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# A Western Diet Pattern Is Associated with Higher Concentrations of Blood and Bone Lead among Middle-Aged and Elderly Men

Xin Wang,[1] Ning Ding,[1] Katherine L Tucker,[3] Marc G Weisskopf,[4] David Sparrow,[5,6] Howard Hu,[7] and Sung Kyun Park[1,2]

Departments of [1]Epidemiology and [2]Department of Environmental Health Sciences, School of Public Health, University of Michigan, Ann Arbor, MI; [3]Department of Clinical Laboratory and Nutritional Sciences, University of Massachusetts at Lowell, Lowell, MA; [4]Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; [5]Normative Aging Study, Veterans Affairs Boston Healthcare System, Boston, MA; [6]Department of Medicine, Boston University School of Medicine, Boston, MA; and [7]Dalla Lana School of Public Health, University of Toronto, Toronto, ON

## Abstract

**Background:** Little is known about the effects of overall dietary pattern on lead concentration.

**Objective:** We examined the association of overall dietary patterns, derived from a semiquantitative food frequency questionnaire, with bone and blood lead concentrations.

**Methods:** These longitudinal analyses included mostly non-Hispanic white, middle-aged-to-elderly men from the Veterans Affairs Normative Aging Study. Long-term lead exposures were measured as tibia and patella lead concentrations by using K-shell-X-ray fluorescence. Short-term lead exposures were measured as blood lead concentrations by using graphite furnace atomic absorption spectroscopy. Dietary pattern scores were derived by using factor analysis. Linear mixed-effects models were utilized to predict blood lead concentrations among 983 men, aged 44–92 y at baseline, with a total of 3273 observations (during 1987–2008). We constructed linear regression models to determine the relations between dietary patterns and bone lead concentrations among 649 participants with an age range of 49–93 y.

**Results:** Two major dietary patterns were identified: a prudent dietary pattern, characterized by high intakes of fruit, legumes, vegetables, whole grains, poultry, and seafood; and a Western dietary pattern, characterized by high intakes of processed meat, red meat, refined grains, high-fat dairy products, French fries, butter, and eggs. After adjusting for age, smoking status, body mass index, total energy intake, education, occupation, neighborhood-based education and income level, men in the highest tertile of the Western pattern score (compared with the lowest) had 0.91 μg/dL (95% CI: 0.41, 1.42 μg/dL) higher blood lead, 5.96 μg/g (95% CI: 1.76, 10.16 μg/g) higher patella lead, and 3.83 μg/g (95% CI: 0.97, 6.70 μg/g) higher tibia lead. No significant association was detected with the prudent dietary pattern in the adjusted model.

**Conclusions:** These findings suggest that the Western diet is associated with a greater lead body burden among the middle-aged-to-elderly men. More studies are needed to examine the underlying mechanisms by which dietary patterns are associated with lead concentrations. *J Nutr* 2017;147:1374–83.

**Keywords:** dietary patterns, bone lead concentrations, patella lead, tibia lead, blood lead concentrations, elderly men, Normative Aging Study

## Introduction

Lead toxicity is a prevalent and persistent public health problem. Lead is known to affect the central nervous system and has been associated with adverse health outcomes, such as hypertension, cardiovascular disease, and impaired renal function (1–5). Environmental exposure to lead occurs through various routes, including air, dust, paint, water, and food (5). With the removal of lead from gasoline and the elimination of lead solder from food and beverage cans, there has been a remarkable reduction in environmental sources of lead (6). However, lead stored in bones can still contribute to cognitive decline, kidney failure, hearing loss, and heart disease among older adults (3, 7–10). In adults, >95% of the total lead body burden is found in the bone (11). Bone lead is, therefore, considered a better biomarker than blood lead for characterizing cumulative lead exposure (3, 7).

Nutritional factors may affect lead body burdens, including short-term lead exposures captured by blood lead concentration and long-term exposures captured by bone lead concentration. In animal models, rats with higher levels of supplemented vitamin C and vitamin B-6 had lower lead concentrations in the blood and organs (12, 13), although a strong positive



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association was observed between blood lead and high fat and high energy intakes in rats (14). In epidemiological studies, dietary intakes of iron, calcium, and vitamin C have been inversely associated with blood lead concentration (15–17). In the Normative Aging Study (NAS), low dietary intakes of vitamin D and phosphorus were also linked to a higher bone lead concentration (15). In addition, findings from human studies showed that dietary protein intake was positively associated with blood lead concentration (18). However, a limitation shared by all of these previous studies is the failure to assess the effects of the combined consumption of nutrients because they occur naturally in foods.

Given the complexity in the correlations of nutrients with each other, it is often difficult to separate the effect of a specific nutrient from others in the diet. Moreover, the specific effects of a single nutrient may be too small to be detected. Therefore, dietary patterns may better represent nutritional exposures. Further, overall patterns may be easier for the public to interpret and translate into their daily eating habits. The patterns can enhance our conceptual understanding of human dietary practice and provide guidance for nutrition intervention to alleviate effects of lead exposure. Thus, dietary patterns emerge as an alternative and complementary approach to analyzing the effects of individual nutrient intakes.

Different approaches have been used to define dietary patterns. One is based on a priori knowledge of nutritional needs, in which dietary patterns are predefined based on foods and nutrients previously identified as necessary components to support the human body. The other method is a posteriori, in which food intake data, attained from an FFQ or diet records, are used to identify patterns in the population sample. A common statistical technique for quantifying dietary patterns is principal components factor analysis, which is a useful tool of multivariate analysis to identify unobserved factors to account for the variations found in observed and correlated foods or food groups. For example, Hu et al. (19) showed that eating patterns derived from an FFQ (i.e., the prudent dietary pattern characterized by high intakes of fruits, vegetables, seafood, poultry, and whole grains and the Western dietary pattern characterized by high intakes of processed meat, red meat, high-fat dairy products, sweets and desserts, French fries, and refined grains) were significantly associated with incident coronary heart disease.

