Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: The Framingham Osteoporosis Study[1–3]

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ABSTRACT

Background: Soft drink consumption may have adverse effects on bone mineral density (BMD), but studies have shown mixed results. In addition to displacing healthier beverages, colas contain caffeine and phosphoric acid (H_3PO_4), which may adversely affect bone.

Objective: We hypothesized that consumption of cola is associated with lower BMD.

Design: BMD was measured at the spine and 3 hip sites in 1413 women and 1125 men in the Framingham Osteoporosis Study by using dual-energy X-ray absorptiometry. Dietary intake was assessed by food-frequency questionnaire. We regressed each BMD measure on the frequency of soft drink consumption for men and women after adjustment for body mass index, height, age, energy intake, physical activity score, smoking, alcohol use, total calcium intake, total vitamin D intake, caffeine from noncola sources, season of measurement, and, for women, menopausal status and estrogen use.

Results: Cola intake was associated with significantly lower ($P <$ 0.001–0.05) BMD at each hip site, but not the spine, in women but not in men. The mean BMD of those with daily cola intake was 3.7% lower at the femoral neck and 5.4% lower at Ward's area than of those who consumed <1 serving cola/mo. Similar results were seen for diet cola and, although weaker, for decaffeinated cola. No significant relations between noncola carbonated beverage consumption and BMD were observed. Total phosphorus intake was not significantly higher in daily cola consumers than in nonconsumers; however, the calcium-to-phosphorus ratios were lower.

Conclusions: Intake of cola, but not of other carbonated soft drinks, is associated with low BMD in women. Additional research is needed to confirm these findings. *Am J Clin Nutr* 2006;84: 936–42.

KEY WORDS Bone, epidemiology, cola, phosphoric acid, adults

INTRODUCTION

Osteoporosis and related fractures represent major public health problems. With the aging of the population, the health care burden from fractures is expected to increase dramatically during the next few decades. The lifetime risk of fracture exceeds 40% for women and 13% for men, and hip fractures have been associated with an excess mortality of up to 20% (1, 2). Most survivors require costly long-term nursing home care (2). It is, therefore, of great importance to identify modifiable risk factors for osteoporosis. Increasingly, numerous dietary behaviors and components have been identified as important contributors to the risk of loss of bone mineral density (BMD) with aging (3). Soft drink consumption has increased rapidly in the general population in recent years. This behavior has been found to be associated with low BMD and fractures in adolescent girls (4–6), although some suggest that such associations may be due to displacement of milk consumption more than to any direct effect of soft drink components (7). Few studies have examined these associations in adults.

In addition to the displacement of more nutrient-dense beverages, there are several reasons to hypothesize that carbonated soft drinks, and colas in particular, may be associated with lower BMD. Caffeine is an ingredient in most colas and has been identified as a risk factor for osteoporosis (8–10). Furthermore, colas contain phosphoric acid, which was shown to interfere with calcium absorption and to contribute to imbalances that lead to additional loss of calcium (11). It has also been suggested that the high fructose corn syrup used to sweeten carbonated beverages may negatively affect bone (12).

Therefore, we examined the association between consumption of carbonated beverages, overall and divided specifically into cola and noncola types, and BMD at several sites using data from >2500 men and pre- and postmenopausal women who participated in the Framingham Osteoporosis Study. We also examined associations with BMD by cola subtype, ie, sweetened, diet, caffeinated, and decaffeinated colas.

