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Milk and Other Dairy Foods and Risk of Hip Fracture in Men and Women

Diane Feskanich[1], **Haakon E. Meyer**[2,3], **Teresa T. Fung**[4], **Heike A. Bischoff-Ferrari**[5], **Walter C. Willett**[1,6]

[1]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA [2]Department of Community Medicine and Global Health, University of Oslo, Norway [3]Norwegian Institute of Public Health [4]Department of Nutrition, Simmons College, Boston, MA, USA [5]Department of Geriatrics and Aging Research, University Hospital and University of Zurich, Switzerland [6]Departments of Nutrition and Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA

Abstract

Purpose—To examine whether higher milk and dairy food consumption are associated with risk of hip fracture in older adults following a report of an increased risk for milk in Swedish women

Methods—In two U.S. cohorts, 80600 postmenopausal women and 43306 men over 50 years of age were followed for up to 32 years. Cox proportional hazards models were used to calculate the relative risks (RR) of hip fracture per daily serving of milk (240 mL) and other dairy foods that were assessed every four years, controlling for other dietary intakes, BMI, height, smoking, activity, medications and disease diagnoses.

Results—2138 incident hip fractures were identified in women and 694 in men. Each serving of milk per day was associated with a significant 8% lower risk of hip fracture in men and women combined (RR=0.92, 95% confidence interval (CI) 0.87 to 0.97). A suggestive inverse association was found for cheese in women only (RR=0.91, CI 0.81 to 1.02). Yogurt consumption was low and not associated with risk. Total dairy food intake, of which milk contributed about half, was associated with a significant 6% lower risk of hip fracture per daily serving in men and women (RR=0.94, CI 0.90 to 0.98). Calcium, vitamin D and protein from non-dairy sources did not modify the association between milk and hip fracture, nor was it explained by contributions of these nutrients from milk.

Conclusions—In this group of older U.S. adults, higher milk consumption was associated with a lower risk of hip fracture.

Corresponding author: Dr. Diane Feskanich, 181 Longwood Drive, Boston, MA 02115, diane.feskanich@channing.harvard.edu telephone: (386) 872-6541.

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Haakon E. Meyer – no conflicts of interest

Teresa T. Fung – no conflicts of interest

Heike A. Bischoff-Ferrari – no conflicts of interest

Walter C. Willett – no conflicts of interest

Mini Abstract

The role of dairy foods for hip fracture prevention remains controversial. In this study among U.S. men and women, a glass of milk per day was associated with an 8% lower risk of hip fracture. This contrasts with a reported increased risk with higher milk intake in Swedish women.

Keywords

milk; dairy; hip fracture; cohort; men; women

INTRODUCTION

Hip fractures are a serious consequence of low bone density as they require costly surgery and long stays in a rehabilitation facility and subsequently increase risk of death, particularly for men [1]. The number of adults in the U.S. with low bone density at the femoral neck was estimated to be about 39 million in 2010 [2] and the count will climb as the elderly population grows. To protect aging bone, the 2015 Dietary Guidelines for Americans recommends that adults consume 2 to 3 cups of milk or equivalent dairy foods per day [3], whereas actual consumption among adults 50–71 years of age is 1.4 per day in women and 1.7 in men [3].

Milk is a likely food for maintaining bone health as it is a significant source of calcium and protein and also supplies vitamin D due to fortification in the U.S. However, the benefit of milk consumption for the prevention of hip fractures has not been established and it is unclear to what extent other dairy foods may or may not lower fracture risk. In 2005, a meta-analysis of data from six cohorts found a non-significant 17% increase in risk of hip fracture for men and women consuming less than one glass of milk per day compared with all others [4], whereas a 2010 meta-analysis of data with six additional cohort studies reported no overall association between milk and hip fractures [5]. In both analyses, a benefit from milk appeared to be stronger for men, though the results were too imprecise to draw a conclusion due to the much smaller number of male participants and fractures. More recently, a non-significant 40% lower risk of hip fracture was reported in elderly men and women in the Framingham Original Cohort who consumed more than one serving of milk per week compared with those with lower intakes [6]. On the other hand, in two large Swedish cohorts, women had a significant 9% greater risk of hip fracture for every glass of milk consumed per day whereas no association was observed men [7].

To compare with these results from the Swedish study and to address the relative lack of data in men, we examined long-term consumption of milk and other dairy foods and risk of hip fracture in two large U.S. cohorts, the Nurses' Health Study (NHS) of women and the Health Professionals Follow-up Study (HPFS) of men. We previously reported no significant associations between milk consumption and hip fractures in these cohorts [8–10], though statistical power was low. In this investigation with additional years of follow-up and hip fracture cases, we expanded analyses to explore whether a benefit from dairy foods may vary by sex, age, timing of dairy food consumption in relation to fracture occurrence, or other dietary intakes in order to determine whether differences in these factors between

previous studies could help to explain differences in results. Our hypothesis was that milk would be protective against hip fracture when assessed as a long-term measure and may be limited to those with lower intakes of calcium, vitamin D and protein from non-dairy sources if these nutrient contributions from milk were responsible for the protective effect.

METHODS

Study Population

The NHS began in June of 1976 when 121,700 female registered nurses, 30 to 55 years of age, responded to a mailed questionnaire. The HPFS was formed ten years later in January of 1986 with 51,529 male health professionals who were 40 to 75 years of age. On the initial questionnaires, participants provided a medical history and information on lifestyle and disease risk factors. Follow-up questionnaires have been mailed every two years to update individual characteristics and to identify incident diagnoses. Dietary intake was first assessed in 1980 in NHS and at 1986 baseline in HPFS. Deaths were ascertained from family members and the postal service and confirmed through the National Death Index [11,12].

This longitudinal analysis included follow-up from the initial cohort dietary assessment through 2012. Women did not enter into analysis until they reached menopause, and for consistency, men did not enter until they reached 50 years of age. Participants were excluded at entry if they reported a prior hip fracture (144 women; 15 men) or a diagnosis of osteoporosis (2,933 women; 186 men) or were African American or Asian (3,630 women; 1,405 men). In our primary analyses using long-term dietary measures, participants were also excluded if they did not respond to the dietary questionnaire at entry (27,315 women; 4,831 men). A total of 80,600 women and 43,306 men contributed to this analysis. Follow-up rates for these study populations were more than 90% over the time period of this analysis. This investigation was approved by the Institutional Review Board at Brigham and Women’s Hospital in Boston, MA.

Hip Fractures

On every biennial questionnaire, participants were asked to report any hip fracture with the date of occurrence and a description of the circumstances. As health professionals, cohort members were capable of accurately reporting these event, as demonstrated in a small validation study in which all 30 self-reports were confirmed by medical records [13]. Fractures due to malignancy or major traumatic events (e.g., motor vehicle accidents, skiing, horseback riding) were not included as outcomes in this study. The majority of the fracture cases occurred when slipping, tripping, falling from the height of a chair, or similar low trauma event (96% in women, 91% in men). Hip fractures were also identified from death records in both cohorts.

Diet and Supplement Use

Diet was assessed with a semiquantitative food frequency questionnaire (FFQ) in 1980 and 1984 in the NHS and in1986 and every four years thereafter in both cohorts, totaling nine FFQs in the NHS and seven in the HPFS over follow-up. Participants reported their

frequency of consumption over the previous year for specified serving sizes of more than 130 foods by selecting from among nine categories: never or < 1/month, 1–3/month, 1/week, 2–4/week, 5–6/week, 1/day, 2–3/day, 4–5/day, ≥ 6/day. Skim, low fat and whole fat varieties of milk were assessed separately and reported per 1 cup (240 mL) serving. Yogurt was assessed as plain, regularly sweetened, or artificially sweetened and each was reported per1 cup serving. Hard cheese and cream cheese were reported per 1 oz (28 g) and cottage or ricotta cheese per ½ cup serving. Other dairy foods on the FFQ included regular ice cream per ½ cup, frozen yogurt or low fat ice cream per ½ cup, and cream or sour cream per 1 tablespoon (15 mL). Daily energy and nutrient intakes, including calcium, vitamin D, protein, vitamin K, caffeine and alcohol, were calculated from all reported frequencies of food consumption and the nutrient contents of these foods, which were derived primarily from U.S. Department of Agriculture sources and supplemented with data from food manufacturers and published research.

