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Higher dairy food intake is associated with higher spine Quantitative Computed Tomography (QCT) bone measures in the Framingham Study for men but not women.

Laura H. van Dongen, MS[1], **Douglas P. Kiel, MD, MPH**[2], **Sabita S. Soedamah-Muthu, PhD**[3], **Mary L. Bouxsein, PhD**[4], **Marian T. Hannan, DSc, MPH**[2], **Shivani Sahni, PhD**[2]

[1]Division of Human Nutrition, Wageningen University and Research Centre, the Netherlands [2]Institute for Aging Research, Hebrew SeniorLife, Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA [3]Center of Research on Psychology in Somatic Diseases, Department of Medical and Clinical Psychology, Tilburg University, the Netherlands [4]Center for Advanced Orthopaedic Studies, Beth Israel Deaconess Medical Center, Department of Orthopedic Surgery, Harvard Medical School, Boston, MA

Abstract

Previous studies found that dairy foods were associated with higher areal bone mineral density (BMD). However, data on bone geometry or compartment specific bone density is lacking. In this cross-sectional study, the association of milk, yogurt, cheese, cream, milk+yogurt and milk+yogurt+cheese intakes with quantitative computed tomography (QCT) measures of bone were examined and we determined if associations were modified by serum vitamin D (25-OH D, tertiles) or age (<50 vs. ≥50yr). Participants were 1,522 men and 1,104 women [aged 32-81y, mean 50y (men); 55y (women)] from the Framingham Heart Study with measures of dairy food intake (servings/wk.) from a food frequency questionnaire, volumetric BMD (vBMD, integral and trabecular, g/cm^3), cross-sectional area (CSA, cm^2) and estimated vertebral compressive strength (VCS, N) and 25-OH D (radioimmuno-assay). Sex-specific multivariable linear regression was used to calculate the association of dairy food intake (energy adjusted) with each QCT measure adjusting for covariates Mean milk intake ±SD was 6±7 servings/week in both men and women. In men, higher intake of milk, milk+yogurt and milk+yogurt+cheese was associated with higher integral (P=0.001-0.006) and trabecular vBMD (P=0.006-0.057) and VCS (P=0.001-0.010). Further, a higher cheese intake was related with higher CSA (P=0.049). In these women with high dairy intake, no significant results were observed for the dairy foods, except for a positive association of cream intake with CSA (P=0.016). The associations appeared to be stronger in older men. Across both 25-OH D groups, dairy was positively associated with bone health. In summary, men with higher intakes of milk, milk+yogurt and milk+yogurt+cheese had higher trabecular and integral

Corresponding author: Shivani Sahni, PhD, Director, Nutrition Program, Associate Scientist, Institute for Aging Research, Hebrew SeniorLife, Assistant Professor of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, 1200 Centre Street, Boston, MA 02131, USA, Telephone number: +1 617 971 5382, Fax: 617-971-5339, ShivaniSahni@hsl.harvard.edu.
Authors' roles: SS, MTH and DPK designed the study; DPK and MLB collected part of the data; LHVD conducted the data analyses and drafted the manuscript. LHVD, SS, MTH, MLB and DPK conducted data interpretation. SS, SSM, MLB, MTH and DPK provided a critical review of the content. LHVD, SS, SSM, MLB, MTH and DPK read and approved the final manuscript. LHVD and SS take responsibility for the integrity of the data analysis.

vBMD and VCS, but not CSA. Dairy intake seems to be most beneficial for older men and dairy continued to have positive associations among all 25-OH D levels.

Keywords

QCT; dairy food; bone; vitamin D; older adults

Introduction

In the US more than 50% of the adults older than 50 years are estimated to have either osteoporosis or a low bone mass.(1) Postmenopausal women have a higher prevalence than older men, putting them at risk for fractures, loss of physical function, decreased quality of life and increased morbidity and mortality.(2) Dietary factors represent an important and growing area of interest for bone health, as these factors could be easily modified for optimum bone health. Dairy products, rich in bone-beneficial nutrients such as calcium, vitamin D, protein, magnesium and potassium, have been positively associated with dual energy X-ray absorptiometry (DXA) derived areal bone mineral density (aBMD).(3–9) Yet, few studies have directly compared specific types of dairy foods.(10, 11) even though not all dairy products have a similar effect on bone health.(12) Consequently, it is important to study the individual roles of dairy products on bone health. The majority of studies examining dairy intake and bone health have used aBMD, a surrogate for bone strength, which does not provide information on geometry or compartment specific bone density, key determinants of bone strength.(13) In contrast, three-dimensional quantitative computed tomography (QCT) can provide true volumetric measures of bone strength for specific compartments, not confounded by individual differences in bone size,(14) which enables us to address the associations of dairy intake with bone strength.

