Association of dietary oxidative balance score, dietary inflammatory potential and fractures among adults aged ≥40 years in the United States in 1999-2018

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ABSTRACT

Background and Objectives: The Dietary Oxidative Balance Score (DOBS) and Dietary Inflammatory Index (DII) reflect dietary oxidative and inflammatory status. This study investigated their associations with the prevalence of wrist, hip, and spine fractures. **Methods and Study Design:** DOBS and DII were scored based on 16 and 28 dietary factors, respectively. Multivariate logistic regression models and restricted cubic spline (RCS) models were used to assess the associations of DOBS and DII with the prevalence of wrist, hip, and spine fractures. Temporal trends of DOBS and DII and their associations with fracture trends were also analyzed, with subgroup analyses for robustness. **Results:** Compared with the lowest DOBS tertile, the highest DOBS tertile was associated with lower prevalence of hip and spine fractures [OR = 0.57 (0.32, 0.72); OR = 0.79 (0.48, 1.00)]. In contrast, the highest DII tertile was associated with an increased prevalence of hip and spine fractures compared with the lowest DII tertile [OR = 1.85 (1.49, 2.72); OR = 1.75 (1.18, 2.58)]. Anti-inflammatory and antioxidant diets were associated with lower prevalence of hip and spine fractures compared with pro-inflammatory and pro-oxidative diets [OR = 0.45 (0.24, 0.85); OR = 0.66 (0.44, 0.84)]. No significant associations were observed for wrist fractures. The overall DOBS trended upward among U.S. adults, while the DII showed opposite trend during the same period, with consistent results observed in subgroup analyses. **Conclusion:** Higher DOBS and/or lower DII were significantly associated with lower hip and spine fracture prevalence, but not with wrist fracture prevalence.

Key words: dietary oxidative balance score, dietary inflammatory index, fracture, oxidative stress, inflammation, NHANES

INTRODUCTION

Fractures are a major global public health concern, especially regarding disability and quality of life, with a notably high incidence in middle-aged and older adults.[1] As the global population ages, the incidence of osteoporosis and associated fractures is expected to increase steadily.[2] This imposes a substantial public health burden,

especially in the context of global aging.[3] Osteoporotic fractures—including those of the hip, spine, and wrist—occur in approximately 50% of women and 20% of men aged 50 years and older.[4] These fractures not only cause significant disability and mortality but also markedly reduce patients' quality of life.

Among the numerous factors associated with the prevalence of fractures, dietary pattern is a critical modifiable determinant. By providing essential nutrients and bioactive components, dietary intake modulates skeletal health and systemic metabolism.[5, 6] Oxidative stress and inflammation are physiological responses of an organism to external stimuli; however, chronic or excessive levels of these processes may induce tissue damage and disease progression, including osteoporosis and fractures.[7] In recent decades, a growing body of evidence has examined the association between dietary antioxidant intake and bone health.[8-11] Dietary antioxidants, such as carotenoids, vitamin C, and vitamin E, may exert beneficial effects on bone health by mitigating oxidative stress.[12-14] Furthermore, the influence of dietary patterns on bone health has garnered considerable research attention. For instance, dietary patterns abundant in fruits, vegetables, low-fat dairy products, whole grains, poultry, fish, nuts, and legumes have been demonstrated to confer beneficial effects on bone health, and are correspondingly linked to higher bone density and a lower prevalence of fractures.[15] In contrast, the Western dietary pattern—characterized by high intake of processed foods, refined grains, and added sugars—is associated with lower bone density and a higher prevalence of fractures.[16] Similarly, diet serves as a key driver of inflammation.[17] Numerous studies have shown that diet, as a primary source of bioactive components, can modulate the inflammatory response.[18] Specific nutrients—including carotenoids, vitamins A, C, and E, as well as minerals such as selenium and zinc—have been reported to exhibit anti-inflammatory properties.[19, 20] In contrast, the intake of red meat—which is high in cholesterol and saturated fats—may exert pro-inflammatory effects.[21-23]

The Dietary Oxidative Balance Score (DOBS) and the Dietary Inflammatory Index (DII) are indices calculated based on the oxidative and inflammatory effects of dietary nutrients, respectively, serving to evaluate the impact of diet on oxidative stress and

inflammation.[24, 25] Generally, a higher DOBS score indicates a greater antioxidant capacity of the diet. Diets with a high DII and a low DOBS typically involve high intake of added sugars, fat, salt, and cholesterol, which promote inflammation and oxidative stress. Conversely, diets with a low DII and high DOBS are typically associated with high intake of vegetables, fruits, protein, and dietary fiber, factors that can reduce inflammation and oxidative stress levels.[26, 27] Although previous studies have separately evaluated the associations between dietary inflammation or oxidative stress and fracture incidence, few have simultaneously examined these factors using comprehensive dietary indices in a nationally representative sample.[28, 29] Therefore, this study aims to explore the joint associations of DOBS and DII with fracture prevalence among U.S. adults using data from the National Health and Nutrition Examination Survey (NHANES). Using a cross-sectional study design and data from NHANES (1999-2018), we systematically examined these associations in a nationally representative adult population.

MATERIALS AND METHODS

Data source and study population

This study used data from the NHANES, a cross-sectional, nationally representative survey conducted by the National Center for Health Statistics (NCHS) in the United States. NHANES employs a rigorous, multistage, stratified sampling method to ensure that the findings accurately reflect the health and nutritional status of the U.S. population. All data collection procedures were approved by the NCHS Ethics Review Board, and participants provided written informed consent. The data for this study were derived from NHANES cycles conducted between 1999 and 2018 inclusive. Cycles from 2011–2012 and 2015–2016 were excluded due to the lack of relevant fracture data. Initially, a total of 101,316 participants were surveyed during the included years. Of these, 22,145 participants were excluded due to missing DOBS/DII data. Additionally, 49,896 participants were excluded because they were younger than 40 years of age. A further 6,348 participants were excluded due to the absence of fracture data. Ultimately, 22,927 participants were included in this study (Figure 1),

among whom 11,141 were female and 11,786 were male.