Current use of nutrient supplements, including calcium, vitamin D, retinol and multivitamins, was ascertained on every biennial questionnaire. Participants provided the brand name and number of tablets per week for multivitamins and dosage per day for calcium, vitamin D and retinol supplements so that an accurate daily intake of could be calculated.

In validation studies, the FFQ was shown to be a suitable instrument for discriminating between levels of dietary intakes. In a comparison of the FFQ with diet records collected seasonally over the previous year, the correlation for skim and low fat milk consumption was 0.88 among 127 HPFS men [14] and 0.81 among 173 NHS women [15].

Non-dietary Measures

Non-dietary measures, including weight, smoking status and number of cigarettes smoked per day, menopausal status and use of postmenopausal hormones (women), diagnoses of cancer, cardiovascular disease, diabetes and osteoporosis, hours per week spent in recreational activities, and use of thiazide diuretics, furosemide-like diuretics (e.g., Lasix®, Bumex®) and oral steroids were assessed on biennial questionnaires. Total metabolic energy expenditure (MET-hours/week) was calculated from the reported recreational activities [16]. Body mass index (kg/m^2) was calculated from the current biennial weight and the height reported on the initial cohort questionnaire. In 1986, participants were asked to recall their frequency of milk consumption during teenage years and they also reported their waist circumference to the nearest ¼ inch using the tape measure provided with this questionnaire. Waist assessments were repeated in 1996 and 2000 in women and 1996 and 2008 in men.

Statistical Analysis

NHS participants contributed person-time from the return date of their 1980 questionnaire if they were postmenopausal, either natural or through surgery, or at the first questionnaire after reaching menopause. HPFS participants contributed person-time from the return date of their 1986 questionnaire if they were at least 50 years of age or at the first questionnaire after age 50. Participants were censored at the date of hip fracture or death from hip fracture, last questionnaire response, or the end of follow-up in 2012. In the primary analyses, we

used food and nutrient intakes that were cumulatively averaged over follow-up, i.e., at every dietary assessment, intakes were updated with the mean of all reports up to that time. Participants who did not respond to the baseline FFQ were not included in this analysis and those who were included did not contribute person-time in cycles in which they failed to report their dietary intake on the two most recent FFQs.

In alternate analyses, we used current dairy food intake and baseline intake at study entry as the exposure variables to examine how time between diet assessment and hip fracture might affect the results. The number of hip fracture cases and person-time in these analyses differed from our primary analysis. Current diet was calculated as the mean from the two most recent FFQs and participants did not contribute person-time in cycles in which they were missing both assessments. The baseline analysis included all participants who responded to the FFQ at study entry.

We used Cox proportional hazards models to compute relative risks (RR) for hip fracture within categories of consumption of specific dairy foods, using the same categories as the reports from the FFQ and collapsing the categories to accommodate the distribution of intakes. We also analyzed total dairy foods as the sum of the servings consumed from all dairy foods on the FFQ in pre-determined categories of < 1, 1, 2, 3, ≥ 4 servings/day. All models were conditioned on months of age and questionnaire cycle to account for age and calendar time and controlled for total energy intake (continuous). Multivariable RRs were calculated from models adjusted simultaneously for all dietary and non-dietary covariates, which included all assessed factors associated or thought to be associated with risk of hip fracture and/or consumption of dairy foods: intakes of calcium, vitamin D and protein from non-dairy foods and supplements (quintiles), retinol from supplements (zero, < 400, 400–999, 100–1599, ≥ 1600 μg/day), intakes of vitamin K and caffeine (quintiles), alcohol (< 0.5, 0.5–4.9, 5–9.9, 10–19.9, ≥ 20 g/day), milk intake during teenage years (< 1, 1, 2, ≥ 3 glasses/day, missing), body mass index < 21, 21–22, 23–24, 25–26, 27–28, ≥ 29 kg/m^2, missing), attained height (continuous), physical activity (quintiles, missing), smoking (never smoker, past smoker with < 5, 5–9, ≥ 10 years since quitting, current smoker with < 15, 15–24, ≥ 25 cigarettes/day, missing), use of postmenopausal hormones (never, past, current, missing), use of thiazide diuretics, furosemide-type diuretics and oral steroids (no, yes, missing), and diagnoses of cancer, diabetes and cardiovascular disease (no, yes). The dairy food and covariate data at the beginning of every 2-year questionnaire cycle were used to allocate person-time to the appropriate category for each variable. To assess a dose-response effect, a linear trend was determined by putting dairy food consumption into the model as a continuous value for an increase of one serving per day or per week. There was no evidence that the proportional hazards assumption was violated as the interactions terms between each dairy food (continuous) and age (continuous) were non-significant. We examined the possibility of nonlinear relations between dairy foods and risk of hip fracture non-parametrically using restricted cubic splines with three knots [17]. Significant curvature was assessed using the likelihood ratio test, comparing the model with only the linear term to the model with the linear and cubic spline terms ($P_{\text{curvature}}$). The results from the two cohorts were pooled using a fixed effects model for the log of the relative risks [18]. Heterogeneity between the cohorts was assessed using the Q statistic ($P_{\text{heterogeneity}}$).

To determine whether the associations between dairy food consumption and hip fracture varied within the populations, we stratified analyses by age, intakes of non-dairy calcium, vitamin D and protein, and other risk factors. Multiplicative interactions between the dairy food and the stratifying variables were assessed using the Wald test for continuous data or the likelihood ratio test for categorical data ($P_{interaction}$). Statistical significance was set at $p<0.05$ for tests of interaction and curvature and $p<0.10$ for tests of heterogeneity.

RESULTS

Mean age at study entry was 53.6 years (range 34–60) in the women and 57.7 years (range 50–75) in the men and mean follow-up times were 20.8 years among 80,600 women and 17.5 years among 43,306 men. Over follow-up in our primary analyses, 2138 low to moderate trauma hip fractures were identified in the women (median age 74 years, range 39–91) and 694 in the men (median age 78 years, range 51 to 96). Mean milk consumption dropped from 6.3 to 5.3 servings per week between 1986 and 2010 in both cohorts and 89% of the milk consumed was skim or low fat.

Age-standardized characteristics of the study populations are shown by frequency of milk consumption at baseline (Table 1). In both cohorts, more frequent consumption was associated with lower alcohol intake, higher total energy intake, and more frequent milk consumption during teenage years. Women with less frequent consumption were more likely to smoke, whereas smoking rates were low among the men overall. On average, women consumed more calcium from supplements than men.

In the primary analysis in which dairy food intakes were cumulatively averaged over follow-up, each additional serving of milk per day was associated with a significant 8% lower risk of hip fracture in women (RR=0.92, 95% CI 0.86–0.98), a non-significant 9% lower risk in men (RR=0.91, 95% CI 0.82–1.02), and a significant 8% lower risk for the pooled results (RR=0.92, 95% CI 0.87–0.97) after adjusting for yogurt and cheese intakes and all assessed covariates in the multivariable models (Table 2). In the categorical analyses for milk in which <1/week was the reference group, those consuming 1/day had a 17% lower risk of hip fracture (RR=0.83, 95% CI 0.73–0.96) and those consuming ≥2/day had a 23% lower risk (RR=0.77, 95% CI 0.65–0.91) when results from the two cohorts were pooled. In women, results for milk from the basic model adjusted only for age, follow-up cycle and total energy intake were somewhat attenuated in the multivariable model primarily due to confounding by physical activity, BMI and smoking; in men, the basic model results were strengthened after adding height, alcohol, non-dairy protein, and milk consumption during teenage years, which we previously found to be associated with a higher risk of hip fracture in men [19]. For cheese, a lower risk associated with higher intake was observed in women only and was not significant (RR=0.91, 95% CI 0.81–1.02 per 1 a day). Yogurt was not associated with a lower risk of hip fracture, though consumption was infrequent in both cohorts. Consumption was also low for cream and ice cream and neither one was associated with hip fracture in either cohort (data now shown). Higher total dairy food consumption (comprised of milk, cheese, yogurt, cream and ice cream) was associated with a significant 7% lower risk of hip fracture in women (RR=0.93, 95% CI 0.88–0.98 per 1 a day), largely due to the fact that milk contributed approximately half to the total, whereas the association exhibited

significant curvature in men. When the cohort results were pooled, risk of hip fracture declined by a significant 6% per daily serving of dairy foods (RR=0.94, 95% CI 0.90–0.98). Spline curves for hip fracture risk by the cumulative averaged food intakes are in Supplemental Figure 1.

