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Effects of beer, wine, and liquor intakes on bone mineral density in older men and women[1–3]

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ABSTRACT

Background: Moderate intake of alcohol has been reported to have beneficial effects on bone. However, different classes of alcoholic beverages have not been investigated.

Objective: Our aim was to determine the association between intake of total alcohol or individual alcoholic beverages and bone mineral density (BMD).

Design: Adjusting for potential confounding factors, we examined alcohol intakes and BMD at 3 hip sites and the lumbar spine in 1182 men and in 1289 postmenopausal and 248 premenopausal women in the population-based Framingham Offspring cohort (age: 29–86 y).

Results: Men were predominantly beer drinkers, and women were predominantly wine drinkers. Compared with nondrinkers, hip BMD was greater (3.4–4.5%) in men consuming 1–2 drinks/d of total alcohol or beer, whereas hip and spine BMD were significantly greater (5.0–8.3%) in postmenopausal women consuming >2 drinks/d of total alcohol or wine. Intake of >2 drinks/d of liquor in men was associated with significantly lower (3.0–5.2%) hip and spine BMD than was intake of 1–2 drinks/d of liquor in men. After adjustment for silicon intake, all intergroup differences for beer were no longer significant; differences for other alcohol sources remained significant. Power was low for premenopausal women, and the associations were not significant.

Conclusions: Moderate consumption of alcohol may be beneficial to bone in men and postmenopausal women. However, in men, high liquor intakes (>2 drinks/d) were associated with significantly lower BMD. The tendency toward stronger associations between BMD and beer or wine, relative to liquor, suggests that constituents other than ethanol may contribute to bone health. Silicon appears to mediate the association of beer, but not that of wine or liquor, with BMD. Other components need further investigation. *Am J Clin Nutr* 2009;89:1188–96.

INTRODUCTION

Although alcoholism is known to have negative effects on bone (1), a positive association between alcohol intake and bone mineral density (BMD) in older women has been reported in the original Framingham Osteoporosis Study (2) and others (3–6). However, few studies have been conducted in men or in younger women. Further, few have considered past drinkers and there is concern that combining this group with individuals who have never consumed alcohol may lead to a possible false impression that moderate alcohol consumption is protective when past drinkers, who may have lower BMD due to past alcohol abuse or other illness, are included as nondrinkers (7). In addition, many have used simple linear models to test for associations when the relation between alcohol consumption and health status has clearly been described as inverted J- or U-shaped (7, 8). However, a recent study of men aged ≥65 y found that alcohol intake was linearly related to BMD at the hip and spine and, further, that greater alcohol intake was not related to risk of fracture (9). In another recent study, Wosje and Kalkwarf (10) reported on data in men and women aged ≥20 y in the third National Health and Nutrition Examination Survey, 1988–1994, and found that BMD at the total hip and femoral neck was significantly higher in men who had ≥5 drinking occasions/month, relative to fewer occasions or none, and a tendency ($P = 0.06$) for postmenopausal women who had ≥29 drinking occasions/month to have higher femoral neck BMD than those who abstained from alcohol. There were no associations between alcohol intake and BMD in premenopausal women. Similarly, the Cardiovascular Health Study recently reported a graded positive relation with BMD at the hip, but a significant U-shaped relation between

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alcohol intake and risk of hip fracture in adults aged ≥65 y. This study (11) found significant protective effects with consumption up to 2 drinks/d, but a tendency toward higher risk with >2 drinks/d. These differences suggest that the actual relation between alcohol intake and bone requires further confirmation and that it may differ by age and sex.

Furthermore, the individual effects of the different classes of alcoholic beverages (beer, wine, liquor) on BMD have not been studied, and the importance of alcoholic beverage choice on health is still disputed (12). Different types of alcoholic beverage may behave differently such that associations with BMD differ. It has been suggested that wine drinkers may have a lower incidence of cardiovascular disease than drinkers of other alcoholic beverages, which suggests that components other than ethanol, such as polyphenols (eg, resveratrol), may be important (13). We previously showed a positive association between silicon intake and BMD in older men and premenopausal women (14). As beer is a good source of silicon, it is possible that part of the observed beneficial effect of alcoholic beverages on BMD is through exposure to this mineral. We therefore examined the association between both total alcohol intake and the intake of different types of alcoholic beverages on BMD in older men, postmenopausal women, and premenopausal women participating in the Framingham Offspring Osteoporosis Study.

SUBJECTS AND METHODS

Subjects in this study were participants in the Framingham Osteoporosis Study, drawn from the Framingham Offspring cohort. The original population-based Framingham Heart Study was initiated in 1948 to examine the risk factors for heart disease and constituted a two-thirds sampling of the households in Framingham, MA (15). The Offspring cohort was established in 1971 and consists of the adult children (and their spouses) of the original cohort members. Members return every 4 y for a physical examination and to complete a series of questionnaires and tests. In the fifth (1991–1995) and sixth (1995–1999) study visits (or examination cycles), there were 2919 participants (1280 men and 1639 women aged 29–86 y) with BMD measurements. Framingham Offspring participants were first seen for the osteoporosis study between 1996 and 2001. BMD measures therefore followed the regular examination in the sixth study visit for most individuals, but continued into the beginning of the seventh visit to complete BMD scans in the cohort. Potential confounding variables were obtained from the most recent Framingham exam before BMD measurement (either exam 6 or 7). Of those with BMD measures, 1182 men and 1537 women also completed at least 1 of the 2 semiquantitative food-frequency questionnaires (FFQ) and completed questionnaires for covariate information. Alcohol intake and other dietary measures were averaged from these 2 exams when both were available (86%); otherwise the single FFQ data were used. Time between the last available FFQ and measurement of BMD averaged at 1.8 y and ranged from the same day to a maximum of 5.5 y. All participants with dietary intake data and BMD measurement were included in this study, with no additional exclusion criteria. Comparison of cohort participants who completed the BMD scan with those who did not revealed few differences, with the exception that the Osteoporosis Study participants were somewhat younger, heavier, and taller than those Offspring Cohort participants who did not join the study. The study was approved by the Institutional Review Boards for Human Research at Boston University (Boston, MA) and the Hebrew Rehabilitation Center (Boston, MA). Written informed consent was obtained from all participants.

