Dietary Saturated Fat Intake Is Inversely Associated with Bone Density in Humans: Analysis of NHANES III[1,2]

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ABSTRACT Mounting evidence indicates that the amount and type of fat in the diet can have important effects on bone health. Most of this evidence is derived from animal studies. Of the few human studies that have been conducted, relatively small numbers of subjects and/or primarily female subjects were included. The present study assessed the relation of dietary fat to hip bone mineral density (BMD) in men and women using NHANES III data ($n =$ 14,850). Multivariate models using SAS-callable SUDAAN were used to adjust for the sampling scheme. Models were adjusted for age, sex, weight, height, race, total energy and calcium intakes, smoking, and weight-bearing exercise. Data from women were further adjusted for use of hormone replacement therapy. Including dietary protein, vitamin C, and β-carotene in the model did not influence the outcome. Analysis of covariance was used to generate mean BMD by quintile of total and saturated fat intake for 4 sex/age groups. Saturated fat intake was negatively associated with BMD at several hip sites. The greatest effects were seen among men $<$ 50 y old (linear trend $P = 0.004$ for the femoral neck). For the femoral neck, adjusted mean BMD was 4.3% less among men with the highest compared with the lowest quintile of saturated fat intake (BMD, 95% CI: highest quintile: 0.922 g/cm^2, 0.909–0.935; lowest quintile: 0.963 g/cm^2, 95% CI: 0.950–0.976). These data indicate that BMD is negatively associated with saturated fat intake, and that men may be particularly vulnerable to these effects. J. Nutr. 136: 159–165, 2006.

KEY WORDS: • *bone density* • *osteoporosis* • *dietary fat* • *saturated fat* • *NHANES*

Evidence has been accumulating over the past several years that dietary fats can have important effects on bone health. Studies in animals indicate that high-fat diets can adversely affect bone (1–5) and that the specific fatty acids in the diet are important [(6–12) see also (13–15) for reviews]. Saturated fatty acids (SFA),[4] in particular, may have effects that could impair bone health (5,16,17). A variety of mechanisms may account for the effects of dietary fats on bone, including alterations in calcium absorption, prostaglandin synthesis, osteoblast formation, and lipid oxidation [see (14,15,17,18) for reviews].

Despite strong evidence from animal and in vitro studies implicating dietary fats in bone health, few studies have been conducted in humans. In women, the available evidence parallels results obtained in animals. That is, the total amount of fat consumed is positively associated with fracture risk, and negatively associated with bone density (19–21). Furthermore, specific fatty acids may be important, with saturated fats, in particular, being potentially harmful. In one study, women administered a coconut oil supplement, which is high in saturated fatty acids (SFA), experienced loss of bone density in the lumbar spine, and no increase in femur bone density, relative to subjects administered evening primrose oil and fish oil [good sources of (n-6) and (n-3) PUFA, respectively] (22). These results provide intriguing evidence that dietary fats can have potentially important effects on bone health in women.

Although low bone density is more common in women than in men, a recent report suggests that men also may be sensitive to the effects of fats on bone. That study utilized a controlled feeding protocol, and the majority of the subjects were men (20 men, 3 women). Significant reductions in N-telopeptide, a key marker of bone resorption, were obtained when subjects consumed diets containing ~8% SFA and ~17% PUFA, compared with consumption of a diet containing ~13% SFA and ~9% PUFA (23). These data indicate that variables relevant to bone health can be improved in men by reducing consumption of dietary SFA and increasing consumption of dietary PUFA. In addition, others showed a positive association between dietary monounsaturated fatty acids (MUFA) and a negative association between dietary linoleic acid (n-6):α-linolenic acid (n-3) ratios, and bone mineral density (BMD) in both men and women (24,25). Approximately 3–6% of American men are estimated to have osteoporosis and 28–47% are estimated to have osteopenia (26). Furthermore, health care costs in the United States due to osteoporosis-related fractures in men were ~2.5 billion dollars in 1995 (27). Because the percentage of

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[4] Abbreviations used: BMD, bone mineral density; HRT, hormone replacement therapy; MUFA, monounsaturated fatty acid; NHANES III, National Health and Nutrition Examination Survey III; Q, quintile; SFA, saturated fatty acid.

