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Association between dietary fiber intake and bone loss in the Framingham Offspring Study

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Abstract

Dietary fiber may increase calcium absorption, but its role in bone mineralization is unclear. Furthermore, the health effect of dietary fiber may be different between genders. We examined the association between dietary fiber (total fiber and fiber from cereal, fruits, vegetables, nuts and legumes) and bone loss at the femoral neck, trochanter and lumbar spine (L2–4) in older men and women. In the Framingham Offspring Study, at baseline (1996–2001), diet was assessed using the Willett food frequency questionnaire and bone mineral density (BMD) was measured using dual-energy X-ray absorptiometry. Follow-up BMD was measured in 2001–2005 and 2005–2008 among 792 men (mean age, 58.1yr; BMI, 28.6kg/m^2) and 1,065 women (57.3yr; 27.2kg/m^2). We used sex-specific generalized estimating equations in multivariable regressions to estimate the difference (β) of annualized BMD change in percent (%ΔBMD) at each skeletal site per 5 g/d increase in dietary fiber. We further estimated the adjusted mean for bone loss (annualized %ΔBMD) among participants in each higher quartile (Q2, Q3 or Q4) compared with those in the lowest quartile (Q1) of fiber intake. Higher dietary total fiber (β=0.06, p=0.003) and fruit fiber (β=0.04, p=0.008) was protective against bone loss at the femoral neck in men but not in women. When examined in quartiles, men in Q2–Q4 of total fiber had significantly less bone loss at the femoral neck versus those in Q1 (all p<0.04). Fiber from vegetables appeared to be protective against spine bone loss in women but not men. There were no associations with cereal fiber or nut and legume fiber and bone loss in men or women. Our findings suggest that higher dietary fiber may modestly reduce bone loss in men at the hip.

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Keywords

Dietary fiber; Bone mineral density; bone loss; Sex-specific difference; Framingham Study

Introduction

Osteoporosis is a common skeletal disorder leading to increasing bone fragility and fracture risk that poses a substantial healthcare burden and affects physical function, comorbidity and mortality in both men and women with advancing age[1,2]. Dietary contributors to osteoporosis have focused on vitamin D and calcium, but nutrients beyond these[3,4] may also affect bone health. Intake of fruits and vegetables[5] and a fruit, vegetable and cereal pattern[6] in the Framingham cohorts have been suggested to be positively related to change in hip BMD in men but not in women. Even though these food sources are major contributors of dietary fiber, studies on dietary fiber per se are limited.

Recent experimental studies suggest that dietary fiber may benefit mineral absorption, BMD, and bone turnover[7–9]. According to the Institute of Medicine, dietary fiber is defined as non-digestible carbohydrates and lignin that are intrinsic and intact in plants[10]. Studies have shown increased calcium absorption in rodent models treated with various fermentable dietary fiber[11–15]. Some[15–17] but not all[12,13,18] of these studies reported a positive effect on BMD. Data from human controlled trials have demonstrated that dietary fiber increased calcium absorption[19,20] and bone mineralization[20] in children/adolescents. The only cross-sectional observational study[21], to our knowledge, reported that dietary fiber was positively related to forearm BMD in children but not in adolescents. However, results from clinical trials in postmenopausal women are inconsistent: Although a positive association has been shown between fiber intake and calcium absorption[22–25], this does not translate to change in BMD[26,27]. Different directions of bone turnover markers were also reported[24,25,27]. To our knowledge, no study has examined the associations of fiber intake with fractures.

Ultimately, the effect of dietary fiber on bone health in older adults is unclear, which may involve various factors including calcium intake and hormones. Previous studies suggested that higher dietary fiber was related to lower estrogen levels in women[28–30] and that the duration of menopause affected calcium absorption with fiber intake[23]. Further, dietary fiber may exert its health effects via change of gut microbiome[8], which is different between sexes[31]. Additionally, sex-specific differences are known in genetics in bone physiology, bone geometry and bone gonadal hormone response. These sex differences point to the importance of conducting sex-specific analysis for genes and environmental factors in association studies on osteoporosis[32]. Together, we hypothesized a sex difference in the inverse association between dietary fiber and bone loss.

In this study, we examined the longitudinal association between intake of dietary fiber and change in BMD in the Framingham Offspring Study. We further examined fiber sub-types including cereal, fruits, vegetables, nuts and legumes because the type of fiber may have different bone health effects such that cereal grain fiber was suggested to be more beneficial in cardiovascular diseases and type 2 diabetes[33–35].