Vitamin D regulates calcium absorption and skeletal homeostasis, suggesting that both adequate levels of calcium and vitamin D are needed to ensure optimal absorption.(15) However, the effect of vitamin D on BMD remains unclear. A recent meta-analysis(16) and a randomized controlled trial (RCT),(17) showed no evidence of an overall benefit of vitamin D supplementation on aBMD, but there was a small but relevant effect on calcium absorption. Our recent study supported this by showing that higher intake of dairy foods was associated with higher aBMD and slower bone loss in vitamin D supplement users.(11) This suggests that the benefits of dairy intake might be dependent on vitamin D intake or status.

The aim of this cross-sectional study was to determine the relation of dairy food intake [milk, yogurt, cheese, cream, milk+yogurt and milk+yogurt+cheese in servings per week] with QCT volumetric measures of bone [vBMD (g/cm^3), integral and trabecular vBMD], cross-sectional area (CSA, cm^2) and vertebral compressive strength (VCS, N) at the L3 level of the spine in men and women from the Framingham Heart Study. Associations were further examined within sub-groups of age (<50 and ≥50 years) and 25-OH D levels (lowest tertile vs. the two highest tertiles). Our hypothesis was that intakes of all dairy foods, except cream, would be favourably associated with QCT-derived bone measures in men and women, and that these associations would be stronger in older adults and those with higher 25-OH D levels.

Methods

Participants and study design

The “Framingham Heart Study Offspring and Generation 3 QCT Study”, initiated in 2002, was designed to measure coronary, aortic and valvular calcification, as well as subcutaneous and visceral fat, to investigate their links with cardiovascular risk.(18) Members of the Offspring and Generation 3 cohorts include second-generation (and spouses) and third-generation offspring of the original Framingham Heart Study cohort initiated in 1948. Information on dietary intake was collected by a food frequency questionnaire (FFQ) in 1998-2001 (Offspring Cohort) and in 2002-2005 (Gen3 cohort). QCT assessment was performed in 2002-2005. Inclusion criteria was men aged >35 years, women aged >40 years, weight <160 kg, and a negative pregnancy test for pre-menopausal women. Of the 3,529 participants enrolled in the QCT study, participants were excluded due to missing CT scans at spinal level L3 (n=186), missing or invalid FFQ [energy intake <2.51 or >16.74 MJ (<600 or >4,000 kcal/d)] (n=318) or missing covariates: body mass index (BMI, n=4), smoking (n=1), calcium supplement use (n=53) and for women, estrogen use (n=341). The final analytic sample of this cross-sectional study was 2,626 (1,522 men and 1,104 women) including 1,205 participants from the Offspring Cohort and 1,421 participants from the Gen3 Cohort. This study was approved by the Institutional Review Board at the Institute for Aging Research, Hebrew SeniorLife.

Bone measurements

Volumetric computed tomography scans were obtained using an 8-slice multi-detector CT scanner (Lightspeed Ultra, General Electric Medical Systems, Milwaukee, WI, USA) in 2002-2005.(14) Cross-sectional area (CSA) of the L3 vertebral bodies was assessed at the mid-vertebral body in cm^2. Analysis of the images was performed using previously described custom software.(19) QCT images were used to assess vBMD at L3 as 98% of the subjects have measures for this vertebral level. Integral vBMD included the entire vertebral body (both cortical and trabecular compartments), but excluded the transverse and posterior processes. The volume of interest for trabecular vBMD measurements was an elliptical region encompassing the anterior vertebral body, centered at the mid-vertebral level and including 70% of the volume between vertebral endplates. Integral and trabecular vBMD (g/cm^3) were measured using previously published methods.(14, 20) Vertebral compressive strength (N, VCS) is estimated using engineering beam theory(21) and calculated as $0.0068 \times E_{ave} \times$cross-sectional area. E_{ave} is the average elastic modulus in megapascals, derived from vBMD using a previously published, empirically derived relationship between QCT vBMD and the elastic modulus of vertebral trabecular bone.(22)