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dietary energy derived from fat is comparable in men and women, but men typically consume more grams of fat (28), the association between fat intake and bone health in men, as well as women, merits investigation.

The present study used data from National Health and Nutrition Examination Survey III (NHANES III) to assess the association between total dietary fat, as well as selected fatty acids, and hip BMD in men and women of different ages.

SUBJECTS AND METHODS

NHANES III is a national survey with data from ~40,000 civilian noninstitutionalized Americans, aged 2 mo to >90 y, conducted from 1988 to 1994. BMD of the proximal femur (the hip region including the femoral neck, intertrochanter, trochanter, and total hip) was measured by dual X-ray absorptiometry in NHANES participants ≥20 y old (29). Dietary data were obtained from a single 24-h recall and were analyzed using the USDA Nutrient Database as described previously (30). The recalls included all 7 d of the week (30,31). Individuals who were bedridden or in wheel chairs, those who reported implausibly low [<2093 kJ/d (<500 kcal/d)] or high [>20,930 kJ/d (>5000 kcal/d)] dietary intakes, as well as women who were currently pregnant or reported pregnancy in the previous 2 y or who were breast-feeding were excluded from the analysis ($n = 1566$). Of the remaining 14,850 subjects, bone data were not available for 1278. Thus, 13,572 subjects were included in the final analysis of the relation between dietary fat (total fat, SFA) and BMD. Characteristics of the subjects included in the final analysis are presented in **Table 1**.

Multivariate models using SAS-callable SUDAAN were used to adjust for the sample weighting and complex sampling scheme. The final models were adjusted for age (y), sex, weight (kg), height (cm), race (black, white, other), total energy (kJ) and calcium intakes (g), smoking (coded as none, past, current), and weight-bearing exercise (yes, no). Data from women were further adjusted for use of hormone replacement therapy (HRT) (ever used: yes, no). Other covariates that were evaluated for possible inclusion in the models, but were not included in the final models, were dietary protein (g) and potassium (g) intake, alcohol consumption (g), serum vitamin C (mmol/L), and β-carotene (μmol/L) levels, history of chronic conditions likely to result in reduced activity (e.g., serious heart disease, stroke) and recent weight loss (yes, no). In some situations, intakes of specific nutrients were observed to be potentially related to bone variables but covaried with other nutrients (e.g., monounsaturated and polyunsaturated fat with saturated fat) and therefore were not included. Other variables that were significant predictors ($P < 0.05$) or produced a material (>10%) change in the coefficient for another covariate were retained in the models. Dietary variables were energy adjusted by the residual method of Willett and Stampfer (32). To develop categorical variables, dietary fat variables were grouped into quintiles (Q) based on the weighted distribution among the study population without missing end points and were entered into models as indicator variables defined by the 2nd through 5th quintiles of energy-adjusted intake, with the lowest quintile as the referent group. To conduct linear trend tests across levels of nutrients, we created variables using exposure scores based on the median values for each quintile and used these in regression models. Analysis of covariance was used to analyze mean BMD by quintile of energy-adjusted fat intake for 4 sex/age groups (male/female, <50 y/≥50 y). Two-sided P-values were used with α set at 0.05. Least-square means are reported after adjustment for covariates.