The objective of this study was to evaluate the association between dietary patterns and blood lead and bone lead concentrations and to establish whether dietary pattern is a predictor of blood lead and/or bone lead, independent of other known factors [e.g., age, smoking, total energy intake, BMI (in kg/m$^2$), occupation, and education]. In the NAS, we derived dietary patterns from FFQ data and tested their association with lead concentrations in older men, who may have had high accumulations of lead because of long-term exposure. Because dietary pattern assessment is a data-driven approach, it is difficult to specify the hypotheses about the number of factors (i.e., dietary patterns) and the directions of the associations of diet with bone and blood lead concentrations. However, we did expect that healthier overall dietary patterns would be associated with lower lead concentrations.

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Supplemental Material, Supplemental Figure 1, and Supplemental Tables 1–5 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

XW and ND contributed equally to this work.

Address correspondence to SKP (e-mail: sungkyun@umich.edu).

## Methods

*Ethics.* All participants provided written, informed consent. This study was reviewed and approved by the Institutional Review Boards of each participating institute, the University of Michigan School of Public Health, the Harvard School of Public Health, and the Department of Veterans Affairs Boston Healthcare System.

*Study population.* Participants were from the NAS, a prospective cohort established by the Veterans Affairs in 1963. A total of 2280 men from Boston, Massachusetts, participated. They were mostly non-Hispanic white and ranged in age from 21 to 80 y at baseline. At the time of enrollment, participants were free of past or present chronic medical conditions, including heart disease, cancer, diabetes, peptic ulcer, gout, bronchitis, sinusitis, recurrent asthma, and hypertension. They returned for regular examinations every 3–5 y. At each visit, self-administered questionnaires were used to record demographic characteristics including age, sex, race/ethnicity, smoking status, household income, education, occupation, medical history, and psychiatric history. Blood samples were also collected to measure blood lead concentration.

Beginning in 1987, self-administered semiquantitative FFQs were mailed to participants, who were asked to complete these questionnaires and bring them back at the time of their regular visits. Of the 1326 participants who actively attended regular NAS examinations between 5 February 1987 and 23 July 2008, 1030 returned FFQs. After the exclusion of 47 participants with missing covariates, 983 men with 3273 observations were available for blood lead analysis (**Supplemental Figure 1**).

Beginning in August 1991, NAS participants who gave informed consent had K-shell-X-ray fluorescence (KXRF) bone lead measurement at the Ambulatory Clinical Research Center of Brigham and Women's Hospital in Boston, Massachusetts. Eight hundred sixty-five men had their patella lead and 869 men had their tibia lead measured between 1 August 1991 and 8 August 1999. After exclusion of participants with high bone lead uncertainty (3 for patella and 6 for tibia), with negative bone lead (4 for patella and 6 for tibia), without a completed FFQ (21 for both patella and tibia), with missing values of potential confounding factors (52 for both patella and tibia), or returning their FFQs after KXRF bone lead measurement (134 for both patella and tibia), 649 participants were included for patella lead and tibia lead analysis (Supplemental Figure 1).

*Blood lead and bone lead measurements.* Whole-blood samples were collected in trace metal-free tubes containing EDTA and analyzed to obtain blood lead concentration by graphite furnace atomic absorption spectroscopy (ESA Laboratories). Detailed measurement procedures were described elsewhere (20). The minimum detection limit of blood lead was 1 μg/dL, and 6 observations with values below this limit were coded as $1/\sqrt{2}$ μg/dL.

A KXRF instrument (ABIOMED, Inc.) was used to measure bone lead of the patella and midtibia shaft, as previously described (21). Both patella and tibia lead are biological markers of cumulative lead exposures in humans. The patella consists almost entirely of trabecular-type bone, whereas the mid-tibia is composed of cortical-type bone. Lead accumulates much more rapidly in trabecular bone with a half-life of a few years compared with lead retention in cortical bone with a half-life of decades. Thus, in general, tibia bone lead has been viewed as an indicator of lifetime cumulative exposure to lead, whereas patella bone lead has been identified as more current, mobilizable lead reserves (22). The KXRF instrument provides an unbiased estimate of bone lead (standardized by bone mineral content) expressed as microgram per gram bone mineral with an estimate of uncertainty. Three participants had patella lead uncertainty >10 μg/g, and 6 participants had tibia lead uncertainty >15 μg/g. These were excluded because these large measurement errors suggest a degraded X-ray signal (23).

*Semiquantitative FFQ.* Starting 1 February 1987, participants were invited to answer a detailed semiquantitative FFQ adapted from the one used in the Harvard Nurses' Health Study (24). Each food item in the FFQ contained 9 possible choices, ranging from "never or <1 time per month" to "6 or more times per day." The participants completed the FFQ every 4 y. They received the form before their regular visit and returned it at the examination. The initial FFQ included 122 food items with specific serving sizes defined by using natural portions (e.g., 1 cup chowder or cream soup, 1 slice of pizza) or standard weight and volume measures of the servings per day commonly used for each food. The FFQ was expanded in 1991 with the addition of 13 food items, including light beer, candy without chocolate, raw carrots, celery, chicken or turkey liver, charred meat, other nuts, oat bran, olive oil and vinegar dressing, onions, onions as a garnish, peppers, tortilla, and turkey. Each food category was converted to number of servings per day from the reported intake frequency. Serving sizes for each food or food group are shown in **Supplemental Material**.

*Dietary pattern assessment.* To minimize within-person variation in intake of individual food items, we first classified 135 food items into 40 groups (**Supplemental Table 1**). Exploratory principal components factor analysis was used to derive dietary patterns based on these 40 food groups. To best represent dietary consumption during long-term follow-up, dietary patterns were treated as time-varying variables in the blood lead analysis. Dietary patterns were derived by using 5 cycles of FFQs respectively from 1987 to 2008. Note that the FFQ information collection and blood lead measurements were conducted simultaneously during each 3- to 5-y regular visit. In the bone lead analysis, dietary patterns were identified by using FFQs collected before KXRF bone lead measurements during 1991–1999. The number of factors was determined based on the Kaiser-Guttman rule (eigenvalue > 1), the Scree test, and interpretability. Factors were rotated with an orthogonal transformation to achieve better interpretability and simpler structure. Compared with dietary indexes based on recommended intake, factor analysis generates statistically independent patterns (factors) on the basis of actual eating habits, rather than a priori knowledge. A factor score for each dietary pattern was calculated by summing the standardized value of intake of each food item with weights proportional to their factor loading (25). Reproducibility and validity of this FFQ for estimating daily nutrient intakes were published elsewhere (24, 26). The analyses were conducted by using PROC FACTOR in SAS, version 9.4 (SAS Institute, Inc.).