BMD

BMD was measured once for each participant during the sixth and seventh examinations (1996–2001), using dual-energy X-ray absorptiometry (Lunar DPX-L; Lunar Radiation, Madison, WI). BMD was measured at the right hip (total hip, trochanter, and femoral neck) and at the lumbar spine (L2–L4). We used standard positioning as recommended by the manufacturer, including medial rotation of the femur to ensure a clear scan of the femoral neck region. Monthly measurements of a bone phantom over the study period showed no machine drift across time.

Dietary intake

Usual dietary intake was assessed using the Willett semiquantitative 126-item FFQ. This questionnaire has been validated for many nutrients and in several populations (16). Before the fifth (1991–1995) and sixth (1995–1999) study visits, questionnaires were mailed to the subjects, who were asked to complete them on the basis of their pattern of intake over the previous year and to bring them to their appointments (visits). A completed FFQ was available from both study visits. The average intake from the 2 questionnaires was used. Completed questionnaires were excluded, as previously reported (17), if calculated energy intakes were considered implausible (<2.51 MJ/d or >16.74 for women or 17.57 MJ/d for men) or if >12 food items were left blank. Processing of the forms to obtain total daily energy intakes and food intake was carried out at Harvard University (Boston, MA).

For each subject, servings of beer, wine, and liquor per day were averaged from the two 126-item FFQs. One serving of beer represented one 356-mL glass, bottle, or can, whereas one serving of wine (red or white) represented 118 mL (one 4-oz glass) and one serving of liquor represented 42 mL (one drink or ''shot''). The average servings per day and the average amount of alcohol ingested in grams/day for the different classes of alcoholic beverages were calculated for each subject. In addition, we checked for any reported past use of alcohol from the previous exams (1–4) to identify ''former drinkers'' compared with ''never drinkers'' during this period. Silicon values/100 g of the edible portion of each of the 278 food items in the FFQ were obtained as previously described (14). These values (mg Si/100 g food) were entered into a database program in the Dietary Assessment and Epidemiology Research Program at Tufts University (Boston, MA) and corrected for the weight of each food item reported for each individual participant. The values (mg silicon) for each food item were then summed to obtain total silicon intake per person per day in each of 2 study visits (1991–1995 and 1995–1999). The average silicon intake (mg/d) from the 2 visits was used for each subject. From our silicon database, we estimated that beer contains ≈7 mg Si/356-mL can, and wine ≈1 mg/118-mL glass. For comparison, a 236-mL glass of carbonated water is estimated to have 0.2 mg Si, whereas 90 g (1/2 cup) of cooked spinach has ≈5 mg.

Potential confounding variables

Potentially confounding variables measured at the time of the BMD measurements were obtained for each participant, along with overall medical history. Menopausal status was assessed by questionnaire. At each examination, women were asked at what age they had ceased menstruating for a full year and whether or not they were taking hormone replacement therapy. Those who had stopped menstruating were also asked the reason (natural, surgical, or due to hormone medication). Any inconsistencies over time were carefully checked and resolved through chart review to ensure correct age at menopause. Age (y), height (m), and weight (kg) were measured, from which body mass index (BMI; in kg/m^2) was calculated. Physical activity was examined using the Physical Activity Scale for the Elderly questionnaire, which is a 7-d record of household activities and the number of hours spent on usual daily activities and on light, moderate, and strenuous sports and recreation. Time spent (h/d) in each activity is multiplied by a defined weight for that activity, and these are summed to obtain a score for each individual (18). Smoking status (current, past, or nonsmoker) and previous alcohol use (yes/no) were determined from the cohort questionnaire, which asks about current and past smoking and drinking at each cycle. Medication use was assessed at the time of BMD measurement. Estrogen use in women was defined as current use of estrogen with continuous use for $\geq$1 y. Use of osteoporosis medication (eg, bisphosphonates, calcitonin) was categorized as a yes/no variable. Total intake of energy (MJ), dietary calcium (mg), dietary vitamin D (IU), magnesium (mg), potassium (mg), and vitamin K (mg) were averaged from the 2 FFQs. Use of calcium (mg) and/or vitamin D supplements (IU) was obtained from the supplement section of the FFQs. To control for potential seasonal effects on BMD measures, a 4-season categorical variable based on month of BMD measurement was also created.

