Original Investigation

Milk Consumption During Teenage Years and Risk of Hip Fractures in Older Adults

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IMPORTANCE Milk consumption during adolescence is recommended to promote peak bone mass and thereby reduce fracture risk in later life. However, its role in hip fracture prevention is not established and high consumption may adversely influence risk by increasing height.

OBJECTIVES To determine whether milk consumption during teenage years influences risk of hip fracture in older adults and to investigate the role of attained height in this association.

DESIGN, SETTING, AND PARTICIPANTS Prospective cohort study over 22 years of follow-up in more than 96 000 white postmenopausal women from the Nurses' Health Study and men aged 50 years and older from the Health Professionals Follow-up Study in the United States.

EXPOSURES Frequency of consumption of milk and other foods during ages 13 to 18 years and attained height were reported at baseline. Current diet, weight, smoking, physical activity, medication use, and other risk factors for hip fractures were reported on biennial questionnaires.

MAIN OUTCOMES AND MEASURES Cox proportional hazards models were used to calculate relative risks (RRs) of first incidence of hip fracture from low-trauma events per glass (8 fl oz or 240 mL) of milk consumed per day during teenage years.

RESULTS During follow-up, 1226 hip fractures were identified in women and 490 in men. After controlling for known risk factors and current milk consumption, each additional glass of milk per day during teenage years was associated with a significant 9% higher risk of hip fracture in men (RR = 1.09; 95% CI, 1.01-1.17). The association was attenuated when height was added to the model (RR = 1.06; 95% CI, 0.98-1.14). Teenage milk consumption was not associated with hip fractures in women (RR = 1.00 per glass per day; 95% CI, 0.95-1.05).

CONCLUSIONS AND RELEVANCE Greater milk consumption during teenage years was not associated with a lower risk of hip fracture in older adults. The positive association observed in men was partially mediated through attained height.

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Adolescence is a time of rapid skeletal growth, with more than 95% of adult bone mineral content attained by the end of this age period.[1,2] Although genetics play a major role in determining peak bone mass and height,[3] lifestyle factors are essential for maximizing genetic potential.[4] Calcium intake during the adolescent growth spurt is a critical factor because the demand for calcium accretion in bone is high.[5,6] Most reviews of the extensive research in this area conclude that bone mass is increased with higher calcium intake during childhood and adolescence,[7-10] although the optimal amount of calcium and the role of milk and dairy foods remain controversial.[11]

Risk of osteoporosis and osteoporotic fractures in older adults is dependent on the amount of bone mass accrued and the subsequent rate of bone loss. Therefore, achieving peak bone mass during adolescence is recommended to withstand losses during later life.[12-14] As longitudinal data suggest that the annual rate of individual bone loss is relatively constant during adult years,[15] achieving peak bone mass during adolescence may have the more important role in fracture prevention.[16] However, although higher milk consumption during formative years can contribute to greater bone density, it is also associated with greater height,[17,18] which is an independent risk factor for hip fracture.[19,20]

In this prospective study over 22 years in older adults with repeated assessments of current milk intake, we hypothesized that greater milk consumption during teenage years would not be associated with a lower risk of hip fracture. We considered attained height as a possible intermediate variable in the association.

Methods

Study Population

The Nurses' Health Study began in 1976 with 121 700 female nurses aged 30 to 55 years, and the Health Professionals Follow-up Study was formed 10 years later with 51 529 male health professionals aged 40 to 75 years. Participants provided their medical history and information on lifestyle and disease risk factors on the initial questionnaire and have updated this information and reported incident diagnoses on subsequent biennial questionnaires. Deaths were ascertained from family members, the postal service, and the National Death Index.[21,22]

Follow-up for this investigation began with the participants who reported their teenage milk consumption in 1986 in the Nurses' Health Study and 1988 in the Health Professionals Follow-up Study. Women did not enter into analysis until they reached menopause, and for consistency, men did not enter until they reached age 50 years. Participants were excluded at entry if they had reported a prior hip fracture, a diagnosis of osteoporosis or cancer, or being of nonwhite race/ethnicity (<3% of participants). A total of 35 349 men and 61 578 women contributed to this analysis, with follow-up rates of 97% and 92%, respectively. This investigation was approved by the institutional review board at Brigham and Women's Hospital, Boston, Massachusetts. Completion and return of the self-administered questionnaires constituted informed consent.