In the multivariable analyses, all covariates for diet, disease diagnoses and height had no missing data. In both cohorts, less than 4% of the observations were missing data for physical activity, BMI, smoking, and use of medications, whereas 16% were missing data for milk consumption during teenage years as it was asked on only one questionnaire. In alternate analyses, we excluded all observations with any missing data rather than including them in separate categories, leaving 1621 hip fractures in the women and 541 in the men. The results were essentially the same as those from the models that included missing covariate data, e.g., the RR for each additional serving of milk per day was 0.89 (95% CI 0.82–0.96) in women and 0.90 (95% CI 0.79–1.02) in men. Results also remained unchanged when covariates were entered into the models as continuous rather than categorical data (data now shown).

We conducted several secondary analyses. In one, we included total intakes of calcium, vitamin D, and protein in our multivariable models instead of the non-dairy sources of these nutrients, expecting the results to be attenuated if the benefit from milk could be attributed to one or more of these nutrient components, but we did not observe this. For example, the RR for hip fracture per daily serving of milk was 0.90 (95% CI 0.83–0.98) in women and 0.89 (95% CI 0.77–1.02) in men. In another analysis, women were censored (n=18,325) upon reported use of any osteoporosis drug, specifically bisphosphonates, raloxifene, calcitonin and tamoxifen, which were added to the biennial questionnaires in 1998 and later. All results were essentially the same as the primary results (data not shown). Finally, we controlled for whether participants reported difficulty with their balance or limited ability to walk several blocks or climb a flight of stairs, which were initially assessed in 1990. Again, results remained unchanged (data not shown).

We examined whether current diet or an early diet assessment would show different associations between dairy foods and hip fracture compared with our cumulative average measure (Table 2). For both men and women, results for current and cumulative average dairy food intakes were very similar. For example, for the pooled cohort results for milk, both measures were associated with a significant 8% lower risk per daily serving. In contrast, we observed only a non-significant 4% lower risk when the baseline diet assessment was used in relation to hip fracture over the full follow-up period. Results for baseline cheese and total dairy food intakes were similarly attenuated in comparison with the cumulative average and current measures in women. Pooled cohort results from the categorical food intake models in Table 2 are in Supplemental Table 1.

Associations between milk and hip fracture did not differ significantly by age ($P_{\text{interaction}}$ = 0.54 in women and 0.29 in men) (Table 3). Nevertheless, there was a significant linear trend in lower risk with increasing milk consumption in men under 75 years of age (RR=0.82, 95% CI 0.69–0.98 per 1 a day) but not in older men. We also did not find clear support for our hypothesis that a benefit from higher milk consumption may be limited to adults with a

lower intake of calcium, vitamin D or protein from non-dairy sources (all $P_{interaction} > 0.05$). Spline curves for the models in Table 3 are in Supplemental Figure 2. Results for cheese and total dairy intake also showed no significant differences between strata of non-dairy calcium, vitamin D and protein (data now shown).

In an exploratory analysis, we observed a strong interaction between milk and BMI in men ($P_{interaction} < 0.001$) (Table 4). Risk of hip fracture was 53% lower per daily serving in obese men with BMI ≥ 30 kg/m^2 (RR=0.47, 95% CI 0.25–0.87) but showed no benefit in the lower BMI categories. A similar pattern was seen for cheese ($P_{interaction}$= 0.02) and total dairy foods ($P_{interaction} < 0.001$) in men. In women, a significant interaction with BMI was only observed for cheese ($P_{interaction}$=0.002), with lower risks in the BMI categories ≥ 25 but no benefit and significant curvature in the lower BMI categories. Risk of hip fracture was also a significant 21% lower among the obese women per daily serving of both milk and total dairy foods. We also examined associations between dairy foods and hip fracture stratified by waist circumference, which was available for 63% of the follow-up in women and 80% in men. In men, we observed some similarity to the BMI stratified results in that risk per daily serving was lower for cheese ($P_{interaction}$=0.05), total dairy foods ($P_{interaction}$=0.01), and somewhat for milk ($P_{interaction}$=0.19) in those with a larger waist circumference. However, this was not observed for any of the dairy food and hip fracture associations in women. In other exploratory analyses, we did not find any evidence that associations between dairy intakes and risk of hip fracture were modified by physical activity, alcohol, smoking, postmenopausal hormone use, height, or milk consumption during teenage years.

DISCUSSION

In this investigation among Caucasian men 50 years of age and older and women past menopause, each additional serving of milk per day was associated with a significant 8% lower risk of hip fracture when milk was assessed as a long-term cumulative average that was updated every four years. In women, the data suggested that higher cheese intake may also contribute to a lower hip fracture risk but the result was not statistically significant. Yogurt, cream and ice cream were not associated with risk of hip fracture in either cohort, though consumption was low and did not provide adequate distribution of intakes for analyses. For total dairy food consumption, risk of hip fracture was a significant 6% lower per daily serving in men and women. Analyses based on current dairy food intakes yielded similar results to those based on the cumulative average measures, whereas results were attenuated if only a baseline measure was used, indicating the importance of current diet for assessing hip fracture risk.

No clinical trials have been conducted to investigate milk or dairy food consumption and hip fractures and previous cohort studies do not generally support an inverse association. In a meta-analysis by Bischoff-Ferrari, et al [5], which included a previous meta-analysis [4], our earlier reports from HPFS [8] and NHS [10], and four additional studies, there was no association between milk and hip fracture in women, whereas each glass of milk per day was associated with a marginally significant 9% lower risk in men (RR=0.91, 95% CI 0.81–1.01). The result for men was imprecise as the data included only 195 hip fractures. Nevertheless, it supports the similar inverse association that we observed in HPFS. The

results for women were heavily influenced by the large Swedish Mammography Cohort [20], which was the only study with a positive association between milk and hip fracture risk. After excluding this study, the meta-analysis resulted in a marginally significant 5% lower risk per glass of milk per day in women (RR=0.95, 95% CI 0.90–1.00). A subsequent study among men and women in the U.S. Framingham cohort reported a threshold association between milk and hip fracture, with a marginally significant 40% lower risk for those consuming > 1 versus ≤ 1 serving/week (RR=0.60, 95% CI 0.36–1.02) that was partially attributed to increased bone mineral density [6].