Statistical analyses

There was a significant interaction ($P < 0.0001$) between alcohol intake and sex, both when men, premenopausal, and postmenopausal women were included and when only men and postmenopausal women were included. Therefore, analyses were conducted separately for men and for pre- and postmenopausal women in SAS (version 9.1; SAS Institute, Cary, NC). We first separated nondrinkers at the time of BMD testing into past and never drinkers on the basis of reports of alcohol use (yes/no) from all of the prior examinations. Those who said ''yes'' at any of the previous exams, but ''no'' at both exam 5 and 6 were categorized as past drinkers. In contrast to the hypothesis that the past drinkers might have lower BMD than never drinkers, and that they could drive the apparent protective association with moderate alcohol intake, there were no statistical differences in BMD for past and never drinkers (eg, for total hip for postmenopausal women: 0.884 $\pm$ 0.009 and 0.864 $\pm$ 0.016 g/cm^2, $P = 0.82$; for men: 1.035 $\pm$ 0.010 and 1.020 $\pm$ 0.022 g/cm^2, $P = 0.99$). Therefore, these groups were combined into nondrinkers for subsequent analysis. To explore, in these cohorts, whether the relations between alcohol intakes and BMD were linear or had an inverted U-shape as suggested in other cohorts, BMD measures (at the 3 hip sites and lumbar spine) were regressed onto categories of alcohol intake (none and >0–0.5, >0.5–1, >1–2, and >2 drinks/d) by using the general linear models procedure in SAS. Categories were defined to identify never, occasional, moderate, and heavy drinkers based on current US recommendations of up to 1 drink/d for women and up to 2 drinks/d for men (19). Models were adjusted for age, height, BMI, physical activity score, smoking status, calcium intake (dietary and supplement use), vitamin D intake (dietary and supplement use), energy intake, magnesium intake (as an indicator of dietary quality), use of osteoporosis medication, season of BMD measurement, and, for postmenopausal women, estrogen use. In several cases, there were few individuals in the highest category such that, when there were <30 individuals, they were collapsed into the next-lower category. Silicon intake was then added and the models were rerun with this variable to determine whether silicon intake contributed to the association between alcohol intake and BMD. A reduction in the β coefficient for alcohol intake (and concomitant reduction in P value) is expected if silicon strongly mediates the association. Associations with adjusted BMD were examined for total alcohol intake (sum of intake from beer, wine, and liquor), and in models that included each of these beverage classes, with adjustment for total remaining alcohol intake (g) from the other 2. To check the possibility of confounding from other nutritional factors, the models were also run replacing magnesium by potassium and by vitamin K.

Adjusted least-squares means were compared between intake categories using post hoc t tests, with Tukey adjustment for multiple comparisons. We also report the overall P value for analysis of covariance (ANCOVA) and P for trend, the latter by assigning the mean intake per category and running as a linear variable. Number of drinks/d was also categorized within type (beer, wine, and liquor), and the analyses described above were repeated for each type, with the remaining grams of alcohol from the other 2 categories adjusted in the analysis. These models were, again, adjusted for age, height, BMI, physical activity score, smoking status, calcium intake (dietary and supplement use), vitamin D intake (dietary and supplement use), energy intake, magnesium intake, use of osteoporosis medication, season of BMD measurement, and, for postmenopausal women, estrogen use. As above, they were also examined with the addition of silicon and the replacement of magnesium with potassium and vitamin K.

RESULTS

The mean age of the men in this analysis was 61 y, of postmenopausal women 62 y, and of premenopausal women 48 y (**Table 1**). The mean BMI was in the overweight range (27–29) for all groups. Only 11–13% of the subjects were current smokers. Very few men or premenopausal women, but 4.1% of postmenopausal women, were taking medications for osteoporosis. The majority of these older adults were moderate drinkers, reporting intake of none to 1 drink/d (44% of men, 56% of postmenopausal women, and 62% of premenopausal women). Twenty-one percent of men, 7% of postmenopausal women, and 7% of premenopausal women consumed >2 drinks /d. Among men, beer was most commonly consumed, whereas among women, wine was the most used alcoholic beverage. Most wine consumers used both red and white wine. For men these were divided approximately equally; for women, ≈75% of the reported wine intake was white.

TABLE 1
Characteristics of the participants[1]

	Men ($n = 1182$)	Postmenopausal women ($n = 1289$)	Premenopausal women ($n = 248$)
Age (y)	61.5 ± 9.3[a,2]	62.5 ± 8.1[b]	48.3 ± 4.7[c]
BMI (kg/m^2)[3]	28.8 ± 5.1[a]	27.5 ± 5.4[b]	26.7 ± 5.6[c]
Height (in)[3,4]	68.8 ± 2.4[a]	63.2 ± 2.5[b]	63.7 ± 2.7[c]
Smoking status (%)[5]			
Never smokers	30	38	43
Current	11	13	13
Former	59	49	44
Physical activity index[3,6]	159 ± 72[a]	136 ± 73[b]	120 ± 79[c]
Energy intake (MJ)[3]	8.2 ± 2.3[a]	7.3 ± 2.3[b]	7.1 ± 2.5[b]
Protein (g)[7]	75 ± 13[a]	79 ± 14[b]	80 ± 15[b]
Dietary calcium (mg)[7,8]	711 ± 253[a]	773 ± 254[b]	823 ± 274[c]
Dietary vitamin D (IU)[7,8]	206 ± 106[a]	220 ± 107[b]	236 ± 115[b]
Calcium supplement use (%)			
≤250 mg	20.1	23.4	23.4
>250 mg[5]	3.2	29.2	16.1
Vitamin D supplement use (%)			
≤15 μg[5]	33.0	48.3	47.6
>15 μg	2.7	2.7	2.4
Osteoporosis medication use (%)[5,9]	0.2	4.1	0.4
Silicon intake (mg)[7]	26 ± 7[a]	25 ± 3[b]	25 ± 8
Magnesium intake (mg)[7]	295 ± 70[a]	313 ± 70[b]	312 ± 75[b]
Potassium intake (mg)[7]	2876 ± 572[a]	3105 ± 574[b]	3158 ± 628[b]
Vitamin K intake (μg)[7]	142 ± 93[a]	182 ± 93[b]	182 ± 100[b]
Alcohol intake			
Total alcohol (servings/d)[7]	1.1 ± 1.1[a]	0.6 ± 1.1[b]	0.6 ± 1.2[b]
Beer[7]	0.5 ± 0.6[a]	0.1 ± 0.6[b]	0.1 ± 0.7[b]
Wine[7]	0.3 ± 0.6	0.3 ± 0.6	0.4 ± 0.7
Liquor[7]	0.3 ± 0.6[a]	0.2 ± 0.6[b]	0.1 ± 0.6[b]