Combination of DOBS and DII

To comprehensively assess dietary intake, all participants completed two 24-hour dietary recall interviews administered by trained interviewers. At the Mobile Examination Center (MEC), images and charts were used to help participants quantitatively report their dietary intake over the previous 24 hours. A second dietary recall was conducted via telephone 3 to 10 days later. Before the interview, a set of measuring tools—including a guidebook, ruler, and spoon—was provided to ensure reporting accuracy. Both interviews were administered using dedicated computer software developed by NHANES. Dietary nutrient intake used for DOBS calculation was the average across the two recalls. On the basis of previous studies,[30] we identified both pro-oxidants and antioxidants from dietary sources. In this study, a total of 16 dietary nutrients were examined, including 2 pro-oxidants (total fat and iron) and 14 antioxidants (dietary fiber, carotene, riboflavin, niacin, vitamin B6, total folate, vitamin B12, vitamin C, vitamin E, calcium, magnesium, zinc, copper, and selenium). Based on prior evidence[30], nutrient intake was categorized into tertiles (highest, middle, lowest). Antioxidants were scored 2, 1, and 0 points for the highest to lowest tertiles, respectively, while pro-oxidants were scored inversely (0, 1, and 2 points). The DOBS was calculated as the sum of scores across all nutrients, with a higher score indicating a greater dietary antioxidant advantage. The detailed scoring scheme is presented in Supplementary Table 1. The theoretical range of DOBS was 1–33.

Detailed descriptions of the DII are available in the literature.[31] This index was developed using a literature review and population-based data, encompassing 45 dietary components with inflammatory potential and their representative intake levels. In this study, we followed established calculation protocols and selected 28 components from these 45 for DII calculation. The 28 dietary components included were (Supplementary Table 2): alcohol, vitamin B-12, vitamin B-6, β-carotene, caffeine, carbohydrate, cholesterol, energy, total fat, fiber, folic acid, iron, magnesium,

monounsaturated fatty acids, niacin, n-3 fatty acids, n-6 fatty acids, protein, polyunsaturated fatty acids, vitamin B-2, saturated fat, selenium, vitamin B-1, vitamin A, vitamin C, vitamin D, vitamin E, and zinc. The DII for a given dietary component = (Daily intake of the dietary component - Global daily mean intake of the dietary component) / Standard Deviation of the global daily intake for the dietary component * Overall inflammatory effect score of the dietary component. The sum of the DII values for all 28 dietary components yielded each participant's overall DII. A higher DII indicates a diet with greater pro-inflammatory potential, such as foods rich in carbohydrates and saturated fats, while diets abundant in fruits, leafy vegetables, and whole grains typically exhibit lower DII values. In the present study, participants with a DII score in the highest tertile were defined as having a pro-inflammatory diet.

To investigate the potential effects of pro-inflammatory and pro-oxidative diets compared with anti-inflammatory and antioxidant diets on fracture prevalence in adults, we constructed a composite variable integrating DOBS and DII. Specifically, participants in the lowest DOBS tertile and highest DII tertile were classified as having a pro-inflammatory and pro-oxidative dietary pattern. Conversely, those in the highest DOBS tertile and lowest DII tertile were classified as having an anti-inflammatory and antioxidant dietary pattern to better capture the synergistic effects of dietary inflammatory and oxidative balance, which may be associated with lower fracture prevalence than either factor alone. All remaining participants were assigned to the mixed composite dietary category.

Assessment of fracture

In the NHANES questionnaire, under the osteoporosis section of the household survey, all participants were asked, "Has a doctor ever told you that you had broken or fractured wrist/hip/spine?" The possible responses included "yes", "no", "don't know", "refused", and "missing". Individuals who either refused to answer, answered "don't know," or had missing responses were excluded from the study. Fracture status was self-reported, which may introduce recall bias. Nevertheless, previous validation

studies of NHANES self-reported fracture data have demonstrated acceptable accuracy, supporting the reliability of this assessment.[32]

Covariates

Data were collected via household interviews and physical examinations performed at the MEC. To adjust for potential confounding variables, this study included the following covariates. Participant characteristics included age, sex, race, educational level, marital status, poverty status, body mass index (BMI), hypertension, diabetes, smoking status, history of prednisone or cortisone use (yes/no), thyroid disorders (yes/no), and liver conditions (yes/no). The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[33] Race was categorized as non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, or other race. Educational attainment was categorized into three levels: less than high school, high school or equivalent, and more than high school. On the basis of existing literature, smoking status was classified into three groups: never smokers (those who smoked fewer than 100 cigarettes), current smokers, and former smokers (those who smoked more than 100 cigarettes but quit).[34] Diabetes was defined as either a self-reported diagnosis, fasting plasma glucose ≥7.0 mmol/L, glycosylated hemoglobin (HbA1c) ≥6.5%, or the use of diabetes medications. Hypertension was defined as having a systolic blood pressure of 140 mmHg or higher, or a diastolic blood pressure of 90 mmHg or higher, measured on three separate occasions using a mercury sphygmomanometer, along with a doctor's or healthcare provider's diagnosis of high blood pressure, or the use of hypertension medications. Covariates were selected based on previous literature demonstrating their associations with fracture prevalence and dietary patterns, ensuring comprehensive confounder adjustment.

Statistical analysis

To preserve the representativeness of NHANES data for the U.S. non-institutionalized civilian population, all estimates were weighted in accordance with the analytical

guidelines provided by the NCHS. Dietary weights were applied in our study. For the pooled calculation of weights, the weights for 1999-2000 and 2001-2002 were multiplied by 2/8; the weights for the remaining years were multiplied by 1/8. We used the masked variance unit variables (SDMVPSU and SDMVSTRA) as the clustering and stratification variables, respectively, and all analyses were performed using survey procedures. Continuous variables were described as means with 95% confidence intervals (CIs), while categorical variables were presented as counts and percentages. For continuous variables, weighted Student's t-tests were used for normally distributed data, and Kruskal–Wallis tests were employed for non-normally distributed data. Group differences in categorical variables were analyzed using weighted chi-square tests. Given the cross-sectional nature of NHANES data and the binary self-reported fracture outcomes, multivariable logistic regression models were used to determine the associations of DOBS, DII, and their different combinations with fracture prevalence. Three models were constructed for this analysis: Model 1 (no covariate adjustment), Model 2 (adjusted for age, sex, and race), and Model 3 (further adjusted for educational level, BMI, poverty status, smoking status, hypertension, diabetes, eGFR, prednisone or cortisone use, thyroid disorders, and liver conditions). To explore potential associations, DOBS, DII, and their different combinations were categorized into tertiles, and trend tests were performed to assess linear trends. Restricted cubic spline (RCS) models were employed to assess the dose-response relationships between the DOBS, DII, and fractures, with potential confounding factors controlled for via multivariable adjustment. The models included four knots, which were set at the 5th, 35th, 65th, and 95th percentiles of the observed values (with the 5th percentile as the reference value). Logistic regression with year as the predictor was employed to assess the temporal trends in fracture prevalence, DOBS, DII, and the individual components of DII and DOBS from 1999 to 2018. Additionally, multiple stratified analyses were conducted to evaluate the potential effect modification by the following factors: age (<60 vs. ≥60 years), sex (male vs. female), race (non-Hispanic White vs. others), BMI (<30 vs. ≥30), poverty-income ratio (<3 vs. ≥3), education (college or above vs. others), smoking status