Hip Fractures

On every biennial questionnaire, participants reported their hip fractures with the date of occurrence and a description of the circumstances. As health professionals, participants were capable of accurately reporting these events.[23] During the 22 years of follow-up, 549 hip fractures were reported in the Health Professionals Follow-up Study population and 1309 in the Nurses' Health Study population. Fractures due to malignancy or major traumatic events (eg, motor vehicle crash, skiing) were not included as outcomes for this study, leaving 490 hip fracture cases in men and 1226 in women. More than 90% of these fractures occurred when tripping, falling from the height of a chair, or similar low-trauma event. The median age at hip fracture was 78 years in men and 73 years in women (range, 47-96 years).

Teenage and Current Adult Diet

On a short 23-item food frequency questionnaire to assess diet during teenage years (ages 13-18 years),[24,25] participants reported the frequency with which they consumed a glass of whole milk (8 fl oz or 240 mL), a glass of skim or low-fat milk, and 1 serving of cheese (1 oz) using 9 categories ranging from never to 6 or more per day. Ninety-two percent of the milk consumption was whole fat. In a reproducibility study in which

this food frequency questionnaire was completed again 8 years later by 249 women in the Nurses' Health Study, the correlation for whole milk was 0.71.[26] Validity was assessed among 270 women aged 34 to 53 years; the correlation between their reported teenage milk intakes and information provided by their mothers 5 years later was 0.44.[27]

Current diet was assessed in 1986 and every 4 years thereafter with a food frequency questionnaire on which participants reported their frequency of consumption for more than 130 foods, including skim, low-fat (1% and 2%), and whole-fat varieties of milk. Current use of multivitamins and calcium, retinol, and vitamin D supplements was ascertained on every biennial questionnaire. To generate estimates of long-term diet, milk consumption and nutrient intakes were updated at every dietary assessment with the mean of all reported intakes.

Nondietary Measures

Height was reported at cohort initiation and was found to be highly valid when compared with college or nursing school records.[28] All other nondietary measures, including weight, smoking, a diagnosis of osteoporosis or cancer, physical activity, and current use of thiazide diuretics, were assessed on most biennial questionnaires. Use of furosemide-like diuretics (eg, Lasix, Bumex) and oral steroids was assessed every cycle in men but was not reported by women until 1994. Questions on menopausal status and use of hormone replacement therapy were part of every biennial assessment, and uses of drugs that affect osteoporosis, specifically bisphosphonate, alendronate, raloxifene, and tamoxifen, were added to the questionnaires beginning in 1998. Activity during high school was assessed in women as the average hours per week spent walking and in moderate and strenuous activity; in men, this was assessed as the number of months per year of participation in aerobic activity or sports at least twice per week. Young adult weight was reported for age 18 years in women and age 21 years in men.

Statistical Analysis

Men and women were analyzed separately to examine possible differences. Each participant contributed person-time from the return date of the questionnaire on which teenage milk consumption was reported (1988 for men; 1986 for women) or a later questionnaire when men attained age 50 years or women entered menopause. Participants were censored at the date of hip fracture or death, last questionnaire response, or the end of follow-up (2010 for men; 2008 for women).