[1] Values in the same row with different superscript letters are significantly different, $P < 0.05$.
[2] Mean ± SD (all such values).
[3] Adjusted for age.
[4] 1 inch = 2.54 cm.
[5] Significant overall by chi-square analysis ($P < 0.05$).
[6] Score measured with the Physical Activity Scale for the Elderly questionnaire.
[7] Adjusted for age and energy intake.
[8] Dietary variables are from the average of 2 food-frequency questionnaires, ≈4 y apart.
[9] Self-reported use of medications for the treatment of low bone mineral density at time of bone measurement.

In men, significant ($P < 0.05$) associations between BMD and total alcohol intake were seen at the total hip, femoral neck, and trochanter (**Table 2**). Both the *P* values across categories and the *P* values for trend were significant ($P < 0.05$). Nonconsumers and those consuming up to 0.5 drinks/d tended to have significantly lower BMD relative to those consuming 1–2 drinks/d. Intakes of >2 drinks/d of beer or liquor were associated with nonsignificantly lower average BMD, relative to 1–2/d. When examined separately, significant associations (both *P* values for ANCOVA and for trend) were seen at the total hip and trochanter for beer intake and at the lumbar spine for wine intake. For liquor, the *P* value for ANCOVA was significant at all sites, but in this case, the lowest BMD was seen in men consuming >2 drinks/d relative to those consuming 1–2 drinks/d. As expected, adjustment for silicon attenuated the associations with beer, but did not affect results with wine or liquor. Replacement of magnesium with either potassium or vitamin K had no meaningful effect on the results presented.

The associations between total alcohol intake and BMD tended to be stronger for postmenopausal women than for men; the *P* values for trend and for ANCOVA were significant ($P = 0.001–<0.0001$ and $P = 0.03–0.003$, respectively) at all 4 bone sites (**Table 3**). However, the intergroup comparisons showed significantly higher BMD in those consuming >2 drinks/d (rather than 1–2/d in men) relative to nondrinkers. When the type of alcoholic drink was examined separately, the *P* values for trend were significant at all 4 sites for wine intake ($P = 0.02–0.002$). The *P* values for ANCOVA were significant at the trochanter and lumbar spine ($P = 0.01–0.006$) and approached significance for the total hip ($P = 0.09$) and femoral neck ($P = 0.08$). Beer intake was significantly associated with BMD only at the femoral neck, but there were too few numbers to differentiate beer intake >0.5 drinks/d. Differences in intake of liquor were significantly associated with BMD only at the lumbar spine, although the *P* value for trend at the trochanter was also significant. No form of alcohol was significantly associated with BMD in premenopausal women, but power was low in this group (**Table 4**).

The magnitude of the differences across intake categories is shown in **Figure 1** for the total hip. In men, the highest BMD

TABLE 2
Bone mineral density in men by alcohol intake category[1]