Dietary assessment

Usual dietary intake over the past year was assessed with a semi-quantitative 126-item Willett FFQ,(23) which has been validated against multiple diet records and blood measures for many nutrients(24, 25) Participants received the questionnaires via email prior to their scheduled clinical visit and they were asked to bring them to the next examination, where they were reviewed by the clinical staff. The FFQ included questions on frequency with a standard serving size and 9 categories ranging from never or <1 serving/mo. to >6 servings/d. Dairy intake (servings per week), total calcium intake (mg/d), multivitamin/calcium/vitamin D supplement use (yes/no) were assessed using the food list section of the FFQ. The serving size for each dairy food is as follows: skim/low fat/whole milk (8 oz. glass), ice milk (1/2 cup), cottage or ricotta cheese (1/2 cup), other cheese (1 slice or 1 oz. serving), cream (1 tbsp.), sour cream (1 tbsp.), ice cream (1/2 cup), cream cheese (1 oz.), and yogurt (1 cup).

Milk intake was calculated as the sum of intake of skim milk, low fat milk, whole milk, and ice milk. Cheese intake was calculated as the sum of intake of cottage/ricotta cheese and other cheeses (including cheeses from mixed dishes such as pizza or lasagna). Cream intake was calculated as the sum of intake of cream, sour cream, ice cream, and cream cheese. Yogurt intake was estimated in servings per week. A variable for milk+yogurt was created which is calculated as the sum of milk and yogurt intake in servings per week and a variable for milk+yogurt+cheese intake was created, which included intake of milk, yogurt, and cheese in servings per week. These combination variables were created to examine the fluid dairy products (milk+yogurt) and the dairy products with a potential beneficial association (milk+yogurt+cheese).

Covariates

Data on age (years), sex, height (m), weight (kg), physical activity, smoking (current/non-current), total energy (kcal/d), alcohol (g/d), multivitamin/calcium/vitamin D supplement use (yes/no), other dietary factors and for women only menopause status (yes/no) and estrogen use (yes/no) were measured at the baseline examination (1998-2001 for Offspring and 2002-2005 for Gen3). Serum 25-OH D was determined from fasting blood samples after overnight fasting in ng/ml. Total energy (kcal/d), fruit/vegetable intake (serv./wk.), multivitamin/calcium/vitamin D supplement use (yes/no), dietary vitamin D (IU/d), alcohol intake (g/d) and cola beverages (serv./wk.), were assessed using the FFQ's food-list section.

Height was measured while participants were shoeless; weight was measured with a standardized balance-beam scale. BMI is calculated from weight and height in kg/m^2. Physical activity was measured with the Physical Activity Index (PAI) (26) for the Offspring cohort and the Physical Activity Scale for the Elderly (PASE) (27) in Gen3. Z-scores for physical activity were calculated separately for each cohort before analyses. Information on smoking (current cigarette smoker vs. former or never smoker), current estrogen users vs. never or former users and menopause status (cessation of menses for at least 1 year) was determined by a questionnaire. 25-OH D was determined by radioimmunoassay (DiaDorin, Stillwater, Minn) in both the cohorts. All samples were run in duplicate and the values averaged. Total (intra-assay and inter-assay) coefficients of variation for control values of 14.4 and 54.7 ng/mL were 8.5% and 13.2% respectively.(28, 29)

Statistical analysis

For this study we combined the data from the Offspring and Gen3 cohorts and performed analyses by sex. The primary exposure variables were milk, yogurt, cheese, cream, milk +yogurt and milk+yogurt+cheese intake. Cream was non-normally distributed and therefore logarithmic transformation was applied to cream intake prior to analyses. T-tests were used to calculate differences in means between men and women while chi-square test was used for categorical variables. Dairy food variables were adjusted for total energy intake by the residual method (30) and modeled as continuous variables (in servings per week) and in quartile categories, except for yogurt which was categorized using the energy-adjusted values as low (0-0.4 servings/wk., raw mean=0), medium (>0.4-3.3 servings/wk., raw mean=0.5) or high intake (>3.3 servings/wk., raw mean=3). Multivariable linear regression was used to calculate regression coefficients (β) estimating the difference in bone measures associated with a 1-unit increase in dairy intake per week. In the categorical analyses, we estimated least squares adjusted means of each bone variable across quartiles or categories of each dairy food variable. Test for trends was conducted using the median measure for each category.