A more recent analysis of the Swedish Mammography Cohort with the addition of the Cohort of Swedish Men [7] reported a significant 9% increase in risk of hip fracture per glass of milk per day in women, although after controlling for the intake of other dairy foods as we did, the result was attenuated to a 6% increase in risk but remained significant. The authors suggested that milk may indeed have an undesirable effect because it is the main dietary source of D-galactose, which causes premature aging in animal models through oxidative stress and chronic inflammation [22], factors that contribute to bone and muscle loss in humans [22–24]. In contrast to milk, fermented milk and yogurt were associated with a significant 11% lower risk of hip fracture per daily serving in women, despite the galactose content of these foods [25]. Cheese, which is typically low in galactose, was associated with a 14% lower risk. None of these dairy foods were associated with hip fracture in the men. It is difficult to know why the results from this Swedish study should contrast with what we observed in our U.S. cohorts, though some differences are worth noting. The prevalence of obesity in adults is much higher in the U.S. than in Sweden (36% and 17%, respectively) [26,27], and we found some evidence that milk and dairy foods may be more likely to reduce risk of for hip fracture among those with higher BMI. In addition, Scandinavia has the highest reported incidence of hip fracture worldwide [28], and particular factors contributing to this high incidence may influence the risk associated with dairy consumption. Fortification of milk with vitamin D also differs, with levels in Sweden about half that in the U.S. and does not include all milk types. In terms of study design, the follow-up period for the Swedish women was over 20 years and diet was updated only once and only for a portion of the population. In our cohort, we found that current milk and dairy food intakes were most important, with the inverse association with hip fracture attenuating as the diet assessment became more distant in time, albeit never showing a positive association as seen in the Swedish study.

We anticipated that the relationship between dairy and hip fractures would change with age. We found some support for this in men, as milk was associated with a lower risk of hip fracture in those younger than 75 years but not at older ages. However, the evidence was weak and not confirmed in the women. We also expected that a benefit from dairy foods could be at least partially attributed to its calcium, vitamin D, and/or protein content. The data did not support this hypothesis, as non-dairy sources of these nutrients did not significantly modify the association between milk intake and hip fracture and the association was not attenuated when controlled for total intakes, including dairy sources, of these three nutrients. For vitamin D, it may be that the amount provided by milk (2.5 μg/glass) is too low to contribute to hip fracture reduction [29,30]. For protein, it may be that in these U.S.

cohorts where protein consumption is high, an additional 8 g per glass of milk does not further improve fracture risk.

The inverse associations between dairy food consumption and risk of hip fracture may be stronger or even limited to those with a larger body size, as measured by BMI and waist circumference. Body fat can have a negative impact on bone as it induces a chronic inflammatory state [31] that can both accelerate bone resorption and inhibit bone formation [32] and may also negatively influence bone microarchitecture [33]. Indeed, although risk of hip fracture decreases with higher BMI, no additional benefit may occur with obesity [34–36]. Abdominal obesity-related inflammation may be particularly detrimental for bone, as we previously reported that risk of hip fracture in women increased with increasing waist circumference, independent of BMI [37]. Dairy food consumption might help to protect against hip fractures in the obese by reducing inflammation [38]. However, although some studies have shown that adding milk proteins to the diet can reduce markers of inflammation and oxidative stress, others have reported no effect [39]. It has also been suggested that an increase in dietary calcium and dairy foods may promote loss of body fat [40], although the preponderance of research indicates that this only occurs in energy-restricted weight loss diets [41–42].

The major strength of the present study is the multiple measures of milk and dairy food intakes for up to 32 years of follow-up, which allowed us to calculate long-term average intakes and to reduce measurement error. We also assessed most major risk factors for hip fractures to control for confounding. Another strength is the large number of hip fractures for analysis that provided statistical power to observe associations. One limitation of the study was that we were unable to assess the influence of yogurt on risk of hip fractures due to low consumption. Another limitation was that hip fractures were mostly self-reported, and elderly participants in particular may have failed to respond to questionnaires to report their fracture. However, we also identified hip fractures that were a contributing cause of death on a death certificate. Misclassification of hip fractures could have attenuated our results. As the study populations were Caucasian, results may not be applicable to other races.

In conclusion, we found that higher long-term milk consumption in older adults was associated with a lower risk of hip fracture. The benefit was not explained by the calcium, vitamin D or protein content of milk. The impact of other specific dairy foods in hip fracture prevention and the role of obesity require more detailed study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Haentjens P, Magaziner J, Colón-Emeric CS, Vanderschueren D, Milisen K, Velkeniers B, Boonen S. Meta-analysis: excess mortality after hip fracture among older women and men. Ann Intern Med 2010;152(6):380–90. [PubMed: 20231569]
2. Wright NC, Looker AC, Saag KG, Curtis JR, Delzell ES, Randall S, Dawson-Hughes B. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. J Bone Miner Res 2014;29(11):2520–6. [PubMed: 24771492]
3. U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans, 8th Edition 12 2015 Available at http://health.gov/dietaryguidelines/2015/guidelines/.
4. Kanis JA, Johansson H, Oden A, De Laet C, Johnell O, Eisman JA, Mc Closkey E, Mellstrom D, Pols H, Reeve J, Silman A, Tenenhouse A. A meta-analysis of milk intake and fracture risk: low utility for case finding. Osteoporos Int 2005;16:799–804. [PubMed: 15502959]
5. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, Kanis JA, Orav EJ, Staehelin HB, Kiel DP, Burckhardt P, Henschkowski J, Spiegelman D, Li R, Wong JB, Feskanich D, Willett WC. Milk intake and risk of hip fracture in men and women; a meta-analysis of prospective cohort studies. J Bone Miner Res 2011;26(4):833–9. [PubMed: 20949604]
6. Sahni S, Mangano KM,1 Tucker KL, Kiel DP,1 Casey VA, Hannan MT. Protective association of milk intake on the risk of hip fracture: results from the Framingham Original Cohort. J Bone Miner Res 2014;29(8):1756–62. [PubMed: 24760749]
7. Michaëlsson K, Wolk A, Langenskiöld S, Basu S, Eva Lemming W, Melhus H, Byberg L. Milk intake and risk of mortality and fractures in women and men: cohort studies. BMJ 2014;10 28;349:g6015. [PubMed: 25352269]
8. Owusu W, Willett WC, Feskanich D, Ascherio A, Spiegelman D, Colditz GA. Calcium intake and the incidence of forearm and hip fractures among men. J Nutr 1997;127(9):1782–7. [PubMed: 9278560]
9. Feskanich D, Willett WC, Stampfer MJ, Colditz GA. Milk, dietary calcium, and bone fractures in women: a 12-year prospective study. Am J Public Health 1997;87(6):992–7. [PubMed: 9224182]
10. Feskanich D, Willett WC, Colditz GA. Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. Am J Clin Nutr 2003;77(2):504– [PubMed: 12540414]
11. Stampfer MJ, Willett WC, Speizer FE, Dyserrt DC, Lipnick R, Rosner B, Hennekens CH. Test of the National Death Index. Am J Epidemiol 1984;119(5):837–9. [PubMed: 6720679]
12. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax Nationwide Death Search. Am J Epidemiol 1994;140(11):10016–19.
13. Colditz GA, Martin P, Stampfer MJ, Willett WC, Sampson L, Rosner B, Hennekens CH, Speizer FE. Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort study of women. Am J Epidemiol 1986;123(5):894–900. [PubMed: 3962971]
14. Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, Willett WC. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc 1993;93(7):790–6. [PubMed: 8320406]
15. Salvini S, Hunter DJ, Sampson L, Stampfer MJ, Colditz GA, Rosner B, Willett WC. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. Int J Epidemiol 1989;18(4):858–67. [PubMed: 2621022]
16. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis JF, Paffenbarger RS. Compendium of Physical Activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993;25(1):71–80. [PubMed: 8292105]
17. Durrleman S, and Simon R. Flexible regression models with cubic splines. Statistics in Medicine 1989;8:551–561. [PubMed: 2657958]
18. DerSimonian R and Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7(3):177–188. [PubMed: 3802833]

