Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women¹⁻³

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ABSTRACT

Background: Calcium supplements increase bone mass in children, but the effect does not persist once supplementation is discontinued. **Objective:** The objective of this study was to determine whether milk intake during childhood and adolescence, when controlled for current calcium intake, is associated with adult bone mass (ie, bone mineral content), bone mineral density, and the incidence of osteoporotic fracture.

Design: We used data from the third National Health and Nutrition Examination Survey of 3251 non-Hispanic, white women age ≥ 20 y. Bone density was measured at the hip. History of fracture of the hip, spine, or forearm was classified as a lifetime fracture (occurring after age 13 y) or an osteoporotic fracture (occurring after age 50 y). Subjects reported frequency of milk consumption during childhood (aged 5–12 y) and during adolescence (aged 13–17 y). Regression models controlled for weight, height, age, menopause and use of estrogen, physical activity, smoking, and current calcium intake.

Results: Among women aged 20–49 y, bone mineral content was 5.6% lower in those who consumed < 1 serving of milk/wk (low intake) than in those who consumed > 1 serving/d (high intake) during childhood (P < 0.01). Low milk intake during adolescence was associated with a 3% reduction in hip bone mineral content and bone mineral density (P < 0.02). Among women aged ≥ 50 y, there was a nonlinear association between milk intake during childhood and adolescence and hip bone mineral content and bone mineral density (P < 0.04). Low milk intake during childhood was associated with a 2-fold greater risk of fracture (P < 0.05).

Conclusion: Women with low milk intake during childhood and adolescence have less bone mass in adulthood and greater risk of fracture. *Am J Clin Nutr* 2003;77:257–65.

KEY WORDS Bone density, milk intake during childhood and adolescence, calcium intake, osteoporosis, peak bone mass, fracture, women

INTRODUCTION

Recommendations for dietary calcium intake have been increased for children and adolescents to maximize peak bone mass and ultimately reduce the risk of osteoporotic fracture (1). The long-term benefit of increased calcium intake during growth for reducing disease risk many decades later is uncertain. Calcium supplementation of children and adolescents increases bone mass and density (2–9). This benefit, however, appears to be transient, and bone mass in children supplemented with calcium is similar

to that in children given placebo after supplementation is discontinued (10–12). Because this effect does not persist, the long-term benefit of promoting higher calcium intake in children and adolescents, specifically, is questionable. In contrast, studies supplementing the diet with milk or milk-derived calcium showed persistent effects on bone mass 1.5–3.5 y after the supplementation was discontinued (13, 14).

Although some (15–20), but not all (21–25), epidemiologic studies have found a relation between lifetime calcium intake and adult bone mineral density (BMD), few studies have investigated the independent effects of calcium or milk intake during childhood and adolescence. Dietary behaviors such as milk and calcium intakes developed in childhood have been shown to persist into adulthood (17, 18, 26, 27). Thus, adjustment for current calcium intake is necessary for the examination of the independent effects of intake during childhood or adolescence. Results of studies that examined the effects of milk or calcium intake during childhood or adolescence and adjusted for current calcium intake were inconsistent, possibly because of differences in study sample characteristics. One study found that milk intake in childhood $(\leq 12 \text{ y})$ was independently related to spine and hip BMD in women aged 45-49 y (28). Another study found no association between childhood milk intake and BMD of the total body, hip, spine, or mid-radius in young women (aged 18-31 y) (27). This latter study, however, did find that milk intake during adolescence (13–19 y) was independently associated with total body and radial shaft BMD but not with spine and hip BMD in young women (27). In contrast, another study found no significant association between calcium intake during adolescence and spine, hip, mid-radius, or distal radius BMD among women aged 30-39 y after adjustment for current calcium intake (29).

Few studies have examined the relation between childhood diet and the risk of osteoporotic fracture. Two studies found no association between milk intake during adolescence and the incidence of fracture of the forearm and hip in adulthood (30, 31), whereas

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Identification of the independent effects of milk and or calcium intake during specific periods of life is important for efficient targeting of interventions to maximize their long-term benefit. The objective of this study was to determine whether milk intakes during childhood and adolescence are independently associated with bone mass, bone density, and bone size (area) of the hip during adulthood after control for current milk and calcium intake in a nationally representative sample of white women in the United States. We hypothesized that lower milk intake would be associated with lower bone mass and density. We also examined the relation between milk intake during childhood and adolescence and the risk of lifetime fracture.

SUBJECTS AND METHODS

We used data from the third National Health and Nutrition Examination Survey (NHANES III) for this study. NHANES III, conducted by the National Center for Health Statistics, is a cross-sectional survey of noninstitutionalized persons in the United States that was conducted between 1988 and 1994 (33). The survey used a stratified, multistage probability design to select a nationally representative sample. Children aged 2 mo–5 y, adults aged > 60 y, and African Americans and Mexican Americans were oversampled. The survey included a household interview and a physical examination conducted in a mobile examination center (MEC).

Bone mineral content (BMC), BMD, and bone area of the left hip were measured by dual-energy X-ray absorptiometry (DXA) at the MEC. Bone area (cm2) was the projected or two-dimensional bone area determined from the DXA scan (34). Measurements were made on the right hip in subjects whose left hip was previously fractured (1%). DXA scans were acquired with the use of a densitometer (QDR 1000; Hologic, Waltham, MA) in pencil-beam mode. Quality-control measures were described elsewhere (35). Measurements were obtained for the total hip and 4 subregions (ie, femoral neck, trochanter, Ward's triangle, and intertrochanter). We restricted our analyses to the total hip because the hip subregions were highly correlated with the total hip measurements (r = 0.76-0.98). Bone measurements were obtained on 14 646 persons, or 88% of persons reporting to the MEC who were ≥20 y old and eligible for a BMD measurement. Measurements were not obtained on persons aged < 20 y, on women who were pregnant or who may be pregnant, or on persons who had a history of fractures of both hips. Of the DXA scans performed, \approx 2% were considered unacceptable because of motion artifacts, incomplete scans, and grossly abnormal scans (35, 36).