Sub-group analyses

To test for the effect modification by 25-OH D, we examined the interaction between 25-OH D and each dairy food variable in separate models. If the interaction term was significant at P<0.05 then stratification by 25-OH D was performed. We wanted to use predefined clinical cut-offs for 25-OH D (<20 ng/ml and ≥20 ng/ml), but due to small sample size in the low 25-OH D group, we decided to use cut-offs based on tertiles (lowest tertile vs. higher two tertiles).(31) Similarly, interaction by age was tested and associations were then examined in subgroups of age (<50 and ≥50y).

Initially, crude linear regression models were examined. Subsequent models were adjusted for age, BMI, height and energy intake. Height was not included in the analyses for CSA. These models were further adjusted for current smoking, calcium and vitamin D supplement use. To determine the best model, following covariates were also considered: fruit, vegetables, physical activity, multivitamin supplement use, cola, alcohol and in women menopause status and estrogen use. These covariates were added one at a time and if any covariate changed the β coefficients by >10%, it was included in the final parsimonious model. In a previous study, cola beverages were found to be associated with low BMD (32) this could be due to the displacement of milk in the diet by carbonated beverages.(33) Therefore, we examined whether cola could be a potential confounder. Of the variables tested, only estrogen use (in women alone) and multivitamin supplement use were included in the final parsimonious model. In the sub-group analyses by 25-OH D, models were not adjusted for vitamin D supplement use, but models were adjusted for season in which blood was drawn for 25-OH D measurement.

All analyses were performed using statistical software program SAS (version 9.4, SAS Institute Inc.). Two-sided P values of 0.05 were considered statistically significant.

Results

The mean age was 50 years (SD 10.6; range 32-80) for men and 55 years (SD of 9.2; range 36-81) for women (Table 1). Sixty-four percent of the men and 70% of the women reached the recommendation of 3 servings of dairy per day. Thirty-three percent of men and 48% of women did not have adequate blood levels of 25-OH D (20 ng/ml) and 68% of men and 51% women did not achieve recommended dietary allowance (RDA) of calcium intake for their age and gender-group. On average men drank more alcohol and cola beverages, consumed more cheese and cream and had higher bone measures (Table 1, P-range <0.0001-0.001). Women were more frequent users of calcium, multivitamin and vitamin D supplements, current smokers and they consumed more yogurt, fruits and vegetables (P <0.0001). Ninety nine percent of the women were post-menopausal of which 27% were current estrogen users.

Association of dairy food intake and bone measures

In the multivariate-adjusted models, dairy intake (serv./wk.), when analyzed on a continuous scale, was associated with multiple bone measures in men. Integral vBMD, trabecular vBMD and VCS were positively associated with higher intake of milk (P range: 0.006-0.057), milk+yogurt (P range: 0.006-0.041) and milk+yogurt+cheese (P=0.001-0.006) in men (Table 2). No significant association was seen for yogurt, cheese and cream with integral vBMD, trabecular vBMD or VCS (P-range: 0.06-0.61). A higher cheese intake was positively associated with CSA (P=0.049). However, other dairy intakes were not significantly associated with CSA (P-range 0.13-0.96). In women, no significant associations were seen for dairy intake with bone health, except a higher cream intake was positively associated with CSA in women (P=0.016). Similar results were observed for the analyses with dairy as a categorical variable, however the associations were attenuated (supplemental tables 1–2).

Sub-group analyses

Interaction with serum 25-OH D: Significant interactions were observed for serum 25-OH D and milk, milk+yogurt and milk+yogurt+cheese in men for trabecular vBMD (P range: 0.02-0.007), integral vBMD (P range: 0.001-0.004) and VCS (P=0.003 each). No interaction was observed for 25-OH D and dairy intake in women (P-range 0.14-0.97). Consequently, the analyses in men were stratified by 25-OH D [lowest tertile (≤24.2 ng/ml) vs. higher two tertiles (>24.2 ng/ml)]. Men in the lowest tertile of 25-OH D were older, current smokers and had lower dairy food intake and calcium intake (mean±SD: age: 53±11y, 7% current smokers, milk+yogurt+cheese intake: 9.1±7.4 servings/wk. and calcium intake: 840±406 mg/d) compared to those with 25-OH D >24.2 ng/ml (mean±SD: age: 45±8y, 0.5% current smokers, milk+yogurt+cheese intake: 10.6±9.0 servings/wk. and calcium intake: 939±459 mg/d).