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Subjects and Methods

Study population

Participants from the Framingham Offspring cohort, which was assembled in 1971 consisting of adult children of the Original Framingham Heart Study and spouses of the offspring participants, were enrolled and subsequently examined approximately every 4 years to investigate familial risk factors for cardiovascular diseases[36]. In 1996–2001, as part of the Framingham Osteoporosis Study, BMD measures of the hip and lumbar spine (LS; L2–L4) were obtained in 3,072 Offspring participants. Follow-up BMD measurements were obtained in 2002–2005 (n=1,311) and in 2005–2008 (n=1,830), of whom 786 persons had three BMD measures at the hip and 778 persons had three BMD measures at the LS. The current study comprised 792 men and 1,065 women who had at least one follow-up BMD measure and valid dietary assessments completed in either 1995–1998 or 1998–2001 (Figure 1). All participants provided informed written consent and the study was approved by the Institutional Review Boards at Boston University and Hebrew SeniorLife.

Baseline dietary assessment

At baseline, habitual dietary intake was assessed using the semi-quantitative Willett validated food frequency questionnaire (FFQ)[37–39]. The FFQ listed 126 food items with frequency of consumption and standard serving sizes. Participants were also allowed to add up to three additional foods, types of breakfast cereal and cooking oil that are not listed in the FFQ. The nutrient values were estimated primarily based on the USDA food composition database and supplemented by other published data[39]. Estimates from the FFQ reflected a long-term average dietary fiber intake based on several weeks of formal diet records with a correlation coefficient of 0.68 for dietary fiber[37–39]. Total fiber intake in grams/day was derived as the sum of fiber from cereal, fruits, vegetables, and nuts and legumes. We only included participants whose FFQs had less than 12 food items left blank, those with no missing values for dietary total fiber and calorie intakes ≥500 kcal and <4,200 kcal for men and <4,000 kcal for women.

Measurements of BMD

BMD (g/cm^2) of the femoral neck (FN) and trochanter (TR) and of the LS, L2–L4 was measured at the baseline exam and at least one follow-up exam. BMD measurements completed at baseline in 1996–2001 were obtained using a LUNAR DPX-L dual-energy X-ray absorptiometry (Lunar Corp., Madison, WI, USA) and were repeated using a GE Lunar Prodigy (GE Lunar, Madison, WI, USA) in 2002–2005 and in 2005–2008. For Lunar DPX-L, the precision was 1.7% at the femoral neck, 2.5% at the trochanter, and 0.9% at the spine, which is similar to the range of 1.8% to 1.9% reported by others[40,41]. For Lunar Prodigy, the % coefficient of variances were 1.8, 2.3, 1.2 and 1.1 for the femoral neck, trochanter, total hip and L2–4 regions, respectively[42]. The right hip was scanned unless there was a history of fracture or hip replacement (there were 4 hip fracture prevalent cases in total with 2 fractures per sex), in which case the left hip was scanned. Percentage change in BMD over the follow-up was calculated as: %ΔBMD = [(BMD at follow-up – BMD at baseline) / BMD at baseline] × 100 (1) as described earlier[43] with adjustment for change in technology from DPX-L to Lunar Prodigy based on the previous calibration study[42]. Annualized %ΔBMD

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was then calculated using formula (1) divided by time difference (years) between the baseline and follow-up BMD measures. Alternatively, we used rate of bone loss per year (g/cm^2/year) estimated by [(BMD at follow-up – BMD at baseline)] divided by time difference described as above.

Other covariates

Body weight (pounds) and height (inches) were measured at baseline and every four years without shoes. Weight was measured in light-weight clothing and height was measured using a wall mounted stadiometer. Body mass index (BMI) (kg/m^2) was calculated as weight (kg) divided by height (m) squared. Cigarette smoking was assessed via questionnaire as current cigarette smoker (smoked regularly in the past year), former smoker or never smoker; we combined former and never smokers into a group of current non-smokers. For estrogen use, women were divided into current estrogen users at the time of the exam and non-current users including those who had never used or formerly used estrogen. Physical activity was measured with use of the Physical Activity Scale in the Elderly (PASE), which has been previously validated in older adults[44,45]. If PASE was missing at baseline (n=16), we used values at the previous exam (1991–1995) as an estimate. Furthermore, menopause status (yes versus no) and use of estrogen (yes versus no) were determined at each visit as the BMD measurement. The Dietary Guidelines Adherence Index (DGAI-2010) score was applied to the baseline FFQ to determine participants' diet quality according to the Dietary Guidelines for Americans 2010[46,47] and ranged from 0 (lowest adherence) to 100 (highest adherence). If the DGAI-2010 was missing at baseline (n=377), values at the previous exam (1991–1995) were used. Because dietary fiber is one of the 24 components in the DGAI-2010, we modified the DGAI-2010 by subtracting the fiber component.