Because of the known sex, racial, and ethnic differences in BMD and risk of osteoporotic fracture (34), we restricted our sample for these analyses to non-Hispanic, white women—the group at greatest risk of osteoporosis—with acceptable bone measurements (n = 3251).

Subjects reported whether they had ever experienced a fracture of the hip, wrist, or spine and specified their age when the fracture occurred. We created 2 fracture variables. Lifetime fractures included fractures that occurred at age 13 y and later. The cutoff of age 13 y was chosen so that milk-intake information pertained to the period either before or concurrent with the fracture. Osteoporotic fractures were those that occurred at age 50 y and later.

This variable was created only for women ≥ 50 y old. Information on the severity of trauma associated with the fracture was obtained only for fractures that occurred at age 50 y and later. Of the women classified with an osteoporotic fracture, only 6% had fractures due solely to severe trauma. Exclusion of fractures associated with severe trauma did not affect the results.

Milk intake

Questions regarding milk consumption during specific periods of life were asked in the household interview. The questionnaire targeted 5 distinct age periods: childhood (5-12 y), adolescence (13–17 y), young adulthood (18–35 y), middle adulthood (36–65 y), and later adulthood (>65 y). Subjects were asked to recall how often they consumed any type of milk, including milk added to cereal but not including small amounts added to coffee or tea, during each age period. Possible responses included: more than once a day, once a day, less than once a day but more than once a week, once a week, less than once a week, never, and don't know. To facilitate analyses, responses were collapsed into 4 categories: > 1/d, 1/d, 1–6/wk, and < 1/wk. "Don't know" responses were classified as missing. Information on current milk intake was derived from the food-frequency questionnaire (FFQ) that also was administered as part of the household interview. Information from the FFQ included the number of servings in the last month of both regular and chocolate milk. Information on portion size was not collected. We categorized current milk intake information into the same categories as the historical milk intake information.

Quantitative information on calcium intake was obtained from the 24-h recall conducted during the MEC visit. The 24-h recall was conducted with the use of an automated, interactive dietary data-collection system that was developed by the University of Minnesota Nutrition Coordinating Center (33). Food composition data were based on the US Department of Agriculture data files specific for that time period. Nutrient intake from the 24-recall does not include intakes from nutritional supplements and antacids. Specific questions regarding the use of antacids and vitamins were asked as part of the household questionnaire. Subjects reported the brand name of vitamin, mineral, and antacids that they regularly consumed and the frequency of use in the last month. We calculated the amount of calcium in the vitamin and mineral supplement preparations by using data from the NHANES III CD ROM 11, no. 2A (National Center for Health Statistics, 1998) and the amount of calcium in the antacids by using information from the Physicians' Desk Reference for Nonprescription Drugs (37) and from product labels. Total calcium intake was calculated from the sum of the 24-h food recalls plus all the aforementioned supplements.

Potential covariates

To control for potential confounding and to reduce overall variability in the data, we evaluated other variables known to affect BMC or BMD in our analyses. These variables included age, weight, height, menopausal status, tobacco use, alcohol consumption, physical activity, and medications used, including estrogen replacement therapy. Age, weight, and height were directly available from the household and MEC interviews. Other variables were constructed by combining information from several sources as described below.

There was no direct question regarding menopausal status on the questionnaire. We categorized women as premenopausal or postmenopausal according to an iterative procedure involving 8



criteria using information on age, occurrence of a menstrual period or pregnancy in the previous year, hormonal contraceptive or other estrogen use, and serum follicle-stimulating hormone concentration. Serum follicle-stimulating hormone was measured only in women aged 35-60 y (33). The criteria were assessed in sequential order so that the successive rules were applied only to those women not already categorized. The decision rules were as follows: I) age > 61 y = postmenopausal; 2) bilateral oophorectomy = postmenopausal; 3) period/pregnancy in the previous year = premenopausal; 4) follicle-stimulating hormone > 40 IU/L = postmenopausal; 5) age < 35 y = premenopausal; 6) birth control pills in the previous year = premenopausal; 7) age > 50 y = postmenopausal; and 8) age < 50 y = premenopausal. To account for the fact that some postmenopausal women were taking estrogen, we further categorized women as estrogen-deficient if they were postmenopausal and were not taking some form of estrogen.

Information on the use of cigarettes, pipe, cigar, chewing tobacco, snuff, and nicotine gum was obtained in the household interview. These questions were redefined into current or not current smoker, ever or never a smoker, and the number of years a smoker. Most persons (34/44 or 77.3%) who smoked a pipe or cigar or used chewing tobacco also smoked cigarettes.

Alcohol intake was assessed as part of the FFQ. Subjects reported the frequency of beer, liquor, and wine consumption in the previous month. We coded alcohol consumption as the total number of servings of beer, wine, and hard liquor into categories: 0, <5, 5-29, and ≥ 30 servings in the previous month.