Milk, milk+yogurt and milk+yogurt+cheese was positively associated with higher integral vBMD (P=0.01, 0.01 and 0.01 respectively, Table 3), trabecular vBMD (P=0.04, 0.03 and 0.02 respectively) and VCS (P=0.01, 0.02 and 0.004 respectively) in men with serum 25-OH D> 24.2ng/dl. In men with low 25-OH D, a higher dairy intake showed larger magnitude of association for some but not all bone health measures as compared to men with a higher 25-OH D level.

Interaction by age: In men, statistically significant interactions were observed for age and cream intake (integral BMD, P=0.015 and VCS, P=0.03). Stratification by age 50 years (Supplemental table 3) showed slightly stronger associations between bone health measures and dairy intake in men aged 50 or older as compared to the younger population of men. In women there was a significant interaction between age, cheese intake and VCS (P=0.04); the same was true for cream (P=0.008). In women, younger than age 50 years, higher intakes of yogurt were associated with lower integral BMD (P=0.033), trabecular BMD (P=0.034) and VCS (P=0.013).

Discussion

In this cross-sectional study of 2,626 participants, higher intakes of milk, milk+yogurt and milk+yogurt+cheese were associated with higher trabecular and integral vBMD, and VCS in men, but not in women. Further, men with 25-OH D ≤24.2ng/dl showed stronger positive associations for some of the dairy variables. However, even among menwith 25-OH D>24.2 ng/dl, dairy continued to have positive associations for milk, milk+yogurt and milk+yogurt +cheese and vBMD and VCS. Also these associations were stronger in men aged ≥50y compared to younger men. No interaction with serum 25-OH D was observed for women. In younger women, higher yogurt intakes were associated with lower vBMD and VCS.

Previously the skeletal effects of dairy foods have mostly been studied using DXA-derived bone measures.(5–7, 10, 11, 34–37) The majority of these studies focused only on milk intake. A recent cross-sectional study (7) showed that a higher dairy intake was associated with a greater hip aBMD in men ≥60 y, but not in women. In the Framingham Offspring Study,(10) milk was associated with hip but not spine aBMD in men and women (mean age: 55y). However, no association was observed between dairy food intakes with either femur or spine aBMD in older men and women (aged 67-93) from the Framingham Original cohort. (11) While higher dairy protein intake has been linked with higher failure load and stiffness at the distal radius and tibia in a cross-sectional study of older women (38) to date, only one study (9) directly examined dairy food intake (defined as sum of milk, yogurt and cheese products) in context of pQCT bone measures at the distal tibia in women (aged 70–85) from the Calcium Intake Fracture Outcome Study/CAIFOS Aged Extension Study (CAIFOS/CARES) cohort.(9) This study reported that a dairy intake of ≥2.2 servings/d was associated with higher total and trabecular vBMD as compared to women with an intake of ≤1.5 servings/d. Similarly, in previous studies on women, dairy food intakes have been found to be beneficial for bone health particularly among those with low dairy and or calcium intakes. (39, 40) The main findings of the current study showed that milk and a combination of dairy products were associated with trabecular and integral vBMD in the spine in men, but not in women. This discrepancy in outcome could be explained by the different age range of the study population or the use of a different bone site. Furthermore, 70% of women in the current study had dairy food intake (milk+yogurt+cheese) ≥3servings/d while in the CAIFOS/CARES cohort only 8.7% of women had dairy food intake of ≥3servings/d. Overall, women in the current study seem to consume more dairy, are younger, use more calcium supplements and have higher total calcium intake than women in the CAIFOS/CARES cohort, which could explain lack of association in these women who may be calcium replete.

Fermented milk products may have advantages for the gut microbiota (41), however the effects on bone health are unclear. Few epidemiologic studies have examined yogurt and cheese in relation to bone health. Nevertheless, in previous studies in older adults from the Framingham Study higher yogurt intake was associated with higher aBMD,(10) but cheese was not.(10, 11) The current study showed negative associations with yogurt on several bone measures in women aged ≤50y. However, the associations between yogurt or cheese and vBMD were not significant. The reason for these negative patterns of association are unclear. Cream was previously reported to have a negative effect on aBMD due to its low nutrient density,(12, 42) but surprisingly the proposed negative associations were not observed in the current study.