Cox proportional hazards models were used to compute relative risks (RRs) with 95% confidence intervals within categories of milk consumption during teenage years. The basic models were conditioned on age and questionnaire cycle, and multivariable RRs were calculated after adjusting simultaneously for the other dietary and nondietary risk factors for hip fracture. The most recent covariate data were used to allocate person-time to the appropriate category for each variable at the beginning of every biennial questionnaire cycle. To assess a dose-response effect, teenage milk consumption was entered into the model as a continuous value for an increase of 1 glass per day. Interactions between milk and other risk factors for hip fracture were assessed using the Wald test for con-

Table 1. Age and Age-Adjusted Characteristics at Entry Into Study Within Low, Middle, and High Categories of Frequency of Milk Consumption During Teenage Years Among Men Aged 50 Years and Older in the Health Professionals Follow-up Study and Postmenopausal Women in the Nurses' Health Study

Characteristic	Teenage Milk Consumption, Glasses[a]					
	Men			Women		
	<2/wk	1/d	≥4/d	<2/wk	1/d	≥4/d
Participants, %	10	16	15	17	19	6
Current adult measures						
Age, mean, y	60.4	59.7	57.2	56.4	56.4	56.2
Attained height, mean, cm	177.6	177.8	179.5	163.1	163.7	164.8
Milk, mean, glasses/wk[a]	3.2	4.7	9.6	3.3	5.7	10.4
Supplements, mean						
Calcium, mg/d	108	102	101	355	357	325
Vitamin D, μg/d	3.7	3.9	3.7	3.4	3.8	3.9
Retinol, μg/d	775	834	836	603	693	700
Protein, mean, g/d	90.3	91.1	93.8	73.5	74.6	76.5
Caffeine, mean, mg/d	243	224	229	295	276	285
Alcohol, mean, g/d	11.4	10.9	11.5	5.6	6.0	6.6
Energy, mean, kcal/d	1886	1920	2161	1640	1736	1957
BMI, mean	26.1	25.6	25.9	26.1	26.1	25.9
Physical activity, mean, MET-h/wk	28.7	28.5	32.8	13.4	14.3	15.0
Current smoker, %	8	7	8	21	19	20
Use, %						
HRT[b]	NA	NA	NA	34	36	34
Diuretic						
Thiazide	8	9	8	17	16	15
Furosemide[c]	2	1	1	3	2	2
Oral steroid[c]	1	1	1	2	2	2
Calcium supplement	16	16	15	50	50	47
Multivitamin	44	45	42	39	44	46
Teenage measures						
Intake, servings/wk						
Cheese[d]	1.5	2.1	2.6	1.6	2.0	2.3
Fruits and vegetables[e]	6.8	9.9	11.3	8.1	9.9	11.9
Meat and fish[f]	4.6	6.0	7.2	5.1	5.4	6.1
BMI at age 21 y (men) or 18 y (women)	23.0	22.8	23.3	21.6	21.5	21.1
Physical activity[g]	6.7	6.9	8.1	8.0	8.4	10.6
Vitamin pill use, %	12	18	21	9	15	20

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HRT, hormone replacement therapy; MET, metabolic equivalents; NA, not applicable.

[a] Milk includes all whole, low-fat, and skim varieties (1 glass = 8 fl oz or 240 mL).

[b] With estrogen alone or combined with progesterone.

[c] In women, use of furosemide diuretics and oral steroids was assessed in 1994 rather than at entry into study.

[d] One serving is equivalent to 1 slice or 1 oz.

[e] Includes apples (1), oranges (1), cabbage or cole slaw (½ cup), broccoli or cauliflower (½ cup), carrots (1 raw or ½ cup cooked), and spinach (½ cup cooked).

[f] Includes beef, pork, or lamb (3-5 oz) and fish or tuna fish (3-5 oz).

[g] Teenage activity was assessed as months per year of participation in vigorous exercise or sports in men and as hours per week of walking and moderate and strenuous exercise in women.

tinuous data or by comparing the difference in −2 log likelihood from models with and without interaction terms to a χ^2 distribution.