Information on leisure-time physical activity was obtained from self-reports. Subjects reported the frequency of participation in specific activities: walking at least 1 mile, jogging or running, bicycling, aerobics, dancing, calisthenics, weight lifting, and other activities. Information coded under "other activities" also was included if the activity fell into the following categories: bicycling, conditioning, dancing, running, team sports, walking, and winter activities. The frequency of each event was combined to create a total activity frequency, which was then categorized for analysis as 0, 1-8, 9-31, and ≥ 32 episodes/mo.

We examined the reported use of medications known to affect BMD. Categories of medications that were considered in this study were anticoagulants and thrombolytics, metabolic drugs and nutrients, medications that affect calcium metabolism, adrenal corticosteroids, and thyroid and antithyroid medications (study drug codes 409, 900, 916, 1032, and 1027). Only thyroid medications had an incidence high enough (ie, > 5%) for meaningful inclusion in further analyses.

Statistical analysis

Multiple regression was used to examine the relations between milk intake during childhood and adolescence and adult BMC, BMD, and bone area of the hip. All analyses were conducted with SUDAAN software (Research Triangle Institute, Research Triangle Park, NC) to account for the complex sample design and allow calculation of appropriate variance estimates. The MEC sample weights were used for statistical analyses. These are the sample weights recommended for use in analysis of data collected at the MEC (33). Models were developed separately for BMC, BMD, and bone area. The sample was divided by age into 2 categories, 20–49 y and ≥50 y, because earlier reports of these data showed that age-related trends in BMC and BMD were not linear. A greater rate of decline in BMC and BMD was associated with increasing age after 50 y, which coincides with the average age of

menopause (34). The relation between milk intake during child-hood and adolescence and BMC, BMD, and bone area was first tested with an overall F test. If the overall test was significant (P < 0.05), the 3 lowest categories were compared with the highest category by the use of Dunnett's test to account for multiple comparisons (38).

A two-step modeling strategy was used to adjust for potential confounding and to improve the precision in estimating the effects of milk intake on BMC, BMD, and bone area. First, we examined the bivariate relations between potential covariates and bone measurements. Potential covariates that were considered included age, weight, height, menopausal and estrogen status, physical activity, alcohol consumption, tobacco use, and current milk or current calcium intake. Age, weight, height, and current calcium intake were fitted as continuous variables. Menopausal and estrogen status, physical activity, alcohol consumption, and tobacco use were fitted as categorical variables. Variables that were associated with BMC or BMD with $P \le 0.25$ in bivariate analyses were included in the full model for that bone measure. In addition to childhood or adolescent milk intake variables, all final models included variables for age, weight, estrogen deficiency or menopause, and current calcium intake (either current milk intake or total mg of calcium) because of their known associations with BMC and BMD. A backward-elimination approach was used to exclude other potential covariates (smoking, alcohol intake, medication use, and physical activity) from the final models. Covariates were retained in the final model if the P value was ≤ 0.10 or if exclusion of that variable affected the coefficients for childhood or adolescent milk intake by > 10%. Height was not included in the models for bone area to prevent an overcorrection of the potential mediating effects of linear growth on hip bone area.

Logistic regression was used to assess the relation between milk intake during childhood and adolescence and fracture occurrence, lifetime fractures (all women), and osteoporotic fractures (for women ≥ 50 y old). Models were computed with SUDAAN software using the MEC sample weights. Potential confounders considered in the models were age, height, weight, smoking, and estrogen deficiency. Criteria for inclusion in the logistic regression models were as described above for the multiple regression. The proportion of fracture cases that could be attributed to low milk intake during childhood, also known as the population attributable risk, was estimated by use of the weighted prevalence estimate of low milk intake during childhood and the odds ratio from the logistic regression model.

RESULTS

There were 3251 non-Hispanic, white women \geq 20 y old with an acceptable DXA scan of the hip. Of these, 1371 (42.2%) were aged 20–49 y ($\overline{x}\pm$ SD: 35 \pm 8) and 1880 (57.8%) were aged \geq 50 y (69 \pm 11; range: 50–90). Women aged 20–49 y had mean (\pm SE) weight of 67.6 \pm 0.6 kg and height of 163.9 \pm 0.2 cm, and women aged \geq 50 y had mean (\pm SE) weight of 69.9 \pm 0.5 kg and height of 160.1 \pm 0.2 cm.

Most women reported consuming ≥ 1 glasses of milk/d during childhood (84.2%) and adolescence (70.4%) (**Table 1**). Reported current milk intake was lower: only 41.8% of women aged 20–49 y and 52.2% of women aged ≥ 50 y reported drinking ≥ 1 glasses of milk/d. Overall, the degree of concordance between milk intake during childhood and adolescence and current milk intake was low. For women aged 20–49 y, the kappa statistics for the comparison of current milk intake with childhood and adolescence

TABLE 1

Distribution of milk and calcium intake among non-Hispanic, white women¹

	Age group	
	20–49 y	≥50 y
	%	
Childhood milk intake (servings)		
<1/wk	5.6	9.8
1–6 wk	8.8	7.8
1/d	27.2	26.5
>1/d	58.4	55.8
Adolescent milk intake (servings)		
<1/wk	13.2	16.0
1–6 wk	17.1	12.4
1/d	29.8	29.5
>1/d	39.8	42.1
Current milk intake (servings)		
<1/wk	27.2	25.1
1–6 wk	31.0	22.7
1/d	19.8	32.1
>1/d	22.0	20.1
Current calcium intake (mg/d) ²		
Dietary intake ³	630 (617, 658)	565 (544, 587)
Mineral supplements and antacids ⁴	143 (124, 166)	223 (195, 257)
Total calcium intake	699 (669, 730)	672 (644, 701)

¹The unweighted sample size for women aged 20–49 y was n = 1371 and that for women aged ≥50 y was n = 1880. The results presented reflect the weighted sample.

milk intakes were 0.14 and 0.25, respectively. For women aged ≥ 50 y, the kappa statistics were 0.13 and 0.22, respectively. The geometric mean dietary calcium intakes determined from the 24-h recall were 630 mg/d (95% CI: 617, 658 mg/d) and 565 mg/d (95% CI: 544, 587 mg/d) for women aged 20–49 and ≥ 50 y, respectively. Calcium from mineral supplements and antacids increased the mean calcium intake by 11% for women aged 20–49 y and by 19% for women aged ≥ 50 y.