Additionally, our study found that men with 25-OH D ≤24.2 ng/ml had stronger associations though they did not reach statistical. Men with 25-OH D >24.2 ng/dl also showed positive associations for dairy intake with integral and trabecular vBMD though effect estimates were smaller than the low vitamin D group. This might be explained by our observation of an interaction with age, where associations were stronger in older men. Men with low vitamin D status tended to be older and had other risk factors for osteoporosis such as low physical activity, current smoking and lower intakes of calcium and vitamin D. This particularly vulnerable group could have therefore shown stronger associations with higher dairy intakes. Our previous work in older adults also showed that in an older population with a higher vitamin D intake, through supplements, specific dairy foods were protective against bone loss.(11) Overall, these results suggest that vitamin D provides substantial beneficial effects for BMD and supplementation in this population might have potential beneficial effects. Currently it is believed that serum 25-OH D levels ≥20 ng/ml are adequate to prevent loss of bone mass in the healthy elderly population.(43) Vitamin D is involved in calcium homeostasis and absorption. Calcium in bone has two main purposes: skeletal strength and dynamic storage for the maintenance of intra- and extracellular calcium pools. The calcium balance is predominantly determined by dietary calcium intake. A decrease of serum calcium results in an increase of 1,25-dihydroxyvitamin D which acts on the vitamin D receptor in the gut, increasing calcium absorption and resorption in the bone.(43) Dairy foods are good sources of dietary calcium, vitamin D and many other bone-beneficial nutrients essential to achieve peak bone mass during skeletal growth and to prevent bone loss in elderly.(39–41, 44–46)

Strengths of the current study includes use of a population-based cohort with data on specific types of dairy foods and supplement use. Measurements of serum 25-OH D were available, which made it possible to examine effect modification by 25-OH D status. 25-OH D is a better measure for vitamin D status than measures from dietary records since it also accounts for the vitamin D formation due to sun exposure. This study examines the association between dairy intake and QCT-derived bone measures, which provide volumetric measures of bone density and estimated strength that are not confounded by individual differences in bone size or body composition. Lastly, this study describes sex specific differences in volumetric spine indices in context of dairy foods. However, this study has potential limitations. Our study population contained primarily white men and women, which may limit generalizability. Mis-specification of dietary intake might have occurred due to the use of a semi-quantitative FFQ and for 46% of the participants, the FFQ data was collected ~4 years prior to the QCT assessment. However, we checked whether participants' intake changed between FFQ measurements, which was not the case. Residual confounding may have occurred despite our attempts to control for possible confounding factors. Moreover, the cross-sectional nature of this study cannot infer causality.

In conclusion, the results suggest that a higher milk, milk+yogurt and milk+yogurt+ cheese intake are associated with higher vBMD and estimated vertebral strength in men. The associations appeared to be stronger in older men and dairy continued to have positive associations among all 25-OH levels though future studies with larger sample sizes should be conducted to confirm these sub-group findings. Future studies should also consider nutrient profiles of specific dairy groups and serum vitamin D concentrations whilst researching the association with bone health. Moreover, more research is needed to better understand the sex specific differences.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline characteristics of the men and women in the dairy foods and QCT sample from the Framingham Study.