19. Feskanich D, Bischoff-Ferrari HA, Frazier AL, Willett WC. Milk consumption during teenage years and risk of hip fracture in older adults. JAMA Pediatr 2014;168(1):54–60. [PubMed: 24247817]
20. Michaelsson K, Melhus H, Bellocco R, Wolk A. Dietary calcium and vitamin D intake in relation to osteoporotic fracture risk. Bone 2003;32(6):694–703. [PubMed: 12810177]
21. Cui X, Zuo P, Zhang Q, Li X, Hu Y, Long J, Packer L, Liu J. Chronic systemic D-galactose exposure induces memory loss, neurodegeneration, and oxidative damage in mice: protective effects of R-alpha-lipoic acid. J Neurosci Res 2006;83(8):1584–90. [PubMed: 16555301]
22. Hardy RR and Cooper MS. Bone loss in inflammatory disorders. J Endocrinol 209;201(3): 309–20. [PubMed: 19443863]
23. Berglundh S, Malmgren L, Luthman H, McGuigan F, Akesson K. C-reactive protein, bone loss, fracture, and mortality in elderly women: a longitudinal study in the OPRA cohort. Osteoporos Int 2015;26(2):727–35. [PubMed: 25410434]
24. Roubenoff R Physical activity, inflammation and muscle loss. Nutrition Reviews 2007;65(12 suppl 3):S208–12. [PubMed: 18240550]
25. Abrahamson A Galactose in dairy products. Available at http://stud.epsilon.slu.se/7718/1/abrahamson_a_150317.pdf
26. Ogden CL, Carroll MD, Fryar CD, Flegal KM. Prevalence of obesity among adults and youth: United States, 2011–2014. NCHS data brief, no 219. Hyattsville, MD: National Center for Health Statistics 2015.
27. Molarius A, Lindén-Boström M, Granström F, Jan Karlsson J. Obesity continues to increase in the majority of the population in mid-Sweden - a 12-year follow-up. Eur J Public Health 2016;26(4): 622–7. [PubMed: 27074794]
28. Kanis JA, Johnell O, De Laet C, Jonsson B, Oden A, Ogelsby AK. International variations in hip fracture probabilities: implications for risk assessment. J Bone Miner Res 2002;17(7):1237– [PubMed: 12096837]
29. Bischoff-Ferrari HA, Willett WC, Wong JB, Stuck AE, Staehelin HB, Orav EJ, Thoma A, Kiel DP, Henschkowski J. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med 2009;169(6):551– [PubMed: 19307517]
30. Bischoff-Ferrari HA, Willett WC, Orav EJ, Lips P, Meunier PJ, Lyons RA, Flicker L, Wark J, Jackson RD, Cauley JA, Meyer HE, Pfeifer M, Sanders KM, Stähelin HB, Theiler R, Dawson-Hughes B. A pooled analysis of vitamin D dose requirements for fracture prevention. N Engl J Med 2012;367(1):40–9. [PubMed: 22762317]
31. Das UN. Is obesity an inflammatory condition? Nutrition 2001;17(11–12):953–66. [PubMed: 11744348]
32. Baker-LePain JC, Nakamurab MC, Lane NE. Effects of inflammation on bone: an update. Curr Opin Rheumatol 2011;23(4):389–395. [PubMed: 21532485]
33. Rolland T, Boutroy S, Vilayphiou N, Blaizot S, Chapurlat R, Szulc P. Poor trabecular microarchitecture at the distal radius in older men with increased concentration of high-sensitivity C-reactive protein - the STRAMBO study. Calcif Tissue Int 2012;90(6):496–506. [PubMed: 22527204]
34. De Laet C, Kanis JA, Odén A, Johanson H, Johnell O, Delmas P, Eisman JA, Kroger H, Fujiwara S, Garnero P, McCloskey EV, Mellstrom D, Melton LJ 3rd, Meunier PJ, Pols HAP, Reeve J, Silman A, Tenenhouse A. Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int 2005;16(11):1330–8. [PubMed: 15928804]
35. Armstrong ME, Spencer EA, Cairns BJ, Banks E, Pirie K, Green J, Wright FL, Reeves GK, Beral V. Body mass index and physical activity in relation to the incidence of hip fracture in postmenopausal women. J Bone Miner Res. 2011 6;26(6):1330–8 [PubMed: 21611971]
36. Nielson CM, Marshall LM, Adams AL, LeBlanc ES, Cawthon PM, Ensrud K, Stefanick ML, Barrett-Connor E, Orwoll ES. BMI and fracture risk in older men: The Osteoporotic Fractures in Men Study (MrOS). J Bone Miner Res 2011; 26(3):496–502. [PubMed: 20814955]

37. Meyer HE, Willett WC, Flint AJ, Feskanich D. Abdominal obesity and hip fracture: results from the Nurses' Health Study and the Health Professionals Follow-up Study. Osteoporos Int 2016; 27(6):2127–36. [PubMed: 26849456]

38. Sharples AP, Hughes DC, Deane CS, Saini A, Selman C, Stewart CE. Longevity and skeletal muscle mass: the role of IGF signalling, the sirtuins, dietary restriction and protein intake. Aging Cell 2015;14(4):511–23. [PubMed: 25866088]

39. Fekete ÁA, Givens DI, Lovegrove JA. Can milk proteins be a useful tool in the management of cardiometabolic health? An updated review of human intervention trials. Proc Nutr Soc 2016;75(3):328–41. [PubMed: 27150497]

40. Barba G and Russo P. Dairy foods, dietary calcium and obesity: a short review of the evidence. Nutr Metab Cardiovasc Dis 2006;16(6):445–51. [PubMed: 16928440]

41. Abargouei AS, Janghorbani M, Salehi-Marzijarani M, Esmaillzadeh A. Effect of dairy consumption on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Int J Obes 2012;36(12):1485–93.

42. Booth AO, Huggins CE, Wattanapenpaiboon N, Nowson CA. Effect of increasing dietary calcium through supplements and dairy food on body weight and body composition: a meta-analysis of randomized controlled trials. Brit J Nutr 2015;114(7):1013–25. [PubMed: 26234296]

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Table 1.

Age and age-standardized characteristics of the study populations of postmenopausal women and men 50 years of age and older by frequency of milk consumption at baseline [a]

	WOMEN, milk consumption [b], servings						MEN, milk consumption [b], servings					
	< 1/week	1/week	2–4/week	5–6/week	1/day	≥ 2/day	< 1/week	1/week	2–4/week	5–6/week	1/day	≥ 2/day
% of population	23	8	18	8	26	17	23	7	20	12	21	17
age, years	53.4	53.3	53.7	53.9	53.7	53.8	57.3	56.4	57.7	58.5	57.6	58.3
food consumption [b], servings/week												
cheese	5.1	5.0	5.0	4.9	5.3	5.1	3.5	3.6	3.7	3.7	3.8	4.2
yogurt	0.7	0.8	0.8	1.0	1.0	1.1	0.4	0.5	0.5	0.6	0.6	0.6
ice cream	1.0	1.1	1.2	1.1	1.2	1.2	0.9	1.1	1.1	1.1	1.2	1.3
cream	1.4	1.4	1.2	1.1	1.0	1.0	1.0	1.0	0.8	0.8	0.8	0.9
total dairy foods	7.4	8.7	10.9	13.7	15.4	25.9	6.8	8.0	10.2	12.8	14.6	26.3
milk in teenage years [c], servings/week	7.7	9.1	10.5	11.9	12.6	16.1	11.9	12.6	13.3	14.7	16.1	20.3
calcium, mg/day												
from dairy foods	201	245	335	457	524	1020	192	237	327	439	508	1057
from non-dairy foods	273	281	289	305	305	333	310	315	322	331	345	367
from supplements	182	184	192	200	172	160	121	97	96	96	99	87
vitamin D, μg/day												
from dairy foods	0.4	0.7	1.5	2.4	3.0	7.4	0.4	0.8	1.5	2.5	3.1	7.8
from non-dairy foods	2.5	2.6	2.7	2.8	2.8	2.8	3.8	3.9	4.0	4.0	4.0	3.6
from supplements	3.2	3.2	3.4	3.7	3.6	3.8	3.8	3.5	3.6	3.8	3.8	3.7
protein, g/day												
from dairy foods	8	10	12	16	18	32	8	9	12	15	17	32
from non-dairy foods	59	60	61	63	63	66	73	74	74	76	77	78
retinol from supplements, μg/day	650	612	633	694	669	732	803	792	816	834	838	814
vitamin K, μg/day	188	183	180	178	181	173	200	191	189	187	185	166
alcohol, g/day	7.8	7.0	6.4	6.0	5.6	4.7	12.9	12.8	12.0	11.3	10.8	9.7
caffeine, mg/day	354	340	328	319	324	307	238	247	234	224	214	214
total energy, kcal/day	1490	1551	1617	1704	1729	1963	1795	1865	1896	1974	2043	2312