The numbers of women successively categorized as postmenopausal by each criterion are shown in **Table 2**. Descriptive

TABLE 2 Categorization of menopause¹

Criteria	Postmenopausal	No. of subjects
		n (%)
Age > 61 y	Yes	1385 (42.6%)
Bilateral oophorectomy	Yes	147 (4.5%)
Period or pregnancy in previous year	No	1275 (39.2%)
Follicle-stimulating hormone > 40 IU/L for women aged 35–60 y	Yes	274 (8.4%)
Age < 35 y	No	18 (0.5%)
Use of birth control pills in previous yea	r No	101 (3.1%)
Age $\geq 50 \text{ y}$	Yes	30 (0.9%)
Age 20–49 y	No	21 (0.6%)

¹Women (total n = 3251) were categorized as premenopausal or postmenopausal according to 8 criteria, in sequential order as listed above, so that the successive rules were applied only to those women not already categorized.

TABLE 3Distribution of covariates among study subjects²

	Age group	
	20–49 y	≥50 y
Postmenopausal (%) ²	7.0	90.1
Estrogen deficient (%) ³	3.3	73.8
Ever a smoker (%)	51.8	45.0
Number of years a smoker (%) ⁴	12 (1–36)	25 (1-71)
Current smoker (%)	33.5	15.8
Leisure-time physical activity, episodes/mo (%)		
0	19.9	36.7
1–8	28.6	19.3
9–31	32.3	30.6
≥ 32	19.2	13.4
Alcohol, servings in the previous mo (%)		
0	39.0	63.9
<5	25.3	15.5
5–29	30.4	12.1
≥ 30	5.2	8.5

¹The unweighted sample size for women aged 20–49 y was n = 1371 and that for women aged ≥ 50 y was n = 1880. The results presented reflect the weighted sample.

information on menopausal and estrogen status and the other potential covariates by age group is given in **Table 3**. Estrogen usage was reported by 16.3% of postmenopausal women \geq 50 y old.

Milk intake and bone density among women aged 20-49 y

Among women aged 20–49 y, final regression models predicting total hip BMC and BMD included current calcium intake, age, weight, height (BMC model only), estrogen deficiency, and physical activity. Models for bone area included weight, age, menopausal status, and current dietary calcium intake. Current dietary calcium intake was positively associated with BMC, BMD, and bone area in all models (*P* values, 0.007–0.12). Total calcium intake (dietary calcium + supplements) was less consistently associated with bone measures; therefore, dietary calcium intake was used for all analyses. Results for current milk intake determined from the FFQ were similar to those for current dietary calcium intake.

Milk intake during childhood, adjusted for confounders, was associated (P = 0.003) with total hip BMC. Hip BMC was 5.6% lower among women who consumed < 1 serving of milk/wk than among women who consumed > 1 serving of milk/d during childhood (P < 0.01). In contrast, the BMC of women who consumed intermediate frequencies of milk was not lower than that of women with the highest consumption frequency (Figure 1). There was no association between childhood milk intake and hip BMD (overall P = 0.31). Childhood milk intake was associated with bone area (P = 0.003). Bone area was 4.6% less among women with the lowest milk intake than among women with the highest intake (P < 0.01) during childhood. Milk intake during adolescence was associated ($P \le 0.02$) with hip BMC and BMD, and the greater values were associated with greater milk intake. The mean BMC and BMD of women who consumed < 1 serving of milk/wk was $\approx 3\%$ lower than those of women who consumed > 1 serving of milk/d during adolescence (P < 0.02). Milk intake during adolescence was not associated with bone area (P = 0.13).



²Geometric mean (95% CI).

³According to the 24-h recall.

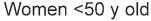
⁴Among those who reported consumption of supplemental calcium in the previous month (31% of women aged ≥50 y).

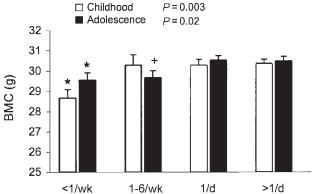
²Percentage of total group.

 $^{^3}$ Postmenopausal and not using some form of estrogen.

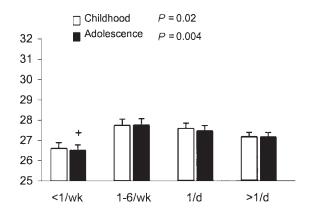
⁴Median (range) among those who ever were smokers.