Results

Characteristics of the men and women at baseline are shown within the low, middle, and high categories of frequency of teenage milk consumption (**Table 1**). Among those who consumed at least 4 glasses of milk per day, men were on average 1.9 cm taller and women were 1.7 cm taller than those who consumed fewer than 2 glasses per week. In both cohorts, milk consumption during teenage years and during adult years was positively correlated ($r = 0.32$ in men; $r = 0.37$ in women). Those who consumed at least 4 glasses of milk per day as teenagers were the most active, had higher intakes of cheese, fruits and vegetables, and meat and fish, and were most likely to take a

Table 2. Relative Risks of Hip Fracture by Frequency of Milk Consumption During Teenage Years Among Men Aged 50 Years and Older in the Health Professionals Follow-up Study, 1988 to 2010, and Among Postmenopausal Women in the Nurses' Health Study, 1986 to 2008

Outcome	Teenage Milk Consumption, Glasses[a]					
	<2/wk	2-6/wk	1/d	2-3/d	≥4/d	Per 1/d[b]
Men						
Hip fracture cases, No.	39	68	87	224	72	490
Person-years	53 364	80 094	92 630	263 168	86 914	576 171
RR (95% CI)						
Basic model[c]	0.82 (0.55-1.20)	0.99 (0.71-1.37)	1 [Reference]	1.04 (0.81-1.35)	1.19 (0.86-1.64)	1.06 (0.99-1.14)
Adult milk intake added[d]	0.75 (0.51-1.12)	0.97 (0.70-1.34)	1 [Reference]	1.06 (0.82-1.38)	1.21 (0.87-1.69)	1.08 (1.01-1.16)
Multivariable model[e]	0.75 (0.50-1.12)	0.97 (0.69-1.35)	1 [Reference]	1.07 (0.84-1.39)	1.21 (0.86-1.69)	1.09 (1.01-1.17)
Women						
Hip fracture cases, No.	225	197	250	474	80	1226
Person-years	176 056	190 898	197 054	414 803	66 013	1 044 824
RR (95% CI)						
Basic model[c]	1.03 (0.86-1.24)	0.86 (0.72-1.04)	1 [Reference]	0.96 (0.82-1.12)	1.01 (0.78-1.30)	1.00 (0.96-1.05)
Adult milk intake added[d]	1.00 (0.83-1.20)	0.87 (0.72-1.05)	1 [Reference]	0.97 (0.83-1.13)	1.02 (0.79-1.32)	1.01 (0.97-1.06)
Multivariable model[e]	1.03 (0.85-1.24)	0.89 (0.73-1.07)	1 [Reference]	0.95 (0.81-1.12)	1.01 (0.78-1.31)	1.00 (0.95-1.05)

Abbreviation: RR, relative risk.

[a] Milk includes skim, low-fat, and whole-fat varieties (1 glass = 8 fl oz or 240 mL).

[b] Increase in risk for each additional glass of milk per day during teenage years.

[c] Adjusted for age and questionnaire cycle.

[d] Adjusted for age, questionnaire cycle, and adult milk consumption.

[e] Adjusted for age, questionnaire cycle, adult milk consumption, adult measures (intakes of calcium from supplements, vitamin D from supplements, and retinol from supplements, total protein, alcohol, and caffeine intakes, total energy intake, physical activity, body mass index [calculated as weight in kilograms divided by height in meters squared], smoking, use of thiazide diuretics, use of furosemide diuretics and oral steroids [men only], use of hormone replacement therapy [women only], and incident diagnoses of osteoporosis and cancer), and teenage measures (consumption of cheese, fruits and vegetables, and meat and fish, physical activity, vitamin use, and body mass index at age 21 years [men] or 18 years [women]).

vitamin pill during these same years. On average, men reported higher milk consumption during their teenage years than women (mean, 2.1 and 1.6 glasses of milk per day, respectively). During follow-up, 1332 men (4%) and 18 810 women (30%) reported a diagnosis of osteoporosis or low bone density, primarily in the later years.

