

Soda consumption and risk of hip fractures in postmenopausal women in the Nurses' Health Study^{1–4}

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ABSTRACT

Background: The frequency of soda consumption remains high in the United States. Soda consumption has been associated with poor bone health in children, but few studies have examined this relation in adults, and to our knowledge, no study has examined the relation of soda consumption with risk of hip fractures.

Objective: We examined the association of soda, including specific types of soda, and risk of hip fracture in postmenopausal women.

Design: An analysis was conducted in postmenopausal women from the Nurses' Health Study cohort ($n = 73,572$). Diet was assessed at baseline by using a semiquantitative food-frequency questionnaire and updated approximately every 4 y. In ≤ 30 y of follow-up, we identified 1873 incident hip fractures. We computed RRs for hip fractures by the amount of soda consumption by using Cox proportional hazards models with adjustment for potential confounders.

Results: In multivariable models, each additional serving of total soda per day was associated with a significant 14% increased risk of hip fracture (RR: 1.14; 95% CI: 1.06, 1.23). The attributable risk in our cohort for total soda consumption was 12.5%. Risk was significantly elevated in consumers of both regular soda (RR: 1.19; 95% CI: 1.02, 1.38) and diet soda (RR: 1.12; 95% CI: 1.03, 1.21) and also did not significantly differ between colas and noncolas or sodas with or without caffeine. The association between soda and hip fractures did not differ by body mass index or diagnosis of diabetes.

Conclusion: Increased soda consumption of all types may be associated with increased risk of hip fracture in postmenopausal women; however, a clear mechanism was not apparent on the basis of these observational data. *Am J Clin Nutr* 2014;100:953–8.

INTRODUCTION

Soda consumption in the United States remains high (1). Despite some decline in the past 10 y, adults continued to consume close to 100 kcal sweetened soda/d in 2010. At the same time, diet soda consumption has increased, with 28.3% of women aged 40–59 y and 23.1% of women aged ≥ 60 y consuming diet soda on any given day (2). Concurrently, 8.9% of women aged ≥ 50 y have osteoporosis (3). By 2025, the worldwide incidence of hip fracture is expected to increase by as much as 250% in men and 220% in women (4).

Most research on the relation between soda consumption and bone health has been conducted in animal models and children. In animals, a significant decrease in bone mineral

density (BMD)⁵ and significant hypercalciuria was observed in groups given cola and/or glucose-sweetened beverages (5, 6). In adolescents, greater overall soda intake has been associated with lower BMD, although the relation was more consistent in girls than boys and may have been explained by the replacement of milk intake with soda; findings have been inconsistent for specific soda subtypes because of vast differences in the sample size and diet-assessment method (7–9).

In adults, the limited number of epidemiologic studies on soda consumption and long-term bone health has not permitted any conclusions, and existing prospective studies have only addressed BMD (10, 11) rather than fracture (12). Nonetheless, several mechanisms have been suggested to explain a potential association between soda consumption and bone health, some of which involve effects on calcium balance. First, diets high in phosphorus and low in calcium can reduce serum calcium, stimulate parathyroid hormone, and, turn, cause bone resorption (13). High phosphorus intake also increases the secretion of fibroblast growth factor-23 from bone, which has been shown to reduce the renal activation of 25-hydroxyvitamin D (14). Furthermore, inorganic phosphoric acid, as shown in some sodas, is absorbed from the small intestine much more efficiently than is phosphates bound to other compounds, and thus, the consequences of the dietary phosphorus are magnified. Second, caffeine is an ingredient in many sodas and an identified risk factor for osteoporosis via the interference with calcium absorption and

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³ Supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (grant nos. T32 AR 055885, P60 AR 47782, AG30521) and the NIH (grant no. CA87969).

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⁵ Abbreviations used: BMD, bone mineral density; FFQ, food-frequency questionnaire; NHS, Nurses' Health Study

Received January 7, 2014. Accepted for publication June 23, 2014.

First published online August 6, 2014; doi: 10.3945/ajcn.114.083352.

excretion (15). Third, sugars, which are a main ingredient in regular sodas, have been identified as an important factor in the macromineral homeostasis and bone density in children (16), men (17), and middle-aged women (11). It may be that these factors work in combination on similar mechanisms or that other, as yet unexplored, biologic mechanisms exist. The primary objective of this analysis was to evaluate the association of total and subtypes of soda consumption with risk of hip fractures in postmenopausal women.