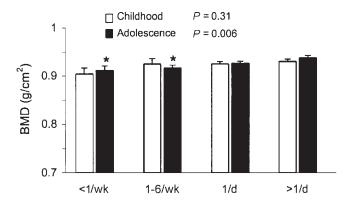
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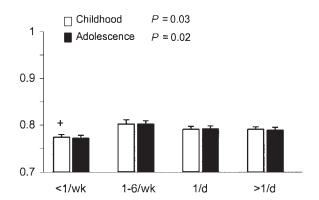


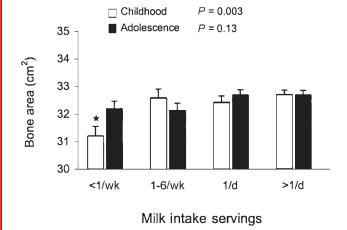


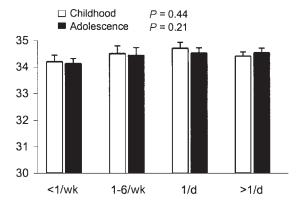
Women ≥50 y old











Milk intake servings

FIGURE 1. Mean total hip bone mineral content (BMC), bone mineral density (BMD), and bone area according to milk intake during childhood and adolescence among non-Hispanic, white women who participated in the third National Health and Nutrition Examination Survey. For women aged 20-49 y (n = 1371), BMC and BMD means were adjusted for current calcium intake, age, weight, height (BMC only), estrogen deficiency, and physical activity. Regression models for women aged ≥ 50 y (n = 1880) also included alcohol intake and any history as a smoker. Regression models for bone area included age, weight, current calcium intake, and menopause. P values in the graph are for the overall F test comparing groups. Follow-up analyses comparing the 3 lowest milk-intake categories with the highest milk-intake category were performed with the use of Dunnett's test to account for multiple comparisons (38) and a two-sided test of significance. ${}^*P \le 0.05$, ${}^+P \le 0.10$.



TABLE 4

Milk intake during childhood and adolescence and fracture occurrence in women aged $\geq 50 \text{ y}$

	Odds ratio (95% CI)	
	Lifetime fractures ¹	Osteoporotic fractures ²
Child milk intake	$P = 0.008^3$	P = 0.04
<1 serving/wk	2.02 (1.13, 3.59)	2.25 (1.26, 4.00)
1-6 servings/wk	1.72 (0.84, 3.54)	1.39 (0.67, 2.89)
1 serving/d	1.39 (0.97, 1.99)	1.00 (0.67, 1.49)
>1 serving/d	1.00	1.00
Adolescent milk intake	P = 0.02	P = 0.29
<1 serving/wk	1.49 (0.90, 2.46)	1.29 (0.75, 2.19)
1-6 servings/wk	2.07 (1.27, 3.37)	1.59 (0.84, 3.04)
1 serving/d	1.13 (0.78, 1.64)	0.87 (0.57, 1.29)
>1 serving/d	1.00	1.00
Childhood and adolescent milk intake	P = 0.008	P = 0.36
Childhood and adolescence ≤1/wk	1.60 (1.17, 2.18)	1.19 (0.83, 1.70)
Childhood > 1/wk and adolescence, ≤ 1/wk	0.96 (0.58, 1.57)	0.85 (0.49, 1.48)
Childhood and adolescence > 1/wk	1.00	1.00

¹Fractures that occurred at ≥13 y of age. Odds ratios are adjusted for age and weight.

To investigate the association between different patterns of milk intake during childhood and adolescence and adult BMD, we categorized women according to whether they had consistently low $(\leq 1 \text{ serving/d})$ or high (> 1 serving/d) milk intake during both childhood and adolescence or whether their milk intakes during the 2 periods of growth differed. Women were categorized into 3 groups: 1) low milk intake during both childhood and adolescence (42.0% of sample); 2) high milk intake during childhood but low intake during adolescence (18.9%); and 3) high milk intake during both childhood and adolescence (38.4%). The proportion of women with low intake during childhood and high intake during adolescence (0.7%) was too small to permit meaningful analysis of this group. Hip BMD, adjusted for potential confounders, was 1.7% lower among women in group 1 (low intake in childhood and adolescence) and 2.1% lower among women in group 2 (high intake in childhood, low intake in adolescence) than among women in group 3 (high intake in childhood and adolescence) $(P \le 0.05)$. There was no association between milk-intake group and hip BMC (P = 0.41) or bone area (P = 0.11).

Milk intake and bone density among women aged ≥ 50 y

Among women aged \geq 50 y, final regression models predicting total hip BMC and BMD included current calcium intake, age, weight, height (BMC model only), estrogen deficiency, physical activity, ever a smoker, and alcohol intake. Models for bone area included age, weight, menopause, and dietary calcium intake. Current dietary calcium intake was positively associated with BMC, BMD, and bone area in all models (P values, 0.004-0.11).

Total hip BMC and BMD differed significantly (P < 0.02) according to milk intake during childhood and adolescence, but the relations were not linear (Figure 1). BMC was 2.0% lower and BMD was 2.1% lower (P = 0.10) among women with the lowest frequency of milk intake (< 1 serving/wk) than among those with

the highest frequency of milk intake (>1 serving/d) during childhood. This same pattern of association was apparent for milk intake during adolescence: women reporting the lowest intakes had hip BMC that was 2.4% lower (P < 0.10) and BMD that was 2.2% lower than those measures in women reporting the highest frequency of milk intake. Milk intake during childhood (P = 0.44) and adolescence (P = 0.21) was not associated with total hip bone area in women ≥ 50 y old.

There was no significant association between the combined classification of high or low milk intake during both childhood and adolescence (the 3 groups outlined above) and hip BMC (P = 0.58), BMD (P = 0.98), or bone area (P = 0.09) among women aged ≥ 50 y.