(current/former/never), hypertension (yes/no), and diabetes (yes/no). Sensitivity analyses were performed by additionally adjusting for additional confounding factors: physical activity and the use of calcium/vitamin D supplements, to ensure the robustness of the results. All analyses were performed using R software (version 4.1.2), with statistical significance determined by a two-sided *p* value threshold of less than 0.05.

RESULTS

Participant characteristics

Baseline characteristics of participants are presented in Table 1. A total of 22,927 participants were included in the study, of whom 2,153 had wrist fractures, 425 had hip fractures, and 636 had spine fractures. Participants with a pro-inflammatory/pro-oxidative diet were older, more often female, non-Hispanic Black, less educated, had a higher BMI (≥30), a lower eGFR (<60), a higher prevalence of smoking, hypertension, and diabetes, and had a greater likelihood of hip or spine fractures compared with those with an anti-inflammatory and antioxidant diets.

Associations of wrist, hip, and spine fractures with DOBS/DII and baseline characteristics

As shown in Supplementary Tables 3–5, participants with wrist fractures were more likely to be older, male, non-Hispanic Black, to have educational attainment above high school, to be current smokers, and to report prednisone or cortisone use and liver disease than those without wrist fractures. Supplementary Tables 6–8 demonstrated that participants with hip fractures were more likely to be older, to have a lower poverty-income ratio, to have less than high school educational attainment, to have a BMI < 25, to have an eGFR <60, and to smoke, as well as to report prednisone or cortisone use, thyroid disorders, and liver disease than those without hip fractures. Furthermore, participants with hip fractures exhibited lower DOBS and higher DII levels. Supplementary Tables 9–11 revealed that participants with spine fractures were

more likely to be older, male, non-Hispanic Black, to have a lower poverty-income ratio, to have a BMI ≥ 30, to have an eGFR < 60, and to be current smokers, as well as to report prednisone or cortisone use and liver disease than those without spine fractures. Consistent with hip fracture participants, those with spine fractures also had lower DOBS and higher DII levels.

Temporal trends in DOBS/DII and prevalence of wrist, hip, and spine fractures

As shown in Supplementary Table 12, the overall estimated DOBS trended upward from 1999 to 2018, a trend opposite to that of DII over the same period. In the DOBS grouping, the overall trends were similar between males and females (Supplementary Figure 1). In the DII grouping, females had overall higher DII levels than males across the same survey years (Supplementary Figure 2). When participants were categorized by DOBS tertiles, the estimated proportion of U.S. adults aged ≥40 years in the lowest DOBS tertile decreased from 38.55% (1999–2000) to 25.83% (2017–2018), whereas the proportion in the highest tertile increased from 32.05% (1999–2000) to 40.00% (2017–2018) (Supplementary Table 13). When categorized by DII tertiles, the estimated proportion of U.S. adults in the lowest DII tertile decreased from 40.90% (1999–2000) to 35.54% (2017–2018), whereas the proportion in the highest tertile increased from 21.89% (1999–2000) to 32.67% (2017–2018) (Supplementary Table 13). Statistically significant changes were also observed in the individual components of DOBS and DII (Supplementary Tables 14–15).

As shown in Supplementary Tables 16–18, the estimated fracture prevalence among U.S. adults aged ≥40 years changed significantly in relation to DOBS and DII from 1999 to 2018. DOBS reached its highest levels during 2009–2010 and 2013–2014, whereas DII reached its lowest levels during these same periods (second only to 1999–2000). Correspondingly, fracture prevalence decreased significantly during these intervals (Supplementary Figure 3). In the analyses of hip and spine fractures, a significant decrease in fracture prevalence was observed in the highest DOBS tertile compared with the lowest tertile, whereas the opposite trend was observed for DII. However, this trend was not observed for wrist fractures.

Associations of DOBS, DII, and different combinations of DII and DOBS with fractures

The results indicated that DOBS, DII, and different combinations of DII and DOBS were significantly associated with the prevalence of hip and spine fractures (Supplementary Tables 19–21). For DOBS, participants in the highest tertile had a significantly lower prevalence of hip fracture (OR = 0.57, 95% CI: 0.32–0.72) and spine fracture (OR = 0.79, 95% CI: 0.48–1.00) compared with those in the lowest tertile (Supplementary Table 19). Conversely, participants in the highest DII tertile had a significantly higher prevalence of hip fracture (OR = 1.85, 95% CI: 1.49–2.72) and spine fracture (OR = 1.75, 95% CI: 1.18–2.58) compared with those in the lowest tertile (Supplementary Table 20). Similarly, compared with a pro-inflammatory and pro-oxidative diet pattern, an anti-inflammatory and antioxidant diet pattern was associated with a lower prevalence of hip fracture (OR = 0.45, 95% CI: 0.24–0.85) and spine fracture (OR = 0.66, 95% CI: 0.44–0.84) (Supplementary Table 21). In Model 3, participants in the highest versus lowest DOBS tertile had an OR of 1.16 (95% CI: 0.80–1.35) for wrist fracture, with a *p*-trend of 0.071; those in the highest versus lowest DII tertile had an OR of 1.12 (95% CI: 0.87–1.45), with a *p*-trend of 0.376; and the anti-inflammatory and antioxidant diet pattern versus the pro-inflammatory and pro-oxidative diet pattern yielded an OR of 0.88 (95% CI: 0.59–1.07), with a *p*-trend of 0.098. None of these associations reached statistical significance (Supplementary Tables 19–21). When these fracture outcomes were analyzed as continuous variables, the results remained essentially unchanged. We further observed that participants in the highest DOBS tertile, the highest DII tertile, or those with an anti-inflammatory and antioxidant diet pattern exhibited more pronounced changes in hip fracture prevalence.