SUBJECTS AND METHODS

Subjects

Data from participants in the Framingham Osteoporosis Study, which drew from the Framingham Offspring Cohort, was

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used for the present study. The original population-based Framingham Heart Study began in 1948 to examine risk factors for heart disease and included a two-thirds systematic sample of the households in Framingham, MA (13). The Offspring Cohort, established in 1971, consists of the adult offspring (and their spouses) of the original cohort members. At the first examination (1971 to 1975), 5124 participants were enrolled. Offspring participants return every 4 y for an extensive physical examination, comprehensive questionnaires, anthropometric measurements, blood chemistries, and assessment of cardiovascular disease and other risk factors, which are all conducted by trained clinical personnel. At the 6th examination cycle (1995 to 1998), there were 3532 participants (1657 men and 1875 women aged 30–87 y). BMD measurements were conducted from 1996 to 2001 during the end of the 6th and beginning of the 7th examination cycles. A total of 1137 men and 1485 women completed food-frequency questionnaires during the 6th examination cycle and also had BMD measurements taken. Of these, 84 participants were excluded because they were using bisphosphonates, selective estrogen receptor modulators, or calcitonin, which left 1125 men and 1413 women for the final analysis. The present study was approved by the Institutional Review Board for Human Research at Boston University and the Institutional Review Board at the Hebrew Rehabilitation Center for Aged (Boston, MA). Written, informed consent was obtained from all participants.

Bone mineral density measurements

BMD was measured by using dual X-ray absorptiometry (Lunar DPX-L; Lunar Radiation Corp, Madison, WI) at the right hip (total hip, trochanter, Ward's area, and femoral neck) and the lumbar spine (L2-L4). The precision (CV) was 1.7% at the femoral neck, 2.5% at the trochanter, and 0.9% at the spine, which is similar to the range of 1.8–1.9% reported by others (14, 15).

Intake of carbonated beverages

Usual dietary intakes of foods and nutrients were assessed with a semiquantitative 126-item food-frequency questionnaire (16, 17). The questionnaires were mailed to the participants before each examination, and the participants were asked to complete them and bring them to the exam. For beverage consumption, responses ranged from never or <1 serving/mo to ≥ 4 servings/d. A serving was defined on the questionnaire as one glass, bottle, or can. For consistency, these responses were converted to number of servings per week. Among these items were the following: sugared caffeinated cola beverages, sugared decaffeinated cola beverages, diet caffeinated cola beverages, diet decaffeinated cola beverages, other sugared carbonated soft drinks, and other diet soft drinks. For this analysis, we grouped drinks to obtain variables for total noncola and cola soft drinks. Colas were further divided into subgroups of sugared cola, decaffeinated cola, and diet cola. This food-frequency questionnaire has been validated for many foods and nutrients and against multiple diet records or blood measures in several populations (16–19). Questionnaires that resulted in energy intakes of <600 or >4000 kilocalories (<2.51 or >16.74 MJ, respectively) per day or those with >12 food items left blank were considered invalid and excluded from additional analysis.

Measurement of confounders

Variables that could potentially confound the relation between carbonated beverage consumption and BMD were obtained from information collected at the 6th examination. These included the following: age; body mass index (BMI); height; smoking; average daily intakes of alcohol, calcium, caffeine; total energy intake; physical activity; season of measurement; and, in women, estrogen use and menopause status. Height was measured to the nearest 0.25 inch (0.64 cm) with the use of a stadiometer while the participants wore no shoes. Weight was measured in pounds with the use of a standard balance-beam scale. These measures were converted to meters and kilograms, respectively, and BMI was then calculated as weight (in kg)/height^2 (in m).

Usual dietary intakes of calcium, vitamin D, caffeine, and total energy were assessed with the food-frequency questionnaire described above. The questionnaire included use of vitamin and mineral supplements, which allowed for the calculation of total nutrient intakes.

The participants also quantified their usual intake of liquor, wine, and beer in the food-frequency questionnaire. From this information, the total grams of alcohol consumed per week were estimated. We created a variable in which participants were classified as nondrinkers, moderate drinkers (based on the current recommendations for moderate intake–ie, ≤ 1 drink/d for women and ≤ 2 drinks/d for men), or heavy drinkers (intakes that were greater than the cutoffs for moderate intake). Smoking status was defined as current smoker, past smoker, or nonsmoker and was based on questionnaire responses. Physical activity was measured with the Physical Activity Scale for the Elderly (PASE) (20, 21). Because previous research has shown that there are seasonal changes in BMD in New England, we created a categorical variable for season of BMD measurement (22, 23). July, August, and September were coded as summer; October, November, and December as fall; January, February, and March as winter; and April, May, and June as spring.