Milk intake and fracture

Among women aged 20–49 y, 4.7% reported a fracture of the hip, spine, or forearm at age 13 or later (lifetime fracture). Among women aged ≥ 50 y, 12.9% reported a fracture at age 13 or later, and 8.4% reported a fracture after age 50 ("osteoporotic" fracture). There was no association between milk intake in childhood and adolescence and the incidence of lifetime fracture among women aged 20–49 y ($P \geq 0.39$). Among women aged ≥ 50 y, milk intake during childhood and adolescence was associated with a significantly greater incidence of lifetime fracture (P < 0.05), but only low childhood milk intake was significantly (P = 0.04) associated with an increased risk of osteoporotic fractures. Odds ratios, adjusted for age, weight, and estrogen deficiency (osteoporotic fractures only), are presented in **Table 4**. Among women aged ≥ 50 y, low milk intake during childhood was associated with 11% of osteoporotic fractures.

DISCUSSION

Current dietary recommendations for calcium intake are designed to maximize bone mass accretion during growth and peak bone mass to reduce risk of osteoporotic fracture many decades later. There is, however, growing evidence that some of the benefit of increased calcium intake is transient and that the gain in BMD is lost once supplemental calcium intake is discontinued (10-12). This calls into question the long-term benefit of promoting higher calcium intake during childhood to reduce osteoporosis many decades later. In a nationally representative sample of women, we found that low milk intake during childhood and adolescence was associated with low BMC or BMD of the hip in adulthood. Hip BMD was 2-3% lower in women who reported consuming < 1 serving of milk/wk than in women who consumed > 1 serving/d during childhood and adolescence. This presumably represents a persistent negative effect of low milk intake during growth on bone mass and density of the hip that is not completely ameliorated by current calcium or milk intake. Furthermore, among women ≥ 50 y of age, those with low milk intake during childhood had a 2-fold greater risk of fracture than did women with high milk intake during childhood, and this greater risk could account for 11% of osteoporotic fractures in this population. It is important that these relations were found in a sample of non-Hispanic, white women—the subset of the population with the greatest risk of osteoporotic fracture. These findings provide support for the potential benefit of nutritional interventions during childhood and adolescence to reduce the risk of osteoporosis in later years.

Although several studies have examined the relation between childhood milk intake and adult bone mass or fracture risk, few



²Fractures that occurred at ≥50 y of age. Odds ratios are adjusted for age and estrogen deficiency.

 $^{^{3}}P$ values are for the overall F test comparing groups.

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have accounted for current dietary calcium or milk intake. Dietary intake of calcium and dairy products shows a moderate degree of tracking from childhood to adulthood (26, 39), so that the assessment of the independent effects of childhood and adolescence intake necessitates control for current dietary intake. New et al (28) found that childhood milk intake was positively related to spine and hip BMD in 1230 women (aged 45-49 y) after control for current intake. Nieves et al (29) found that calcium intake during adolescence was associated with hip BMD but not with spine, mid-radius, or distal radius BMD among 139 young women after adjustment for current calcium intake. Teegarden (1999) found that milk intake during adolescence, but not during childhood, was independently associated with BMC and BMD of the total body and radial shaft but not with those of the spine and hip in 224 young women after control for current calcium intake (27). Our findings extend prior observations in that we found an association between low milk intake during both childhood and adolescence and the hip BMD or BMC or both in a large representative sample of women. Furthermore, we found that low milk intake during childhood was associated with an increased incidence of selfreported fractures among women aged ≥ 50 y.

Bone mass and density in adulthood are the net result of factors that affect both bone mineralization and bone size. Sufficient calcium intake during growth is essential to support rapid mineralization of the skeleton. Peak bone mineral accretion, which occurs during puberty, averages 322 g/y in girls (40). This is approximately twice the bone mineral accretion rate in the years before puberty (41). Although positive effects of calcium or milk supplementation on bone mass and density have been found in prepubertal (3, 6, 7) and pubertal (4, 5, 9) children and adolescents, there has been controversy as to whether interventions during childhood or adolescence are more efficacious. Lloyd et al (42) found that calcium supplementation was most beneficial in adolescents in a more advanced Tanner stage. In contrast, Johnson et al (2) found that supplementation was beneficial for prepubertal children but not for pubertal children. Our results provide evidence of beneficial effects on adult BMD of milk intake during both periods of growth.

Milk provides a variety of nutrients (eg, protein, phosphorous, vitamin D, zinc, and magnesium) in addition to calcium that may have positive effects on bone growth and mineralization. In a randomized milk-supplementation trial, girls consuming additional milk had higher serum insulin-like growth factor I concentrations, which may have affected bone growth (4). Bonjour et al (3) found that children who received a milk-derived calcium supplement containing phosphorous had larger bone area and greater vertebral height as well as greater BMC than were seen in children who did not receive the supplement, which implies that the supplement affected bone growth (3). It is important that this effect on bone area and BMC was still apparent 3.5 y after supplementation was stopped (14). A review of calcium-supplementation trials in children found that positive effects of calcium supplementation on BMD were usually a result of increased BMC, not increased bone area (43), although increases in bone area with nonmilk calcium supplementation have been reported (42). We found an association between bone area and milk intake during childhood, but not during adolescence, among women aged < 50 y. This likely reflects that fact that relatively more growth occurs during childhood than during adolescence in girls.

Although women with the lowest level of milk intake had the lowest BMC and BMD, a dose-response relation for adolescent

milk intake was apparent only in women aged < 50 y. The reason for our not finding a dose-response relation in older women is not clear. One possibility is the greater degree of error in reporting childhood and adolescent milk intake among older women that results from the longer recall interval (44).