	Alcohol intake (drinks/d)[2]						
	0	0–0.5	0.5–1	1–2	>2	*P* (ANCOVA)	*P* for trend
Total alcohol[3]							
No. of subjects	220	333	191	201	237		
Total hip (g/cm^2)	1.033 (1.015, 1.051)	1.026[a] (1.010, 1.041)	1.035 (1.015, 1.054)	1.068[b] (1.049, 1.087)	1.046 (1.028, 1.064)	0.008	0.048
Femoral neck (g/cm^2)	0.970 (0.953, 0.987)	0.957[a] (0.943, 0.972)	0.965 (0.947, 0.983)	0.994[b] (0.975, 1.011)	0.979 (0.962, 0.997)	0.02	0.055
Trochanter (g/cm^2)	0.865[a] (0.848, 0.883)	0.867[a] (0.851, 0.882)	0.877 (0.859, 0.896)	0.911[b] (0.893, 0.930)	0.893 (0.875, 0.911)	0.007	0.003
Spine (g/cm^2)	1.337 (1.310, 1.365)	1.304 (1.280, 1.327)	1.335 (1.305, 1.364)	1.328 (1.299, 1.357)	1.339 (1.311, 1.368)	0.20	0.25
Beer[3,4]							
No. of subjects	412	504	127	46	93		
Total hip (g/cm^2)	1.025 (1.011, 1.039)	1.044 (1.031, 1.057)	1.050 (1.026, 1.073)	1.071 (1.033, 1.109)	1.055 (1.026, 1.084)	0.05	0.03
Femoral neck (g/cm^2)	0.960 (0.947, 0.973)	0.972 (0.960, 0.985)	0.986 (0.963, 1.008)	0.997 (0.960, 1.033)	0.988 (0.960, 1.014)	0.10	0.03
Trochanter (g/cm^2)	0.862 (0.848, 0.875)	0.886 (0.873, 0.899)	0.890 (0.867, 0.914)	0.922 (0.884, 0.959)	0.904 (0.876, 0.932)	0.002	0.005
Spine (g/cm^2)	1.320 (1.299, 1.341)	1.324 (1.304, 1.344)	1.329 (1.293, 1.365)	1.366 (1.308, 1.425)	1.353 (1.310, 1.397)	0.46	0.09
Wine[3,4]							
No. of subjects	493	467	122	61	39		
Total hip (g/cm^2)	1.038 (1.025, 1.050)	1.035 (1.022, 1.049)	1.058 (1.034, 1.082)	1.038 (1.005, 1.072)	1.059 (1.016, 1.102)	0.46	0.23
Femoral neck (g/cm^2)	0.970 (0.958, 0.982)	0.970 (0.957, 0.983)	0.988 (0.965, 1.011)	0.961 (0.929, 0.993)	0.974 (0.933, 1.015)	0.60	0.80
Trochanter (g/cm^2)	0.874 (0.861, 0.886)	0.878 (0.865, 0.891)	0.902 (0.878, 0.926)	0.893 (0.860, 0.926)	0.910 (0.868, 0.953)	0.14	0.02
Spine (g/cm^2)	1.327 (1.308, 1.347)	1.313 (1.292, 1.333)	1.357 (1.320, 1.394)	1.314 (1.263, 1.364)	1.398 (1.333, 1.464)	0.04	0.046
Liquor[3,4]							
No. of subjects	582	428	89	45	60		
Total hip (g/cm^2)	1.038 (1.027, 1.051)	1.034 (1.021, 1.048)	1.065 (1.034, 1.082)	1.039[a] (1.037, 1.093)	1.009[b] (0.976, 1.043)	0.008	0.86
Femoral neck (g/cm^2)	0.971 (0.959, 0.982)	0.967 (0.954, 0.980)	1.000 (0.974, 1.027)	1.007 (0.971, 1.044)	0.945 (0.913, 0.976)	0.02	0.93
Trochanter (g/cm^2)	0.878 (0.866, 0.890)	0.879 (0.865, 0.892)	0.898 (0.871, 0.926)	0.926[a] (0.888, 0.963)	0.850[b] (0.816, 0.883)	0.03	0.95
Spine (g/cm^2)	1.332 (1.314, 1.336)	1.315 (1.294, 1.336)	1.370[a] (1.328, 1.400)	1.342 (1.283, 1.400)	1.276[b] (1.225, 1.327)	0.04	0.33

[1] All values are least-squares means (95% CIs). Values in the same row with different superscript letters are significantly different, $P < 0.05$.
[2] One drink = 13.2 g alcohol.
[3] Adjusted for age, sex, smoking, osteoporosis medication use, BMI, height, physical activity, and calcium, vitamin D, magnesium, protein, and total energy intakes.
[4] Also adjusted for grams of alcohol from other sources.

was seen among men consuming 1–2 drinks/d, with a notable tendency toward lower BMD at intakes greater than this amount. For sites with significant results, BMD for men was 2.5% (femoral neck) to 5.3% (trochanter) greater among those consuming 1–2 alcoholic drinks/d relative to none and 4.5% (total hip) to 7.0% (trochanter) greater for those consuming 1–2 beers/d compared with none. In contrast, for liquor intake, BMD for those consuming >2 drinks/d was 3.0% (total hip) to 8.9% (trochanter) lower than those consuming 1–2 drinks/d. Linear trends were more pronounced among postmenopausal women. For postmenopausal women, when related to nondrinkers, BMD was 5.0% (total hip) to 7.4% (spine) greater for those consuming >2 alcoholic drinks/d, 8.3% (spine) to 10.7% (trochanter) greater for >2 glasses of wine/d, and 7.9% (spine only) greater for >2 glasses of liquor/d.

DISCUSSION

To our knowledge this is the first study to examine the association between BMD and intakes of the different classes of alcoholic beverages in men and post- and premenopausal women. These data support earlier observations that moderate alcohol intake may protect BMD in postmenopausal women and older men. However, they illustrate that the benefits appear most clearly from beer and wine intake, which suggests that factors in addition to ethanol may exert protective effects. They also extend earlier findings to suggest that the positive effect of alcohol intake in men peaks at 1–2/d and provide evidence that these benefits decline with higher intakes. In contrast, there were clear linear benefits of alcohol intake in postmenopausal women that were most significant at intakes of >2 glasses/d This was especially apparent for wine intake and possibly for liquor intake and consistent but not discernible for beer intake, for which the highest category was >0.5 servings/d (Figure 1). It is possible that we would see an inverse J-shaped curve, as seen in men consuming >2 drinks/d of liquor, if we had more women who were very heavy alcohol consumers.