Statistical analysis

Descriptive statistics were generated using means and standard deviations for normal distribution otherwise median (interquartile range) of continuous measures and frequencies and percentages for categorical measures. For continuous variables, Shapiro-Wilk W test was used to test normality and ANOVA was tested for differences among quartiles of total fiber. Dietary fiber, including total fiber and sub-group fiber was modeled as both a continuous variable as well as a categorical variable in quartiles. We first calculated the residuals of dietary fiber for men and women separately by regressing fiber intake on total calories[48] to obtain sex-specific quartiles of dietary fiber. We further calculated average T score based on the BMD of women aged 20–29 years in the NHANES[49] and had standardized the BMD values[50].

Dietary fiber may interact with sex hormones to impact bone loss, therefore we first assessed whether there sex modified this association by including a cross product term of each dietary fiber variable and sex in separate regression models. Because dietary total fiber and femoral bone loss was suggested to be modified by sex (p for interaction=0.05), we performed the analyses using a linear regression model in men and women separately. In the unadjusted model, only exam period was adjusted as part of the GEE regression for repeated measure[51] (model 1). In the base model (model 2), we controlled for age (years), BMI (kg/m^2), height (m) and exam period for repeated BMD measures. In the full model (Model

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3), we further adjusted for current cigarette smoking (yes, no), physical activity (PASE, continuous), modified DGAI 2010 (continuous), calcium supplement intake (yes, no), vitamin D supplement intake (yes, no), caffeine intake (mg/day), dietary calcium (in quartile, mg/day), dietary vitamin D (in quartile, I.U./day), menopausal status (yes, no, in women only), and estrogen therapy use (yes, no, in women only). These covariates have been suggested as significant factors for BMD in the Framingham Osteoporosis Study[6,43,52]. As fiber may be related to diet quality, we included a dietary index to reduce possible confounding by a potential healthy diet effect in those who consume higher dietary fiber. No evidence suggested that any of the covariates were mediators. We used the Generalized Estimating Equations in the regression models to account for the correlation between the repeated BMD measurements. The difference (β) in %ΔBMD at each bone site per 5 g/day increase in dietary fiber on a continuous scale and the least squares adjusted mean (β) comparing a higher quartile (Q2, Q3 or Q4) with the lowest quartile Q1 (reference) were obtained from the regression models. We took the same approach to examine dietary fiber intake in relation to annual rate of bone loss (g/cm^2/year).

Menopause and hormone therapy are known risk factors for osteoporosis[53,54]. A previous study reported that women who experienced menopause for >6 years had higher calcium absorption in the fiber group than the placebo group, but no difference was observed in women who experienced menopause for 2–6 years[23]. Therefore, we conducted stratified analyses by i) menopausal status (premenopausal versus postmenopausal, defined as menstrual periods stopped at least one year), and among postmenopausal women; ii) by estrogen users (yes/no); and iii) by stage of menopause (early postmenopausal, i.e. menstrual periods stopped less or equal to 5 years versus late postmenopausal, i.e. menstrual periods stopped more than 5 years).

All statistical analyses were conducted using SAS Version 9.3 (SAS Institute, Inc., Cary, North Carolina). Based on the scientific evidence from the literature, we had *a priori* hypothesis that higher versus lower intake of the same type of dietary fiber (total or sub-group) was associated with greater change in BMD. We also limited the BMD measurements to three skeletal sites. Hence, the p values in this study were not adjusted for multiple testing.[55] A two-sided p value less than 0.05 was considered statistically significant.

Results

Among the 3,072 participants with baseline BMD, the 1,008 participants who were dead or lost of contact were not included in this study. The distribution of deaths or loss of contact did not vary across the quartiles of dietary total fiber with chi-square tests ranged from 0.08 to 0.20. Baseline characteristics are described in Table 1 across quartiles of dietary total fiber by sex. The ratio of males and females in each follow-up group in 2002–2005 or in 2005–2008 was similar (p=0.30) with 44.1% and 46.3 % as men, respectively. The mean (standard deviation) for age was 58.1 (8.9) years and for BMI was 28.6 (4.2) kg/m^2 in men and 57.3 (9.0) years and 27.2 (5.6) kg/m^2 in women. Dietary fiber intake was similar in both genders with 19.7 (7.9) g/day for men and 19.5 (8.1) g/day for women. BMI, height, PASE, vitamin

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D supplementation use did not differ across the quartiles of total fiber intake in either gender.