TABLE 1

Subject characteristics[1]

Characteristic	Men $n = 6547$	Women $n = 7025$
Age, *y*	47.8 ± 19.0	48.0 ± 18.7
Weight, *kg*	80.2 ± 15.8	70.9 ± 17.3
Height, *cm*	173.4 ± 7.5	160.3 ± 7.1
BMI, *kg/m²*	26.6 ± 4.6	27.6 ± 6.5
Dietary variables[2]		
Energy, *kJ/d*	9907 ± 3893	7174 ± 2955
Energy, *kcal/d*	2367 ± 930	1714 ± 706
Total fat, *g*	89.5 ± 46.7	65.3 ± 36.6
Saturated fat, *g*	29.6 ± 16.8	21.5 ± 13.0
Monounsaturated fat, *g*	33.9 ± 18.8	24.4 ± 14.3
Polyunsaturated fat, *g*	18.8 ± 12.7	14.4 ± 10.5
Calcium, *mg*	843 ± 537	658 ± 420
Bone variables (selected)		
Total femoral mineral density, *g/cm²*	1.01 ± 0.17	0.90 ± 0.17
Total femoral mineral concentration, *g*	43.2 ± 9.0	32.6 ± 6.5
Smoking, %		
Nonsmoker	36	61
Past smoker	30	17
Current smoker	34	22
Any weight bearing exercise, %	33	28
Race/Ethnicity, %		
Caucasian	69	68
African American	27	30
Other	4	3
Age, % ≥ *50 y*	42	42

[1] Values are means ± SD or %.
[2] Dietary variables are adjusted for total energy intake.

RESULTS

There was no significant association between total fat intake and BMD at any of the sites analyzed. Fat intake across quintiles ranged from ≤39.8 g in Q1 to 109.2–310.9 g in Q5. In contrast, saturated fat intake was negatively associated with BMD in the femoral neck across all subjects (linear trend $P = 0.004$). BMD decreased 2.3% from the lowest to the highest quintile of saturated fat intake (BMD, 95% CI: lowest quintile: 0.843 g/cm^2, 0.838–0.849; highest quintile: 0.824 g/cm^2, 0.818–0.830). Saturated fat intake across all subjects ranged from ≤12.4 g in Q1 to 36.4–130.3 g in Q5 (median 24.4 g). Including dietary protein, vitamin C, and β-carotene in the model did not influence the outcome. Given the association between saturated fat and femoral neck BMD in the population as a whole, additional analyses were conducted to determine effects in specific age/sex groups.

The negative relation between saturated fats and BMD were more pronounced in men than in women. Across all men (<50 y old and ≥50 y old), saturated fat intake was negatively associated with BMD in the femoral neck, trochanter, and total hip (linear trend for the femoral neck: $P = 0.001$, trochanter: $P = 0.04$, total hip $P = 0.0005$). BMD decreased ~2–4% from Q1 to Q5 at these sites, with the greatest effects occurring in the femoral neck (**Table 2**). Among all men, the median intake of saturated fat was 29.5 g.

In men <50 y old, saturated fat intake was negatively associated with BMD in the femoral neck (linear trend $P = 0.004$). Median saturated fat intake in men <50 y of age was 35 g (**Table 3**).

There were no significant trends in men ≥50 y of age. However, there were tendencies for saturated fat intake to be negatively associated with BMD in the femoral neck, intertrochanter, and total hip in the older men (linear trend for the femoral neck $P = 0.08$, intertrochanter $P = 0.07$, total hip $P = 0.08$). Although these trends were not significant, the reductions in BMD from Q1 to Q5 were moderately large (~3% or more) (Table 3). The older men consumed less

TABLE 2

Association between saturated fat intake and BMD of different hip bone regions in all men[1]