SUBJECTS AND METHODS

Nurses' Health Study

The Nurses' Health Study (NHS) is an ongoing, prospective cohort study of women initiated in 1976 when 121,700 nurses aged 30–55 y who were living in 11 US states responded to a questionnaire (18). Since 1976, participants have completed follow-up questionnaires every 2 y to update exposure, lifestyle, and disease information. A food-frequency questionnaire (FFQ) was completed in 1980, 1984, 1986, and every 4 y thereafter to update dietary information. A follow-up rate ~90% has been achieved in each follow-up cycle. This study was approved by the Institution Review Board of the Brigham and Women's Hospital.

Analytic population

Women who were postmenopausal at the initial 1980 FFQ entered the study population follow-up at that time; other women entered at the biennial questionnaire when they reached menopause, including surgical menopause. Participants were excluded at entry if they did not have the most-recent dietary assessment, had previously reported a hip fracture or diagnosis of cancer or osteoporosis, or were nonwhite (<3% of the cohort). Therefore, 73,572 white women were included in the analysis.

Ascertainment of hip fractures

Participants reported hip fractures on biennial questionnaires, which also included information on the bone site and month and year of the fracture. Only fractures of the proximal femur were classified as a hip fractures for the analysis. A textual description of the circumstances under which the fracture occurred was also requested to categorize the fracture by the level of trauma during the event of the fracture; fractures that resulted from motor vehicle accidents, horseback riding, skiing, and other high-trauma events were excluded because these events could have resulted in a fracture even in the absence of osteoporosis. Because all participants were nurses, the self-reporting of fractures was likely highly accurate. In a validation study in the NHS, a medical record review confirmed all reported fractures in all 30 sampled cases (19).

Dietary assessment

Soda and other food and supplement intakes were assessed repeatedly via a validated semi-quantitative FFQ (20). The FFQs were designed to assess the average intake of >130 foods and beverages in the previous year. Participants could choose from 9 categories of frequency for a standard portion size of one 12-oz

(355-mL) can of soda (never or <1 or 1–3 servings/mo; 1, 2–4 or 5–6 servings/wk; and 1, 2–3, 4–5, or ≥6 servings/d). The FFQ included items on carbonated beverages that were regular (sugar-sweetened) or diet, with or without caffeine, and as a cola or noncola type. Generally, colas are brown colas and not clear sodas such as Sprite (The Coca-Cola Company), which often use citric acid as the primary acidulant. Seltzers and other nonsweet carbonated beverages were not included in this analysis.

Soda consumption was well reported in our cohorts. In a validation study of the FFQ that used four 1-wk diet records in the NHS, corrected correlation coefficients between the FFQ and diet records were 0.84 for sugar-sweetened cola and 0.40 for noncola carbonated beverages (21). Total energy and nutrient intakes were computed by summing contributions from all foods and nutritional supplements on the FFQ.

Nondietary measures

Height (cm, continuous) was evaluated at baseline. Weight and the calculated BMI (in kg/m², continuous), recreational activity, smoking, thiazide diuretic use (yes or no), postmenopausal hormone use (never, past, or current), and diagnosis of osteoporosis and diabetes (yes or no) were assessed on all biennial questionnaires. Recreational physical activity was assessed with 10 activities that were assigned a metabolic equivalent task score for energy expenditure in relation to sitting, and reported hours per week were multiplied by these scores and summed over all activities to create a value in metabolic equivalent task hours per week.

Statistics

In this cohort of women, follow-up began with the date of return of the 1980 questionnaire or the first questionnaire after reaching menopause. The date of censoring corresponded to whichever of the following occurred first: date of hip fracture, death, last questionnaire response, or end of follow-up on 1 June 2010. For the analysis of caffeinated and noncaffeinated sodas, follow-up could not begin until 1984 because that was the first FFQ that captured intakes of these subtypes. For colas and noncolas, the end of follow-up was 2002 because FFQs at that point no longer distinguished between these 2 types of soda.