Non-linear analysis using RCS and sensitivity analyses and subgroup analyses

As shown in Figure 2, after multivariate adjustment, DOBS was associated with a decreased prevalence of hip fracture in an approximately linear manner (*p* for overall = 0.004, *p* for nonlinear = 0.450), and also with a decreased prevalence of spine

fracture in an approximately linear manner (p for overall = 0.008, p for nonlinear = 0.364). Similarly, DII was associated with an increased prevalence of hip fracture in an approximately linear manner (p for overall <0.001, p for nonlinear = 0.151), and also with an increased prevalence of spine fracture in an approximately linear manner (p for overall <0.001, p for nonlinear = 0.476). In the sensitivity analysis, we adjusted for the confounding effects of physical activity and calcium/vitamin D supplement use. The associations between fracture prevalence and DOBS/DII, as well as different combinations of DII and DOBS, remained unchanged, confirming the robustness of the study findings (Supplementary Table 22). Subgroup analyses based on age, sex, race, BMI, poverty-income ratio, education level, smoking, hypertension, and diabetes revealed similar associations (Supplementary Tables 23–31). In the subgroup analysis results, we found that the associations with hip and spine fractures were more pronounced specifically among participants aged ≤60 years, female, non-Hispanic White, with BMI <30, poverty income ratio ≥3, higher education level, non-smoking status, and no history of hypertension or diabetes (Supplementary Tables 23–31).

DISCUSSION

Using data from NHANES of 22,927 U.S. adults, we calculated the DII (based on 28 dietary components) and DOBS (based on 16 nutrients) to reflect dietary inflammatory and oxidative balance. We analyzed their associations with fractures (wrist, hip, and spine) in adults aged ≥40 years, as well as temporal trends in these indices and fracture prevalence. After covariate adjustment, lower DOBS or higher DII was associated with an increased prevalence of hip and spine fractures. DOBS peaked, and DII reached a trough, in 2009–2010 and 2013–2014, which was accompanied by a concurrent reduction in hip and spine fracture prevalence. Notably, among participants aged ≤60 years, who were female, non-Hispanic White, with BMI <30, poverty income ratio ≥3, higher educational level, non-smoking status, and no history of hypertension or diabetes, those adhering to diets rich in anti-inflammatory and antioxidant components had a lower prevalence of hip and spine fractures.

To our knowledge, few studies have jointly examined oxidative balance and inflammatory potential, as well as their combined effects on different skeletal sites in a nationally representative sample. Chronic low-grade inflammation and oxidative stress play critical roles in the development of osteoporosis and other skeletal disorders.[35-37] Numerous studies have demonstrated that oxidative stress negatively impacts bone remodeling, resulting in reduced bone mineral density (BMD).[38-41] Recent evidence also indicates that inflammation associated with oxidative stress may partially contribute to the pathogenesis of osteoporosis.[42] Oxidative stress can be induced by a variety of factors, including endogenous and physiological processes (such as metabolic alterations, hormonal changes, and aging), environmental factors (such as dietary intake and pollution),[43, 44] and pathological conditions related to inflammatory cytokines or prolonged pharmacological interventions such as corticosteroid therapy.[45] The potential effects of pro-inflammatory diets on skeletal disorders have been elucidated through multiple biological mechanisms. Long-term intake of pro-inflammatory dietary components has been shown to increase systemic inflammatory status. Studies have indicated that diets high in saturated fat may stimulate the production of interleukin-1 (IL-1) and IL-6.[21] Red meat intake has been shown to increase plasma concentrations of C-reactive protein (CRP) and other pro-inflammatory cytokines.[18] Furthermore, evidence has shown that pro-inflammatory factors contribute to bone erosion and subsequent bone loss by inhibiting osteoblast function and promoting osteoclast activity.[46, 47]

The association between dietary inflammation (assessed by the DII) and fractures has been confirmed in multiple population-based studies.[48, 49] Previous studies have shown that higher dietary inflammatory potential is associated with osteoporosis or lower baseline BMD, as well as an increased fracture prevalence over 10 years in older men,[50] even after adjusting for the competing risk of death. Furthermore, studies have shown that higher DII levels correlate with an elevated fall risk score and reduced appendicular lean mass.[51] On the other hand, oxidative stress exerts a significant impact on fracture occurrence and progression.[52] Emerging evidence indicates that antioxidants—obtainable through dietary intake or exogenous

supplementation—counteract reactive oxygen species (ROS), with plant-based foods exhibiting the strongest antioxidant capacity.[53] These foods are often compared based on their oxygen radical absorbance capacity (ORAC) values.[54] The higher the ORAC value, the stronger the food's ability to scavenge oxygen free radicals. Antioxidant supplements are commonly used in clinical practice to mitigate ROS. A substantial body of research has explored the potential benefits of vitamins and minerals, highlighting their role as both exogenous and endogenous protectors against ROS damage.[14, 55-58]

Our study indicates that dietary patterns with both anti-inflammatory and antioxidant properties were associated with a lower prevalence of hip and spine fractures compared with individual dietary components. This superiority may be attributed to the combined effects of enhancing anti-inflammatory and antioxidant capacities,[59] providing a more comprehensive spectrum of nutrients,[60] and targeting multiple pathways (such as inflammation, immune dysfunction, free radical generation, and oxidative stress) that influence fracture.[61] Our findings underscore the importance of incorporating both anti-inflammatory and antioxidant dietary components into dietary interventions for fracture prevention. Compared with individuals in the lowest tertile, those in the highest tertile of DOBS exhibited a 43% lower prevalence of hip fracture and a 21% lower prevalence of spine fracture. Conversely, participants in the highest tertile of DII had an 85% higher prevalence of hip fracture and a 75% higher prevalence of spine fracture than those in the lowest tertile. Notably, individuals adhering to anti-inflammatory and antioxidant diets had a 55% lower prevalence of hip fracture and a 34% lower prevalence of spine fracture compared with those consuming pro-inflammatory and pro-oxidative diets. The combined effects of anti-inflammatory and antioxidant diets were more pronounced than those of either diet alone, even though the individual effects of anti-inflammatory and antioxidant diets were similar. The reliability and robustness of these findings are supported by consistent results from stratified analyses.