For the women, estrogen use was defined as either current use or never and past users; these categories were based on evidence that past use does not sustain bone benefits (24). Postmenopausal status was defined as women who reported no menstrual period during the preceding year (with no pregnancy). We included 2 indicator variables—women who were menopausal but were not using estrogen, and women who were menopausal and were using estrogen. Both of these were then compared with premenopausal women.

Statistical analyses

All statistical analyses were performed with the use of SAS for WINDOWS (version 9.1; SAS Institute, Cary, NC). Because interactions between sex and cola intake were significantly associated ($P < 0.05$) or nearly significantly associated ($P < 0.10$) with BMD at several sites, measures of BMD at the hip and spine were regressed on carbonated beverage variables separately for men and women after adjustment for a full set of potential confounders by using the regression procedure in SAS. These beverage variables included total noncola carbonated beverage intake, total cola intake, sugared cola intake, decaffeinated cola intake, and diet cola intake. Confounders, which were described above, included age, BMI, physical activity score, alcohol use, smoking status, total calcium intake, total vitamin D intake, energy intake, caffeine intake from sources other than cola, season

of bone measurement, and, for women, menopausal status and current estrogen use. These analyses were repeated to include fruit juice consumption and any soft drink consumption other than that being analyzed. Additional models were run adding, one at a time, the calcium-to-phosphorus intake ratio, total fruit and vegetable intake, and the protein-to-potassium intake ratio. The interaction between menopausal status and cola intake on each BMD measure was also tested. Because none of these interactions were significant, all women were included in the same models after adjustment for menopausal status, as described above.

For visual presentation and to assess the form of the relation, we also created intake categories for cola consumption ranging from never or <1 serving/mo to daily, depending on frequency of use. Bone measures were each regressed on these intake categories, along with the set of confounding variables, by using the general linear models procedure in SAS to obtain least-squares means by cola intake category. Categories were compared for significant differences with post-hoc comparisons and Tukey-Kramer adjustment for multiple comparisons.

RESULTS

Means (±SDs) for all continuous independent variables and potential confounders used in these analyses are presented in **Table 1**. For the categorical variables, percentages are presented by category. The women in the study ranged in age from 29 to 83 y, and the men's ages ranged from 35 to 86 y. This group of men and women tended to be overweight, to be former smokers, and to consume alcohol moderately. Mean calcium intakes were ≈800 mg/d for the men and 1000 mg/d for the women, which is lower than the current recommendation of 1200 mg/d for older adults (25). Of the women in this analysis, 80% were postmenopausal and 29% of these were using estrogen.

Mean intake of carbonated beverages was 6 servings/wk for the men and 5 servings/wk for the women (**Table 2**); cola was the most commonly selected choice at almost 5 and 4 servings/wk for the men and women, respectively. Women were equally likely to consume caffeinated and noncaffeinated cola but more likely to consume diet than sugared cola (2.7 compared with 0.9 servings/wk, respectively), although intakes were variable, as evidenced by the large SDs.