	Q1 (low fat)	Q2	Q3	Q4	Q5 (high fat)
Intake, *g*	≤15.3	15.4–22.5	22.6–30.8	30.9–42.3	42.4–130.3
All men, *n*	1410	1417	1402	1416	1411
Femoral neck	0.897	0.885	0.875	0.878	0.858
$P = 0.001$; $R^2 = 0.43$	(0.889–0.906)	(0.878–0.893)	(0.868–0.882)	(0.870–0.885)	(0.848–0.867)
Q5 − Q1 = −4.3%					
Trochanter	0.765	0.758	0.754	0.758	0.747
$P = 0.04$; $R^2 = 0.25$	(0.758–0.773)	(0.752–0.765)	(0.748–0.760)	(0.748–0.760)	(0.739–0.775)
Q5 − Q1 = −2.4%					
Intertrochanter	1.150	1.130	1.135	1.137	1.138
$P = 0.09$; $R^2 = 0.36$	(1.138–1.161)	(1.120–1.141)	(1.126–1.147)	(1.127–1.147)	(1.125–1.151)
Q5 − Q1 = −1.0%					
Total hip	1.028	1.018	1.010	1.013	0.995
$P = 0.0005$; $R^2 = 0.40$	(1.019–1.036)	(1.010–1.025)	(1.003–1.017)	(1.006–1.020)	(0.986–1.004)
Q5 − Q1 = −2.7%					

[1] These models were adjusted for age, weight, height, race (white, black, other), total energy, calcium, smoking (none, past, current), and weight bearing exercise (yes/no). Saturated fat is an energy-adjusted variable. BMD data are presented as least-square means [g/cm^2 (95% CI)]; *P*-values were derived from linear trend analyses as described in the methods. R^2 is for the entire model.

saturated fat than the younger men; the median saturated fat intake in the older men was 25.8 g.

There were no statistically reliable associations between saturated fat intake and BMD in the total group of women or in the 2 age groups of women (**Tables 4** and **5**). Median saturated fat intake in the overall group of women was 21.6 g. In women <50 and ≥50 y old, median saturated fat intakes were 23.4 g and 19.0 g, respectively.

TABLE 3

Association between saturated fat intake and bone mineral density of different hip bone regions in men of different ages[1]

	Q1 (low fat)	Q2	Q3	Q4	Q5 (high fat)
Men <50 y					
Intake, *g*	≤17.8	17.9–25.8	25.9–34.9	35.0–46.3	46.4–130.3
n	796	794	801	792	797
Femoral neck	0.963	0.947	0.938	0.939	0.922
$P = 0.004$; $R^2 = 0.21$	(0.950–0.976)	(0.936–0.957)	(0.928–0.948)	(0.929–0.950)	(0.909–0.935)
Q5 − Q1 = −4.3%					
Trochanter	0.790	0.780	0.777	0.779	0.779
$P = 0.31$; $R^2 = 0.18$	(0.780–0.800)	(0.771–0.788)	(0.769–0.788)	(0.770–0.787)	(0.769–0.790)
Q5 − Q1 = −1.4%					
Intertrochanter	1.251	1.239	1.231	1.227	1.224
$P = 0.13$; $R^2 = 0.31$	(1.237–1.265)	(1.227–1.250)	(1.219–1.242)	(1.216–1.239)	(1.210–1.239)
Q5 − Q1 = −2.2%					
Total hip	1.073	1.060	1.055	1.054	1.049
$P = 0.14$; $R^2 = 0.29$	(1.061–1.084)	(1.051–1.070)	(1.045–1.064)	(1.044–1.063)	(1.037–1.062)
Q5 − Q1 = −2.2%					
Men ≥50 y					
Intake, *g*	≤12.9	13.0–19.1	19.2–25.8	25.9–35.6	35.7–102.2
n	613	619	616	610	618
Femoral neck	0.811	0.800	0.795	0.787	0.782
$P = 0.08$; $R^2 = 0.27$	(0.798–0.824)	(0.789–0.811)	(0.784–0.806)	(0.776–0.798)	(0.768–0.796)
Q5 − Q1 = −3.6%					
Trochanter	0.735	0.726	0.723	0.724	0.714
$P = 0.34$; $R^2 = 0.20$	(0.723–0.747)	(0.715–0.736)	(0.713–0.732)	(0.714–0.734)	(0.702–0.727)
Q5 − Q1 = −2.9%					
Intertrochanter	1.132	1.128	1.113	1.107	1.095
$P = 0.07$; $R^2 = 0.33$	(1.116–1.148	(1.113–1.142)	(1.100–1.127)	(1.093–1.121)	(1.077–1.113)
Q5 − Q1 = −3.3%					
Total hip	0.967	0.961	0.951	0.946	0.936
$P = 0.08$; $R^2 = 0.33$	(0.954–0.981)	(0.949–0.973)	(0.940–0.963)	(0.934–0.957)	(0.921–0.950)
Q5 − Q1 = −3.2%					