In this study, we also identified dietary trends among U.S. adults, characterized by an overall upward trend in DOBS and no significant sex disparity. Conversely, DII

exhibited an opposing trend to DOBS, with females showing significantly higher DII levels than males. This finding is consistent with results from large-scale cohort studies, which suggest that the association between inflammation and fracture is more pronounced in females than in males. [29, 62, 63] According to the data, DOBS and DII reached their peak and trough values during 2009–2014, respectively (with DII levels second only to those in 1999–2000). Concomitantly, hip fracture prevalence decreased significantly, while spine fracture prevalence reached its minimum. Although concurrent changes in DOBS/DII and fracture prevalence were observed, the temporal trend analysis of DOBS/DII and fracture prevalence in this study is an ecological descriptive analysis. It only reflects population-level trends in dietary patterns and fracture prevalence. Given the many other factors affecting fracture trends (including diagnosis, treatment, prevention, and population aging), this analysis cannot verify individual-level associations, nor can causal effects be inferred. Causal relationships and specific mechanisms require further validation in subsequent prospective cohort studies. Furthermore, we observed that higher DOBS or lower DII was significantly associated with lower prevalence of hip and spine fractures, whereas no significant association was observed with wrist fractures. This discrepancy may be attributed to differences in bone composition and mechanical loading across these skeletal sites. The hip and spine are primarily composed of trabecular bone, which has a high metabolic rate and large surface area, rendering it particularly susceptible to oxidative damage. A diet rich in antioxidants—including dietary fiber, carotenoids, vitamin C, calcium, and magnesium—may counteract age-related increases in oxidative stress and chronic low-grade inflammation. The potential mechanisms of action include direct effects on bone tissue and indirect effects through the reduction of oxidative stress and inflammation; these processes upregulate osteoblastogenesis and downregulate osteoclastogenesis, thereby increasing bone mass and strength and reducing the prevalence of fracture.[64-66] In contrast, the wrist is predominantly composed of cortical bone, which is denser and less metabolically active—potentially reducing its susceptibility to oxidative stress and inflammation. Furthermore, wrist fractures are often caused by external factors such as falls, where mechanical

trauma—rather than bone quality—may play a more dominant role. These site-specific differences underscore the importance of accounting for skeletal heterogeneity when assessing the impact of dietary factors on the prevalence of fracture.

The subgroup analyses in our study further confirmed the adverse effects of pro-inflammatory and/or pro-oxidative dietary patterns on fracture prevalence, as well as on increased inflammatory and oxidative stress markers. Furthermore, stronger associations were observed among participants aged ≤60 years, who were female, non-Hispanic White, with BMI <30, poverty-income ratio ≥3, higher educational level, non-smoking status, and no history of hypertension or diabetes. These findings were consistent with those reported in previous studies.[67, 68] These findings suggest that an individual's healthy lifestyle, lower disease risk, and physiological and metabolic differences make the relationship between diet quality and health risks more pronounced. Additionally, previous studies have shown that advanced age and current smoking are both associated with elevated levels of inflammation and oxidative stress.[69, 70] Therefore, our findings further emphasize the importance of modifying unhealthy lifestyles in individuals consuming pro-inflammatory and pro-oxidative dietary patterns for fracture prevention.

Although previous studies have shown that diet affects fracture prevalence, our study adds several new advantages to the existing literature: First, drawing on established methodologies, we constructed two comprehensive dietary indices—DOBS and DII—to evaluate dietary oxidative stress and inflammatory status; this approach prioritizes the combined effects of multiple dietary components rather than the impact of single dietary factors on fracture. Second, we used a complex multistage probability sampling method to ensure that the participants in this study accurately reflect the non-institutionalized civilian population, thus enabling the study results to be generalized to the entire U.S. population. Finally, we also conducted subgroup analyses to account for the impact of multiple clinical indicators on fractures. However, this study has several limitations. First, because this is a cross-sectional study, it is impossible to infer causality between DOBS, DII, and

fracture prevalence, and further prospective studies are needed to validate these results. Meanwhile, dietary intake was assessed at the time of the survey, whereas fracture history reflected previous diagnoses made by doctors. It was therefore impossible to determine the temporal sequence between dietary factors and fracture occurrence, leading to the potential for reverse causation bias. Second, the dietary data used to calculate DOBS and DII, as well as the definition of fractures, were self-reported, which may introduce recall bias and affect the accuracy of the scores. Although DOBS and DII provide comprehensive measures of dietary oxidative balance and inflammation, they do not cover all relevant dietary components (such as anthocyanins,[71] polyphenols,[72] and flavonoids).[73] Future studies expanding the components included in DOBS and DII may enhance their predictive validity. However, compared with similar published studies, our study included as many relevant components as possible. Third, this study focused on wrist, hip, and spine fractures, which may not fully represent all fracture types associated with osteoporosis. In addition, misclassification of fractures may occur due to self-reporting. Fourth, regarding unconsidered potential confounders: although adjustments were made for a wide range of confounding variables, several important potential confounders, including menopausal status, hormone therapy, BMD and osteoporosis, were not incorporated due to data availability and year limitations. Finally, the study was conducted in a U.S. adult sample that is predominantly non-Hispanic White and characterized by Western dietary patterns; thus, the findings may not be generalizable to other ethnicities or regions.