We used Cox proportional hazards models to examine the relation between soda consumption and hip fractures. We computed cumulative averages for beverage, food, and nutrient intakes from available FFQs to reduce the within-person variation and represent long-term intake (22). For example, for a woman who became postmenopausal in 1984, the soda exposure in 1994 was calculated as the average of 1984, 1990, and 1994 intakes. We did not use information from the 1986 FFQ because soda consumption was not assessed in detail. Exposure variables for the consumption of total soda and the various subtypes were modeled as categorical variables on the basis of frequency. No soda intake of any kind was used as the common reference group for all of these categorical analyses. We also assessed a linear trend in hip-fracture risk with increasing soda consumption by assigning the median intake per day of each category to minimize the influence of outliers. We also modeled this continuous variable as risk per each additional serving per day. For soda

subtypes, the trend did not include women who reported no soda intake of any kind.

In multivariable analysis, we adjusted for age (in mo), physical activity (5 categories), thiazide use (yes or no), smoking (10 categories to represent smoking history and number of cigarettes per day), energy intake (quintiles), alcohol (5 categories), caffeine (quintiles), and the following nutrients in energy-adjusted quintiles: calcium, potassium, protein, retinol, vitamin D, and vitamin K (23). We also adjusted for the Alternate Mediterranean diet score (24) as a measure of a generally healthy diet as a continuous variable that did not include soda consumption in the scoring scheme. These variables were updated at each questionnaire follow-up period. For categorical variables, missing data were assigned into a separate category. We did not adjust for self-reported diagnoses of osteoporosis or diabetes because they may have been in the causal pathway of soda consumption and fracture development. In our cohort, soda consumption was associated with higher risk of diabetes (25), and diabetes was a risk factor for hip fractures (26). Instead, we conducted analyses stratified by these factors. In other secondary analyses, we stratified by postmenopausal hormone use (user compared with nonuser), BMI (<25 compared with ≥25), age (<75 compared with ≥75 y), and physical activity (above or below the median) to explore whether the influence of soda on fracture risk varied by the level of these variables.

RESULTS

During ≤30 of follow-up, we identified 1873 cases of incident hip fractures. A total of 81.3% of women consumed some

soda at menopause. In soda drinkers, 29.0% of women drank regular soda only, 45.7% of women drank diet soda only, and 25.3% of women drank both. Women with higher intake of total soda tended to have higher BMI and consumed more calories (Table 1).

In age-adjusted models, we did not observe any significant association between total soda consumption and hip fractures when women who consumed ≥10 servings/wk were compared with nonconsumers (Table 2). However, adjustment for BMI unmasked positive associations. For example, for ≥10 servings total soda/wk, the age-adjusted RR of 1.10 (95% CI: 0.90, 1.35) increased to 1.42 (95% CI: 1.16, 1.75) after adjustment for BMI, and risk of hip fracture associated with each additional serving per day increased from 5% (RR: 1.05; 95% CI: 0.98, 1.13) to 16% (RR: 1.16; 95% CI: 1.08, 1.25). Risk of hip fracture remained significantly elevated after adjustment for other confounders; specifically, the RR associated with the intake of ≥10 sodas/wk was 1.42 (95% CI: 1.15, 1.74), and the RR per daily serving of total soda was 1.14 (95% CI: 1.06, 1.23). The attributable risk in our cohort for total soda consumption was 12.5%.

Risk of hip fracture was elevated with a higher consumption of all soda subtypes. For each additional daily serving, the RR was 1.19 (95% CI: 1.02, 1.38) for regular soda, 1.12 (95% CI: 1.03, 1.21) for diet soda, 1.15 (95% CI: 1.02, 1.29) for caffeinated soda, 1.08 (95% CI: 0.97, 1.20) for noncaffeinated soda, 1.12 (95% CI: 0.99, 1.26) for colas, and 1.32 (95% CI: 1.08, 1.62) for noncaffeinated colas. Tests for differences in risk of hip fractures by soda subtypes were not significant when regular soda was compared with diet soda, caffeinated soda compared with noncaffeinated soda, or cola compared with noncolas. Phosphorus,

TABLE 1

Diet and lifestyle characteristics of the postmenopausal participants at entry into analysis by categories of total soda intake