In men, risk of hip fracture increased 6% for each additional glass of milk per day during teenage years (RR = 1.06; 95% CI, 0.99-1.14) in the basic model (**Table 2**). After adding current adult milk consumption to the model, risk of hip fracture increased to 8%, and further adjustment for all other risk factors raised the risk to 9% per glass per day (RR = 1.09; 95% CI, 1.01-1.17). In the multivariable categorical analyses, men who consumed at least 4 glasses per day had an RR of 1.21 for hip fracture (95% CI, 0.86-1.69) compared with those who consumed 1 glass per day, and risk was lowest in those who consumed the least amount of milk. Height was not included in the multivariable models because it was hypothesized to be an intermediate factor between teenage milk consumption and adult hip fracture. There was evidence for this, as the association was attenuated when adjusted for height: for each additional glass of milk per day, RR = 1.06 (95% CI, 0.98-1.14); for men who consumed at least 4 glasses per day, RR = 1.12 (95% CI, 0.80-1.57). Further evidence of this intermediary role is illustrated by the modest, though significant, increase in height (0.47 cm in men and 0.38 cm in women) for each additional glass of milk consumed during teenage years and the significant increased risk of hip fracture (4.5% in men and 5.0% in women) for every additional centimeter of height.

In women, no association was observed between teenage milk consumption and risk of hip fracture (multivariable RR = 1.00 per glass of milk per day; 95% CI, 0.95-1.05) (Table 2). In an alternative analysis, we censored women at the first reported use of a bisphosphonate (n = 12 288), raloxifene (n = 3422), or tamoxifen (n = 1170) and still found no evidence of an association.

Cheese consumption during teenage years was not associated with risk of hip fracture in either men or women, although intake was low during this age period. For an increase of 2 servings per week (mean intake), the RR for hip fracture was 0.96 (95% CI, 0.89-1.03) in men and 1.01 (95% CI, 0.96-1.05) in women. Cheese consumption during teenage years had little effect on attained height. Men were 0.06 cm shorter and women were 0.07 cm taller, on average, for each additional 2 servings per week.

We further examined the association between teenage milk consumption and hip fractures in men and women in categories below and above the median adult intakes of milk, calcium, and vitamin D but found little evidence that these were modifying factors. A strong positive association was observed in men with low intakes of both calcium (<875 mg/d) and vitamin D (<10 μg/d) (RR = 1.21 per glass per day; 95% CI,

1.06-1.39), whereas the association was much weaker in men with higher intakes of both nutrients (RR = 1.07; 95% CI, 0.95-1.20). However, the interaction was not significant (P = .16). Age, physical activity (teenage or adult), body mass index (calculated as weight in kilograms divided by height in meters squared; ages 18 and 20 years or current adult), and use of hormone replacement therapy did not modify associations between teenage milk consumption and risk of hip fracture (data not shown).

Discussion

Greater milk consumption during childhood and adolescence contributes to peak bone mass and is therefore expected to help avoid osteoporosis and bone fractures in later life. However, milk consumption during teenage years was not associated with a lower risk of hip fracture in older adults in our cohorts. Instead, a significant 9% increase in risk was observed in men for each additional glass of milk consumed per day during teenage years.

Milk consumption in early life not only builds bone mass but also increases height,[17,18] and height is a risk factor for hip fractures in later life.[19,20] This was true in our cohorts, where risk was increased by approximately 5% per centimeter. A mediating effect of height can partially account for our observed positive association between teenage milk consumption and hip fractures in men as risk was attenuated when height was added to the model. To our knowledge, no studies have examined whether milk consumption during childhood and adolescence is associated with other bone measures that increase risk of hip fracture independent of height, such as hip axis length or femoral neck width.[29-32] If an effect of milk on fracture risk were primarily mediated by other bone measures, adjustment for height could only be indirect and incomplete in accounting for this mediating role. Unlike milk, cheese consumption during teenage years was not associated with hip fractures in men or women, perhaps because it was not associated with attained height and has not been shown to affect growth in children.[17] Alternatively, it may be explained by the limited reported intake of cheese.

We did not see an increased risk of hip fracture with teenage milk consumption in women as we did in men. One explanation may be the competing benefit of an increase in bone mass with an adverse effect of greater height. Women are at higher risk for osteoporosis than men, hence the benefit of greater bone mass balanced the increased risk related to height. Men are not exposed to rapid bone loss as women are during menopause, and therefore the effect on bone length dominated. It is also possible that lack of any association among women may be because an assessment of milk consumption during preteen years would have been more relevant, as girls reach maximal height about 2 years before boys[33] and are younger when they enter puberty, a time when the bone mineral accretion rate approximately doubles.[5] Support for this hypothesis comes from retrospective data from the Third National Health and Nutrition Examination Survey[34] in which risk of osteoporotic fractures was more than twice as high in women

older than 50 years who drank milk less than once per week compared with higher intakes during ages 5 to 12 years, whereas milk intake during ages 13 to 17 years showed no significant association.