[1] These age- and sex-stratified models are adjusted for weight, height, race (white, black, other), total energy, calcium, smoking (none, past, current), weight-bearing exercise (yes/no). Saturated fat is an energy-adjusted variable. BMD data are presented as least-square means [g/cm^2 (95% CI)]; *P*-values were derived from linear trend analyses (see methods). R^2 is for the entire model.

TABLE 4

Association between saturated fat intake and bone mineral density of different hip bone regions in all women[1]

	Q1 (low fat)	Q2	Q3	Q4	Q5 (high fat)
Intake, *g*	≤10.8	10.9–16.0	16.1–22.1	22.2–30.2	30.3–124.6
All women, *n*	1572	1536	1575	1551	1560
Femoral neck	0.779	0.793	0.794	0.798	0.789
$P = 0.23$; $R^2 = 0.56$	(0.792–0.806)	(0.787–0.799)	(0.788–0.800)	(0.792–0.804)	(0.781–0.796)
Q5 − Q1 = +1.3%					
Trochanter	0.662	0.661	0.663	0.664	0.658
$P = 0.66$; $R^2 = 0.43$	(0.656–0.668)	(0.656–0.667)	(0.658–0.668)	(0.659–0.670)	(0.652–0.665)
Q5 − Q1 = −0.6%					
Intertrochanter	1.063	1.057	1.058	1.058	1.052
$P = 0.71$; $R^2 = 0.52$	(1.054–1.072)	(1.049–1.065)	(1.057–1.066)	(1.051–1.066)	(1.042–1.062)
Q5 − Q1 = −1.0%					
Total hip	0.900	0.895	0.897	0.898	0.891
$P = 0.58$; $R^2 = 0.54$	(0.892–0.907)	(0.889–0.902)	(0.890–0.903)	(0.892–0.904)	(0.883–0.889)
Q5 − Q1 = −1.0%					

[1] These models were adjusted for age, weight, height, race (white, black, other), total energy, calcium, smoking (none, past, current), weight bearing exercise (yes/no) and HRT. Saturated fat is an energy-adjusted variable. BMD data are presented as least-square means [g/cm^2 (95% CI)]; *P*-values were derived from linear trend analyses (see methods). R^2 is for the entire model.

DISCUSSION

In this study, associations between dietary fat intake and BMD in several regions of the hip were examined in a nationally representative large sample of American men and women. Saturated fat intake was negatively associated with bone density, and the strongest effects were seen among men <50 y old.

The present results indicate that diets high in saturated fats may increase the risk of bone disease, in addition to their already well-documented effects on cardiovascular health (33). The fact that dietary fat was negatively associated with bone density in the femoral neck region of the hip is important because this is a vulnerable fracture site. Hip fractures induce serious consequences, including pain, reduced mobility, reduced quality of life, premature mortality, and increased health care costs (34). Reductions in bone density are consistently associated with increased fracture risk; a 16% (1 SD) decrease in bone density is associated with an increase in the relative fracture risk of ~50% or more on a population basis (35–37). In the present study, there was >4% difference in bone density in the femoral neck between the lowest and highest quintiles of saturated fat intake among the men. Based upon the previously reported estimates (above), this difference would be associated with an increase in relative fracture risk of ~12%.