No significant negative associations of BMD with noncola carbonated beverage intake were observed for either men or women (**Table 3**). In the men, no significant associations were observed between BMD and cola intake. For the women, however, significant negative linear associations were seen for cola consumption at each of the hip sites ($P < 0.001$ for total hip, femoral neck, and Ward's area, and $P < 0.01$ for trochanter). No significant associations with spine BMD were observed for either men or women (data not shown). Additional analysis of cola subgroups for the women showed that the trends were not unique to the sugared, caffeinated colas, but were evident for all cola subgroups tested, with the exception of sugared decaffeinated cola (**Table 4**). The latter was consumed by <16% of women; only 1% reported consumption of ≥3 times/wk. Each of the hip sites was significantly associated with sugared cola intake as well as with diet cola intake ($P < 0.05$–0.01). Total caffeinated cola showed stronger associations with hip BMD ($P < 0.01$–0.001) than did total decaffeinated cola ($P < 0.05$ at Ward's area and approaching significance, ie, $P < 0.1$, at total hip and femoral neck). Sugared decaffeinated soda intake was not significant at any site, but it should be noted that this was the least commonly used form of cola by the women (Table 2). Additional adjustment for the calcium-to-phosphorus intake ratio, total fruit and vegetable intake, and the protein-to-potassium intake ratio did not change the significance level or materially change the coefficient of association between cola and BMD, with the exception of the femoral neck and Ward's area for sugared cola. In each of these cases, significance changed from $P < 0.05$ to $P = 0.06$.

In the women, a greater intake of cola was not associated with significantly lower intake of milk, but regular cola consumers did consume less fruit juice than did noncola consumers (**Table 5**). Regular cola consumers also had significantly lower intakes of calcium and lower calcium-to-phosphorus intake ratios (for both total and dietary calcium) than did nonconsumers. We repeated all models with the addition, one at a time, of milk intake, fruit juice intake, the calcium-to-phosphorus intake ratio, total fruit and vegetable intake, and the protein-to-potassium intake ratio. None of these additions had meaningful effects on the results presented.

TABLE 1
Subject characteristics

	Men (n = 1125)	Women (n = 1413)
Age (y)	59.4 ± 9.5[1,2]	58.2 ± 9.4
BMI (kg/m^2)	28.7 ± 4.4[2]	27.3 ± 5.6
Smoking (%)[2]		
Current	12	14
Former	67	52
Alcohol use (%)[2]		
Moderate[3]	57	53
Heavy	20	15
Physical activity score[4]	155 ± 86[2]	136 ± 72
Energy intake (MJ)	8.2 ± 2.6[2]	7.3 ± 2.4
Calcium intake (mg)	807 ± 402[2]	1008 ± 537
Vitamin D intake (μg)	9.3 ± 7.3[2]	10.3 ± 7.4
Caffeine intake (mg)	270 ± 208[2]	235 ± 194
Postmenopausal (%)	—	80
Estrogen use (%)	—	29
Season (% of measurements)[5]		
Fall	24.1	22.5
Winter	24.7	30.7
Spring	25.8	25.5
Summer	25.3	21.3
Bone mineral density (g/cm^2)		
Total hip	1.05 ± 0.15[2]	0.92 ± 0.15
Femoral neck	0.98 ± 0.14[2]	0.88 ± 0.14
Trochanter	0.89 ± 0.14[2]	0.72 ± 0.14
Ward's area	0.78 ± 0.16[2]	0.74 ± 0.17

[1] $\bar{x}$ ± SD (all such values).
[2] Significantly different from women, $P < 0.05$ (t test for continuous variables, chi-square for categorical variables).
[3] Defined as alcohol consumption of ≥1 drink/mo and ≤1 drink/d for women or 2 drinks/d for men.
[4] Measured with the Physical Activity Scale for the Elderly (PASE) questionnaire (20).
[5] Seasons were divided as follows: Fall (October, November, and December), winter (January, February, and March), spring (April, May, and June), and summer (July, August, and September).

TABLE 2
Carbonated beverage consumption[1]

	Men (n = 1125)		Women (n = 1413)	
	$\bar{x}$ ± SD	Median	$\bar{x}$ ± SD	Median
All carbonated beverages	6.3 ± 7.7[2]	3.9	5.0 ± 7.6	2.0
Cola	4.7 ± 6.8[2]	2.5	3.6 ± 6.4	0.9
Noncola	1.6 ± 3.2	0.5	1.5 ± 3.4	0.5
Sugared cola[3]	1.8 ± 4.4[2]	0.5	0.9 ± 2.8	0
Diet cola[4]	3.0 ± 5.8	0	2.7 ± 5.7	0
Caffeinated cola[5]	3.1 ± 5.7[2]	0.9	1.8 ± 4.4	0
Decaffeinated cola[5]	1.6 ± 3.8	0	1.8 ± 4.3	0