Conclusion

In conclusion, this study provides evidence from a nationally representative sample that combined assessment of dietary oxidative balance and inflammatory potential, as well as their composite impact on different skeletal sites. Higher DOBS and/or lower DII was associated with lower prevalence of hip and spine fractures. However, no statistically significant association with wrist fracture was observed for any of the dietary indices examined. This suggests that the relationship between diet and fracture

prevalence may not be consistent across all skeletal sites. Prospective studies are needed in the future to confirm these site-specific associations and to elucidate the potential mechanisms linking dietary patterns to different skeletal outcomes. Participants with diets that are both anti-inflammatory and antioxidant had a lower prevalence of hip and spine fractures, particularly among those aged ≤60 years, who were female, non-Hispanic White, with a BMI <30, poverty income ratio ≥3, higher education level, non-smoking status, and no history of hypertension or diabetes. These findings confirm the results of previous studies and suggest that DOBS and DII may be valuable tools for assessing the impact of dietary factors related to oxidative stress and inflammation on fractures. Further research is needed to understand the exact underlying mechanisms.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare that they have no known competing financial interests or personal relationships.

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Table 1. Baseline characteristics of participants

	Total	Dietary oxidative balance score (DOBS) (N = 22927)				Dietary inflammatory index (DII) (N = 22927)				Different combinations of DII and DOBS (N = 22927)			
		≤12 (n=7643)	13-18 (n=7642)	≥19 (n=7642)	*p*	≤0.78 (n=7643)	0.79-2.45 (n=7642)	≥2.46 (n=7642)	*p*	Anti-inflammatory and antioxidant diet (n=5773)	Composite diet category (n=11255)	Pro-inflammatory and pro-oxidative diet (n=5899)	*p*
Age	57.79 (57.49, 58.09)	58.85 (58.47, 59.22)	58.02 (57.62, 58.42)	56.83 (56.41, 57.26)	<0.001	57.43 (57.00, 57.86)	57.52 (57.12, 57.93)	58.53 (58.13, 58.94)	<0.001	57.07 (56.61, 57.53)	57.78 (57.43, 58.13)	58.82 (58.38, 59.25)	<0.001
Sex (%)					0.060				<0.001				<0.001
Female	11786 (53.38)	3656 (51.47)	4024 (53.96)	4106 (54.25)		3046 (41.55)	3964 (54.70)	4776 (66.50)		2711 (46.30)	5858 (54.75)	3217 (60.12)	
Male	11141 (46.62)	3987 (48.53)	3618 (46.04)	3536 (45.75)		4597 (58.45)	3678 (45.30)	2866 (33.50)		3188 (53.70)	5397 (45.25)	2556 (39.88)	
Poverty	3.22 (3.16, 3.29)	2.79 (2.72, 2.87)	3.24 (3.16, 3.31)	3.52 (3.44, 3.59)	<0.001	3.56 (3.49, 3.63)	3.24 (3.16, 3.31)	2.79 (2.72, 2.87)	<0.001	3.58 (3.51, 3.66)	3.23 (3.16, 3.30)	2.71 (2.62, 2.79)	<0.001
Race (%)					<0.001				<0.001				<0.001
Non-Hispanic White	11777 (75.82)	3356 (68.94)	4014 (75.84)	4407 (80.74)		4279 (79.84)	3946 (75.56)	3552 (71.16)		3397 (80.88)	5853 (75.88)	2527 (68.58)	
Non-Hispanic Black	4567 (9.84)	2059 (15.23)	1435 (9.49)	1073 (6.27)		1125 (6.51)	1496 (9.78)	1946 (14.03)		825 (6.09)	2156 (9.59)	1586 (15.70)	
Mexican American	3839 (5.24)	1384 (5.69)	1280 (5.47)	1175 (4.72)		1260 (5.06)	1325 (5.45)	1254 (5.23)		908 (4.75)	1925 (5.37)	1006 (5.61)	
Other Hispanic	1549 (4.26)	529 (5.34)	505 (4.12)	515 (3.61)		479 (3.68)	492 (4.12)	578 (5.15)		384 (3.53)	738 (4.16)	427 (5.53)	
Other race	1195 (4.83)	315 (4.79)	408 (5.08)	472 (4.66)		500 (4.92)	383 (5.09)	312 (4.44)		385 (4.74)	583 (5.00)	227 (4.58)	
Education (%)					<0.001				<0.001				<0.001
More than high school	10722 (56.68)	2655 (42.98)	3646 (56.83)	4421 (66.39)		4393 (66.78)	3531 (56.23)	2798 (44.72)		3515 (68.28)	5270 (56.36)	1937 (41.14)	
High school or equivalent	5379 (25.35)	1899 (29.51)	1822 (25.69)	1658 (22.07)		1596 (21.37)	1831 (25.89)	1952 (29.65)		1218 (20.79)	2685 (25.88)	1476 (30.49)	
Less than high school	6790 (17.88)	3073 (27.36)	2163 (17.40)	1554 (11.50)		1645 (11.79)	2264 (17.79)	2881 (25.51)		1161 (10.90)	3277 (17.64)	2352 (28.25)	
Marital (%)					<0.001				<0.001				<0.001
Married	13485 (64.31)	4231 (59.96)	4534 (64.89)	4720 (66.93)		4948 (68.70)	4542 (65.25)	3995 (57.80)		3743 (67.91)	6690 (64.81)	3052 (58.07)	