Thus, although qualitatively consistent with earlier reports (2, 6, 10, 20–24), our results suggest that the protective effects seen in postmenopausal women extend to intakes that are higher than those currently considered as moderate in the United States, namely >2 drinks/d. Why this should be is not clear, as the mechanism of action of moderate alcohol consumption on BMD remains poorly established. A protective effect has been hypothesized to be due to the effects of alcohol on adrenal androgens or estrogen concentrations (25). The effect may be stronger among postmenopausal women and in men than in premenopausal women because the low estrogen concentrations, particularly in postmenopausal women, are increased by alcohol (22, 25). However, in a recent review (23), a case was made for the acute suppression of bone resorption as the primary effect of moderate ethanol ingestion rather than an alcohol–hormone–bone

TABLE 3
Bone mineral density in postmenopausal women by alcohol intake category[1]

	Intake (drinks/d)[2]						
	0	0–0.5	0.5–1	1–2	>2	*P* (ANCOVA)	*P* for trend
Total alcohol[3]							
No. of subjects	339	548	176	132	94		
Total hip (g/cm^2)	0.880[a] (0.863, 0.897)	0.890 (0.875, 0.905)	0.900 (0.879, 0.920)	0.901 (0.878, 0.923)	0.924[b] (0.898, 0.950)	0.03	0.001
Femoral neck (g/cm^2)	0.836[a] (0.819, 0.853)	0.848 (0.833, 0.863)	0.852 (0.832, 0.872)	0.854 (0.832, 0.877)	0.883[b] (0.857, 0.909)	0.02	0.001
Trochanter (g/cm^2)	0.687[a] (0.672, 0.703)	0.697 (0.683, 0.710)	0.710 (0.691, 0.728)	0.709 (0.688, 0.729)	0.733[b] (0.710, 0.757)	0.004	0.0002
Spine (g/cm^2)	1.107[a] (1.081, 1.133)	1.126 (1.104, 1.149)	1.146 (1.115, 1.177)	1.146 (1.112, 1.181)	1.189[b] (1.149, 1.228)	0.003	<0.0001
Beer[3,4]							
No. of subjects	983	263	43[5]	—	—		
Total hip (g/cm^2)	0.889 (0.876, 0.902)	0.900 (0.882, 0.918)	0.916 (0.880, 0.953)	—	—	0.17	0.16
Femoral neck (g/cm^2)	0.844 (0.830, 0.857)	0.858 (0.840, 0.876)	0.885 (0.849, 0.921)	—	—	0.03	0.03
Trochanter (g/cm^2)	0.698 (0.685, 0.710)	0.704 (0.687, 0.720)	0.721 (0.688, 0.755)	—	—	0.34	0.21
Spine (g/cm^2)	1.126 (1.105, 1.146)	1.141 (1.113, 1.169)	1.158 (1.102, 1.213)	—	—	0.31	0.19
Wine[3,4]							
No. of subjects	474	608	115	61	31		
Total hip (g/cm^2)	0.886 (0.870, 0.901)	0.895 (0.880, 0.910)	0.904 (0.880, 0.928)	0.905 (0.874, 0.937)	0.938 (0.895, 0.980)	0.09	0.02
Femoral neck (g/cm^2)	0.840 (0.825, 0.856)	0.853 (0.838, 0.867)	0.853 (0.829, 0.877)	0.858 (0.826, 0.889)	0.891 (0.849, 0.933)	0.08	0.048
Trochanter (g/cm^2)	0.681[a] (0.677, 0.706)	0.703 (0.689, 0.716)	0.711 (0.689, 0.733)	0.704 (0.675, 0.733)	0.754[b] (0.715, 0.793)	0.01	0.008
Spine (g/cm^2)	1.114[a] (1.090, 1.138)	1.132 (1.110, 1.155)	1.160 (1.124, 1.197)	1.161 (1.113, 1.209)	1.206[b] (1.142, 1.270)	0.006	0.002
Liquor[3,4]							
No. of subjects	780	377	68	32	32		
Total hip (g/cm^2)	0.888 (0.873, 0.902)	0.899 (0.883, 0.915)	0.897 (0.867, 0.927)	0.905 (0.863, 0.946)	0.918 (0.876, 0.959)	0.37	0.10
Femoral neck (g/cm^2)	0.844 (0.830, 0.859)	0.854 (0.838, 0.870)	0.845 (0.815, 0.875)	0.877 (0.836, 0.919)	0.864 (0.823, 0.905)	0.32	0.13
Trochanter (g/cm^2)	0.696 (0.682, 0.709)	0.703 (0.688, 0.717)	0.708 (0.680, 0.735)	0.709 (0.671, 0.747)	0.730 (0.691, 0.768)	0.35	0.045
Spine (g/cm^2)	1.118[a] (1.096, 1.140)	1.143 (1.118, 1.167)	1.132 (1.086, 1.177)	1.138 (1.075, 1.201)	1.206[b] (1.143, 1.269)	0.03	0.01

[1] All values are least-squares means (95% CIs). Values in the same row with different superscript letters are significantly different, $P < 0.05$.
[2] One drink = 13.2 g alcohol.
[3] Adjusted for age, sex, smoking, osteoporosis medication use, estrogen use, BMI, height, physical activity, and calcium, vitamin D, magnesium, protein, and total energy intakes.
[4] Also adjusted for grams of alcohol from other sources.
[5] There were insufficient numbers of women in the >1 drink/d category; therefore, this category is actually >0.5 drinks/d.

pathway. Whichever is correct, it is possible that the marked effect of postmenopausal bone resorption is partially rescued by alcohol, an effect that would not, of course, be observed in men or premenopausal women. Clearly, this observation must be placed in the context of harmful effects of high alcohol intake in older women, including increased risk of falls—and thus fracture risk—and greater risk of breast cancer (26) and cirrhosis. For premenopausal women, the relation between alcohol intake and BMD remains unclear due to the low number of subjects. However, consistent with our findings, Wosje and Kalkwarf (10) also reported no difference in BMD between premenopausal women who drank alcohol compared with abstainers.