[1] Consumption was measured in mean servings per week; one serving was defined as one glass, can, or bottle.
[2] Significantly different from women, $P < 0.05$ (t test).
[3] Sugared cola includes caffeinated (1.4 ± 3.9 servings for the men and 0.6 ± 2.3 servings for the women) and decaffeinated (0.3 ± 1.5 for the men and 0.3 ± 1.4 for the women) beverages.
[4] Diet cola includes caffeinated (1.7 ± 4.5 servings for the men and 1.2 ± 3.8 for the women) and decaffeinated (1.3 ± 3.5 for the men and 1.5 ± 3.8 for the women) beverages.
[5] Caffeinated and decaffeinated cola categories each contain both sugared and diet colas, as combined from the above figures.

More evidence on the distribution and size of these effects is evident in **Figure 1**. A clear dose response is evident with significantly lower BMD observed at greater cola intakes. The difference in mean femoral neck BMD between those consuming cola daily or more frequently and noncola consumers was 3.8%. For other sites (not shown), differences ranged from 2.1% to 5.4%.

DISCUSSION

In this large population-based cohort, we saw consistent robust associations between cola consumption and low BMD in women. The consistency of pattern across cola types and after adjustment for potential confounding variables, including calcium intake, supports the likelihood that this is not due to displacement of milk or other healthy beverages in the diet. The major differences between cola and other carbonated beverages are caffeine, phosphoric acid, and cola extract. Although caffeine likely contributes to lower BMD, the result also observed for decaffeinated cola, the lack of difference in total caffeine intake across cola intake groups, and the lack of attenuation after adjustment for caffeine content suggest that caffeine does not explain these results. A deleterious effect of phosphoric acid has been proposed (26). Cola beverages contain phosphoric acid, whereas other carbonated soft drinks (with some exceptions) do not. Although cola drinkers did have lower calcium-to-phosphorus intake ratios than did noncola drinkers, adjustment for this variable did not significantly attenuate the results and the ratio itself was not significant. Much less is known about the possible effects of cola extract, which contains catechins, theobromine, and tannins, on BMD (27). Catechins, which are also found in tea, may have a positive effect on bone (28). However, it remains possible that another component in cola extract could have a deleterious effect.

If confirmed, a negative effect of cola intake on bone is of considerable importance. From 1960 to 1990, carbonated beverage consumption increased more than three-fold (29). In our sample, >70% of carbonated beverages consumed were colas, all containing phosphoric acid (H_3PO_4) and one-half (for the women) to three-fourths (for the men) containing caffeine. Caffeine has been associated with bone loss in older women (8–10),

TABLE 3
Linear associations between carbonated beverage intake and bone mineral density[1]

	Total hip	Trochanter	Femoral neck	Ward's area
Women (n = 1410)				
All soft drinks[2]	−0.0014[3]	−0.0011[4]	−0.0014[3]	−0.0020[3]
Adjusted[5]	−0.0014[4]	−0.0011[4]	−0.0014[3]	−0.0019[3]
Noncola[2]	−0.0003	−0.0006	−0.0005	−0.0014
Adjusted[5]	−0.0003	−0.0004	−0.0002	−0.0010
Cola[2]	−0.0019[3]	−0.0014[4]	−0.0019[3]	−0.0024[6]
Adjusted[5]	−0.0018[3]	−0.0014[4]	−0.0018[3]	−0.0022[3]
Men (n = 1122)				
All soft drinks[2]	0.0001	0.00004	0.0008	0.0005
Adjusted[5]	0.0001	0.00004	0.0008	0.0004
Noncola[2]	0.0006	0.00003	0.0022	0.0017
Adjusted[5]	0.0006	0.00003	0.0022	0.0017
Cola[2]	−0.00003	0.00005	0.0004	0.0002
Adjusted[5]	−0.00005	0.00002	0.0004	0.0001