	None	<2 servings/wk	2 to <5 servings/wk	5 to <10 servings/wk	≥10 servings/wk
<i>n</i>	14,323	18,490	14,828	17,544	11,329
Age (y)	53.9 ± 3.9 ¹	53.4 ± 4.1	53.1 ± 4.2	52.9 ± 4.4	52.4 ± 4.5
BMI (kg/m ²)	23.9 ± 3.9	24.7 ± 4.3	25.4 ± 4.5	26.0 ± 4.9	27.0 ± 5.5
Physical activity (MET-h/wk) ²	18 ± 17	15 ± 15	15 ± 15	15 ± 15	14 ± 15
Current smoker (%)	29	22	21	22	25
Postmenopausal hormone use (%)	25	29	31	33	34
History of diabetes (%)	2	2	3	4	5
Energy intake (kcal/d)	1563 ± 501	1617 ± 505	1668 ± 509	1684 ± 515	1777 ± 564
Protein (g/d) ³	76 ± 14	75 ± 13	76 ± 14	76 ± 15	76 ± 17
Alcohol (g/d)	8 ± 12	6 ± 10	6 ± 10	6 ± 10	6 ± 11
Calcium (mg/d) ³	876 ± 436	889 ± 441	887 ± 436	876 ± 447	863 ± 457
Vitamin D (IU/d) ³	359 ± 300	345 ± 271	338 ± 253	336 ± 274	322 ± 262
Phosphorus (mg/d) ³	1179 ± 262	1160 ± 244	1158 ± 241	1169 ± 249	1188 ± 271
Caffeine (mg/d) ³	363 ± 268	342 ± 254	336 ± 246	334 ± 248	353 ± 255
Alternate Mediterranean diet score ⁴	4.2 ± 1.8	4.0 ± 1.8	4.1 ± 1.8	4.0 ± 1.8	3.9 ± 1.8
Milk (servings/d)	0.9 ± 1	0.9 ± 1	0.9 ± 0.9	0.8 ± 0.9	0.8 ± 0.9
Regular soda (servings/wk)	0 ± 0	0.5 ± 0.4	1.3 ± 1.4	2.0 ± 3.2	4.4 ± 7.7
Diet soda (servings/wk)	0 ± 0	0.4 ± 0.4	1.8 ± 1.4	4.8 ± 2.8	15.1 ± 10.6
Colas (servings/wk)	0 ± 0	0.4 ± 0.4	1.4 ± 1.3	3.1 ± 3.0	9.7 ± 10.6
Noncolas (servings/wk)	0 ± 0	0.3 ± 0.3	0.8 ± 1.0	1.2 ± 1.9	2.9 ± 5.4
Caffeinated sodas (servings/wk)	0 ± 0	0.3 ± 0.3	1.2 ± 1.2	2.8 ± 2.7	8.1 ± 8.6
Noncaffeinated sodas (servings/wk)	0 ± 0	0.5 ± 0.4	1.9 ± 1.2	4.0 ± 2.8	10.6 ± 9.2

¹ Mean ± SD (all such values).

² MET-h, metabolic equivalent task-hours. This variable was not available for women who entered the analysis before 1986.

³ Energy adjusted.

⁴ Possible range: 0–9 points.

TABLE 2RRs (95% CIs) for hip fractures in postmenopausal women according to soda intake ($n = 73,572$)¹

