association between adherence to the DASH dietary pattern and OA add new evidence to the existing

literature on potential benefits of the DASH diet for bone and joint health.

Although the association between adherence to the DASH dietary pattern and OA are novel, it is biologically plausible. First the DASH diet is rich in key nutrients required by the bones and tissues of synovial joints, including vitamin D, K, calcium, and magnesium. Compared to adults consuming a typical American diet, continual consumption of the DASH diet over a 30-day period has been associated with a reduction in bone turnover markers and improvement in calcium metabolism (Doyle and Cashman 2004). Deficient dietary consumption of calcium leads to lower bone and cartilage mineral content and bone mineral density, and long-term deficiency can lead to rickets, osteomalacia and osteoporosis (Dermience et al. 2015). Magnesium deficiency may play a role in OA onset and progression. Lower magnesium intake was associated with greater knee pain in individuals with radiographic knee OA (Shmagel et al. 2018). Second, the DASH diet may be beneficial to OA development through an anti-inflammatory pathway (Samadi et al. 2019). There is emerging evidence that the development and progression of OA is associated with low-grade systemic inflammation. A systematic review of 32 studies found that serum levels of hs-CRP were statistically significantly higher in OA patients than in controls (Jin et al. 2015). Inflammation may increase the risk of OA through increased cartilage degeneration and osteophytosis (Kozijn et al. 2019). In a cross-over trial the DASH

diet has been associated with lower levels of hs-CRP/CRP (King et al. 2007). The DASH diet is comprised of many nutrients that may modulate both acute and chronic inflammation (Calder et al. 2009). For example, high dietary saturated fatty acids (Cruz-Teno et al. 2012) have been associated with pro-inflammatory effects, whereas dietary fibre (King et al. 2007) and flavonoids (Saneei et al. 2014) have been associated with anti-inflammatory effects. The DASH diet is rich in flavonoid and fibre but lower in saturated fatty acids (Appel et al. 1997). However, this study was not designed to identify the relationship of each nutrient or food group with OA. Future work is needed to investigate whether this association is causal and to elucidate the underlying mechanisms.

This study has several notable strengths. First, this study included a large nationally representative sample with a wide age range (e.g. 20–80 years). Second, the dietary intakes in NHANES were assessed by two 24-h dietary recalls that were administered by trained research staff and included multiple prompts to reduce the likelihood of missing food or drinks consumed by the participants. Lastly, NHANES had extensive measures of sociodemographic and lifestyle factors, as well as directly measured anthropometric data (e.g. weight, height, and waist circumferences) which allowed us to control for most potential confounders. However, the findings of the current study should be considered with several limitations. NHANES is designed as a cross-sectional study and observational in nature; therefore, causality cannot be determined and residual confounding cannot be completely rule out. Additionally, OA was self-reported and likely to introduce a bias. However, the questionnaire has been widely used in studies to assess self-reported OA (Kojima et al. 2017; Hackney et al. 2019; Parekh et al. 2019).

In conclusion, adherence to the DASH dietary pattern was associated with lower likelihood of having OA among US adults. This is particularly relevant given the increasing prevalence of OA and the cost of treating such chronic conditions. Future studies with prospective designs and more accurate assessment of OA, or clinical trials are needed to confirm the results from current study.

### Authors' contributions

YZ: study conception and design, literature search, interpretation of analyses, drafting the manuscript and major editing; ECF: study conception and design, obtain data, and statistical analysis; XT: statistical

analysis and editing; JW: major editing; KK: major editing; LC: study conception and design, literature search, data obtain and statistical analysis, interpretation of analyses, major editing; All authors read and approved the final manuscript. LC ([cliwei86@ucla.edu](mailto:cliwei86@ucla.edu)) had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

### Disclosure statement

The authors declare that they have no conflict of interest.

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