The annual %ΔBMD between the baseline and each follow-up BMD measures is described by quartile intake of total fiber in Supplemental Table 1. The average time between the baseline BMD and the first follow-up was 4.7 (range 1.8 to 7.9) years, and that between the baseline BMD and the second follow-up was 8.1 (range 4.6 to 11.5) years. In addition, the T-scores at the baseline and the follow-ups (in 2002–2005 and in 2005–2008) were as follows: −0.50, −0.51, −0.57 for men and −1.17, −1.17, −1.26 for women, respectively.

As shown in Table 2, the results from three different models are similar. For men, per 5 g/day increase in dietary total fiber was associated with less bone loss by 0.06% in annual %ΔBMD (p=0.003) at the femoral neck in the fully adjusted model. This corresponds to 0.0005g/cm^2 BMD in lower annual rate of bone loss (p=0.0015) at the femoral neck. A positive association was also observed for fruit fiber (β =0.10, p=0.008), which corresponds to 0.001g/cm^2 in lower annual rate of bone loss at the femoral neck (p=0.004). The positive association of dietary total fiber with change in trochanter BMD had a tendency towards significance (β =0.04, p=0.08). For LS (L2–4) change of BMD, a weak positive association was observed with fruit fiber for men (β =0.07, p=0.10) and a significant association was found with vegetable fiber for women (β =0.12, p=0.01). Fiber from nuts and legumes was not related to change of BMD. However, no protective association between dietary fiber and hip bone loss was observed in women.

When dietary total fiber was analyzed as a categorical variable in quartiles, in men, there was significantly less femoral neck bone loss, represented by either annual %ΔBMD or annual rate of bone loss (g/cm^2/year) comparing a higher quartile (Q2, Q3 or Q4) with Q1 of dietary total fiber (Figure 2). Men in the higher quartiles of dietary total fiber had significantly less bone loss with Least Squared Means ranged −0.009 to −0.003% for annualized change of BMD at the femoral neck versus −0.15% in men in Q1 (all p<0.04). No statistical difference was found for specific types of fiber or at other skeletal sites comparing a higher with the lowest quartile. The results in women were in general null and similar to those in dietary fiber on a continuous scale (See Supplemental Table 2). The β estimates for dietary fiber with annual rate of bone loss were materially the same as for annual %ΔBMD. Hence, we only presented the results in the form of annual %ΔBMD.

In addition, no significant associations were seen between any of the dietary fiber variables and bone loss at femoral neck, trochanter and LS examined (p range: 0.25 to 0.98) in the following sub-groups of women: premenopausal (n=271), late postmenopausal (n=578) and early postmenopausal (n=216); and postmenopausal women who used estrogen therapy (n=297) and those who did not (n=497).

Discussion

The present study reported a longitudinal association between dietary fiber and bone loss among community-dwelling older adults. Our results suggest a possible sex-specific difference such that the observed associations were driven primarily by men in whom higher

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fiber intake was associated with less bone loss at the hip during an 8-year follow-up. For every 5 g per day increase of dietary total fiber and fruit fiber, we found that there was a decrease of 0.06% and 0.04% in annualized change of femoral neck BMD, respectively. For women, we did not observe associations regardless status of menopausal or estrogen use. Such sex differences could be attributed to a hormonal effect that may override a small benefit of dietary fiber against bone loss.

Recent evidence from fiber feeding studies in animals or in children/adolescents and postmenopausal women has suggested prominent results in improved calcium absorption[11–15,19,20,22], but data in bone turnover biomarkers suggested either increase[24], decrease[27] or no changes[25] of bone formation and resorption markers. No long-term studies reported difference in change in BMD in the fiber group versus the placebo group in postmenopausal women[26,27]. One possible biological mechanism for the beneficial effect of dietary fiber on the skeleton is the prebiotic properties of fiber in modulating the microbial composition in the gut to improve calcium absorption due to the release of short-chain fatty acids during fermentation[18,56]. Further, dietary fiber may promote desirable gut microbiota composition to reduce inflammation and stimulate hormones to regulate bone density and signal bone turnover.[8] Other mechanisms include that dietary fiber may enlarge the absorption surface in the intestine lumen to increase mineral absorption[7].

Our data suggested a possible sex difference in dietary fiber in relation to bone loss. The β coefficient per 5 g dietary total fiber with femoral neck BMD change suggested a multiplicative interaction between men and women (the β was 0.025 if adjustment for sex in the model). Earlier studies in women have suggested that dietary fiber reduces estrogen concentration in both postmenopausal women[28] and premenopausal women[29,30], possibly through lowering β-glucuronidase activity in the feces and therefore decreasing reabsorption of estrogen in the colon[29]. In addition, studies have shown a sex difference in the microbiome composition due to the influence of sex hormones[31,57]. The distribution of dietary fiber intake was similar between men and women in this study, although the recommended dietary fiber intake is higher in men than women[10]. It is unclear what may explain the sex difference between dietary fiber and bone loss in our study, it is plausible that dietary fiber may affect bone loss, at least, through the impact of sex-hormones on microbiome.