*Covariates.* Age, smoking status, and education were collected at each study visit with a self-administered questionnaire. Cigarette smoking was categorized (former or current compared with never). Education was categorized as *1*) did not graduate from high school, *2*) graduated from high school but did not attend a 4-y college, *3*) attended some college, and *4*) graduated from 4-y college or higher degree. Total energy intake was obtained from each cycle of the FFQ based on food intake. BMI was calculated using height (centimeters) and weight (kilograms) information collected in regular NAS visits from 1987. Occupation (white collar compared with non–white collar work) was determined based on occupational information collected at each visit from 1962 to 1980. The individual's address was obtained at each bone and blood lead measurement. The NAS cohort has been relatively stable with regard to residential address. All the addresses were sent to a commercial firm (BonData) to be geocoded and converted to county code, census tract number, and block group number, based on geographic areas defined in the 1990 Census of Population and Housing (Bureau of the Census, US Department of Commerce). Census-derived geographic areas were identified as undereducated if ≥25% of residents aged ≥25 y had not graduated from high school (27). Areas were identified as impoverished if ≥10% of residents of the population lived below the federal poverty line (27).

*Statistics.* Univariate statistics were calculated and examined for each tertile of the factor score in each dietary pattern. We used the chi-square test for categorical variables and ANOVA for continuous variables. We used linear mixed models with random intercepts to calculate effect estimates and their 95% CIs for the association between time-varying dietary patterns and blood lead concentration over time. Linear regression models were utilized to compute effect estimates and their 95% CIs for the relation between dietary patterns and bone lead concentration. We included the same set of potential confounders in both linear mixed models and linear regression models to estimate the associations of dietary patterns with bone and blood lead concentrations, independent of age, smoking status, total energy intake, BMI, achieved education level, occupation, and neighborhood-based education and poverty levels. We did not consider individual annual income, because our population was a group of middle-aged to older adults, more than half of whom had retired during the study period. A type I error rate ($\alpha$ level) of 0.05 was used for all tests.

In our study, collider stratification bias may exist, because selection into the KXRF bone lead substudy was linked to previous lead exposure and potential confounders at the time of enrollment (8). To mitigate the bias, we assigned weights to each participant, based on inverse probability weighting per Weisskopf et al. (8). Briefly, a single logistic regression model was constructed to predict the probability of substudy enrollment, with 1 record/study visit at the time of bone lead measurements for those participants in the substudy; for those without bone lead measures, we utilized the last visit before 1999 (the last year of bone lead measurements used in our study). The C statistic for the model is 0.87. All the predictors included in the logistic regression model are presented in **Supplemental Table 2**.

Several sensitivity analyses were conducted to examine analytical consistency and robustness of our findings. We repeated the dietary pattern analysis using maximum likelihood rather than the principal-components method to extract factors. We also repeated the analysis with a different rotation approach, i.e., using oblique transformation (producing correlated factors) instead of orthogonal transformation (producing uncorrelated factors). In addition, we derived the dietary patterns based on 135 food items in the FFQ data, rather than 40 predefined food groups. In addition, bone lead can serve as an endogenous source because, through bone resorption, lead can be released into the bloodstream (28). Thus, we evaluated the influence of adjustment for bone lead in the association between dietary patterns and blood lead to determine if bone lead mediates the association of dietary patterns and blood lead. Finally, we tested the homogeneity of diet effects on bone lead concentrations across age groups. We dichotomized age at 65 y and incorporated the cross-product term between age and diet score in the linear regression models to examine effect modification by age on the association of diet with bone lead concentrations. All analyses were conducted by SAS, version 9.4 (SAS Institute, Inc.). Values are presented as means ± SDs.

## Results

Based on eigenvalues, the Scree test, and interpretability, we extracted 2 factors from 40 predefined food groups to represent eating behavior (i.e., dietary patterns) in this population. Factor loadings for the 2 patterns identified for the blood lead and bone lead study are shown in **Supplemental Tables 3** and **4**, respectively. Factor loadings <0.30 were hidden for simplicity. A positive factor loading indicates a positive association with the factor; whereas a negative factor loading stands for an inverse association. The larger the factor loading, the more the specific food group contributes to the overall pattern. The first factor loaded heavily with fruit, legumes, vegetables, whole grains,

**TABLE 1** Baseline characteristics according to tertiles of prudent and Western diet scores as associated with blood lead in the Normative Aging Study, 1987–2008[1]