	<1 serving/mo					P-trend	Per daily serving ²
	No soda	(specific soda only)	<2 servings/wk	2–4.9 servings/wk	5–9.9 servings/wk		
Total soda							
No. of cases	181	—	679	472	329	212	—
Person-years	153,348	—	462,887	381,891	321,355	206,427	—
Age adjusted	1	—	0.94 (0.80, 1.12)	0.89 (0.75, 1.06)	0.90 (0.75, 1.09)	1.10 (0.90, 1.35)	0.15 1.05 (0.98, 1.13)
Age + BMI	1	—	1.03 (0.87, 1.21)	1.06 (0.88, 1.26)	1.12 (0.93, 1.35)	1.42 (1.16, 1.75)	<0.0001 1.16 (1.08, 1.25)
Multivariable	1	—	1.08 (0.91, 1.28)	1.11 (0.93, 1.33)	1.16 (0.96, 1.40)	1.42 (1.15, 1.74)	0.0004 1.14 (1.06, 1.23)
Regular soda							
No. of cases	181	741	644	194	83	30	—
Person-years	153,348	625,586	487,007	163,926	69,096	26,944	—
Age adjusted	1	0.89 (0.75, 1.05)	0.93 (0.78, 1.10)	0.97 (0.79, 1.19)	1.29 (0.99, 1.68)	1.45 (0.98, 2.14)	<0.0001 1.31 (1.14, 1.50)
Age + BMI	1	1.05 (0.89, 1.24)	1.06 (0.89, 1.25)	1.11 (0.90, 1.36)	1.45 (1.11, 1.88)	1.64 (1.10, 2.42)	0.0005 1.27 (1.11, 1.46)
Multivariable	1	1.06 (0.87, 1.29)	1.06 (0.86, 1.29)	1.05 (0.83, 1.34)	1.28 (0.96, 1.72)	1.37 (0.90, 2.10)	0.03 1.19 (1.02, 1.38)
Diet soda							
No. of cases	181	505	468	327	239	153	—
Person-years	153,348	340,715	345,239	289,187	240,741	156,678	—
Age adjusted	1	1.09 (0.92, 1.29)	0.89 (0.75, 1.06)	0.81 (0.67, 0.98)	0.88 (0.72, 1.07)	1.05 (0.84, 1.30)	0.98 1.00 (0.93, 1.08)
Age + BMI	1	1.13 (0.95, 1.35)	1.02 (0.86, 1.22)	0.99 (0.82, 1.20)	1.11 (0.91, 1.36)	1.37 (1.09, 1.71)	0.01 1.11 (1.02, 1.20)
Multivariable	1	1.10 (0.88, 1.38)	1.08 (0.86, 1.35)	1.05 (0.83, 1.34)	1.17 (0.91, 1.50)	1.38 (1.06, 1.81)	0.007 1.12 (1.03, 1.21)
Caffeinated soda							
No. of cases	176	519	556	260	110	42	—
Person-years	128,524	369,547	450,689	216,271	108,797	50,123	—
Age adjusted	1	0.88 (0.74, 1.04)	0.85 (0.72, 1.01)	0.96 (0.79, 1.17)	1.04 (0.82, 1.32)	1.00 (0.71, 1.41)	0.05 1.12 (1.00, 1.26)
Age + BMI	1	0.98 (0.83, 1.17)	0.98 (0.82, 1.17)	1.17 (0.96, 1.43)	1.27 (1.00, 1.63)	1.25 (0.89, 1.76)	0.003 1.20 (1.06, 1.34)
Multivariable	1	1.04 (0.84, 1.27)	1.03 (0.84, 1.26)	1.22 (0.98, 1.51)	1.29 (0.98, 1.68)	1.18 (0.82, 1.70)	0.02 1.15 (1.02, 1.29)
Noncaffeinated soda							
No. of cases	176	266	639	348	152	82	—
Person-years	128,524	199,597	479,582	284,114	158,370	73,765	—
Age adjusted	1	0.96 (0.79, 1.17)	0.88 (0.74, 1.04)	0.86 (0.72, 1.04)	0.83 (0.66, 1.03)	1.14 (0.88, 1.49)	0.32 1.06 (0.53, 1.17)
Age + BMI	1	1.03 (0.85, 1.25)	0.99 (0.83, 1.18)	1.04 (0.86, 1.26)	1.03 (0.83, 1.29)	1.47 (1.12, 1.92)	0.006 1.16 (1.04, 1.28)
Multivariable	1	1.17 (0.93, 1.48)	1.17 (0.95, 1.44)	1.21 (0.97, 1.50)	1.16 (0.90, 1.48)	1.56 (1.16, 2.09)	0.19 1.08 (0.97, 1.20)
Cola							
No. of cases	173	179	285	167	96	55	—
Person-years	178,531	150,741	313,975	209,960	131,628	74,330	—
Age adjusted	1	0.85 (0.69, 1.06)	0.75 (0.62, 0.92)	0.72 (0.57, 0.90)	0.85 (0.65, 1.10)	0.97 (0.71, 1.33)	0.14 1.09 (0.97, 1.23)
Age + BMI	1	0.90 (0.73, 1.12)	0.84 (0.69, 1.02)	0.85 (0.68, 1.06)	1.03 (0.79, 1.33)	1.21 (0.88, 1.67)	0.009 1.17 (1.04, 1.31)
Multivariable	1	0.96 (0.72, 1.28)	0.90 (0.68, 1.19)	0.90 (0.67, 1.20)	1.07 (0.78, 1.48)	1.18 (0.81, 1.71)	0.07 1.12 (0.99, 1.26)
Noncola							
No. of cases	173	246	381	103	52	—	—
Person-years	178,531	283,835	424,190	124,958	47,651	—	—
Age adjusted	1	0.77 (0.63, 0.94)	0.78 (0.64, 0.94)	0.75 (0.58, 0.96)	1.19 (0.86, 1.63)	—	0.01 1.31 (1.07, 1.60)
Age + BMI	1	0.84 (0.68, 1.03)	0.88 (0.73, 1.06)	0.89 (0.69, 1.15)	1.39 (1.01, 1.92)	—	0.002 1.37 (1.12, 1.68)
Multivariable	1	0.80 (0.62, 1.02)	0.90 (0.71, 1.15)	0.90 (0.67, 1.20)	1.25 (0.87, 1.79)	—	0.007 1.32 (1.08, 1.62)