The percentage difference in BMD between the lowest and highest quintiles of saturated fat intake in the present study is similar to the differences reported for other factors relevant to bone health, including vitamin D (1.2–4.8% difference in hip BMD between lowest and highest quintiles) (38), early milk consumption (~3–5% difference in hip BMD between low and high intakes) (39,40), and jogging (5% difference in femoral BMD between joggers and nonjoggers) (41). The contribution of saturated fat to overall variability in the present study was modest (<1%); however, it was at about the same level, and in some cases stronger than dietary calcium intake in these models. Although modest reductions in bone density are associated with individual factors in isolation, their combined effects are potentially profound. Therefore, any factors that can affect bone density are worthy of attention, especially those that are modifiable (such as diet and lifestyle). The present results suggest that dietary fat should be included in the spectrum of dietary constituents considered important to bone health (42).

Our results indicate that associations between dietary fat and bone health are particularly strong in men. One reason that saturated fats demonstrated a stronger inverse association with bone density in men may be that, in general, men consumed more saturated fat than women. Sex-based differences in the absolute amount of fat in the diet were reported previously across NHANES surveys. That is, although the percentages of total fat and fatty acid fractions are comparable between the sexes, men, in general, consume more grams of fat (including saturated fat) than do women (28). Saturated fat intake ranged from ~13–130 g in men (median ~30 g), and from ~10–125 g in women (median ~22 g). That the total amount consumed is important is also supported by comparisons between the younger and older men. Specifically, the total amount of saturated fat consumed was greater in the younger cohort [~18–130 g in the young men (median 35 g), ~13–102 g in the older men (median ~26 g)], and associations between saturated fat intake and BMD were significant only in the younger cohort. Thus, the total amount of saturated fat consumed may be an important dietary factor relevant to bone health. The effects of fats reported herein represent an important new finding because 28–47% of American men are estimated to have osteopenia (26), and ~20% of healthcare costs due to osteoporotic fractures arise from the treatment of men (27). Furthermore, 1-y post-hip fracture mortality is higher in men than in women (43).

The fact that effects were strongest in the younger cohort of men is of particular concern and may reflect reduced dietary quality in that segment of the population. Other studies provided evidence that younger men are more likely to consume diets higher in fat and of lower quality than women or older men. For instance, when tested in a controlled laboratory environment, young men and women consumed more dietary fat than older men and women, with young men consuming the most (44). These findings were corroborated by a survey of a small sample of healthy free-living older and younger men and women (45). In that study, dietary fat and saturated fat intakes were greatest, and dietary variety was lowest in the young men. The present results, therefore,

TABLE 5

Association between saturated fat intake and bone mineral density of different hip bone regions in women of different ages[1]

