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

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Abstract

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.

Objective—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—Prospective cohort study over 22 years of follow-up

Setting—United States

Participants—Over 96,000 Caucasian postmenopausal women from the Nurses' Health Study and men age 50 and older from the Health Professionals Follow-up Study

Exposures—Frequency of consumption of milk and other foods during ages 13–18 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 Outcome Measures—Cox proportional hazards models were used to calculate relative risks (RR) of first incident hip fracture from low-trauma events per glass (8 fl oz or 240 mL) of milk consumed per day during teenage years.

Results—Over 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

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Author Contributions:

Study concept and design: Feskanich, Willett

Acquisition of data: Feskanich, Willett

Analysis and interpretation of data: Feskanich, Willett, Bischoff-Ferrari, Frazier

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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, 95% CI 0.95–1.05 per glass per day).

Conclusion 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.

Adolescence is a time of rapid skeletal growth, with over 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 height³, lifestyle factors are essential for maximizing genetic potential⁴. 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 controversial¹¹.

Risk of osteoporosis and osteoporotic fractures in older adults is dependent upon 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 years¹⁵, achieving peak bone mass during adolescence may have the more important role in fracture prevention¹⁶. 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 repeat 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 (NHS) began in 1976 with 121,700 female nurses 30 to 55 years of age, and the Health Professionals Follow-up Study (HPFS) was formed ten years later with 51,529 male health professionals 40 to 75 years of age. Participants provided a 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 NHS and 1988 in HPFS. 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 had reported a prior hip fracture, a diagnosis of osteoporosis or cancer, or were of non-Caucasian ancestry (< 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 in Boston, MA.

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 events²³. Over the 22 years of follow-up, 549 hip fractures were reported in the HPFS study population and 1309 in NHS. Fractures due to malignancy or major traumatic events (e.g., motor vehicle accidents, skiing) were not included as outcomes for this study, leaving 490 hip fracture cases in men and 1226 in women. Over 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).

Teenage and Current Adult Diet

On a short 23-item food frequency questionnaire (FFQ) to assess diet during teenage years (ages 13 to 18)^{24,25}, participants reported the frequency with which they consumed a glass of whole milk (8 fluid ounces or 240 mL), a glass of skim or low fat milk, and one serving of cheese (1 oz) using nine categories ranging from never to 6/day. Ninety-two percent of the milk consumption was whole fat. In a reproducibility study in which this FFQ was completed again eight years later by 249 NHS women, the correlation for whole milk was 0.71²⁶. Validity was assessed among 270 women 34–53 years of age, in which the correlation between their reported teenage milk intakes and information provided by their mothers five years later was 0.44²⁷.

Current diet was assessed in 1986 and every four years thereafter with an FFQ 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.

Non-dietary Measures

Height was reported at cohort initiation and was found to be highly valid when compared with college or nursing school records²⁸. All other non-dietary 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 (e.g., Lasix[®], Bumex[®]) and oral steroids were assessed every cycle in men but were not reported by women until 1994. Questions on menopausal status and use hormone replacement therapy were part of every biennial assessment, and uses of drugs that affect osteoporosis, specifically bisphosphonates, alendronates, 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, and in men 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 in women and age 21 in men.

Statistical Analysis

Men and women were analyzed separately in order 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 50 years of age 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 (RR) with 95% confidence intervals (CI) 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 non-dietary 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 one glass per day. Interactions between milk and other risk factors for hip fracture were assessed using the Wald test for continuous data or by comparing the difference in $-2 \log$ likelihood from models with and without interaction terms to a chi-square 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 ≥ 4 glasses/day of milk, men were on average 1.9 cm taller and women were 1.7 cm taller than those who consumed < 2 glasses/week. In both cohorts, milk consumption during teenage years and during adult years were positively correlated ($r=0.32$ in men; $r=0.37$ in women). Those who consumed ≥ 4 glasses/day of milk as teenagers were the most active, had a higher intakes of cheese, fruits and vegetables, and meat and fish, and were most likely to take a 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/day, respectively). Over follow-up, 1,332 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/day of milk 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/day (RR=1.09, 95% CI 1.01–1.17). In the multivariable categorical analyses, men who consumed ≥ 4 glasses/day had an RR of 1.21 for hip fracture (95% CI 0.86–1.69) compared with those who consumed 1 glass/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: RR=1.06 (95% CI 0.98–1.14) per glass/day of milk and RR=1.12 (95% CI 0.80–1.57) among men who consumed ≥ 4 glasses/day versus 1/day. 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 cm of height.