Despite the large and representative sample of subjects who participated in this study, the conclusions of this study are limited by potential error in the measurement of historical milk intake. Milk intake during childhood and adolescence was ascertained by recall, and other calcium sources were not measured. In general, past diet is recalled moderately well to poorly (39, 44, 45), but the intake of milk has been found to be recalled better than that of most foods because of its high frequency and stability in the diet (39, 44). The actual milk intake during childhood and adolescence may be different from the recalled intake, but recalled milk intake may be suitable for ranking persons in this study. Welton et al (45) found that the relative ranking of subjects according to recalled milk intake was moderate; there was exact quartile agreement of 36% to 51% of subjects between the milk intake reported for age 13 and recalled 16 y later. Dwyer et al (39) found a correlation of 0.25 between the intake of dairy foods reported for ages 5-7 y and recalled at age 50. Random error in recalled milk intake will lead to an underestimation of the true magnitude of the relation between milk intake and bone density. Women were aware of their fracture history (but not BMD) at the time of reporting prior and current dietary intake, which could lead to a differential recall bias.

Fracture ascertainment was by self-reporting of fractures of the wrist, spine, and hip, which may be subject to error. Spine fractures may be underestimated, because many go undiagnosed. Hip fracture is associated with increased risk of mortality and institutionalization, and thus hip fractures may be underrepresented in these data. Nevitt et al (46) found that elderly women tended to overreport wrist and hip fractures by 8% to 11%, and that overreporting was greater among women who believed they had osteoporosis and who had lower education.

Because of the observational nature of this study, we statistically adjusted for many factors known to be associated with bone density to prevent possible confounding of our results. It is possible that there were other factors that may have affected bone density that we were not able to account for, such as occupation-related physical activity. In addition, information on current calcium intake was limited to that from a single 24-h recall, which imperfectly characterizes a person's long-term usual intake. The fact that similar results were obtained when milk-intake frequency from the semiquantitative FFQ was used in the analyses provides some assurance that we adequately adjusted for the effects of current calcium intake.

More than half of subjects reported milk intakes during child-hood and adolescence of > 1 serving/d—the highest category included in the survey. Truncation of potential responses limited our ability to investigate the relation between hip BMD and milk intake > 1 serving/d. Current recommendations are for an intake of 2–3 servings of dairy products daily (US Department of Agriculture food guide pyramid) or the consumption of 800–1300 mg of calcium/d, depending on the age group (1).

In summary, we found that milk intake in childhood and adolescence is associated with increased bone mass and density in adulthood, and this effect is independent of current milk or calcium intake. These findings support efforts to promote a diet containing one or more servings of milk/d for girls during childhood

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REFERENCES

- Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. Washington, DC: National Academy Press, 1997.
- Johnston CC Jr, Miller JZ, Slemenda CW, et al. Calcium supplementation and increases in bone mineral density in children. N Engl J Med 1992;327:82-7.
- Bonjour JP, Carrie AL, Ferrari S, et al. Calcium-enriched foods and bone mass growth in prepubertal girls: a randomized, double-blind, placebo-controlled trial. J Clin Invest 1997;99:1287–94.
- Cadogan J, Eastell R, Jones N, Barker ME. Milk intake and bone mineral acquisition in adolescent girls: randomised, controlled intervention trial. BMJ 1997;315:1255–60.
- Chan GM, Hoffman K, McMurry M. Effects of dairy products on bone and body composition in pubertal girls. J Pediatr 1995;126:551–6.
- Dibba B, Prentice A, Ceesay M, Stirling DM, Cole TJ, Poskitt EM. Effect of calcium supplementation on bone mineral accretion in Gambian children accustomed to a low-calcium diet. Am J Clin Nutr 2000; 71:544–9.
- Lee WTK, Leung SSF, Wang S-H, et al. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. Am J Clin Nutr 1994;60:744–50.
- Lloyd T, Andon MB, Rollings N, et al. Calcium supplementation and bone mineral density in adolescent girls. JAMA 1993;270:841

 –4.
- Nowson CA, Green RM, Hopper JL, et al. A co-twin study of the effect of calcium supplementation on bone density during adolescence. Osteoporos Int 1997;7:219–25.
- Lee WT, Leung SS, Leung DM, et al. Bone mineral acquisition in low calcium intake children following the withdrawal of calcium supplement. Acta Paediatr 1997;86:570–6.
- 11. Lee WTK, Leung SSF, Leung DMY, Cheng JCY. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. Am J Clin Nutr 1996;64:71–7.
- Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. J Bone Miner Res 1997;12:676–82.
- Barker M, Lambert H, Cadogan J, Jones N, Wallace F, Eastell R. Milk supplementation and bone growth in adolescent girls: is the effect ephemeral? Bone 1998;23:S606 (abstr).
- Bonjour JP, Chevalley T, Ammann P, Slosman D, Rozzoli R. Gain in bone mineral mass in prepubertal girls 3–5 years after discontinuation of calcium supplementation: a follow-up study. Lancet 2001;358: 1208–12.
- Halioua L, Anderson JJB. Lifetime calcium intake and physical activity habits: independent and combined effects on the radial bone of healthy premenopausal Caucasian women. Am J Clin Nutr 1989;49: 534–41.
- Murphy S, Khaw KT, May H, Compston JE. Milk consumption and bone mineral density in middle aged and elderly women. BMJ 1994; 308:939–41.
- 17. Sandler RB, Slemenda CW, LaPorte RE, et al. Postmenopausal bone