| | | Tertile of prudent diet score | | | Tertile of Western diet score | | |
|---|---|---|---|---|---|---|---|
| Baseline characteristics | Total ($n$ = 983) | 1 (lowest) ($n$ = 327) | 2 ($n$ = 328) | 3 (highest) ($n$ = 328) | 1 (lowest) ($n$ = 327) | 2 ($n$ = 328) | 3 (highest) ($n$ = 328) |
| Diet score median (minimum, maximum) | | −0.77 (−1.3, −0.45) | −0.17 (−0.44, 0.19) | 0.68 (0.20, 7.43) | −0.80 (−2.0, −0.44) | −0.11 (−0.43, 0.25) | 0.74 (0.26, 4.05) |
| Age, y | 65.1 ± 7.7 | 64.2 ± 7.9 | 65.0 ± 7.7 | 66.3 ± 7.2 | 66.9 ± 7.2 | 64.9 ± 7.6 | 63.6 ± 7.8 |
| Blood lead, μg/dL | 6.1 ± 4.2 | 6.5 ± 3.9 | 6.3 ± 4.9 | 5.6 ± 3.4 | 5.9 ± 4.8 | 6.0 ± 3.8 | 6.5 ± 3.8 |
| Patella lead,[2] μg/g | 30.7 ± 19.5 | 32.3 ± 20.6 | 29.4 ± 18.4 | 30.3 ± 19.3 | 29.9 ± 18.0 | 29.8 ± 19.3 | 32.3 ± 20.8 |
| Tibia lead,[2] μg/g | 21.7 ± 13.6 | 23.1 ± 14.5 | 20.9 ± 12.2 | 21.0 ± 14.0 | 21.1 ± 11.5 | 21.1 ± 13.9 | 22.8 ± 15.1 |
| Smoking | | | | | | | |
| Never | 27.4 | 26.0 | 29.3 | 26.8 | 33.3 | 27.1 | 21.7 |
| Former or current | 72.6 | 74.0 | 70.7 | 73.2 | 66.7 | 72.9 | 78.3 |
| Education | | | | | | | |
| Less than high school | 9.8 | 14.1 | 10.7 | 4.6 | 10.4 | 8.2 | 10.7 |
| High school | 36.6 | 39.1 | 37.5 | 33.2 | 35.5 | 34.8 | 39.6 |
| Some college | 26.1 | 25.1 | 22.9 | 30.5 | 26.6 | 27.7 | 24.1 |
| ≥4-y college | 27.5 | 21.7 | 28.9 | 31.7 | 27.5 | 29.3 | 25.6 |
| Occupation | | | | | | | |
| White collar | 34.4 | 29.0 | 33.8 | 40.2 | 34.9 | 38.1 | 30.2 |
| Non–white collar | 65.6 | 71.0 | 66.2 | 59.8 | 65.1 | 61.9 | 69.8 |
| Total energy intake, kcal/d | 1958 ± 593 | 1641 ± 505 | 1933 ± 457 | 2298 ± 612 | 1657 ± 489 | 1913 ± 463 | 2302 ± 625 |
| BMI, kg/m$^2$ | 27.8 ± 3.7 | 28.2 ± 3.6 | 27.8 ± 3.6 | 27.4 ± 3.9 | 27.2 ± 3.6 | 27.8 ± 3.4 | 28.4 ± 4.0 |
| Food intakes, servings/d | | | | | | | |
| Red meat | 0.5 ± 0.3 | 0.4 ± 0.3 | 0.5 ± 0.3 | 0.5 ± 0.4 | 0.2 ± 0.2 | 0.4 ± 0.2 | 0.7 ± 0.4 |
| Processed meat | 0.3 ± 0.4 | 0.3 ± 0.4 | 0.3 ± 0.3 | 0.3 ± 0.4 | 0.1 ± 0.1 | 0.3 ± 0.2 | 0.6 ± 0.5 |
| Seafood | 0.4 ± 0.3 | 0.2 ± 0.2 | 0.3 ± 0.2 | 0.6 ± 0.5 | 0.4 ± 0.4 | 0.4 ± 0.3 | 0.4 ± 0.4 |
| Poultry | 0.4 ± 0.3 | 0.2 ± 0.2 | 0.3 ± 0.2 | 0.5 ± 0.4 | 0.4 ± 0.3 | 0.3 ± 0.3 | 0.4 ± 0.3 |
| Eggs | 0.2 ± 0.3 | 0.2 ± 0.3 | 0.3 ± 0.3 | 0.2 ± 0.3 | 0.1 ± 0.1 | 0.2 ± 0.2 | 0.4 ± 0.4 |
| Butter | 0.3 ± 0.7 | 0.4 ± 0.9 | 0.2 ± 0.5 | 0.2 ± 0.5 | 0.1 ± 0.2 | 0.2 ± 0.5 | 0.6 ± 1.0 |
| Fries | 0.1 ± 0.1 | 0.1 ± 0.1 | 0.1 ± 0.1 | 0.1 ± 0.1 | 0.0 ± 0.1 | 0.1 ± 0.1 | 0.1 ± 0.1 |
| High-fat dairy products | 1.0 ± 1.3 | 1.1 ± 1.3 | 1.2 ± 1.6 | 0.9 ± 1.0 | 0.5 ± 0.6 | 0.9 ± 0.6 | 1.9 ± 1.8 |
| Fruit | 1.5 ± 1.2 | 0.9 ± 0.7 | 1.4 ± 0.9 | 2.2 ± 1.4 | 1.8 ± 1.4 | 1.4 ± 1.0 | 1.2 ± 1.0 |
| Whole grains | 1.5 ± 1.4 | 0.8 ± 0.8 | 1.5 ± 1.2 | 2.1 ± 1.6 | 1.6 ± 1.3 | 1.5 ± 1.4 | 1.3 ± 1.3 |
| Refined grains | 1.5 ± 1.2 | 1.2 ± 1.0 | 1.4 ± 1.2 | 1.8 ± 1.4 | 1.0 ± 0.9 | 1.4 ± 1.0 | 2.0 ± 1.5 |
| Vegetables | 1.7 ± 1.3 | 0.8 ± 0.4 | 1.5 ± 0.5 | 2.9 ± 1.6 | 1.9 ± 1.4 | 1.6 ± 1.2 | 1.7 ± 1.3 |
| Legumes | 0.4 ± 0.3 | 0.2 ± 0.2 | 0.4 ± 0.2 | 0.6 ± 0.4 | 0.4 ± 0.3 | 0.4 ± 0.3 | 0.5 ± 0.4 |
| Tomatoes | 0.6 ± 0.6 | 0.3 ± 0.3 | 0.5 ± 0.5 | 0.9 ± 0.8 | 0.5 ± 0.5 | 0.6 ± 0.5 | 0.7 ± 0.8 |
| Neighborhood-based socioeconomic status, % | | | | | | | |
| Education[3] | 12.0 ± 8.9 | 13.0 ± 9.5 | 12.4 ± 8.9 | 10.4 ± 8.2 | 12.5 ± 9.3 | 11.0 ± 8.1 | 12.3 ± 9.3 |
| Income[4] | 6.3 ± 5.6 | 6.7 ± 6.0 | 6.2 ± 5.2 | 6.0 ± 5.6 | 6.5 ± 6.0 | 5.9 ± 5.3 | 6.5 ± 5.6 |

[1] Values are means ± SEs or percentages unless otherwise indicated.
[2] Patella lead and tibia lead concentrations were measured between 1991 and 1999 ($n$ = 786).
[3] Geographic areas were identified as undereducated if ≥25% of residents age ≥25 y had not completed high school.
[4] Geographic areas were identified as impoverished if ≥10% of residents of the population lived below the federal poverty line.