Peak bone mass is believed to be a major determinant of osteoporosis and age-related fractures.[35] Results from epidemiologic studies and mathematical models suggest that a 10% increase in peak bone mass would delay the onset of osteoporosis by 13 years[16] and reduce the risk of fracture by 50% in women after menopause.[36] However, it is not entirely clear that an early gain in bone mass will persist into adult years as the young skeleton is replaced through many years of remodeling, which may erase any initial advantage.[37] Also, gains in bone mass with calcium or dairy supplementation in children and adolescents may not endure after treatment is discontinued,[38-44] similar to the return to pretreatment levels when physical activity or hormone replacement therapy is discontinued in adults.[45-47] In 2 calcium supplementation trials in girls, the gains in bone mineral density in the treatment groups were no longer evident 2 to 7 years after the trials ended.[43,44] Benefits to bone mass may diminish even when higher calcium intakes are not discontinued, as demonstrated in a clinical trial in girls in which the differences in bone mineral density between the calcium-treated and placebo groups during the pubertal growth spurt became insignificant at most bone sites by early adulthood[48] because the habitual calcium intake in the placebo group was sufficient for bone mineral density to slowly come up to that in the treatment group. This catch-up phenomenon has been reported in animal studies[49,50] and in adolescents with anorexia nervosa who did not retain a deficiency in bone mineral after their weight was restored.[51]

Although the recommendation for milk consumption in children and adolescents focuses primarily on its calcium content, milk contributes in other ways to bone development. Fortified milk is a good source of vitamin D, which can increase spine and hip bone mineral density around puberty.[52] Vitamin D supplementation, however, may only be advantageous in children and adolescents with low baseline 25-hydroxyvitamin D levels[53] and benefit may not persist after supplementation is discontinued.[54] Milk also contributes protein, which promotes bone mineralization in childhood and adolescence.[48,55,56] Insulin-like growth factor 1, a key mediator of bone growth,[57] is regulated by dietary protein, and protein from milk may be superior in this role to that from other sources.[58,59] Nutrients or bioactive factors in milk may also stimulate endogenous production of growth hormone.[60]

The conclusions of this study are limited by error in retrospective reporting of milk consumption during teenage years. Although diet in the distant past may be poorly recalled, long-term recall of milk is better than for many other foods owing to the relative stability in the diet.[61,62] Studies have reported correlations of 0.22[63] and 0.25[64] between documented teenage milk consumption and recalled intake more than 40 years later, which may be sufficient for ranking individuals.[61] Our finding that recalled adolescent milk intake was associated with height in both men and women, consistent with our prospective findings in adolescents,[17] adds important evidence of validity of recalled milk intake in our cohorts. Dairy food con-

sumption exhibits a moderate degree of tracking from childhood to adulthood[65] and distant recall may also be influenced by current intake, although adult milk intake did not confound or modify our observed association between teenage milk consumption and hip fractures.

The major strength of this study is the prospective design in which teenage milk consumption was reported at baseline and current milk consumption was assessed throughout the follow-up period. Another strength is the identification of hip fractures, rather than bone density or other intermediate measures, because they are the true public health concern owing to cost and added morbidity and mortality, and the large number of hip fractures provided statistical power to observe associations. However, the fractures were self-reported and not specific as to bone site at the hip. The generalization of these results may be limited to white adults.

Dietary Guidelines for Americans, 2010 recommends the consumption of 3 cups of milk or equivalent dairy foods per day[66] to promote maximal bone mass in adolescents. In this investigation, higher milk consumption at this age did not translate into a lower risk of hip fracture for older adults, and a positive association was observed among men. Further research is needed to clarify the roles of early milk consumption and height in prevention of hip fractures in older adults.

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