- density and milk consumption in childhood and adolescence. Am J Clin Nutr 1985;42:270-4.
- Soroko S, Holbrook TL, Edelstein S, Barrett-Connor E. Lifetime milk consumption and bone mineral density in older women. Am J Public Health 1994;84:1319–22.
- Stracke H, Renner E, Knie G, Leidig G, Minne H, Federlin K. Osteoporosis and bone metabolic parameters in dependence upon calcium intake through milk and milk products. Eur J Clin Nutr 1993;47: 617–22
- Tylavsky FA, Anderson JJB, Talmage RV, Taft TN. Are calcium intakes and physical acitivity patterns during adolescence related to radial bone mass of white college-age females. Osteoporos Int 1992; 2:232–40.
- Bauer DC, Browner WS, Cauley JA, et al. Factors associated with appendicular bone mass in older women. The Study of Osteoporotic Fractures Research Group. Ann Intern Med 1993;118:657–65.
- Davis JW, Novotny R, Ross PD, Wasnich RD. Anthropometric, lifestyle and menstrual factors influencing size-adjusted bone mineral content in a multiethnic population of premenopausal women. J Nutr 1996;126:2968–76.
- Fehily AM, Coles RJ, Evans WD, Elwood PC. Factors affecting bone density in young adults. Am J Clin Nutr 1992;56:579–86.
- McCulloch RG, Bailey DA, Houston CS, Dodd BL. Effects of physical activity, dietary calcium intake and selected lifestyle factors on bone density in young women. Can Med Assoc J 1990;142:221–7.
- Lloyd T, Chinchilli VM, Johnson-Rollings N, Kieselhorst K, Eggli DF, Marcus R. Adult female hip bone density reflects teenage sportsexercise patterns but not teenage calcium intake. Pediatrics 2000; 106:40–4.
- Welten DC, Kemper HC, Post GB, Van Staveren WA, Twisk JW. Longitudinal development and tracking of calcium and dairy intake from teenager to adult. Eur J Clin Nutr 1997;51:612–8.
- Teegarden D, Lyle RM, Proulx WR, Johnston CC, Weaver CM. Previous milk consumption is associated with greater bone density in young women. Am J Clin Nutr 1999;69:1014–7.
- 28. New SA, Bolton-Smith C, Grubb DA, Reid DM. Nutritional influences on bone mineral density: a cross-sectional study in premenopausal women. Am J Clin Nutr 1997;65:1831–9.
- Nieves JW, Golden AL, Siris E, Kelsey JL, Lindsay R. Teenage and current calcium intake are related to bone mineral density of the hip and forearm in women aged 30–39 years. Am J Epidemiol 1995;141: 342–51.
- 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;87:992–7.
- 31. Nieves JW, Grisso JA, Kelsey JL. A case-control study of hip fracture: evaluation of selected dietary variables and teenage physical activity. Osteoporos Int 1992;2:122–7.
- Kelsey JL, Browner WS, Seeley DG, Nevitt MC, Cummings SR. Risk factors for fractures of the distal forearm and proximal humerus. Am J Epidemiol 1992;135:477–89.
- NCHS. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988–94. Hyattsville, MD: National Center for Health Statistics, 1994.
- Looker AC, Wahner HW, Dunn WL, et al. Proximal femur bone mineral levels of US adults. Osteoporos Int 1995;5:389–409.
- Wahner HW, Looker A, Dunn WL, Walters LC, Hauser MF, Novak C. Quality control of bone densitometry in a national health survey (NHANES III) using three mobile examination centers. J Bone Miner Res 1994:9:951–60.
- Looker AC, Wahner HW, Dunn WL, et al. Updated data on proximal femur bone mineral levels of US adults. Osteoporos Int 1998;8: 468–89.
- Arky R. Physicians' desk reference for nonprescription drugs. Montvale, NJ: Medical Economics, 1994.



- Winer BJ. Statistical principles in experimental design. New York: McGraw-Hill, 1971.
- Dwyer JT, Gardner J, Halvorsen K, Krall EA, Cohen A, Valadian I.
 Memory of food intake in the distant past. Am J Epidemiol 1989;130: 1033–46
- Bailey DB, Martin AD, McKay HM, Whiting S, Mirwald R. Calcium accretion in girls and boys during puberty: a longitudinal analysis. J Bone Miner Res 2000;15:2245–50.
- 41. Martin AD, Bailey DA, McKay HA, Whiting S. Bone mineral and calcium accretion during puberty. Am J Clin Nutr 1997;66:611–5.
- 42. Lloyd T, Martel JK, Rollings N, et al. The effect of calcium supplementation and Tanner stage on bone density, content and area in teenage women. Osteoporos Int 1996;6:276–83.
- 43. Specker B, Wosje K. A critical appraisal of the evidence relating calcium and dairy intake to bone health early in life. In: Burckhardt P, Dawson-Hughes B, Heaney RP, eds. Nutritional aspects of osteoporosis. San Diego: Academic Press, 2001:107–23.
- Friedenreich CM, Slimani N, Riboli E. Measurement of past diet: review of previous and proposed methods. Epidemiol Rev 1992;14: 177–96.
- 45. Welten DC, Kemper HC, Post GB, Van Staveren WA. Relative validity of 16-year recall of calcium intake by a dairy questionnaire in young Dutch adults. J Nutr 1996;126:2843–50.
- 46. Nevitt MC, Cummings SR, Browner WS, et al. The accuracy of self-report of fractures in elderly women: evidence from a prospective study. Am J Epidemiol 1992;135:490–9.