Never married	1540 (6.03)	530 (6.35)	503 (6.06)	507 (5.78)		469 (5.58)	501 (6.07)	570 (6.55)		376 (5.66)	745 (6.10)	419 (6.42)	
Other marital status	7596 (28.21)	2743 (32.12)	2531 (27.93)	2322 (25.64)		2113 (23.72)	2489 (27.19)	2994 (34.91)		1696 (24.41)	3677 (27.76)	2223 (34.59)	
BMI (%)					<0.001				<0.001				<0.001
<25	5769 (26.63)	1823 (25.01)	1835 (25.88)	2111 (29.50)		2137 (29.47)	1838 (26.31)	1794 (24.87)		1709 (30.84)	2681 (25.60)	1379 (25.05)	
25-30	8166 (35.08)	2729 (36.00)	2760 (36.24)	2677 (34.84)		2904 (37.84)	2701 (35.09)	2561 (33.49)		2139 (36.08)	4043 (35.94)	1984 (34.26)	
≥30	8505 (36.74)	2872 (38.99)	2908 (37.88)	2725 (35.66)		2473 (32.69)	2948 (38.60)	3084 (41.64)		1953 (33.08)	4306 (38.45)	2246 (40.69)	
eGFR (%)					<0.001				<0.001				<0.001
<60	3136 (10.72)	1318 (15.00)	1051 (11.52)	767 (8.19)		837 (8.69)	1003 (10.68)	1296 (14.86)		607 (8.32)	1512 (11.03)	1017 (15.61)	
60-90	9835 (45.63)	3171 (45.22)	3314 (47.97)	3350 (48.88)		3470 (49.63)	3273 (48.33)	3092 (44.12)		2648 (49.20)	4847 (48.18)	2340 (43.77)	
≥90	8828 (39.58)	2697 (39.79)	2925 (40.51)	3206 (42.93)		3014 (41.68)	2995 (41.00)	2819 (41.02)		2403 (42.48)	4363 (40.78)	2062 (40.63)	
Smoke (%)					<0.001				<0.001				<0.001
Now	4134 (17.98)	1725 (25.14)	1327 (17.62)	1082 (13.17)		997 (11.79)	1374 (18.73)	1763 (24.80)		761 (11.50)	2028 (18.55)	1345 (25.78)	
Former	7452 (31.72)	2480 (30.63)	2486 (31.48)	2486 (32.74)		2729 (35.55)	2432 (30.04)	2291 (28.93)		2011 (34.26)	3646 (31.10)	1795 (29.67)	
Never	11323 (50.26)	3428 (44.23)	3826 (50.90)	4069 (54.09)		3912 (52.65)	3832 (51.23)	3579 (46.27)		3123 (54.24)	5575 (50.35)	2625 (44.55)	
Hypertension (%)					<0.001				<0.001				<0.001
Yes	13042 (50.68)	4720 (55.27)	4358 (51.69)	3964 (46.56)		4044 (47.20)	4327 (50.83)	4671 (54.86)		3066 (46.44)	6394 (51.06)	3582 (55.82)	
No	9878 (49.29)	2920 (44.73)	3282 (48.31)	3676 (53.44)		3597 (52.80)	3313 (49.17)	2968 (45.14)		2831 (53.56)	4859 (48.94)	2188 (44.18)	
Diabetes (%)					<0.001				<0.001				<0.001
Yes	4087 (13.43)	1546 (15.78)	1400 (13.72)	1141 (11.53)		1166 (11.79)	1375 (13.56)	1546 (15.35)		855 (11.16)	2034 (13.76)	1198 (15.91)	
No	18822 (86.49)	6093 (84.22)	6239 (86.28)	6490 (88.47)		6468 (88.21)	6261 (86.44)	6093 (84.65)		5035 (88.84)	9215 (86.24)	4572 (84.09)	
Prednisone or cortisone (%)					0.003				<0.001				<0.001
Yes	937 (4.35)	301 (8.47)	330 (7.02)	306 (5.94)		257 (5.65)	301 (6.33)	379 (9.10)		211 (5.74)	468 (6.81)	258 (9.02)	
No	13420 (58.71)	3834 (91.53)	4544 (92.98)	5042 (94.06)		4657 (94.35)	4296 (93.67)	4467 (90.90)		3828 (94.26)	6433 (93.19)	3159 (90.98)	
Thyroid problem (%)					0.510				<0.001				0.010
Yes	2377 (11.45)	657 (15.09)	865 (15.61)	855 (14.68)		704 (13.35)	768 (14.44)	905 (17.98)		592 (13.64)	1194 (15.35)	591 (16.74)	
No	14756 (64.40)	4437 (84.91)	5049 (84.39)	5270 (85.32)		5016 (86.65)	4844 (85.56)	4896 (82.02)		4032 (86.36)	7182 (84.65)	3542 (83.26)	
Liver condition (%)					0.190				0.630				0.850
Yes	1072 (4.60)	327 (4.56)	383 (5.05)	362 (4.26)		386 (4.75)	344 (4.35)	342 (4.72)		291 (4.46)	543 (4.71)	238 (4.58)	
No	21796 (95.19)	7297 (95.44)	7239 (94.95)	7260 (95.74)		7235 (95.25)	7277 (95.65)	7284 (95.28)		5591 (95.54)	10684 (95.29)	5521 (95.42)	
Wrist fracture (%)					0.550				0.110				0.710
Yes	2153 (10.87)	692 (10.50)	699 (10.73)	762 (11.25)		755 (11.61)	682 (10.14)	716 (10.78)		590 (11.21)	1030 (10.75)	533 (10.68)	
No	20774 (89.13)	6951 (89.50)	6943 (89.27)	6880 (88.75)		6888 (88.39)	6960 (89.86)	6926 (89.22)		5309 (88.79)	10225 (89.25)	5240 (89.32)	
Hip fracture (%)					<0.001				<0.001				<0.001
Yes	425 (1.56)	173 (2.16)	139 (1.45)	113 (1.23)		111 (1.20)	129 (1.29)	185 (2.32)		81 (1.17)	202 (1.45)	142 (2.37)	
No	22502 (98.44)	7470 (97.84)	7503 (98.55)	7529 (98.77)		7532 (98.80)	7513 (98.71)	7457 (97.68)		5818 (98.83)	11053 (98.55)	5631 (97.63)	
Spine fracture (%)					0.020				0.002				0.430
Yes	636 (3.12)	219 (3.24)	222 (3.61)	195 (2.60)		204 (3.00)	200 (2.55)	232 (3.91)		151 (2.85)	314 (3.15)	171 (3.43)	
No	22291 (96.88)	7424 (96.76)	7420 (96.39)	7447 (97.40)		7439 (97.00)	7442 (97.45)	7410 (96.09)		5748 (97.15)	10941 (96.85)	5602 (96.57)	