The protective association of dietary fiber with bone loss in older men as seen in the current study is in line with male rodents treated with dietary fiber that were found to have enhanced calcium absorption[15,16,58], higher bone mineral content[16] and bone strength[59] as compared to the controls, although animal data may not be translated to humans directly. Furthermore, in our analyses of quartiles of dietary total fiber in men, we observed a potential threshold effect in lower bone loss at the second quartile and above comparing with the lowest quartile. That is men who consumed dietary total fiber in Q2 and above had comparable less bone loss at the femoral neck as compared with men in Q1 (all $p<0.04$). This observation is in agreement with an earlier study in male rodents[16], where the maximum effect of inulin fiber on BMD was found at the concentration from 0 to 5 g/100 g diet ($p <0.001$), but no further BMD increase at a higher dosage from 5 to 10 g/100 g diet ($p= 0.11$)[16].

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The relationship of dietary fiber with bone loss in women in our study was generally null particularly in the hip. In a 2-year randomized clinical trial, postmenopausal women supplemented with prebiotic fiber did not show a difference in change in BMD at 24 months at the femur or LS compared to the group supplemented with calcium alone or with placebo[27], although it is possible that a 2 year duration is not sufficient to detect the effect of dietary fiber on change in BMD. When we stratified women by menopausal status, we did not see associations between dietary fiber and change in BMD, which may indicate that the dominant effects of estrogen deficiency in women may have obscured the smaller effects of fiber on bone loss. In our sample of the Framingham Offspring Study, 94% of the women were over 45 years.

Because our analysis hinted a threshold effect for low dietary total fiber with greater bone loss in men in the quartile analysis (Figure 2), we should be cautious in interpreting the results of test for trend. Due to the relatively small number of participants and a modest protective effect observed in this study, future studies with a larger sample size should evaluate whether the association between dietary fiber and bone loss is better characterized as dose-dependent or as threshold based.

Strengths of this study include the use of a population-based cohort, repeated measures of BMD over 3 time points, and examination of dietary fiber from specific food sources in both men and women to examine the relationship between dietary fiber and change of BMD. One of the limitations of this study is that dietary data is self-reported and may prone to biases, resulting in the potential to underestimate the observed associations. Despite our attempts to control for potential confounders, residual confounding may still occur in observational studies. However, generalizability of our results may be limited to non-Hispanic White populations in the US because Framingham study participants are Caucasian, whose fiber intake and BMD change may be different from other racial ethnic groups.

In conclusion, our data suggest that dietary total fiber and fiber from fruits may protect against bone loss at the hip in older men but not in older women. This protective association in men was modest even though the results reached statistical significance. As femoral neck BMD is the primary BMD measure to predict risk of hip fracture, findings from this study deserve further investigation to elucidate the mechanisms in microbiota composition induced by dietary fiber and sex hormone concentration in relation to bone health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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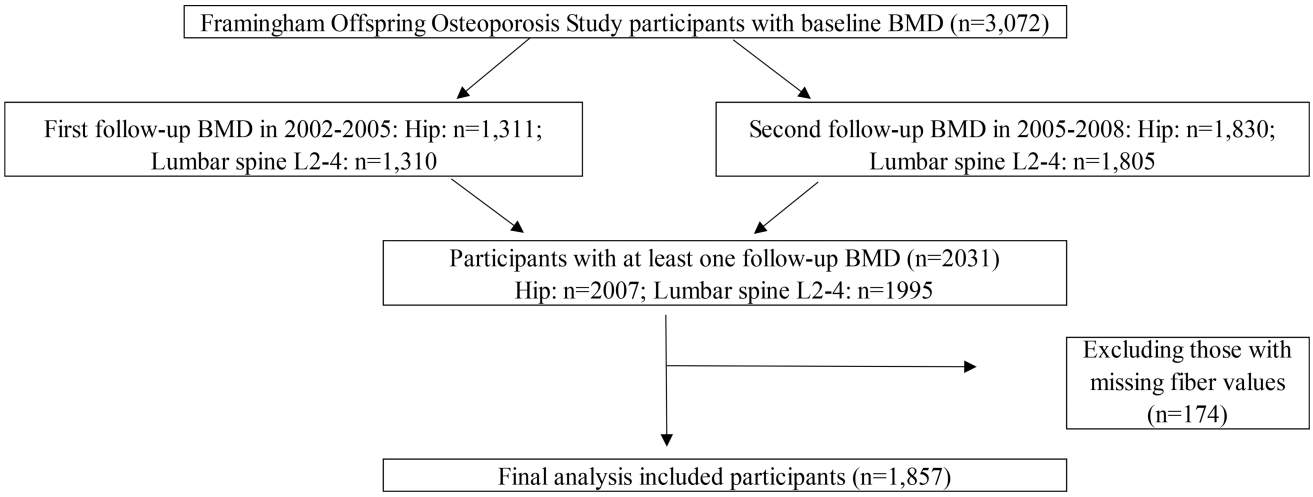

Figure 1.