[1] All values are regression coefficients. In combined models, sex × all soft drinks and sex × cola interactions were significant: $P < 0.05$ at the femoral neck and Ward's area and $P < 0.15$ for cola at the total hip. Sex × noncola interactions were not significant.
[2] Adjusted for BMI, height, smoking, alcohol use, age, physical activity score, season of bone mineral density measurement, and for intakes of total energy, calcium, vitamin D, and caffeine from sources other than carbonated beverages. Also adjusted for menopausal status and estrogen use in the women.
[3] $P < 0.001$.
[4] $P < 0.01$.
[5] Additionally adjusted for consumption of remaining carbonated beverages (if any) and fruit juice. Further adjustment for the calcium-to-phosphorus ratio, total fruit and vegetable intake, or the protein-to-potassium intake ratio did not change the significance level or materially change the coefficient of any association between cola intake and bone mineral density.
[6] $P < 0.0001$.

TABLE 4
Linear associations between carbonated beverage intake and bone mineral density in the women[1]

	Total hip (n = 1410)	Trochanter (n = 1410)	Femoral neck (n = 1410)	Ward's area (n = 1410)
All sugared cola	−0.0027[2]	−0.0027[2]	−0.0025[2]	−0.0030[2]
Caffeinated	−0.0032[2]	−0.0031[2]	−0.0031[2]	−0.0040[2]
Decaffeinated	−0.0019	−0.0020	−0.0014	−0.0009
All diet cola	−0.0016[3]	−0.0011[3]	−0.0017[3]	−0.0021[3]
Caffeinated	−0.0023[3]	−0.0018[2]	−0.0022[2]	−0.0021[2]
Decaffeinated	−0.0013	−0.0005	−0.0015[4]	−0.0026[3]
All caffeinated cola	−0.0027[5]	−0.0024[5]	−0.0026[5]	−0.0028[3]
All decaffeinated cola	−0.0013[4]	−0.0007	−0.0014[4]	−0.0022[2]

[1] All values are regression coefficients. Adjusted for BMI, height, smoking, alcohol use, age, physical activity score, season of bone mineral density measurement, and for intakes of total energy, calcium, vitamin D, and caffeine from sources other than cola. Also adjusted for menopausal status and estrogen use. All associations were additionally adjusted for consumption of fruit juice and any carbonated beverages other than that being analyzed. With this adjustment, the associations for total decaffeinated cola were not significant at the total hip and femoral neck, associations for diet decaffeinated cola were not significant at the femoral neck and were attenuated at Ward's area (to $P < 0.05$), and associations for diet caffeinated cola were attenuated at the femoral neck (to $P < 0.05$) and Ward's area (to $P < 0.1$).
[2] $P < 0.05$.
[3] $P < 0.01$.
[4] $P < 0.1$.
[5] $P < 0.001$.

whereas the association between phosphoric acid and bone loss remains controversial (7). Theoretically, diets high in phosphorus and low in calcium lead to complexes that reduce serum calcium, stimulating parathyroid hormone (PTH), which, in turn, causes bone resorption and returns serum calcium to homeostatic concentrations. Although it was suggested that the amount of phosphoric acid in cola is insufficient to cause this imbalance (7), it remains unclear whether regular exposure to phosphoric acid without exposure to calcium or other beneficial nutrients slowly affects bone remodeling and causes bone loss over time. High dietary phosphorus was shown to cause bone loss in animals (30). In one study, cola was given to immature and adult rats and found that both developed significant hypercalciuria and hyperphosphaturia; the older animals also developed hyperparathyroidism (11). In another study, cola was given to ovariectomized rats; subsequent hypocalcemia and loss of femoral BMD was observed in the rats relative to a control group (31).