Descriptive variables	Men (n=1,522)	Women (n=1,104)	P-value
Age, y	50.0 ± 10.6[a]	55.3 ± 9.2	<0.0001
BMI, kg/m^2	28.4 ± 4.5	27.3 ± 5.7	<0.0001
Height, m	1.8 ± 0.07	1.6 ± 0.06	<0.0001
Serum 25-OH D[b], ng/ml	31.8 ± 14.3	29.9 ± 15.1	0.004
Physical activity, z-score	0.210 ± 1.03	−0.189 ± 0.872	<0.0001
Current smokers, n (%)	438 (28.8)	364 (33.0)	0.0004
Calcium supplement user, n (%)	100 (6.6)	584 (52.9)	<0.0001
Multivitamin supplement user, n (%)	625 (41.3)	644 (59.0)	<0.0001
Vitamin D supplement user, n (%)	19 (1.3)	70 (6.3)	<0.0001
Dairy intake (servings/week)			
Milk	5.9 ± 7.1	5.9 ± 6.8	0.23
Yogurt	0.79 ± 1.8	1.4 ± 2.4	<0.0001
Cheese	4.0 ± 4.4	3.3 ± 3.3	<0.0001
Cream	5.6 ± 7.1	4.7 ± 6.9	0.001
Milk+yogurt	6.7 ± 7.4	7.4 ± 7.3	0.022
Milk+yogurt+cheese	10.7 ± 8.7	10.7 ± 8.1	1.00
Other dietary intakes			
Energy, kcal/d	2,117 ± 691	1,779 ± 555	<0.0001
Alcohol, gm	14.8 ± 17.9	6.8 ± 10.3	<0.0001
Cola, servings/wk.	7.8 ± 3.8	6.7 ± 3.3	<0.0001
Fruit, servings/wk.	1.2 ± 2.4	1.6 ± 2.6	<0.0001
Vegetable, servings/wk.	4.8 ± 4.2	6.0 ± 4.6	<0.0001
Total calcium, mg	905 ± 452	1202 ± 599	<0.0001
Dietary calcium, mg	764 ± 373	757 ± 363	0.60
Total vitamin D, IU/d	377 ± 289	453 ± 304	<0.0001
Dietary vitamin D, IU/d	200 ± 122	204 ± 123	0.41
Bone health measures			
Trabecular vBMD, g/cm^3	0.146 ± 0.04	0.127 ± 0.04	<0.0001
Integral vBMD[c], g/cm^3	0.191 ± 0.04	0.174 ± 0.04	<0.0001
Cross sectional area[c], cm^2	12.40 ± 1.21	10.23 ± 1.37	<0.0001
Vertebral compressive strength[c], N	4,915 ± 1,108	3,678 ± 1,114	<0.0001
Current estrogen users, n (%)	-	295 (26.7)	-
Postmenopausal, n (%)	-	1,089 (98.9)	-

[a] Mean ± SD for all such values.

[b] Serum vitamin D, n=1,286 in men and 791 in women.

[c] n = 1,513 in men and 1,094 in women for integral vBMD, cross-sectional area and vertebral compressive strength.

Table 2

Multivariable adjusted association between bone measures and dairy intake[a] separately for men and women from the Framingham Study.

	Men[b] (n=1,522)		**Women[b,c] (n=1,104)**	
	β ± SE	**P**	**β ± SE**	**P**
Cross-sectional area				
Milk	0.00247 ± 0.0044	0.58	0.00211 ± 0.0063	0.74
Yogurt	0.00093 ± 0.0178	0.96	−0.02939 ± 0.0182	0.11
Cheese	0.01444 ± 0.0073	**0.049**	0.02296 ± 0.0132	0.083
Cream	−0.00538 ± 0.0270	0.84	0.10023 ± 0.0417	**0.016**
Milk+yogurt	0.00231 ± 0.0042	0.58	−0.00127 ± 0.0060	0.83
Milk+yogurt+cheese	0.00571 ± 0.0038	0.13	0.00309 ± 0.0057	0.59
Integral vBMD[d]				
Milk	0.00035 ± 0.0001	**0.006**	0.00013 ± 0.0002	0.42
Yogurt	0.00031 ± 0.0005	0.55	−0.00005 ± 0.0005	0.91
Cheese	0.00031 ± 0.0002	0.14	0.00017 ± 0.0003	0.61
Cream	0.00126 ± 0.0008	0.10	−0.00110 ± 0.0010	0.29
Milk+yogurt	0.00033 ± 0.0001	**0.006**	0.00011 ± 0.0001	0.47
Milk+yogurt+cheese	0.00035 ± 0.0001	**0.001**	0.00013 ± 0.0001	0.37
Trabecular vBMD[d]				
Milk	0.00025 ± 0.0001	0.057	0.00010 ± 0.0002	0.54
Yogurt	0.00051 ± 0.0005	0.34	−0.00020 ± 0.0005	0.66
Cheese	0.00038 ± 0.0002	0.080	0.00030 ± 0.0003	0.37
Cream	0.00110 ± 0.0008	0.17	−0.00043 ± 0.0011	0.68
Milk+yogurt	0.00026 ± 0.0001	**0.041**	0.00007 ± 0.0002	0.67
Milk+yogurt+cheese	0.00031 ± 0.0001	**0.006**	0.00011 ± 0.0001	0.43
Vertebral compressive strength[d]				
Milk	9.9036 ± 3.8441	**0.010**	2.9679 ± 4.2463	0.48
Yogurt	7.9613 ± 15.454	0.61	−12.078 ± 12.273	0.33
Cheese	11.866 ± 6.3875	0.063	9.0436 ± 8.9174	0.31
Cream	32.256 ± 23.496	0.17	14.179 ± 28.129	0.61
Milk+yogurt	9.5032 ± 3.6744	**0.010**	1.3926 ± 4.0499	0.73
Milk+yogurt+cheese	10.823 ± 3.2928	**0.001**	2.9131 ± 3.8250	0.45

[a]Dairy food intakes were energy-adjusted residuals added to a constant, where the constant equaled the dairy food intake for the mean energy intake of the study population.