Flow chart for the Framingham Offspring Study participants who were included in the analyses of dietary fiber and annualized percent change in bone mineral density (%ΔBMD) BMD, bone mineral density; Lumbar spine; LS2–4, location 2 to 4.

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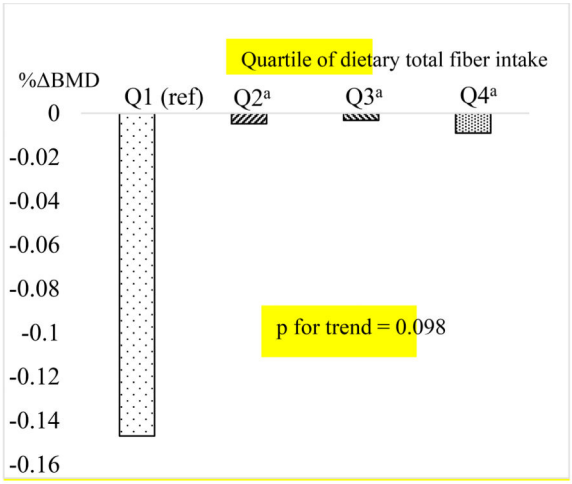
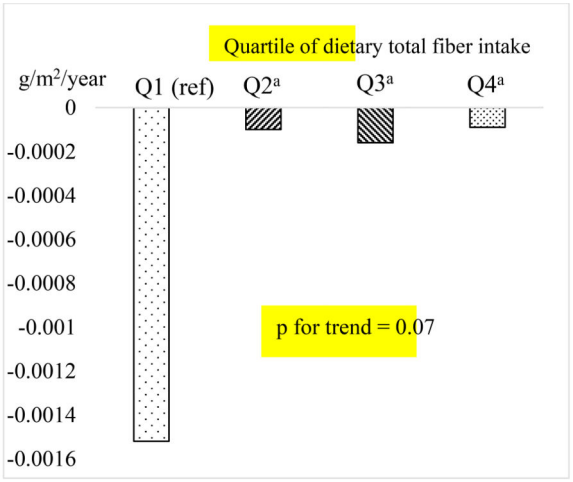


(a) Quartile of dietary total fiber intake in relation to annualized %ΔBMD



(b) Quartile of dietary total fiber intake in relation to bone loss (g/cm^2/year)

Figure 2.

Adjusted least square means of annualized percent change in bone mineral density (%ΔBMD)(Panel a) and annual rate of bone loss (g/cm^2/year, panel b) at the femoral neck by quartiles (Q1, ⬚; Q2, ▨; Q3, ▩; Q4, ▧) of dietary total fiber intake in men (n=792).

[a]indicates statistical significance when compared with Q1 (all $p<0.04$);

Models adjusted for total energy intake (kcal/day), age (year), BMI (kg/m^2), height (m), exam period for repeated measures, current cigarette smoking (yes, no), physical activity (PASE, continuous), modified DGAI 2010 score (continuous), calcium supplement intake (yes, no), vitamin D supplement intake (yes, no), caffeine intake (mg/day), dietary calcium (in quartiles, mg/day), and dietary vitamin D (in quartiles, I.U./day).

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J Bone Miner Res. Author manuscript; available in PMC 2018 June 06.

Table 1

Baseline characteristics of men and women by quartiles of dietary total fiber (g/d) at the baseline examination (1996–2001) in the Framingham Offspring Study.