It has been proposed that many associations between alcohol intake and health may exaggerate the protective effect due to misclassification of nondrinkers by combining never and past drinkers, the latter who may have stopped drinking due to poor health (7). We found that this was not the case for BMD, as there was no difference in BMD across these 2 groups in either men or women. Consistent with these results, Cawthon et al (9) also found that men who reported a history of problem drinking had higher femoral neck and spine BMD than those without such a history, although it is important to note that those men also had a higher risk of falls.

As noted above, it is possible that nutrients obtained from differing forms of moderate alcohol consumption also have contributing effects to BMD. silicon, for example, as orthosilicic acid, is a major constituent of beer (27) that may additionally promote bone formation (28). We previously reported that higher dietary silicon intake was associated with higher BMD in this sample of men and premenopausal women (28), and this has since been confirmed in a sample of women in the United Kingdom (29). Beer is a major source of dietary silicon, especially for men, and adjustment for silicon intake rendered comparisons across beer intake groups nonsignificant. Adjustment for silicon intake had no effect on the associations between wine or liquor intake and BMD. Wine and liquor are lesser and negligible sources of dietary silicon, respectively (30). Taken together, these results suggest that the main effect of moderate alcohol consumption on BMD is likely to be an ethanol effect (23). Our results also provide the first evidence for a nonethanol bone-active component in beer, namely silicon. The silicon effect appears to be moderate and, in contrast to ethanol, is likely to act on bone formation (28, 30).

A major constituent of wine that has been receiving considerable attention, particularly in relation to heart disease, is resveratrol (31, 32). Although little research on this compound in relation to BMD has been conducted, a recent study in an ovariectomized rat model showed that rats treated with resveratrol had significantly greater BMD than those not treated (33). The authors concluded that these results suggest that the

TABLE 4
Bone mineral density in premenopausal women by alcohol intake category[1]

	Intake (drinks/d)[2]					
	0	0–0.5	0.5–1	>1	*P* (ANCOVA)	*P* for trend
Total alcohol[3]						
No. of subjects	49	116	38	45		
Total hip (g/cm^2)	1.009 (0.977, 1.042)	0.991 (0.969, 1.012)	0.988 (0.950, 1.025)	1.026 (0.992, 1.060)	0.24	0.16
Femoral neck (g/cm^2)	0.976 (0.942, 1.009)	0.951 (0.928, 0.973)	0.951 (0.912, 0.9990)	0.989 (0.954, 1.024)	0.21	0.17
Trochanter (g/cm^2)	0.777 (0.747, 0.808)	0.774 (0.753, 0.795)	0.767 (0.731, 0.802)	0.807 (0.775, 0.839)	0.28	0.11
Spine (g/cm^2)	1.297 (1.252, 1.342)	1.239 (1.209, 1.269)	1.258 (1.206, 1.310)	1.265 (1.218, 1.312)	0.17	0.86
Beer[3,4]						
No. of subjects	154	94[5]	—	—		
Total hip (g/cm^2)	1.009 (0.990, 1.029)	0.985 (0.960, 1.011)	—	—	0.11	0.11
Femoral neck (g/cm^2)	0.974 (0.954, 0.994)	0.944 (0.918, 0.970)	—	—	0.05	0.05
Trochanter (g/cm^2)	0.784 (0.766, 0.805)	0.773 (0.749, 0.797)	—	—	0.36	0.44
Spine (g/cm^2)	1.266 (1.239, 1.293)	1.247 (1.211, 1.282)	—	—	0.44	0.36
Wine[3,4]						
No. of subjects	67	131	50[6]	—	—	
Total hip (g/cm^2)	1.010 (0.982, 1.038)	0.988 (0.967, 1.009)	1.022 (0.989, 1.056)	—	0.14	0.21
Femoral neck (g/cm^2)	0.977 (0.948, 1.006)	0.949 (0.926, 0.971)	0.981 (0.947, 1.016)	—	0.12	0.34
Trochanter (g/cm^2)	0.777 (0.750, 0.803)	0.777 (0.757, 0.798)	0.798 (0.767, 0.830)	—	0.47	0.22
Spine (g/cm^2)	1.285 (1.247, 1.324)	1.243 (1.213, 1.272)	1.273 (1.227, 1.319)	—	0.16	0.72
Liquor[3,4]						
No. of subjects	149	99[5]	—	—		
Total hip (g/cm^2)	0.999 (0.979, 1.019)	1.005 (0.981, 1.029)	—	—	0.66	0.66
Femoral neck (g/cm^2)	0.966 (0.946, 0.987)	0.959 (0.934, 0.984)	—	—	0.65	0.65
Trochanter (g/cm^2)	0.778 (0.759, 0.797)	0.786 (0.763, 0.809)	—	—	0.58	0.58
Spine (g/cm^2)	1.257 (1.230, 1.285)	1.269 (1.235, 1.302)	—	—	0.58	0.58

[1] All values are least-squares means (95% CIs). Values in the same row with different superscript letters are significantly different, $P < 0.05$.
[2] One drink = 13.2 g alcohol.
[3] Adjusted for age, sex, smoking, osteoporosis medication use, BMI, height, physical activity, and calcium, vitamin D, magnesium, protein, and total energy intakes.
[4] Also adjusted for grams of alcohol from other sources.
[5] There were insufficient numbers of women in the >1 drink/d category; therefore, this category is actually >0 drinks/d.
[6] There were insufficient numbers of women in the >1 drink/d category; therefore, this category is actually >0.5 drinks/d.

estrogenic resveratrol could play a role in protecting against bone loss in postmenopausal women with low estrogen status. A review of the bioactivity of resveratrol (34) further suggests that its estrogenic activity may help prevent postmenopausal bone loss. These observations are consistent with our finding of a significant effect of wine on BMD, although we were not able to quantify the actual exposure to resveratrol in this group of both red and white wine drinkers.