	Q1 (low fat)	Q2	Q3	Q4	Q5 (high fat)
Women <50 y					
Intake, *g*	≤12.6	12.7–18.4	18.5–24.7	24.8–33.5	33.6–124.6
n	887	899	890	889	893
Femoral neck	0.880	0.866	0.872	0.874	0.870
$P = 0.24$; $R^2 = 0.32$	(0.870–0.889)	(0.858–0.874)	(0.858–0.874)	(0.866–0.882)	(0.859–0.880)
Q5 − Q1 = −1.1%					
Trochanter	0.719	0.712	0.713	0.713	0.711
$P = 0.72$; $R^2 = 0.23$	(0.711–0.727)	(0.705–0.719)	(0.706–0.720)	(0.706–0.720)	(0.702–0.721)
Q5 − Q1 = −1.1%					
Intertrochanter	1.150	1.130	1.135	1.137	1.138
$P = 0.09$; $R^2 = 0.36$	(1.138–1.161)	(1.120–1.141)	(1.126–1.147)	(1.127–1.147)	(1.125–1.151)
Q5 − Q1 = −1.0%					
Total hip	0.977	0.962	0.966	0.968	0.966
$P = 0.76$; $R^2 = 0.35$	(0.967–0.987)	(0.953–0.970)	(0.958–0.974)	(0.961–0.977)	(0.955–0.977)
Q5 − Q1 = −1.2%					
Women ≥50 y					
Intake, *g*	≤9.1	9.2–13.7	13.8–18.5	18.6–25.7	25.8–93.9
n	663	671	668	664	670
Femoral neck	0.688	0.698	0.695	0.692	0.693
$P = 0.46$; $R^2 = 0.59$	(0.678–0.696)	(0.689–0.707)	(0.686–0.703)	(0.683–0.701)	(0.682–0.704)
Q5 − Q1 = +0.7%					
Trochanter	0.598	0.598	0.596	0.595	0.594
$P = 0.64$; $R^2 = 0.37$	(0.580–0.598)	(0.589–0.606)	(0.588–0.603)	(0.587–0.603)	(0.584–0.604)
Q5 − Q1 = −0.7%					
Intertrochanter	0.952	0.955	0.957	0.952	0.949
$P = 0.92$; $R^2 = 0.47$	(0.938–0.965)	(0.942–0.967)	(0.945–0.969)	(0.940–0.964)	(0.934–0.966)
Q5 − Q1 = −0.3%					
Total hip	0.799	0.806	0.815	0.802	0.800
$P = 0.80$; $R^2 = 0.48$	(0.788–0.810)	(0.796–0.816)	(0.795–0.814)	(0.792–0.812)	(0.788–0.812)
Q5 − Q1 = 0%					

[1] These age- and sex-stratified models are adjusted for weight, height, race (white, black, other), total energy, calcium, smoking (none, past, current), weight-bearing exercise (yes/no) and HRT. Saturated fat is an energy-adjusted variable. BMD data are presented as least-square means [g/cm^2 (95% CI)]; *P*-values were derived from linear trend analyses (see methods). R^2 is for the entire model.

corroborate these previous studies, and suggest that dietary choices among younger men may not be optimal for bone health.

The present analysis does not provide direct evidence of the type of foods consumed. However, dietary protein, vitamin C, and β-carotene were evaluated for inclusion in the model and did not influence the outcome, suggesting that consuming large amounts of protein or low quantities of fruits and vegetables cannot account for the inverse association between saturated fat intake and bone density. In addition, calcium was included in the final model, suggesting that consumption of large quantities of full-fat dairy products also cannot account for the results obtained. Finally, MUFA and PUFA covaried with SFA. Thus, reductions in these classes of fatty acids, which are associated with beneficial effects on bone, cannot explain our results (13,24). It appears, therefore, that the effects of saturated fat are strong, even when consumption of other nutrients is taken into account.

The present results are not in agreement with results reported in a smaller epidemiologic study (24). In that study, no effect of saturated fat on forearm BMD was found in either men or women, but MUFA were positively associated with BMD in both sexes. Several factors may account for the different results. First, data were obtained from Greek subjects. The Greek diet is typically higher in foods rich in MUFA (e.g., olive oil) and polyphenols (e.g., vegetables, fruits, and their derivatives), and lower in foods rich in SFA than the American diet (46). Such differences would influence the data analysis in each study. In addition, because the relative proportion of fatty acids in the diet is thought to have important effects on bone health, it is possible that the Greek diet conferred protection and/or reduced risk associated with consumption of different kinds of fats. Unfortunately, fat intake was not reported; thus, direct comparisons to the present findings cannot be made. The presence of polyphenols in the Greek diet also may have contributed to the different results, due to the anti-inflammatory effects of these dietary constituents (47), and the potentially important role of inflammation in the development of bone disease (48). Second, only 118 women and 36 men were included in the study, making it quite small, especially for the men. It is possible that if a greater number of subjects had been studied, significant associations between SFA intake and bone density would have been found. Third, the bone site (forearm) was different. Thus, there are several differences between the study of Trichopoulou et al. (24) and the present investigation. However, the differences do not negate the importance of the present results for people who consume diets similar to the typical American diet. Taken together, these 2 studies point to the potential importance of diets low in SFA and higher in MUFA for optimal bone health.