Several studies have examined the association between carbonated beverages and fracture (4, 32, 33), hypocalcemia (26, 34), or BMD (5, 6) in children. Wyshak et al (32) found a 1.4 (1.1–1.6) greater risk of fracture in former athletes and a 3-fold risk in adolescent girls who consumed carbonated beverages compared with those who did not (4). Few studies have examined this in adults. Higher PTH and hyperphosphaturia have been reported in postmenopausal women with low serum calcium (≤8.8 mg Ca/dL compared with >8.8 mg Ca/dL), and the women with low serum calcium were significantly more likely to consume ≥1 cola/d (odds ratio: 1.28; 95% CI: 1.06, 1.53) (26). However, Kim et al (35) did not find associations between carbonated beverage consumption and BMD in 1000 women aged 44–98 y.

Heaney and Rafferty (36) examined the effect of carbonated beverages on short-term urinary calcium excretion in 20–40-y-old women. Only beverages containing caffeine, regardless of phosphoric acid content, were associated with increases in urinary calcium. Beverages with phosphoric acid but no caffeine did not produce excess calciuria. The authors concluded that the negative effects of carbonated beverage consumption were likely due to milk displacement. They acknowledged, however, that their study examined only short-term calciuria and that another mechanism of effect remained possible.

In the present study, there was no significant difference in milk consumption by level of cola intake. However, total calcium intake was lower in the women with the highest cola intakes, and

TABLE 5
Dietary intake of women by category of cola consumption, adjusted for age and total energy intake[1]

	No cola (n = 449)	0.5–3 servings cola/wk (n = 546)	>3 servings cola/wk (n = 417)
Milk (servings/wk)	5.7 ± 0.3	5.3 ± 0.2	5.2 ± 0.3
Fruit juice (servings/wk)	6.5 ± 0.3	5.7 ± 0.3[2]	5.1 ± 0.3[3]
Total calcium intake (mg)	1057 ± 23	1027 ± 21	928 ± 24[3]
Phosphorus intake (mg)	1202 ± 12	1206 ± 10	1198 ± 12
Total calcium:phosphorus	0.90 ± 0.02	0.85 ± 0.02	0.81 ± 0.02[2]
Dietary calcium:phosphorus	0.63 ± 0.01	0.62 ± 0.01	0.60 ± 0.01[3]
Caffeine intake (mg)	230 ± 9	235 ± 8	242 ± 10

[1] All values are $\bar{x}$ ± SD.
[2,3] Significantly different from no cola (ANOVA with Tukey's): [2]$P < 0.05$, [3]$P < 0.01$.