This study sought to investigate the effect of alcohol intake on BMD in a large, well-described population. Strengths also include the ability to control for important confounders, including other health behaviors, use of nutrient supplements, and season of measurement. Limitations of this study are recognized. First, although the alcohol intake data incorporated 2 time points and preceded the bone measurement, the analysis was cross sectional, so although a relation between moderate alcohol intake and BMD is indicated, caution must be exercised when drawing conclusions about the long-term effects of alcohol intake on bone health. Second, BMD was adjusted for known potential confounders, but we cannot rule out the possibility of residual confounding. Several other potential factors that may result in misclassification have recently been highlighted for epidemiologic analyses with alcohol, including the pattern and frequency of alcohol consumption (12). A steady drinking pattern may be more protective than infrequent binge drinking even though both may be classed under moderate ingestion on the basis of average daily or weekly intakes, as is usual with the FFQ, and as we have done here. Future studies should take into account this potential misclassification by including more detail in questionnaires about alcohol intake patterns. Third, because of the low number of premenopausal women in this cohort/study, the relation between alcohol intake and BMD remains unclear in this group. Finally, the low numbers of women drinking beer limits our ability to draw conclusions regarding the potential effects of beer intake on bone in women.

Overall, however, the positive relation between intake of alcohol and BMD in men and postmenopausal women, the reproducibility of these effects across the different bone sites, and the consistency of these findings with other published studies of total alcohol intake suggest that alcohol intake, particularly from beer and wine, may protect bone health. However, intake of >2 drinks/d of liquor in men was clearly harmful. We did not have sufficient numbers of women who drank heavily to confirm or refute this likely negative effect with heavy drinking. Therefore, caution is advised when interpreting this finding. Although there is likely an effect of ethanol on bone resorption, the relative lower significance of distilled liquors points to a possible role of components other than ethanol in bone resorption in beer and wine. Adjustment for silicon suggests that this component adds a further dimension with beer consumption that is likely to act on

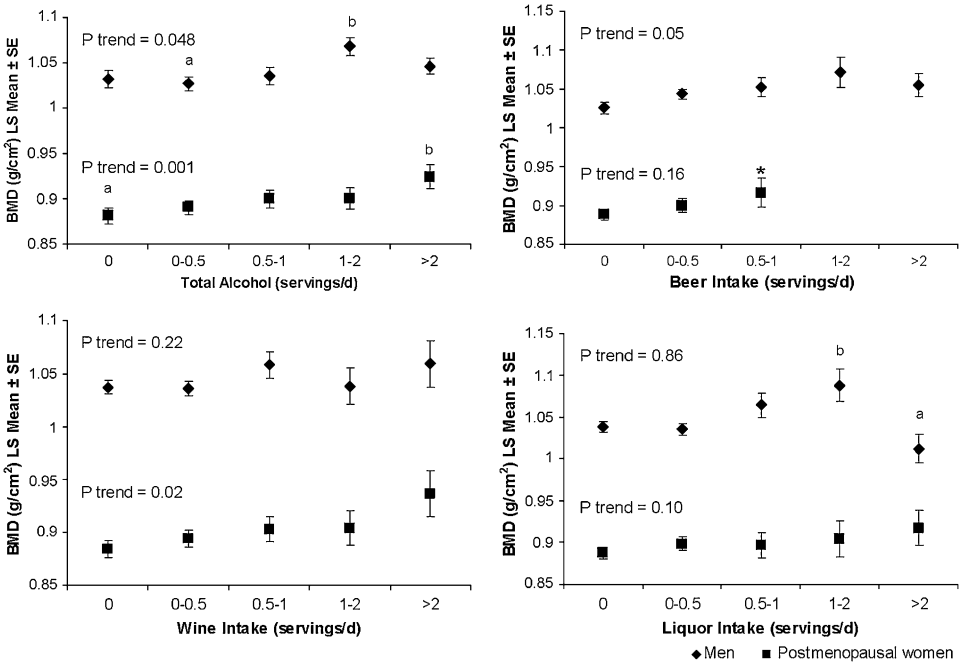

FIGURE 1. Adjusted least-squares (LS) mean bone mineral density (BMD), with bars indicating SEs, at the total hip by intake of total alcohol, beer, wine, and liquor, adjusted for age, height, BMI, physical activity score, smoking status, calcium intake (dietary and supplement use), vitamin D intake (dietary and supplement use), energy intake, magnesium intake, use of osteoporosis medication, season of BMD measurement, and, for postmenopausal women, estrogen use, and, for specific alcohol types, for total grams of alcohol from the other types. Significance between categories was tested by using the post hoc *t* test, with Tukey adjustment for multiple comparisons. Values with different lowercase letters are significantly different from postmenopausal women, $P < 0.05$. The asterisk indicates that the very few women who consumed >1 beer/d were collapsed into the top category as >0.5/d.

bone formation, and more research on other possible components is needed. Confirmation of these findings is required, and human intervention studies that measure changes in bone remodeling markers may help in establishing potential mechanisms.

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