	WOMEN, milk consumption [b], servings						MEN, milk consumption [b], servings					
	< 1/week	1/week	2–4/week	5–6/week	1/day	≥ 2/day	< 1/week	1/week	2–4/week	5–6/week	1/day	≥ 2/day
physical activity [d], met-hours/week	9	9	10	11	10	11	22	22	23	23	24	24
height, cm	164	164	164	164	164	164	178	178	178	178	178	179
body mass index, kg/m^2	25.3	25.7	25.7	25.9	25.8	25.8	25.6	25.9	25.8	25.7	25.5	25.6
waist circumference, cm	78	79	79	79	79	79	96	96	96	96	95	96
current smoker, %	28	25	22	21	21	21	10	10	9	9	8	10
postmenopausal hormone use, %	30	33	34	34	32	32						
thiazide diuretic use, %	13	13	13	12	12	12	10	11	10	9	9	9
furosemide-type diuretic use, %	1	2	2	1	2	1	2	1	1	1	1	1
oral steroid use, %	2	1	2	2	1	2	<1	<1	<1	<1	<1	<1
diabetes, %	3	3	3	4	4	5	3	3	3	4	4	4
cancer, %	7	7	7	7	7	6	5	4	4	4	5	4
cardiovascular disease, %	2	2	2	2	2	3	9	9	9	9	9	8
physical limitations [e], %	17	17	16	16	17	17	8	7	8	8	8	8
difficulty with balance [e], %	5	5	5	5	6	6	4	4	4	4	5	5
fell at least once in past year [f], %	22	22	23	24	24	24						

[a] Baseline is when participants entered into analysis. For NHS women, it is 1980 or the biennial follow-up cycle when they first reported being postmenopausal. For HPFS men, it is 1986 or the biennial follow-up cycle when they first reached 50 y of age.

[b] Milk includes all skim, low fat and full fat varieties with a serving size of 1 cup (240 mL). Cheese includes all types of hard and soft chesses with serving sizes of 1 oz (28 g) for hard cheeses and cream cheese and ½ cup (120 mL) for cottage or ricotta cheese. Yogurt includes all varieties of nonfat, low fat, full fat, plain, sweetened and artificially sweetened with a serving size of 1 cup (240 mL). Ice cream includes all low fat and high fat varieties plus frozen yogurt with a serving size of ½ cup (120 mL). Cream includes sour cream, whipping cream and cream used in coffee with a serving size of 1 tablespoon (15 mL). Total dairy foods are the total servings per week from all of these foods.

[c] Milk consumption during teenage years (ages 13–18) includes all skim, low fat and full fat varieties with a serving size of 1 cup (240 mL).

[d] Physical activity includes only recreational activities and was assessed in metabolic equivalents (1 met-hour is equivalent to 1 hour of sitting).

[e] Limited ability to walk several blocks or climb a flight of stairs and difficulty with balance were first assessed in 1990.

[f] Number of falls to the ground was first assessed in 1998 in women only

Table 2.

Relative risk (95% confidence interval) of hip fracture by frequency of consumption of milk, cheese, yogurt and total dairy foods among postmenopausal women and among men 50 years of age and older

	Cumulative Average Consumption [a]				Current Consumption [a]			Baseline Consumption [a]		
	cases	p-y	basic model [b]	multivariable [c]	cases	p-y	multivariable [c]	cases	p-y	multivariable [c]
Milk [d]										
Women										
< 1 /week	285	249	1.00	1.00	492	350	1.00	413	274	1.00
1 /week	173	140	0.86 (0.71–1.04)	0.89 (0.73–1.08)	184	146	0.89 (0.75–1.05)	348	286	0.95 (0.82–1.09)
2–4 /week	578	422	0.88 (0.76–1.02)	0.94 (0.81–1.09)	591	419	0.96 (0.85–1.08)	382	311	0.92 (0.80–1.07)
5–6 /week	331	240	0.83 (0.71–0.98)	0.90 (0.76–1.07)	352	259	0.91 (0.79–1.05)	176	139	0.97 (0.81–1.16)
1 /day	550	420	0.81 (0.70–0.94)	0.88 (0.75–1.03)	602	491	0.83 (0.73–0.94)	591	453	0.93 (0.81–1.06)
≥ 2 /day	221	207	0.75 (0.62–0.90)	0.77 (0.64–0.94)	334	264	0.82 (0.70–0.95)	361	290	0.87 (0.75–1.02)
per 1 a day	2138	1678	0.91 (0.86–0.97)	0.92 (0.86–0.98)	2555	1929	0.93 (0.88–0.98)	2271	1753	0.96 (0.92–1.01)
Men										
< 1 /week	109	134	1.00	1.00	163	168	1.00	122	119	1.00
1 /week	66	64	0.99 (0.72–1.36)	1.00 (0.72–1.37)	48	61	0.78 (0.56–1.09)	99	123	0.85 (0.64–1.12)
2–4 /week	179	198	0.84 (0.65–1.07)	0.81 (0.63–1.04)	149	182	0.78 (0.62–0.99)	175	164	1.04 (0.81–1.32)
5–6 /week	107	109	0.84 (0.64–1.11)	0.79 (0.59–1.05)	117	111	0.88 (0.68–1.13)	88	90	0.88 (0.66–1.17)
1 /day	142	155	0.80 (0.61–1.04)	0.73 (0.58–0.96)	154	172	0.72 (0.57–0.91)	129	168	0.67 (0.52–0.87)
≥ 2 /day	91	99	0.92 (0.68–1.23)	0.77 (0.58–1.05)	93	105	0.72 (0.54–0.96)	140	134	0.83 (0.63–1.10)
per 1 a day	694	759	0.98 (0.88–1.08)	0.91 (0.82–1.02)	724	799	0.91 (0.82–1.00)	753	798	0.94 (0.86–1.03)
Pooled [e]										
per 1 a day	2832	2437	0.93 (0.88–0.98)	0.92 (0.87–0.97)	3279	2728	0.92 (0.88–0.97)	3024	2551	0.96 (0.92–1.00)
Cheese [d]										
Women										
< 1 /week	126	112	1.00	1.00	391	220	1.00	178	152	1.00
1 /week	323	251	1.02 (0.83–1.26)	1.09 (0.88–1.35)	430	338	0.94 (0.82–1.08)	402	328	1.10 (0.92–1.32)
2–4 /week	1017	740	0.93 (0.77–1.12)	1.03 (0.85–1.24)	1079	825	0.95 (0.84–1.07)	830	639	1.14 (0.97–1.35)
5–6 /week	393	314	0.90 (0.74–1.11)	1.00 (0.81–1.24)	355	292	0.91 (0.78–1.06)	375	279	1.07 (0.89–1.29)