¹P-trend for soda subtypes was computed in soda consumers only. Total, regular, and diet soda analyses were from 1980 to 2010. Caffeinated and noncaffeinated soda analyses were from 1984 to 2010. Cola and noncola analyses were from 1980 to 2002, in which the top category represented intake ≥5 servings/wk for noncola soda only. Multivariable analysis was adjusted for age; energy intake; physical activity; smoking; BMI; thiazide use; postmenopausal hormone use; intakes of vitamin D, calcium, retinol, protein, caffeine, and alcohol; and the Alternate Mediterranean diet score. In addition, regular and diet sodas were adjusted for one another, caffeinated and noncaffeinated sodas were adjusted for one another, and cola and noncola were adjusted for one another. RRs were computed by using a Cox proportional hazard model.

²Risk per serving per day for soda subtypes was computed in soda consumers only. Each daily serving was equivalent to 12 fluid oz (355 mL).

tea, coffee, and milk consumption were not associated with soda intakes and did not affect results when added to the models (data not shown). No significant interaction was observed between milk or phosphorus in any type of soda (data not shown).

Higher BMI is a strong protective factor for hip fracture (27) and also associated with higher soda consumption. Therefore, we examined associations between soda intake and hip fracture in strata of BMI <25 and ≥25 but did not observe any significant interactions in results (data not shown).

We also conducted analyses stratified by diagnoses of diabetes and showed no significant interaction with soda intake. For women without diabetes, each serving of regular soda conferred an additional 19% risk (95% CI: 1.01, 1.40) of hip fractures (1415 cases). A suggestion of increased risk was also noted in women with diabetes (RR for each serving daily: 1.46; 95% CI: 0.96, 2.22), but the number of cases were much fewer (277 cases) and did not reach statistical significance. Results also did not differ by age, physical activity, or postmenopausal hormone use.

DISCUSSION

In this long-term, prospective study with repeated measures of soda intake, we observed a significant increase in hip fracture risk with increased intake of soda in postmenopausal women. However, there did not appear to be notable differences in risks of different subtypes of soda. A review of literature in the past 10 y did not find any previous study on soda consumption and fractures in older adults.

Multiple mechanisms have been proposed regarding an association between soda intake and hip fracture, all of which have been largely based on changes in the calcium balance. One mechanism has focused on the caffeine from sodas, which interferes with calcium absorption and excretion (15). However, there was no statistical difference in risk of hip fractures between caffeinated and noncaffeinated sodas, even after adjustment for coffee and tea consumption; thus, we suggest that the caffeine in sodas is not the primary explanation for increased risk. Our findings add to mixed results in prospective studies that examined caffeine and urinary calcium excretion, bone loss, or fracture risk (28–31). Sugars are another controversial mechanism of action because it may be a relevant factor in mineral homeostasis, specifically through a negative impact on the calcium balance (16, 17). However, similar risks we observed with sweetened and diet soda in our study did not support this biologic explanation as critical in the association between soda consumption and risk of fracture.