In women, no association was observed between teenage milk consumption and risk of hip fracture (multivariable RR=1.00, 95% CI 0.95–1.05 per glass/day) (Table 2). In an alternate analysis, we censored women at the first reported use of a bisphosphonate ($n=12,288$), raloxifene ($n=3,422$), or tamoxifen ($n=1,170$), 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 two servings/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 two servings/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, 95% CI 1.06–1.39 per glass per day) 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=0.16). Neither age, physical activity (teenage or adult), BMI (ages 18 and 20 or current adult), nor use of hormone replacement therapy modified associations between teenage milk consumption and risk of hip fracture (data not shown).

COMMENT

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 children¹⁷. 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 of osteoporosis than men, hence the benefit of greater bone mass balanced the increased risk related to height. Men are not exposed to the 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 pre-teen years would have been more relevant, as girls reach maximum height about two years before boys³³ and are younger when they enter puberty, a time when the bone mineral accretion rate approximately doubles⁵. Support for this hypothesis comes from retrospective NHANES III data³⁴ in which risk of osteoporotic fractures was over twice as high in women over 50 who drank milk less than once per week compared with higher intakes during ages 5–12, whereas milk intake during ages 13–17 showed no significant association.

Peak bone mass is believed to be a major determinant of osteoporosis and age-related fractures³⁵. Results from epidemiologic studies and mathematical models suggest that a 10% increase in peak bone mass would delay the onset of osteoporosis by 13 years¹⁶ and reduce

the risk of fracture by 50% in women after menopause³⁶. 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 advantage³⁷. Also, gains in bone mass with calcium or dairy supplementation in children and adolescents may not endure after treatment is discontinued³⁸⁻⁴⁴, similar to the return to pre-treatment levels when physical activity or hormone replacement therapy are discontinued in adults⁴⁵⁻⁴⁷. In two calcium supplementation trials in girls, the gains in bone mineral density in the treatment groups were no longer evident two to seven 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 adulthood⁴⁸ as 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 restored⁵¹.

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 puberty⁵². Vitamin D supplementation, however, may only be advantageous in children and adolescents with low baseline 25(OH)D levels⁵³ and benefit may not persist after supplementation is discontinued⁵⁴. Milk also contributes protein which promotes bone mineralization in childhood and adolescence^{48,55,56}. IGF-1, a key mediator of bone growth⁵⁷, 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 hormone⁶⁰.

The conclusions of this study are limited by error in retrospective reporting of milk consumption during teenage years. Though diet in the distant past may be poorly recalled, long-term recall of milk is better than for many other foods due to the relative stability in the diet^{61,62}. Studies have reported correlations of 0.22⁶³ and 0.25⁶⁴ between documented teenage milk consumption and recalled intake over 40 years later, which may be sufficient for ranking individuals⁶¹. Our finding that recalled adolescent milk intake was associated with height in both men and women, consistent with our prospective findings in adolescents¹⁷, adds important evidence of validity of recalled milk intake in our cohorts. Dairy food consumption exhibits a moderate degree of tracking from childhood to adulthood⁶⁵ 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 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 due 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 Caucasian adults.

The 2010 Dietary Guidelines for Americans recommends the consumption of three cups of milk or equivalent dairy foods per day⁶⁶ to promote maximum 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 role of early milk consumption and height in prevention of hip fractures in older adults.

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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 age 50 and older in the Health Professionals Follow-up Study and postmenopausal women in the Nurses' Health Study.