BMI, body mass index; eGFR, estimated glomerular filtration rate.

Data were presented as unweighted numbers (weighted percentages) for categorical variables and 95% confidence intervals for continuous variables.

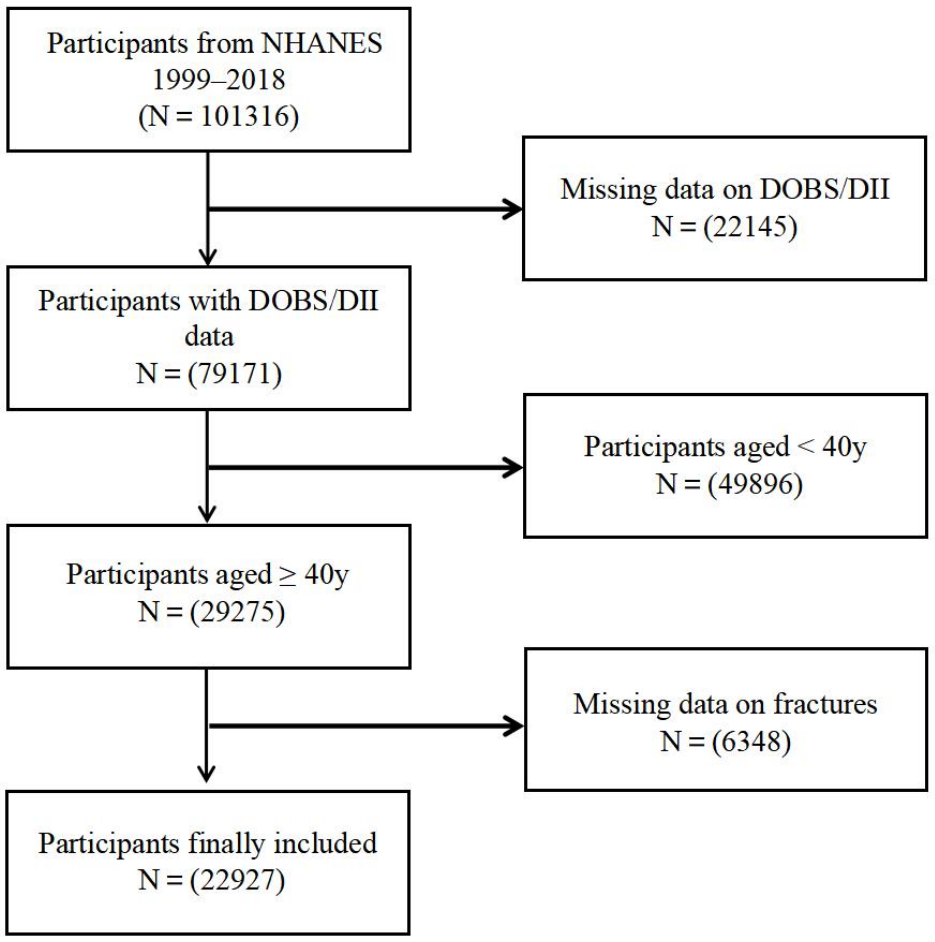

Figure 1. Sample selection process diagram NHANES: National Health and Nutrition Examination Survey; DOBS: dietary oxidative balance score; DII: Dietary Inflammatory Index

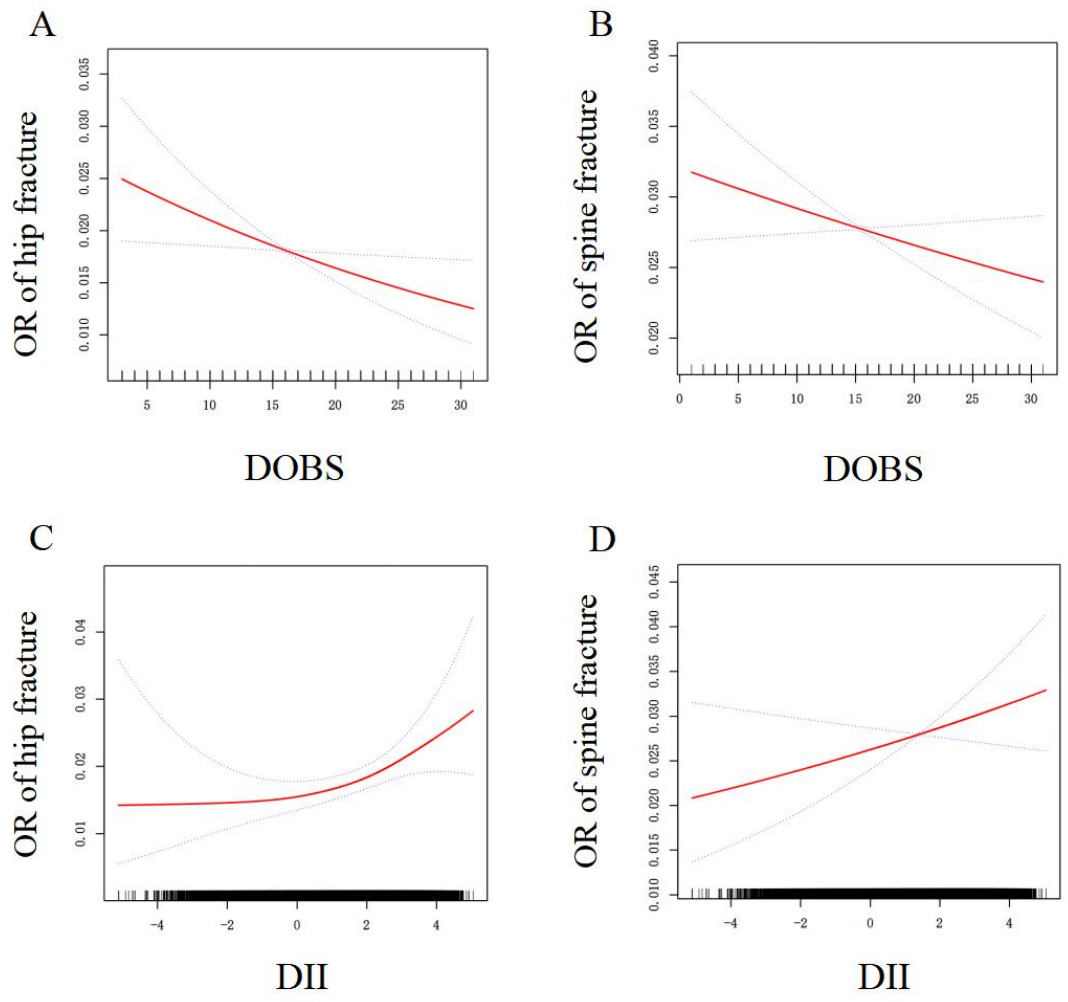

Figure 2. The association of DOBS/DII with prevalence of fracture. A: Association between DOBS and hip fractures; B: Association between DOBS and spine fractures. C: Association between DII and hip fractures; D: Association between DII and spine fractures. Solid and dashed lines represent the predicted value and 99 % confidence intervals.