Another proposed explanation for an unfavorable relation between soda consumption and bone health has been based on the acid-ash or acid-base hypothesis (32, 33). According to this hypothesis, acidic ions, such as phosphate, contribute to the acid load in the body, which is then buffered by calcium from the skeleton, leading to bone demineralization. Animal studies have particularly pointed to colas (which contain phosphoric acid) as a risk factor for hypercalciuria, hyperparathyroidism, and loss of femoral BMD (5, 6). In the Framingham Osteoporosis study, colas, but not other carbonated sodas, were associated with significantly lower BMD at each hip site in women in a cross-sectional study (11). In contrast, a small intervention study in young women reported no acute effect of acidulant on calcium excretion (30). In addition, there was no association between phosphorus-containing carbonated beverages (or any carbonated beverages) and BMD in adult women in the Rancho Bernardo study (10). Thus, evidence has been equivocal on the contribution of sodas in bone health through the acid-base hypothesis.

Phosphorus has been shown to reduce the synthesis of calcitriol in kidneys through the stimulation of fibroblast growth factor-23 secretion (14). However, a meta-analysis of intervention studies of phosphate intake did not show an adverse effect on urinary calcium or calcium balance (34). In our cohort, soda contributed to <3% of phosphorus intake during follow-up, and phosphorus intake did not vary by soda consumption. Additional adjustment for phosphorus in our regression models also did not alter results. Our findings also did not clearly support the hypothesis that phosphoric acid from sodas is a risk factor for bone. However, the phosphorus content of foods may be inaccurately represented in nutrient databases because of the widespread use of phosphorus-containing additives. In addition, the absorption of inorganic phosphorus, such as those in sodas, could be substantially higher than organic phosphorus, and the

bioavailability is not well captured in nutrient databases. Inaccuracies of phosphate content in nutrient databases would limit the ability of the FFQ to rank phosphorus intake in individuals (35). We also failed to find any clear difference in the association between cola and noncola consumption and risk of hip fracture.

Our primary finding of a significant positive association between total soda consumption and risk of hip fracture in women, as well as elevated risk even in women without diabetes or osteoporosis, may have indicated that there is no single biologic mechanism but, rather, a set of contributors that act primarily with higher total intakes, or there may be a factor that has yet to be explored. For example, one common feature of soda is carbonation, which is the process of dissolving carbon dioxide in water, resulting in the formation of carbonic acid. The impact of carbonation on gastric acidity and subsequent ramifications for nutrient absorption is possible, but the impact is unclear (36), and no studies have examined the impact on bone to our knowledge.

The strengths of this study included up to 30 y of follow-up along with repeated measures of soda intake and covariate information. The use of repeated measurements could have reduced measurement error, and cumulative averages provided a good measure of average long-term intake, which was likely the relevant exposure for osteoporosis. Hip fracture is the important clinical outcome of osteoporosis, and it was well reported in our cohort of nurses. To our knowledge, our study was the first large-scale prospective cohort in women to study the relation between soda consumption and hip fractures. Nevertheless, it is necessary to replicate this study in other populations to confirm the results and generalizability.

However, because of the self-reporting nature of our study, some misclassification was unavoidable. Soda drinkers tended to have higher BMI than that of women who drank little soda. However, the NHS has extensive information on a number of dietary and demographic factors, which were included in our multivariable models. Furthermore, there has been no major potential confounder suggested in the current literature that was not controlled for in our analyses.

In conclusion, we showed that a greater consumption of soda was associated with modest increased risk of hip fracture in women. The magnitude of attributable risk in our cohort was not trivial, although we are uncertain of the mechanism. With the high prevalence of osteoporosis in older American women and the popularity of soda consumption, the potential impact could be large. Additional research is needed to confirm our findings and identify biological mechanisms.

We thank the participants and staff of the NHS for their valuable contributions.

The authors' responsibilities were as follows—DF and MHA: designed the analysis plan; MHA and TTF: analyzed data and wrote the manuscript; FG, JNK, WCW, and BR: advised on the analysis and interpretation of data; TTF: had primary responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript. None of the authors had a conflict of interest.

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