	Men (n=792)				Women (n=1,065)			
Quartiles of dietary total fiber	Q1 (low)	Q2	Q3	Q4 (high)	Q1 (low)	Q2	Q3	Q4 (high)
N	198	198	198	198	266	266	267	266
Age (year)[1,*]	56.2 (8.9)	58.2 (8.2)	58.2 (9.0)	59.9 (9.0)	55.8 (9.3)	57.1 (8.4)	57.6 (8.9)	58.8 (9.0)
BMI (kg/m^2)[1]	28.9 (4.2)	28.6 (4.3)	28.7 (4.2)	28.1 (4.1)	27.6 (5.8)	27.1 (5.7)	27.0 (5.6)	27.0 (5.2)
Height (cm)[1]	175.7 (7.0)	174.6 (6.4)	174.9 (6.4)	175.6 (6.7)	161.4 (6.6)	161.9 (6.4)	161.5 (5.9)	161.5 (6.4)
Current smokers, n (%)[*]	29 (14.7)	22 (11.1)	13 (6.6)	8.0 (4.0)	48 (18.1)	14 (5.3)	15 (5.6)	12 (4.5)
Physical activity (PASE)[1]	166.6 (88.1)	171.3 (84.5)	160.3 (81.7)	152.4 (79.9)	135.1 (69.4)	138.5 (66.0)	149.0 (77.0)	142.8 (69.5)
Total energy intake (kcal)[2,*]	2029 (999)	1719 (773.7)	1817 (788)	2031 (688)	1825 (828)	1589 (763)	1610 (713)	1812 (664)
Dietary total fiber(g/d)[2,*]	13.4 (7.9)	15.8 (7.1)	19.9 (6.2)	27.3 (8.3)	13.6 (6.3)	15.5 (7.5)	19 (7.2)	26.1 (8.9)
Cereal fiber (g/d)[2,*]	4.9 (3.8)	5.4 (3.5)	6.9 (3.7)	8.5 (4.6)	5.1 (3.2)	5.2 (3.4)	6 (3.7)	7.4 (4.1)
Fruit fiber (g/d)[2,*]	1.4 (1.7)	2.3 (2.4)	3.8 (2.7)	5.4 (4.4)	1.7 (2.1)	2.5 (2.6)	3.7 (2.7)	5.6 (3.9)
Vegetable fiber (g/d)[2,*]	2.7 (2.1)	3.3 (2.1)	4.2 (2.1)	5.8 (3.7)	2.9 (1.9)	3.7 (2.1)	4.7 (2.5)	6.7 (3.3)
Nut and legume fiber (g/d)[2,]	1.7 (1.6)	1.9 (1.7)	2.2 (1.5)	3.0 (2.8)	1.3 (1.4)	1.7 (1.4)	2.1 (1.6)	2.7 (3.2)
Dietary vitamin D (IU/d)[2,*]	183 (195)	185 (135)	192 (122)	251 (180)	202(192)	189 (158)	202 (160)	253 (132
Vitamin D supplement use, n (%)	2 (1.0)	2 (1.0)	4 (2.0)	2 (1.0)	7 (2.6)	9 (3.4)	15 (5.6)	12 (4.5)
Dietary calcium (mg/d)[2,*]	652.4 (546.7)	625.8 (467.2)	670.5 (368.9)	806.5 (464.1)	677.5 (573.5)	644.2 (440.9)	669.9 (406)	804.9 (422.6)
Calcium supplement use, n (%)[‡]	9 (4.6)	5 (2.5)	10 (5.1)	14 (7.1)	70 (26.3)	80 (30.1)	111 (41.6)	111 (41.7)
Caffeine intake (units/d)[2,*]	347.6 (277.7)	343.6 (237.0)	221.7 (270.0)	158.4 (307.6)	251.6 (244.4)	183.7 (305.7)	167.8 (291.9)	165.0 (305.6)
Modified DGAI 2010 score[3,*]	50.1 (11.9)	53.5 (12.1)	58.3 (11.7)	63.1 (13.5)	54.3 (13.5)	59.9 (12.9)	63.2 (12.2)	68.3 (10.2)
Post-menopausal (yes), n (%)	-	-	-	-	184 (69.2)	197 (74.1)	202 (75.7)	211 (79.3)
Current estrogen use, n (%)	-	-	-	-	90 (33.8)	81 (30.5)	88 (33.0)	85 (32.0)

[1] Values for mean (standard deviation);

[2] Values for median (Interquartile range)

[*] Represents differences of characteristics among quartiles of total fiber intake within each gender are statistically significant at $p<0.05$

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‡Represents differences of characteristics among quartiles of total fiber intake within women only are statistically significant at p<0.05.