The lack of an association between saturated fat intake and bone density in women in the present study was surprising. Others have reported an inverse association between total fat intake and bone density as well as a direct association between

total fat intake and fracture risk in women (19–21). However, saturated fat intake was not assessed in these earlier studies. On the other hand, other fatty acids in the diet may be important. A longitudinal study, for instance, found no association between total fat or saturated fat intake and loss of BMD in women going through the menopausal transition. However, higher intakes of PUFA and MUFA were associated with loss of BMD in that study (49). In the present study, no strong associations between BMD and MUFA or PUFA were found; this may have been due to the cross-sectional nature of the analysis or the covariance with saturated fat.

It is also possible that the lack of effect in women was due to methodological differences between the present study and other reports. One factor to consider is the bone site analyzed. In the present investigation, no association between fat intake and hip variables was found in women. Others reported similar results. Specifically, total fat intake was inversely associated with BMD in the lumbar spine, but not the femoral neck, in 175 pre- and postmenopausal women (21), as well as in 218 postmenopausal women (19). Bone sites vary in their response to dietary fats in animal studies, as well. Bone sites with more cancellous tissue, in particular, appear to be more vulnerable to the negative effects of dietary saturated fats (5). Because bone tissue in the spinal vertebrae is composed of a greater proportion of cancellous tissue than hip regions (50), it is possible that apparent discrepancies between studies may be due to the specific bone region analyzed.

Statistical modeling may also account for differences between studies. In the present report, data from women were adjusted for the use of hormone replacement therapy, as well as age, weight, height, race, total energy and calcium intakes, smoking, and weight-bearing exercise. In a previous report, adjustments were made only for age, weight, and physical activity (19). It is possible, then, that other factors may have contributed to the effects reported.

It is also possible that the lack of correlation in women was due to inaccuracies in the dietary intake data reported. Attempts to assess underreporting of dietary data in NHANES III indicated that underreporting was greater in women than in men, and was associated with diets lower in fat (51). In particular, ~18% of men and ~28% of women were classified as underreporters, i.e., ~10% more women than men were classified as underreporters. Thus, it cannot be ruled out that measurement error may have been greater in women, and may have contributed to the results reported here.

Although not demonstrating a cause/effect relation, the data presented here corroborate evidence from animal and in vitro studies, indicating that dietary fats can have potent effects on bone health. SFA, in particular, may act through several different mechanisms to exert their effects. Dietary fats high in SFA can decrease intestinal membrane fluidity and reduce calcium uptake by brush border membrane vesicles (52,53). In addition, an atherogenic diet high in SFA was reported to reduce bone mineralization and inhibit osteogenic differentiation of marrow stromal cells in mice (54,55). This is thought to be due to the presence of oxidized lipids in bone due to the atherogenic diet (17). In vitro studies showed that minimally oxidized LDL inhibit stromal cell osteoblastic differentiation (bone-forming cells) through a mitogen-activated protein kinase–dependent pathway and by the formation of reactive oxygen species (54,56). Furthermore, oxidized lipids also were reported to enhance osteoclastic differentiation (bone resorption cells) in vitro through a cAMP-mediated pathway (57). Taken together, the available evidence suggests that dietary SFA have direct and indirect effects that may reduce calcium absorption from the intestine, reduce bone formation, and enhance bone resorption, all of which would be deleterious to bone health.

Recommendations cannot yet be made concerning the optimal fatty acid composition of the diet for bone health; however, the present findings provide new evidence supporting dietary recommendations to consume diets low in saturated fat. Further work in this area is clearly warranted given the increasing age of the population, the prevalence of osteoporosis, and the recent popularity of low-carbohydrate, high-fat diets.

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