**TABLE 2** Baseline characteristics according to tertiles of prudent and Western diet scores as associated with bone lead in the Normative Aging Study, 1991–1999[1]

| | | Tertile of prudent diet score | | | Tertile of Western diet score | | |
|---|---|---|---|---|---|---|---|
| Baseline characteristics | Total ($n$ = 649) | 1 (lowest) ($n$ = 216) | 2 ($n$ = 217) | 3 (highest) ($n$ = 216) | 1 (lowest) ($n$ = 216) | 2 ($n$ = 217) | 3 (highest) ($n$ = 216) |
| Diet score median (minimum, maximum) | | −0.81 (−1.81, −0.47) | −0.17 (−0.46, 0.21) | 0.75 (0.23, 5.44) | −0.77 (−1.80, −0.48) | −0.14 (−0.47, 0.24) | 0.76 (0.25, 4.08) |
| Age, y | 67.0 ± 7.2 | 66.0 ± 7.3 | 67.5 ± 7.3 | 67.3 ± 7.1 | 68.0 ± 7.1 | 66.7 ± 7.2 | 66.1 ± 7.2 |
| Blood lead, μg/dL | 5.6 ± 3.6 | 6.1 ± 3.7 | 5.7 ± 4.1 | 5.1 ± 3.0 | 5.4 ± 3.8 | 5.5 ± 3.3 | 6.1 ± 3.8 |
| Patella lead, μg/g | 31.2 ± 20.0 | 33.0 ± 21.0 | 31.7 ± 19.7 | 29.0 ± 19.0 | 30.8 ± 18.2 | 30.0 ± 19.7 | 32.8 ± 21.9 |
| Tibia lead, μg/g | 22.3 ± 13.9 | 23.5 ± 15.0 | 22.2 ± 13.2 | 21.2 ± 13.4 | 21.3 ± 11.4 | 22.0 ± 13.7 | 23.6 ± 16.2 |
| Smoking | | | | | | | |
| Never | 30.0 | 26.4 | 34.6 | 26.9 | 34.7 | 30.0 | 23.2 |
| Former or current | 70.0 | 73.6 | 65.4 | 73.1 | 65.3 | 70.0 | 76.9 |
| Education | | | | | | | |
| Less than high school | 9.9 | 13.9 | 9.7 | 6.0 | 9.3 | 8.8 | 11.6 |
| High school | 37.3 | 39.8 | 38.7 | 33.3 | 38.0 | 33.2 | 40.7 |
| Some college | 23.7 | 23.2 | 20.7 | 27.3 | 23.6 | 29.0 | 18.5 |
| ≥4-y college | 29.1 | 23.1 | 30.9 | 33.3 | 29.2 | 33.3 | 29.2 |
| Occupation | | | | | | | |
| White collar | 36.2 | 29.6 | 63.6 | 42.6 | 37.0 | 37.3 | 34.3 |
| Non–white collar | 63.8 | 70.4 | 36.4 | 57.4 | 63.0 | 62.7 | 65.7 |
| Total energy intake, kcal/d | 1976 ± 627 | 1646 ± 519 | 1931 ± 496 | 2353 ± 643 | 1616 ± 475 | 1937 ± 490 | 2377 ± 651 |
| BMI, kg/m$^2$ | 27.9 ± 3.9 | 28.4 ± 3.9 | 28.0 ± 3.8 | 27.3 ± 3.8 | 27.6 ± 3.8 | 27.7 ± 3.8 | 28.4 ± 4.0 |
| Food intakes, servings/d | | | | | | | |
| Red meat | 0.5 ± 0.3 | 0.4 ± 0.3 | 0.4 ± 0.3 | 0.5 ± 0.4 | 0.2 ± 0.2 | 0.4 ± 0.2 | 0.7 ± 0.4 |
| Processed meat | 0.3 ± 0.4 | 0.3 ± 0.4 | 0.3 ± 0.4 | 0.3 ± 0.4 | 0.1 ± 0.1 | 0.2 ± 0.2 | 0.6 ± 0.5 |
| Seafood | 0.4 ± 0.3 | 0.2 ± 0.2 | 0.3 ± 0.2 | 0.5 ± 0.4 | 0.4 ± 0.3 | 0.3 ± 0.2 | 0.4 ± 0.4 |
| Poultry | 0.4 ± 0.3 | 0.2 ± 0.2 | 0.4 ± 0.2 | 0.5 ± 0.4 | 0.4 ± 0.4 | 0.4 ± 0.2 | 0.4 ± 0.3 |
| Eggs | 0.2 ± 0.3 | 0.2 ± 0.3 | 0.2 ± 0.3 | 0.2 ± 0.2 | 0.1 ± 0.2 | 0.2 ± 0.2 | 0.3 ± 0.3 |
| Butter | 0.3 ± 0.6 | 0.4 ± 0.8 | 0.2 ± 0.5 | 0.2 ± 0.4 | 0.1 ± 0.1 | 0.2 ± 0.4 | 0.6 ± 0.9 |
| Fries | 0.1 ± 0.1 | 0.1 ± 0.1 | 0.1 ± 0.1 | 0.1 ± 0.1 | 0.0 ± 0.1 | 0.1 ± 0.1 | 0.2 ± 0.1 |
| High-fat dairy products | 1.1 ± 1.3 | 1.3 ± 1.7 | 1.1 ± 1.2 | 0.9 ± 0.9 | 0.4 ± 0.5 | 0.8 ± 0.8 | 1.9 ± 1.8 |
| Fruit | 1.5 ± 1.2 | 0.9 ± 0.7 | 1.4 ± 0.9 | 2.3 ± 1.3 | 1.8 ± 1.4 | 1.5 ± 1.1 | 1.2 ± 0.9 |
| Whole grains | 1.4 ± 1.4 | 0.8 ± 0.7 | 1.5 ± 1.2 | 2.0 ± 1.7 | 1.6 ± 1.6 | 1.6 ± 1.3 | 1.2 ± 1.2 |
| Refined grains | 1.4 ± 1.1 | 1.3 ± 1.0 | 1.3 ± 1.0 | 1.7 ± 1.2 | 1.0 ± 0.8 | 1.4 ± 0.9 | 1.9 ± 1.3 |
| Vegetables | 1.7 ± 1.3 | 0.8 ± 0.4 | 1.5 ± 0.5 | 2.9 ± 1.5 | 1.7 ± 1.3 | 1.7 ± 1.2 | 1.8 ± 1.3 |
| Legumes | 0.4 ± 0.3 | 0.2 ± 0.1 | 0.4 ± 0.2 | 0.6 ± 0.4 | 0.4 ± 0.3 | 0.4 ± 0.3 | 0.4 ± 0.3 |
| Tomatoes | 0.6 ± 0.5 | 0.3 ± 0.3 | 0.5 ± 0.4 | 0.8 ± 0.7 | 0.5 ± 0.5 | 0.5 ± 0.4 | 0.6 ± 0.7 |
| Neighborhood-based socioeconomic status, % | | | | | | | |
| Education[2] | 12.3 ± 9.6 | 13.6 ± 10.1 | 12.4 ± 9.7 | 11.3 ± 8.8 | 12.3 ± 9.5 | 12.0 ± 9.2 | 13.0 ± 10.1 |
| Income[3] | 6.4 ± 5.8 | 7.3 ± 6.9 | 6.0 ± 5.3 | 6.1 ± 5.0 | 6.5 ± 6.2 | 6.5 ± 6.0 | 6.3 ± 5.3 |