	Cumulative Average Consumption [a]				Current Consumption [a]			Baseline Consumption [a]		
	cases	p-y	basic model [b]	multivariable [c]	cases	p-y	multivariable [c]	cases	p-y	multivariable [c]
≥ 1 /day	279	261	0.85 (0.68–1.06)	0.94 (0.75–1.17)	300	254	0.94 (0.80–1.11)	486	355	1.06 (0.89–1.27)
per 1 a day	2138	1678	0.88 (0.79–0.99)	0.91 (0.81–1.02)	2555	1929	0.92 (0.86–1.04)	2271	1753	0.97 (0.90–1.04)
Men										
< 1 /week	90	93	1.00	1.00	125	116	1.00	114	108	1.00
1 /week	123	144	0.85 (0.64–1.18)	0.89 (0.67–1.19)	129	146	0.90 (0.69–1.17)	157	170	0.97 (0.75–1.25)
2–4 /week	333	343	0.90 (0.71–1.16)	0.96 (0.75–1.24)	285	334	0.88 (0.70–1.11)	273	308	0.89 (0.70–1.13)
5–6 /week	70	101	0.66 (0.48–0.92)	0.72 (0.51–1.01)	92	109	0.80 (0.60–1.07)	99	105	0.85 (0.63–1.13)
≥ 1 /day	78	78	1.01 (0.73–1.40)	1.08 (0.77–1.51)	93	94	0.96 (0.71–1.29)	110	107	0.96 (0.72–1.28)
per 1 a day	694	759	1.03 (0.84–1.26)	1.04 (0.85–1.28)	724	799	1.01 (0.85–1.20)	753	798	1.01 (0.87–1.17)[g]
Pooled [e]										
per 1 a day	2832	2437	0.93 (0.81–1.07)	0.94 (0.85–1.03)	3279	2728	0.96 (0.88–1.04)	3024	2551	0.98 (0.91–1.04)
Yogurt [d]										
Women										
never	668	560	1.00	1.00	1210	814	1.00	1390	997	1.00
< 1/week	814	567	0.87 (0.78–0.97)	0.97 (0.87–1.08)	593	484	0.93 (0.84–1.03)	402	326	1.06 (0.95–1.19)
1 /week	327	255	0.84 (0.73–0.96)	0.97 (0.84–1.12)	288	237	0.91 (0.80–1.04)	186	168	1.01 (0.86–1.18)
2–4/week	297	247	0.94 (0.81–1.08)	1.08 (0.93–1.26)	359	301	0.91 (0.80–1.03)	192	179	1.02 (0.87–1.19)
≥ 5 /week	32	49	0.68 (0.47–0.98)	0.77 (0.53–1.12)	105	92	0.90 (0.73–1.10)	101	83	1.09 (0.88–1.34)
per 1 a week	2138	1678	0.98 (0.94–1.01)	1.00 (0.97–1.04)	2555	1929	0.98 (0.96–1.01)	2271	1753	1.00 (0.98–1.03)
Men										
never	303	372	1.00	1.00	413	450	1.00	531	534	1.00
< 1/week	244	235	1.05 (0.88–1.25)	1.12 (0.93–1.34)	140	177	1.03 (0.84–1.25)	109	128	0.97 (0.80–1.20)
1 /week	90	76	1.22 (0.96–1.56)	1.29 (1.00–1.66)	72	74	1.15 (0.88–1.50)	40	60	0.82 (0.58–1.16)
≥ 2 /week	57	76	0.88 (0.66–1.18)	0.92 (0.67–1.25)	99	98	1.17 (0.92–1.49)	72	76	1.02 (0.78–1.32)
per 1 a week	694	759	1.04 (0.97–1.10)[g]	1.04 (0.97–1.11)[g]	724	799	1.05 (1.00–1.10)	753	798	1.00 (0.78–1.05)[g]
Pooled [e]										
per 1 a week	2832	2437	0.99 (0.96–1.02)	1.01 (0.98–1.04)	3279	2728	1.01 (0.95–1.08)[f]	3024	2551	1.00 (0.98–1.02)
Total Dairy Foods [d]										

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	Cumulative Average Consumption [a]				Current Consumption [a]			Baseline Consumption [a]		
	cases	p-y	basic model [b]	multivariable [c]	cases	p-y	multivariable [c]	cases	p-y	multivariable [c]
Women										
< 1 /day	306	252	1.00	1.00	490	338	1.00	422	279	1.00
1 /day	873	653	0.91 (0.80–1.04)	0.98 (0.86–1.13)	962	715	0.96 (0.85–1.07)	745	490	1.04 (0.92–1.17)
2 /day	611	461	0.82 (0.71–0.95)	0.90 (0.78–1.05)	598	464	0.89 (0.79–1.01)	364	273	0.93 (0.80–1.07)
3 /day	284	234	0.80 (0.67–0.95)	0.88 (0.73–1.05)	334	273	0.83 (0.71–0.96)	229	180	0.88 (0.74–1.04)
≥ 4 /day	64	78	0.72 (0.54–0.96)	0.76 (0.57–1.02)	171	139	0.82 (0.68–0.99)	511	531	0.90 (0.76–1.05)
per 1 a day	2138	1678	0.91 (0.86–0.96)	0.93 (0.88–0.98)	2555	1929	0.94 (0.90–0.98)	2271	1753	0.97 (0.95–1.00)
Men										
< 1 /day	139	158	1.00	1.00	157	174	1.00	179	171	1.00
1 /day	257	301	0.83 (0.67–1.04)	0.82 (0.66–1.03)	247	302	0.83 (0.67–1.02)	185	200	0.84 (0.68–1.04)
2 /day	166	166	0.82 (0.64–1.05)	0.79 (0.61–1.02)	149	164	0.73 (0.57–0.94)	184	212	0.76 (0.61–0.95)
3 /day	80	90	0.76 (0.56–1.03)	0.68 (0.49–0.98)	104	97	0.85 (0.64–1.12)	91	134	0.61 (0.46–0.80)
≥ 4 /day	62	44	1.31 (0.92–1.87)	1.17 (0.80–1.70)	67	62	0.76 (0.55–1.06)	114	101	0.88 (0.66–1.16)
per 1 a day	694	759	1.00 (0.92–1.08)[g]	0.96 (0.88–1.04)[g]	724	799	0.95 (0.88–1.02)	753	798	0.96 (0.90–1.03)[g]
Pooled [e]										
per 1 a day	2832	2437	0.95 (0.87–1.03)[f]	0.94 (0.90–0.98)	3279	2728	0.94 (0.91–0.98)	3024	2551	0.97 (0.95–0.99)

p-y is person-years, in thousands

[a] Baseline consumption is the diet assessment when participants entered into analysis. Current consumption is an average of the two most recent diet assessments. Cumulative consumption is an average of the dietary assessments beginning at baseline through current consumption.

[b] Basic models are adjusted for age, follow-up cycle and total energy intake.

[c] Multivariable models are adjusted for age, follow-up cycle, total energy intake, calcium and vitamin D from non-dairy foods plus supplements, protein from non-dairy foods, retinol from supplements, vitamin K, caffeine, alcohol, milk during teenage years, body mass index, height, physical activity, smoking, use of postmenopausal hormones (women), use of thiazide diuretics, furosemide-type diuretics and oral steroids, and diagnoses of cancer, diabetes and cardiovascular disease. In addition, milk, cheese and yogurt are adjusted for one another.

[d] See Table 1 footnote for description and serving sizes of dairy foods.

[e] combined results from women and men

[f] $P_{\text{heterogeneity}} < 0.10$

[g] $P_{\text{curvature}} < 0.05$

Table 3.