Table 1

(% of participants)	Teenage Milk Consumption ^b (glasses)			
	Men		Women	
	< 2/week (10%)	1/day (16%)	4/day (15%)	4/day (6%)
<i>Current Adult Measures^a</i>				
Age, yrs	60.4	59.7	57.2	56.2
Attained height, cm	177.6	177.8	179.5	164.8
Milk ^b , glasses/week	3.2	4.7	9.6	10.4
Calcium from supplements, mg/d	108	102	101	325
Vitamin D from supplements, µg/d	3.7	3.9	3.7	3.9
Retinol from supplements, µg/d	775	834	836	700
Protein, g/d	90.3	91.1	93.8	76.5
Caffeine, mg/d	243	224	229	285
Alcohol, g/d	11.4	10.9	11.5	6.6
Energy, kcal/d	1886	1920	2161	1957
BMI, kg/m ²	26.1	25.6	25.9	25.9
Physical activity, MET-h/week ^d	28.7	28.5	32.8	15.0
Current smoker, %	8	7	8	20
HRT use ^c , %	na	na	na	34
Thiazide diuretic use, %	8	9	8	15
Furosemide diuretic use ^d , %	2	1	1	2
Oral steroid use ^e , %	1	1	1	2
Calcium supplement use, %	16	16	15	47
Multivitamin use, %	44	45	42	46
<i>Teenage Measures^a</i>				
Cheese, servings/week ^f	1.5	2.1	2.6	2.3
Fruits and vegetables, servings/week ^g	6.8	9.9	11.3	11.9
Meat and fish, servings/week ^h	4.6	6.0	7.2	6.1

(% of participants)	Teenage Milk Consumption ^b (glasses)					
	Men			Women		
	< 2/week (10%)	1/day (16%)	4/day (15%)	< 2/week (17%)	1/day (19%)	4/day (6%)
BMI, age 21 (men) or 18 (women), kg/m ²	23.0	22.8	23.3	21.6	21.5	21.1
Physical activity ⁱ	6.7	6.9	8.1	8.0	8.4	10.6
Vitamin pill use, %	12	18	21	9	15	20

BMI=body mass index; na=not applicable

^a values are means or percentages

^b milk includes all whole, low fat, and skim varieties (one glass = 8 fl oz or 240 mL)

^c hormone replacement therapy with estrogen alone or combined with progesterone

^d metabolic equivalents

^e in women, use of furosemide diuretics and oral steroids was assessed in 1994 rather than at entry into study

^f cheese consumption: 1 serving = 1 slice or 1 oz

^g fruits and vegetables (with serving sizes) include 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)

^h meat and fish (with serving sizes) includes beef, pork or lamb (3–5 ounces) and fish or tuna fish (3–5 ounces)

ⁱ teenage activity was assessed as months per year of participation in vigorous exercise or sports in the men and as hours per week of walking and moderate and strenuous exercise in the women

Relative risks of hip fracture by frequency of milk consumption during teenage years among men age 50 and older in the Health Professionals Follow-up Study, 1988–2010, and among postmenopausal women in the Nurses' Health Study, 1986–2010.

Table 2

	Teenage Milk Consumption (glasses) ^a					per 1/day ^b
	< 2/week	2–6/week	1/day	2–3/day	4/day	
Men						
hip fracture cases	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)	1.00	1.04 (0.81–1.35)	1.19 (0.86–1.64)	1.06 (0.99–1.14)
• add adult milk intake ^d	0.75 (0.51–1.12)	0.97 (0.70–1.34)	1.00	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)	1.00	1.07 (0.84–1.39)	1.21 (0.86–1.69)	1.09 (1.01–1.17)
Women						
hip fracture cases	225	197	250	474	80	1,226
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)	1.00	0.96 (0.82–1.12)	1.01 (0.78–1.30)	1.00 (0.96–1.05)
• add adult milk intake ^d	1.00 (0.83–1.20)	0.87 (0.72–1.05)	1.00	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)	1.00	0.95 (0.81–1.12)	1.01 (0.78–1.31)	1.00 (0.95–1.05)

RR=relative risk; CI=confidence interval

^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 a 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, plus the following adult measures: intakes of calcium from supplements, vitamin D from supplements, retinol from supplements, total protein, alcohol, and caffeine intakes, total energy intake, physical activity, BMI, 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; plus the following teenage measures: consumption of cheese, fruits and vegetables, and meat and fish, physical activity, vitamin use, and BMI at age 21 (men) or age 18 (women)