[1] Values are means ± SEs or percentages unless otherwise indicated.
[2] Geographic areas were identified as undereducated if ≥25% of residents age ≥25 y had not completed high school.
[3] Geographic areas were identified as impoverished if ≥10% of residents of the population lived below the federal poverty line.

poultry, and seafood and was labeled the prudent diet. The second factor was characterized by high intakes of processed meat, red meat, refined grains, high-fat dairy products, French fries, butter, and eggs, i.e., the Western diet. Correlations between each of the foods or food groups in first 2 waves of FFQs in the NAS are presented in **Supplemental Table 5**, indicating good reproducibility of the FFQs.

**Table 1** shows the distributions of baseline characteristics and food consumption by tertiles of prudent and Western dietary pattern scores among the analytic sample for blood lead ($n$ = 983). Participants were aged 65.1 ± 7.7 y, ranging from 44 to 92 y. Men with higher Western diet scores were more likely to be former or current smokers, and smoking status differed across Western diet score categories ($P$ = 0.03). Men who did not graduate from high school were less likely to have a prudent eating pattern than those with higher education ($P$ = 0.02).

The concentration of blood lead was 6.1 ± 4.2 μg/dL. Blood, patella, and tibia lead concentrations differed significantly across prudent and Western diet categories. Men with a lower prudent diet score or a higher Western diet score were more likely to have elevated blood and bone lead concentrations. Moreover, dietary patterns were associated with area-based measures of socioeconomic position. The prudent pattern was linked to neighborhood-based education level ($P$ = 0.01). Men living in undereducated areas were less likely to consume a diet with high intakes of whole grains, fruit, vegetables, legumes, poultry, and seafood.

Baseline characteristics and food intake in the bone lead study are shown in **Table 2** ($n$ = 649). Participants were also in the middle-to-elderly age groups (67.0 ± 7.2 y, range: 49–93 y). The concentrations of tibia and patella lead were 22.3 ± 13.9 and 31.2 ± 20.0 μg/g, respectively. Men with higher prudent diet scores tended to have lower blood, patella, and tibia lead concentrations. Baseline characteristics found in the analytic sample for the bone were similar to those for blood lead analyses.

**Table 3** summarizes the association between dietary patterns and blood lead concentrations. After adjustment for age, smoking, total energy intake, BMI, occupation, education, and area-level income and education, men in highest tertile of the Western diet score had a 0.91-μg/dL (95% CI: 0.41, 1.42 μg/dL, $P$ < 0.001) higher blood lead concentration than did those in the lowest tertile. In contrast, blood lead concentration was lower with a higher prudent diet score, but a significant association was observed only in the model adjusting for age and smoking *(P* = 0.002).

Patella and tibia lead concentrations were also associated with dietary patterns (**Table 4**). Higher intakes of Western diet foods and lower intakes of prudent foods were associated with an increased patella lead concentration. After adjusting for age, smoking status, total energy intake, BMI, education, occupation, and area-level education and income levels, men with Western scores in the highest tertile had a 5.96-μg/dL (95% CI: 1.76, 10.16 μg/dL, $P$ = 0.005) higher patella lead concentration than did those in the lowest. Again, bone lead concentration was lower with a higher prudent diet score, but a significant association was only observed in the model adjusting for age and smoking. Similar relations were found with tibia lead.

Dietary patterns derived from 40 food groups by using principal components analysis are consistent with findings from sensitivity analyses. To determine whether bone lead is an intermediate in the causal pathway between dietary pattern and

**TABLE 3** Association between blood lead concentration (expressed as μg/dL) and dietary pattern scores in the Normative Aging Study, 1987–2008 ($n$ = 983)

| Dietary pattern | Model adjusting for age and smoking | | | Model adjusting for age, smoking, total energy intake, and BMI | | | Model adjusting for age, smoking, total energy intake, BMI, education,[1] and occupation[2] | | | Model adjusting for age, smoking, total energy intake, BMI, education, occupation, and neighborhood-based education[3] and income[4] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| scores | β | 95% CI | *P*-tertile | β | 95% CI | *P*-tertile | β | 95% CI | *P*-tertile | β | 95% CI | *P*-tertile |
| Prudent pattern score | | | | | | | | | | | | |
| Tertile 1[5] | — | — | — | — | — | — | — | — | — | — | — | — |
| Tertile 2 | −0.33 | (−0.74, 0.08) | 0.11 | −0.27 | (−0.70, 0.15) | 0.21 | −0.20 | (−0.63, 0.22) | 0.35 | −0.17 | (−0.59, 0.24) | 0.41 |
| Tertile 3 | −0.74 | (−1.15, −0.33) | <0.001 | −0.59 | (−1.10, −0.08) | 0.02 | −0.44 | (−0.95, 0.08) | 0.10 | −0.38 | (−0.88, 0.13) | 0.14 |
| *P*-prudent categories | | 0.002 | | | 0.08 | | | 0.25 | | | 0.34 | |
| Western pattern score | | | | | | | | | | | | |
| Tertile 1[5] | — | — | — | — | — | — | — | — | — | — | — | — |
| Tertile 2 | 0.36 | (−0.05, 0.77) | 0.08 | 0.48 | (0.05, 0.91) | 0.03 | 0.49 | (0.06, 0.93) | 0.02 | 0.49 | (0.07, 0.92) | 0.02 |
| Tertile 3 | 0.68 | (0.26, 1.09) | 0.001 | 0.90 | (0.39, 1.41) | <0.001 | 0.92 | (0.41, 1.42) | <0.001 | 0.91 | (0.41, 1.42) | <0.001 |
| *P*-Western categories | | 0.006 | | | 0.002 | | | 0.002 | | | 0.002 | |