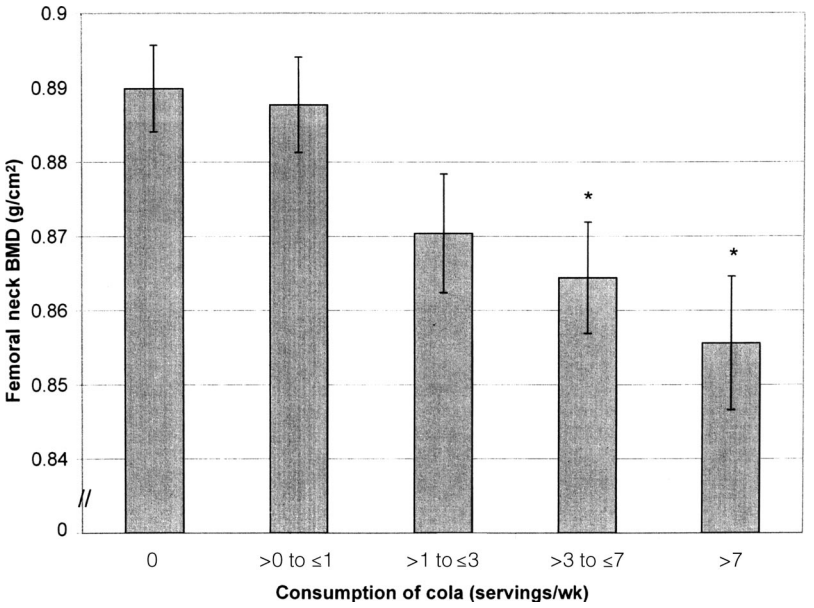

FIGURE 1. Least-squares mean (±SEM) femoral neck bone mineral density (BMD) by total cola intake in the women. The analysis was adjusted for age, height, BMI, smoking status, alcohol use, physical activity score, season of measurement, menopausal status, estrogen use, and intakes of total energy, calcium, vitamin D, caffeine from noncarbonated beverages, and noncola carbonated beverages. *Significantly different from women who consumed <1 serving cola/mo, $P < 0.05$ (analysis of covariance with Tukey's adjustment).

this may contribute to their low BMD. In addition, fruit juice intake was lower in high compared with low cola consumers. We previously showed that BMD was associated with fruit and vegetable intake and the apparent effects of cola consumption may be related to poor dietary quality. However, adjustment for fruit juice intake (or for total fruit and vegetable intake) did not significantly change the results.

The caffeine content of cola may contribute to lower BMD, and results were consistently stronger for intake of caffeinated cola than for intake of decaffeinated cola. Adjustment for caffeine intake from other sources did attenuate, but did not eliminate, the association between decaffeinated cola and loss of BMD. The remaining significance of decaffeinated cola may be due to yet unexplained actions of phosphoric acid. Although adjustment for the overall daily calcium-to-phosphorus intake ratio did not significantly attenuate results, it is less clear how regular use of a beverage containing a dose of phosphoric acid, with no calcium and no other basic forming or neutralizing components, may affect BMD over a long-term exposure. In addition to calciuric effects of high phosphorus and low calcium combinations, phosphoric acid present in the gut may form a complex with dietary calcium to block its absorption. It is possible that this may reduce the calciuric effect but still have a negative effect on bone by reducing total calcium availability. However, the observed associations may also be due to incomplete control of confounding. More research on the potential mechanisms by which phosphoric acid may affect bone is needed.

It is interesting that our findings of an association between cola intake and BMD in women but not men are consistent with several studies that found associations for girls but not boys (4–6). It is not clear why females would be more sensitive to the effects of cola than are males. Girls and women have smaller bones overall, are at higher risk of osteoporosis, and may be more sensitive to nutritional insult. Whiting et al (6) suggested that greater physical activity and higher calcium intakes in boys may protect them against the negative effects of soft drinks. The men in our population had higher physical activity but similar calcium intakes compared with the women. Hormonal interactions may also contribute to these differing results by sex, but additional research is needed.

The results presented here suggest that regular intake of cola, but not of noncola carbonated beverages, may contribute to lower BMD in women. Because BMD is strongly linked with fracture risk, and because cola is a popular beverage, this is of considerable public health importance. However, these associations, which were seen previously in adolescent girls, remain controversial and more research is needed. Although earlier studies have implied that low BMD is due to the displacement of milk in the diet by carbonated beverages, we saw no significant difference in milk intake by cola consumption group. Caffeine may contribute to lower BMD, although low BMD remained after adjustment for caffeine intake and some associations between low BMD and decaffeinated cola were also observed. The role of phosphoric acid on bone loss requires additional investigation. No evidence exists that occasional use of carbonated beverages, including cola, is detrimental to bone. However, unless additional evidence rules out an effect, women who are concerned about osteoporosis may want to avoid the regular use of cola beverages.

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KLT designed the analysis and drafted the manuscript. KM contributed expertise on phosphorus nutrition and conducted the literature review. NQ performed the statistical analysis. MTH contributed to the design and data management of the main study, as well as to the interpretation of bone data. LAC oversaw data management and statistical analysis. DPK directs the Framingham Osteoporosis Study. All authors contributed to the discussion of the design of the study and analysis of the data and reviewed the final manuscript. None of the authors reported any conflicts of interest.

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