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Table 2

Association of dietary total fiber and its sub-types per 5 g/day increase with annualized percent change in BMD (%ΔBMD, g/cm^2)[1] in men (n=792) and women (n=1,065) in the Framingham Offspring Study

	%Δ Femoral neck BMD			%Δ Trochanter BMD			%Δ Lumbar spine 2–4 BMD		
	β[2]	SE	p	β	SE	p	β	SE	p
Dietary total fiber (g/d)									
Men									
Model 1[1]	0.04	0.02	0.02	0.04	0.02	0.03	0.02	0.02	0.31
Model 2[3]	0.04	0.02	0.02	0.04	0.02	0.02	0.018	0.02	0.36
Model 3[4]	0.06	0.02	0.003	0.04	0.02	0.08	−0.008	0.02	0.69
Women									
Model 1	0.011	0.02	0.48	0.004	0.02	0.83	0.03	0.02	0.02
Model 2	0.001	0.02	0.94	0.003	0.02	0.90	0.02	0.01	0.21
Model 3	0.009	0.02	0.58	−0.008	0.03	0.75	0.02	0.02	0.24
Cereal fiber (g/d)									
Men									
Model 1	0.02	0.03	0.44	0.02	0.03	0.63	−0.017	0.04	0.64
Model 2	0.02	0.03	0.47	0.01	0.03	0.71	−0.02	0.034	0.60
Model 3	0.04	0.03	0.22	0.02	0.03	0.56	−0.025	0.04	0.50
Women									
Model 1	0.02	0.03	0.40	0.04	0.04	0.29	−0.01	0.03	0.80
Model 2	0.01	0.03	0.63	0.03	0.04	0.41	−0.02	0.03	0.48
Model 3	0.01	0.03	0.66	0.01	0.04	0.79	−0.02	0.03	0.40
Fruit fiber (g/d)									
Men									
Model 1	0.09	0.03	0.007	0.07	0.04	0.09	0.10	0.04	0.01
Model 2	0.09	0.03	0.009	0.07	0.04	0.07	0.10	0.04	0.02
Model 3	0.10	0.04	0.008	0.04	0.04	0.31	0.07	0.04	0.10
Women									
Model 1	0.04	0.04	0.34	−0.01	0.06	0.83	0.09	0.04	0.04

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	%Δ Femoral neck BMD			%Δ Trochanter BMD			%Δ Lumbar spine 2–4 BMD		
	β[2]	SE	p	β	SE	p	β	SE	p
Model 2	0.01	0.04	0.78	−0.006	0.06	0.91	0.03	0.04	0.41
Model 3	0.02	0.05	0.67	−0.03	0.07	0.61	0.04	0.05	0.36
Vegetable fiber (g/d)									
Men									
Model 1	0.05	0.04	0.18	0.09	0.04	0.02	0.007	0.04	0.87
Model 2	0.05	0.04	0.16	0.10	0.04	0.01	0.008	0.04	0.84
Model 3	0.06	0.04	0.13	0.07	0.04	0.10	−0.057	0.04	0.16
Women									
Model 1	−0.0003	0.04	0.99	−0.006	0.05	0.90	0.13	0.04	0.002
Model 2	−0.01	0.04	0.79	−0.004	0.05	0.93	0.10	0.04	0.006
Model 3	0.01	0.04	0.76	−0.003	0.06	0.96	0.12	0.04	0.01
Nut and legume fiber (g/d)									
Men									
Model 1	−0.04	0.06	0.49	0.01	0.05	0.91	−0.055	0.06	0.33
Model 2	−0.04	0.06	0.51	0.02	0.05	0.65	−0.05	0.06	0.35
Model 3	−0.02	0.06	0.71	0.014	0.06	0.80	−0.085	0.06	0.15
Women									
Model 1	−0.0004	0.05	0.99	−0.06	0.07	0.42	0.0007	0.05	0.99
Model 2	−0.02	0.05	0.74	−0.07	0.07	0.31	−0.006	0.05	0.91
Model 3	0.03	0.05	0.58	−0.04	0.07	0.52	−0.007	0.05	0.90

[1]Percent change in BMD was measured from BMD at the baseline in 1996–2001 and the follow-up exams in 2002–2005 and 2005–2008.

[2]Based on exchangeable correlation matrix using Generalized Estimating Equations; SE, standard error; p, p value; β represent difference of %ΔBMDassociated with per 5 g/d increase in dietary fiber.

[3]Model 1 was unadjusted except exam period as part of the GEE model;

[4]Model 2 was further adjusted for total energy intake (kcal/day), age (year), BMI (kg/m^2), height (m);

[5]Model 3 was further adjusted for current cigarette smoking (yes/no), physical activity (PASE), modified DGAI 2010 excluding fiber component, calcium supplement intake (yes/no), vitamin D supplement intake (yes/no), caffeine intake (mg/d), dietary calcium (in quartiles, mg/d), dietary vitamin D (in quartiles, I.U./d), menopausal status (yes, no, in women only), and current estrogen use (yes, no, in women only).

J Bone Miner Res. Author manuscript; available in PMC 2018 June 06.