[1] Education is categorized as less than high school diploma, high school diploma, some college, or 4-y college or higher.
[2] Occupation is categorized as white-collar occupations and non–white collar occupations.
[3] Geographic areas were identified as undereducated if ≥25% of residents age ≥25 y had not completed high school.
[4] Geographic areas were identified as impoverished if ≥10% of residents of the population lived below the federal poverty line.
[5] Reference group.

**TABLE 4** Associations of patella and tibia lead concentrations with dietary pattern scores in the Normative Aging Study, 1991–1999 ($n$ = 649)

| Dietary pattern scores | Model adjusting for age and smoking | | | Model adjusting for age, smoking, total energy intake, and BMI | | | Model adjusting for age, smoking, total energy intake, BMI, education,[1] and occupation[2] | | | Model adjusting for age, smoking, total energy intake, BMI, education, occupation, and neighborhood-based education[3] and income[4] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | β | 95% CI | *P*-tertile | β | 95% CI | *P*-tertile | β | 95% CI | *P*-tertile | β | 95% CI | *P*-tertile |
| Patella lead concentration, μg/g | | | | | | | | | | | | |
| Prudent pattern score | | | | | | | | | | | | |
| Tertile 1[5] | — | — | — | — | — | — | — | — | — | — | — | — |
| Tertile 2 | −2.10 | (−5.79, 1.59) | 0.26 | −1.20 | (−4.96, 2.57) | 0.53 | −0.52 | (−4.15, 3.11) | 0.78 | −0.28 | (−3.83, 3.27) | 0.87 |
| Tertile 3 | −5.53 | (−9.16, −1.91) | 0.003 | −3.14 | (−7.36, 1.08) | 0.14 | −0.85 | (−4.96, 3.25) | 0.68 | −0.40 | (−4.41, 3.61) | 0.84 |
| *P*-prudent categories | | 0.002 | | | 0.13 | | | 0.65 | | | 0.80 | |
| Western pattern score | | | | | | | | | | | | |
| Tertile 1[5] | — | — | — | — | — | — | — | — | — | — | — | — |
| Tertile 2 | −0.92 | (−4.53, 2.70) | 0.61 | 0.15 | (−3.63, 3.92) | 0.93 | 0.98 | (−2.67, 4.63) | 0.59 | 0.63 | (−2.94, 4.19) | 0.72 |
| Tertile 3 | 3.74 | (0.04, 7.44) | 0.04 | 6.03 | (1.56, 10.50) | 0.008 | 6.15 | (1.85, 10.45) | 0.005 | 5.96 | (1.76, 10.16) | 0.005 |
| *P*-Western categories | | 0.04 | | | 0.008 | | | 0.006 | | | 0.006 | |
| Tibia lead concentration, μg/g | | | | | | | | | | | | |
| Prudent pattern score | | | | | | | | | | | | |
| Tertile 1[5] | — | — | — | — | — | — | — | — | — | — | — | — |
| Tertile 2 | −1.78 | (−4.32, 0.76) | 0.17 | −1.41 | (−4.00, 1.17) | 0.28 | −0.84 | (−3.32, 1.63) | 0.50 | −0.71 | (−3.13, 1.70) | 0.56 |
| Tertile 3 | −3.40 | (−5.91, −0.89) | 0.008 | −2.52 | (−5.45, 0.40) | 0.09 | −0.93 | (−3.76, 1.89) | 0.52 | −0.62 | (−3.37, 2.13) | 0.66 |
| *P*-prudent categories | | 0.008 | | | 0.008 | | | 0.50 | | | 0.63 | |
| Western pattern score | | | | | | | | | | | | |
| Tertile 1[5] | — | — | — | — | — | — | — | — | — | — | — | — |
| Tertile 2 | 0.83 | (−1.67, 3.33) | 0.51 | 0.99 | (−1.61, 3.58) | 0.45 | 1.27 | (−1.22, 3.77) | 0.32 | 1.03 | (−1.40, 3.46) | 0.40 |
| Tertile 3 | 3.70 | (1.14, 6.25) | 0.005 | 4.05 | (0.97, 7.14) | 0.01 | 4.01 | (1.07, 6.96) | 0.008 | 3.83 | (0.97, 6.70) | 0.009 |
| *P*-Western categories | | 0.005 | | | 0.01 | | | 0.009 | | | 0.01 | |

[1] Education is categorized as less than high school diploma, high school diploma, some college, or 4-y college or higher.
[2] Occupation is categorized as white-collar occupations and non–white collar occupations.
[3] Geographic areas were identified as undereducated if ≥25% of residents age ≥25 y had not completed high school.
[4] Geographic areas were identified as impoverished if ≥10% of residents of the population lived below the federal poverty line.
[5] Reference group.

blood lead, we incorporated patella lead and tibia lead in the models. We detected dramatic decreases in the effect estimates and associations between dietary patterns and blood lead concentration after accounting for this internal storage source of lead (data not shown). To examine whether associations between diet and bone lead concentrations were modified by age, cross-product terms between age (dichotomized at 65 y) and diet scores were incorporated into the linear models. We found no statistically significant interactions between age and either the prudent diet ($P$-interaction = 0.87) or the Western diet ($P$-interaction = 0.62), suggesting homogeneity of diet effects on bone lead concentrations across age groups.

## Discussion

We identified 2 dietary patterns in this population of older men: a prudent dietary pattern, characterized by high intakes of fruit, vegetables, legumes, whole grains, poultry, and seafood; and a Western pattern, characterized by high intakes of processed meat, red meat, refined grains, high-fat dairy products, French fries, butter, and eggs. We found significantly positive relations between the Western dietary pattern and both bone and blood lead concentrations. These associations remained significant after adjusting for age, smoking, total energy intake, BMI, attained education, occupation, and area-based education and income levels. The prudent pattern was associated with lower blood and bone lead concentrations only in models adjusted for age and smoking status.