Multivariable relative risk [a] (95% confidence interval) of hip fracture by cumulatively averaged frequency of milk consumption, stratified by age and approximate median nutrient intakes from non-dairy sources, among postmenopausal women and among men 50 years of age and older

			Milk Consumption, servings [b]						
	cases	**p-y**	**< 1 /week**	**1 /week**	**2–4 /week**	**5–6 /week**	**1 /day**	**≥ 2/day**	**per 1 a day**
Age									
women < 75 y	1228	1459	1.00	0.93 (0.73–1.19)	0.99 (0.82–1.19)	0.97 (0.78–1.20)	0.92 (0.75–1.11)	0.78 (0.61–1.00)	0.90 (0.83–0.98)
≥ 75 y	910	219	1.00	0.81 (0.59–1.10)	0.85 (0.67–1.08)	0.80 (0.61–1.05)	0.80 (0.62–1.03)	0.74 (0.54–1.02)	0.94 (0.84–1.05)
men < 75 y	273	617	1.00	0.88 (0.53–1.46)	0.95 (0.65–1.37)	0.97 (0.64–1.49)	0.63 (0.41–0.97)	0.64 (0.41–1.04)	0.82 (0.69–0.98)
≥ 75 y	421	142	1.00	1.08 (0.71–1.66)	0.75 (0.53–1.06)	0.70 (0.48–1.04)	0.80 (0.55–1.15)	0.87 (0.57–1.32)	0.98 (0.85–1.13) [d]
Non-dairy Calcium [c]									
women < 500 mg/d	924	814	1.00	0.81 (0.61–1.09)	1.05 (0.85–1.30)	0.81 (0.63–1.05)	0.94 (0.75–1.19)	0.89 (0.66–1.19)	0.95 (0.85–1.05)
≥ 500 mg/d	1214	864	1.00	0.95 (0.73–1.23)	0.86 (0.70–1.06)	0.94 (0.75–1.17)	0.83 (0.67–1.03)	0.70 (0.54–0.92)	0.90 (0.82–0.98)
men < 400 mg/d	286	379	1.00	1.31 (0.81–2.14)	0.88 (0.60–1.31)	0.97 (0.62–1.52)	0.69 (0.44–1.09)	0.70 (0.41–1.19)	0.85 (0.70–1.02)
≥ 400 mg/d	408	380	1.00	0.78 (0.50–1.23)	0.75 (0.53–1.07)	0.61 (0.41–0.91)	0.67 (0.47–0.97)	0.74 (0.48–1.13)	0.93 (0.81–1.08) [d]
Non-dairy Vitamin D [c]									
women < 6 μg/d	938	835	1.00	0.87 (0.65–1.15)	1.03 (0.83–1.28)	0.95 (0.74–1.22)	0.90 (0.72–1.14)	0.92 (0.69–1.22)	0.95 (0.85–1.05)
≥ 6 μg/d	1200	843	1.00	0.89 (0.68–1.16)	0.87 (0.71–1.07)	0.86 (0.68–1.08)	0.84 (0.68–1.05)	0.69 (0.53–0.90)	0.88 (0.81–0.97)
men < 6 μg/d	261	344	1.00	1.01 (0.57–1.78)	0.85 (0.55–1.31)	1.07 (0.66–1.72)	0.61 (0.38–0.99)	0.76 (0.45–1.27)	0.88 (0.74–1.06)
≥ 6 μg/d	433	413	1.00	1.05 (0.70–1.57)	0.85 (0.61–1.18)	0.71 (0.49–1.05)	0.84 (0.59–1.20)	0.83 (0.54–1.26)	0.95 (0.82–1.11)
Non-dairy Protein									
women < 60 g/d	1171	831	1.00	1.03 (0.80–1.33)	1.15 (0.94–1.40)	1.07 (0.85–1.35)	1.07 (0.86–1.32)	0.79 (0.59–1.05)	0.90 (0.82–0.98) [d]
≥ 60 g/d	967	847	1.00	0.72 (0.53–0.97)	0.70 (0.56–0.88)	0.68 (0.53–0.87)	0.66 (0.53–0.84)	0.65 (0.49–0.85)	0.93 (0.84–1.02) [d]
men < 70 g/d	351	366	1.00	1.17 (0.75–1.80)	0.88 (0.62–1.25)	0.89 (0.59–1.33)	0.63 (0.42–0.94)	0.71 (0.44–1161)	0.86 (0.72–1.02)
≥70 g/d	343	393	1.00	0.83 (0.50–1.39)	0.71 (0.48–1.03)	0.67 (0.43–1.02)	0.74 (0.49–1.09)	0.79 (0.50–1.24)	0.97 (0.83–1.13)

$P_{interaction} > 0.05$ for all stratified analyses.

[a] Multivariable models are adjusted for age, follow-up cycle, total energy intake, yogurt and cheese intakes, calcium and vitamin D from non-dairy foods plus supplements, protein from non-dairy foods, retinol from supplements, vitamin K, caffeine, alcohol, milk during teenage years, body mass index, height, physical activity, smoking, use of postmenopausal hormones (women), use of thiazide diuretics, furosemide-type diuretics and oral steroids, and diagnoses of cancer, diabetes and cardiovascular disease

[b] Milk includes all skim, low fat and full fat varieties with a serving size of 1 cup (240 mL).

[c] includes intake from non-dairy foods plus supplements

[d] $P_{curvature} < 0.05$

Table 4.

Multivariable-adjusted relative risk [a] (95% confidence interval) of hip fracture by cumulatively averaged frequency of consumption of milk, cheese and total dairy foods, stratified by categories of body mass index [b] and by approximate quartiles of waist circumference, among postmenopausal women and among men 50 years of age and older

	cases	p-y	Milk per 1/day [c]	Cheese per 1/day [c]	Total Dairy per 1/day [c]
BMI, kg/m^2					
women < 18.5	142	268	1.17 (0.80–1.69)	1.40 (0.78–2.51) [d]	1.20 (0.90–1.61)
18.5–24.9	1166	754	0.90 (0.82–0.99)	1.00 (0.96–1.05) [d]	0.93 (0.87–1.00)
25–29.9	573	550	0.96 (0.84–1.10)	0.76 (0.59–0.96)	0.92 (0.83–1.03)
≥ 30	229	329	0.79 (0.63–0.95)	0.71 (0.49–1.05)	0.79 (0.66–0.95)
$P_{interaction}$			0.57	0.002	0.12
men < 18.5	9 [e]	25	---	---	---
18.5–24.9	379	304	0.98 (0.84–1.13)	1.22 (0.92–1.62)	1.01 (0.90–1.13)
25–29.9	220	345	0.91 (0.73–1.12)	0.83 (0.55–1.23)	0.95 (0.80–1.12)
≥ 30	62	82	0.47 (0.25–0.87)	0.58 (0.21–1.58)	0.57 (0.36–0.89)
$P_{interaction}$			< 0.001	0.02	< 0.001
Waist Circumference [f] cm					
women < 73	268	214	0.85 (0.68–1.04)	1.02 (0.72–1.46)	0.94 (0.80–1.11)
73–80.9	332	277	0.92 (0.77–1.09)	0.95 (0.70–1.30)	0.92 (0.80–1.06)
81–90.9	387	247	0.80 (0.68–0.95)	0.93 (0.68–1.26)	0.86 (0.74–0.98)
≥ 91	341	223	0.88 (0.74–1.06)	0.85 (0.60–1.20)	0.88 (0.76–1.03)
$P_{interaction}$			0.55	0.23	0.85
men < 91	118	145	1.15 (0.86–1.54)	1.40 (0.75–2.61)	1.16 (0.92–1.46)
91 −95.9	114	134	0.86 (0.62–1.21)	1.70 (0.95–3.06)	0.87 (0.66–1.14)
96–102.9	163	167	0.78 (0.60–1.01)	1.06 (0.65–1.73)	0.83 (0.67–1.02)
≥ 103	148	146	0.89 (0.66–1.19)	0.65 (0.37–1.14)	0.85 (0.68–1.07)
$P_{interaction}$			0.19	0.05	0.01

p-y is person-years, in thousands

[a] Multivariable models are adjusted for age, follow-up cycle, total energy intake, calcium and vitamin D from non-dairy foods plus supplements, protein from non-dairy foods, retinol from supplements, vitamin K, caffeine, alcohol, milk during teenage years, body mass index, height, physical activity, smoking, use of postmenopausal hormones (women), use of thiazide diuretics, furosemide-type diuretics and oral steroids, and diagnoses of cancer, diabetes and cardiovascular disease. In addition, milk is adjusted for yogurt and cheese intakes and cheese is adjusted for milk and yogurt intakes.

[b] BMI categories defined by the World Health Organization.

[c] See Table 1 footnote for descriptions and serving sizes of dairy foods.

[d] $P_{curvature} < 0.05$

[e] too few cases for analysis

[f] Follow-up began in1986 when waist circumference was first assessed in both cohorts.