[b]The models were adjusted for age, BMI, energy intake, current smoking status, calcium supplement use and vitamin D supplement use. n = 1,513 for men and n = 1,094 for women at integral vBMD, cross-sectional area and vertebral compressive strength.

[c]Additional adjustment for estrogen use.

[d]Additional adjustment for height.

Table 3

Multivariable adjusted associations between bone health and dairy intake[a] in men from the Framingham Study stratified by serum vitamin D.

	Tertile 1[b] (n=438) 25-OH D ≤24.2 ng/ml, range (4.6–24.2 ng/ml)		Tertile 2+3[c] (n=877) 25-OH D >24.2 ng/ml, range (24.3–98.1 ng/ml)	
	β ± SE[d]	**P value**	**β ± SE[d]**	**P value**
Cross-sectional area				
Milk	0.00978 ± 0.0095	0.30	0.00312 ± 0.0053	0.56
Yogurt	0.01477 ± 0.0372	0.69	0.00207 ± 0.0211	0.92
Cheese	−0.00565 ± 0.0145	0.70	0.01465 ± 0.0092	0.11
Cream	−0.03735 ± 0.0518	0.47	−0.00361 ± 0.0349	0.92
Milk+yogurt	0.00963 ± 0.0090	0.29	0.00299 ± 0.0051	0.56
Milk+yogurt+cheese	0.00561 ± 0.0078	0.47	0.00615 ± 0.0046	0.18
Integral vBMD[e]				
Milk	0.00051 ± 0.0003	0.08	0.00041 ± 0.0002	**0.01**
Yogurt	0.00138 ± 0.0011	0.23	0.00015 ± 0.0006	0.80
Cheese	0.00058 ± 0.0004	0.19	0.00016 ± 0.0003	0.53
Cream	0.00051 ± 0.0016	0.75	0.00054 ± 0.0010	0.58
Milk+yogurt	0.00053 ± 0.0003	0.05	0.00038 ± 0.0001	**0.010**
Milk+yogurt+cheese	0.00057 ± 0.0002	**0.02**	0.00035 ± 0.0001	**0.010**
Trabecular vBMD[e]				
Milk	0.00014 ± 0.0003	0.64	0.00033 ± 0.0002	**0.04**
Yogurt	0.00127 ± 0.0012	0.29	0.00048 ± 0.0006	0.45
Cheese	0.00056 ± 0.0005	0.23	0.00024 ± 0.0003	0.38
Cream	0.00105 ± 0.0017	0.53	0.00048 ± 0.0010	0.64
Milk+yogurt	0.00020 ± 0.0003	0.49	0.00033 ± 0.0002	**0.03**
Milk+yogurt+cheese	0.00032 ± 0.0003	0.21	0.00033 ± 0.0001	**0.02**
Vertebral compressive strength[e]				
Milk	17.7048 ± 9.0247	0.05	11.38217±4.4988	**0.01**
Yogurt	54.3821 ± 35.372	0.12	0.0028 ± 17.903	1.00
Cheese	11.6446 ± 13.754	0.4	10.1285 ± 7.7917	0.19
Cream	−6.03725 ± 49.340	0.90	21.8920 ± 29.634	0.46
Milk+yogurt	19.0158 ± 8.5232	**0.03**	10.4597 ± 4.3140	**0.02**
Milk+yogurt+cheese	17.7456 ± 7.3938	**0.02**	11.1490 ± 3.9036	**0.004**

[a] Dairy food intakes were energy-adjusted residuals added to a constant, where the constant equaled the dairy food intake for the mean energy intake of the study population.

[b] Mean 17.9 and range 4.6-24.2

[c] Mean 39.0 and range 24.3-98.1

[d] Models were adjusted for age, BMI, energy intake, current smoking status, calcium supplement use and season of blood withdrawal.

[e]Additional adjustment for height.

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