This is the first study, to our knowledge, to test the association of dietary pattern with bone and blood lead. We conducted multiple internal validation assessments and found similar results. It is noteworthy that area-based income and education levels were associated with blood and bone lead concentrations before but not after the addition of dietary patterns in the models suggesting, not surprisingly, that those living in lower-socioeconomic-status neighborhoods were more likely to follow the Western dietary pattern. The Western diet was also significantly associated with smoking status, which has also been linked with an unhealthy food intake (29). In contrast, people following a prudent diet were more likely to be nonsmokers. Moreover, total energy intake, as an indicator for the amount of food consumption, has been related to lead absorption. For example, more lead was shown to be absorbed during fasting states among adults compared with being ingested with food (30). Importantly, the associations of the Western dietary pattern with lead concentrations remained after adjusting for smoking, socioeconomic factors, neighborhood characteristics, and total energy intake, suggesting that dietary patterns are related to blood and bone lead, independent of those factors.

The attenuation of associations between dietary patterns and blood lead after the inclusion of bone lead suggests that bone lead may be another important determinant of blood lead concentration in the human body and that elevations in both may be associated with long-term dietary pattern exposures. It has been shown that lead can be released from bone to re-enter into the circulation (31).

Although the underlying mechanisms are still not well understood, there is biological plausibility for nutritional effects. High fat intakes in the Western diet may contribute to lead accumulation. In rats, increasing dietary fat content from 5% to 40% was significantly associated with higher lead concentrations in both osseous and nonosseous tissues (14). Additionally, Wohl et al. (32) found that adult roosters with a high-fat diet had a lower calcium absorption rate and a faster rate of turnover in trabecular bones, which may further contribute to enhanced bone resorption and lead circulation.

Unlike for the Western dietary pattern, we did not have enough evidence to support a significant association of the prudent diet with bone and blood lead concentrations after adjustment for age, total energy, smoking, BMI, education, occupation, and neighborhood characteristics. The relation was statistically significant only when adjusting for age and smoking, suggesting that the collinearity with socioeconomic factors may make it difficult to disentangle this dietary pattern from its close relation with income, education, occupation, and likelihood of exposure to lead in the environment.

Previous studies have supported the effects of single nutrients in decreasing lead concentration. For example, Vitamin C (ascorbic acid) may act as a natural chelator for lead, with a protective potency to increase lead excretion and reduce blood lead concentration (33). Vitamin C can also act as a low–molecular mass antioxidant that scavenges lead-induced free radicals. When researchers supplemented rats with 500 mg vitamin C/L drinking water, reduced lipid peroxidation was noted in their livers and brains (12). Experimental studies have identified vitamin E as a membrane and lipoprotein protector against lead-induced oxidative stress by elimination of free radicals (34). Folate has been shown to improve lead excretion, lower blood lead concentration, and alleviate lead-induced neurological impairment (35). Minerals including iron and calcium have been associated with a lower lead concentration and may decrease lead absorption by competing for shared absorptive receptors in the intestinal mucosa (36–38). In a randomized, double-blind clinical trial, participants with calcium supplementation had an 11% (0.4 μg/dL) lower blood lead concentration compared with the placebo control group ($P$ = 0.004) (16).

Food contamination may also provide possible explanations for the observed associations of dietary patterns with bone and blood lead concentrations. However, there is no compelling evidence to support that dietary intake of lead contributes to elevated blood lead concentration, as shown in a recent study conducted in NHANES (39).

Our study has several limitations. First, the identification of dietary patterns may be influenced by methodological issues. For example, the classification of foods into 40 groups is an arbitrary decision. However, in sensitivity analyses, we changed the number of factors and rotation method, based on empirical guidelines. Further, the dietary patterns identified in our study are similar to those derived in different populations by factor analysis with the use of a similar methodology (19, 40). Thus, our results are unlikely to suffer from misspecification by statistical methods. Second, the findings of association between diet and bone lead concentrations could be subject to inherent limitations of cross-sectional study designs. Thus, interpretations of results in the bone lead study still need to be cautious given the temporal ambiguity of dietary patterns. Furthermore, the study populations for bone lead and blood lead analyses were not the same, and there may be selection bias based on agreement to participate in the bone lead substudy. To minimize the possibility of selection bias, we assigned weights to participants, using inverse probability weighting, and created a pseudo-population to represent the study population before enrollment into the bone lead substudy. Finally, participants in our study were non-Hispanic white men living in Massachusetts. Because dietary intakes vary greatly by sex, race/ethnicity, and societal factors, it is necessary to replicate our findings in women and other racial/ethnic groups.

In conclusion, we identified 2 dietary patterns from FFQ data, similar to those identified in other studies: the Western diet and the prudent diet. The Western dietary pattern was significantly associated with bone and blood lead concentrations, independent of several other variables. An unhealthy diet, with high intakes of processed meat, red meat, refined grains, butter, high-fat dairy products, eggs, and French fries, may enhance lead accumulation in the bone and concentration in the blood. Our findings suggest that public health efforts to help people adopt healthy overall dietary patterns and to provide guidance for nutrition intervention may help reduce lead concentrations in the body. These findings also suggest the use of overall dietary patterns for future research in the relation of nutritional factors and environmental exposures, and lead burden could be acting as an unmeasured confounder in relation to studies that have been conducted on the association of a Western diet with outcomes such as cardiovascular disease. More studies are needed to examine the underlying mechanisms by which dietary patterns are associated with lead concentrations, e.g., whether diets reflect rates of gastrointestinal uptake or biokinetics resulting in differential internal distribution or excretion patterns.

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The authors' responsibilities were as follows—SKP: was the guarantor of this work, had full access to all the data in the study, and took responsibility for the contents of the manuscript; XW, ND, and SKP: were involved in the design of the analysis plan; XW and ND: conducted the data analyses and wrote the manuscript; KLT, MGW, DS, and HH: contributed to the collection of the data; and all authors: contributed to the interpretation of the data, critically revised the manuscript, and read and approved the final version of the paper.

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