Alcohol consumption and bone mineral density in elderly women

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Abstract

Objective: Findings regarding alcohol consumption and bone mineral density (BMD) in elderly women have been inconsistent. The objective of the present study was to explore the association of alcohol intake with BMD in elderly women.

Design: This cohort study included women from the population-based Kuopio Osteoporosis Risk Factor and Prevention – Fracture Prevention Study (OSTPRE-FPS). Alcohol intake and potential confounders were assessed at baseline and after 3 years of follow-up using a lifestyle questionnaire. In addition, an FFQ was distributed in the third year to measure dietary intake, including alcohol. Women underwent BMD measurements at the femoral neck and lumbar spine at baseline and after 3 years of follow-up.

Setting: Kuopio Province, Finland.

Subjects: Three hundred elderly women (mean age 67.8 years) who provided both BMD measurements and FFQ data.

Results: Alcohol consumption estimated from the FFQ and lifestyle questionnaire was significantly associated with BMD at both measurement sites after adjustment for potential confounders, including lifestyle and dietary factors (P<0.05). Using the FFQ, women drinking >3 alcoholic drinks/week had significantly higher BMD than abstainers, 12.0% at the femoral neck and 9.2% at the lumbar spine. Results based on the lifestyle questionnaire showed higher BMD values for all alcohol-consuming women at the femoral neck and for women drinking 1-3 alcoholic beverages/week at the lumbar spine, compared with non-users. Conclusions: The results from OSTPRE-FPS suggest that low to moderate alcohol intake may exert protective effects on bone health in elderly women.

Keywords Alcohol Bone density Elderly women Osteoporosis

Osteoporosis and related fractures have major consequences for the health of elderly women worldwide. Low bone mineral density (BMD) has been shown to be a strong predictor of an enhanced fracture risk^(1,2). In addition to unmodifiable risk factors such as age and sex, several nutritional and lifestyle factors including low Ca intake and low physical activity are recognized as important risk factors for the development of osteoporosis⁽³⁾. Alcohol intake as a potential contributing factor to osteoporosis

and osteoporotic fractures was first described in 1965⁽⁴⁾. Since then, the negative impact of chronic heavy alcohol consumption on bone health has been recognized⁽⁵⁾. Long-term alcohol use has been shown to exert direct and indirect effects on bone turnover and remodelling, leading to decreased BMD and increased risk of fractures⁽⁶⁾. Alcohol may directly worsen bone health by impairing proliferation and function of osteoblasts⁽⁷⁾, causing malabsorption, increased renal excretion and disruption of Ca-regulating hormones such as parathyroid hormone, calcitonin and vitamin D metabolites. Also, insufficient dietary intake related to alcohol may indirectly interfere with bone homeostasis^(8,9). In contrast to these harmful effects of

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alcohol abuse, several studies have reported that moderate alcohol use may decrease fracture rates and increase bone density, mostly in postmenopausal women^(10–23). However, others showed no significant association between alcohol intake and BMD^(24–28), and one reported a negative relationship between BMD at the lumbar spine and lifetime beer consumption⁽²⁹⁾.

As with CVD, the relationship between alcohol intake and bone health may be U-shaped⁽³⁰⁾. Moderate alcohol consumption has been suggested to increase oestrogen levels in postmenopausal women and subsequently prevent the development of osteoporosis. Studies, especially more recent ones^(31,32), have suggested that moderate alcohol intake may be associated with increased oestrogen levels in postmenopausal women. However, the findings regarding the effect of alcohol intake on BMD in elderly women are inconclusive and more studies with extensive adjustments for potential confounders are needed. To continue this line of investigation, the present study examined the association between alcohol intake and BMD at the lumbar spine and proximal femur in a subsample of the Kuopio Osteoporosis Risk Factor and Prevention Study (OSTPRE) population.

Materials and methods

Study design and participants

The present study was based on the Kuopio Osteoporosis Risk Factor and Prevention - Fracture Prevention Study (OSTPRE-FPS) which began in 2003 in Kuopio, Finland⁽³³⁾. The primary aim of the study was to determine whether vitamin D and Ca supplementation would prevent bone loss in postmenopausal women in a non-placebo-controlled, parallel-group trial. The ethics committee of Kuopio University Hospital approved the OSTPRE-FPS in October 2001. The trial was registered at Clinictrials.gov under identifier NCT00592917 (registration date: 2 January 2008). Written informed consent was obtained from the study participants at baseline enquiry. The OSTPRE-FPS population (n 5407) was selected from the population-based OSTPRE cohort of 13 100 peri- and postmenopausal women born in 1932-1941⁽³⁴⁾. The inclusion criteria for OSTPRE-FPS were: being a minimum of 65 years of age at the end of November 2002; living in Kuopio Province at the onset of the trial; and not having been included in the OSTPRE sample in which BMD measurements were conducted. Willingness to participate in a vitamin D and Ca supplementation trial was enquired via mail. A response rate of 63.5% led to a study population of 3432 women, which was randomized into two groups of equal size. From this study population, a subsample of 750 women was randomly selected to take part in a clinical trial. Of these, a total of 606 participants started the trial.

The baseline measurements took place between February 2003 and May 2004 and the follow-up measurements

between January 2006 and May 2007 (mean follow-up time 2.8 (sp 0.4) years). In both examinations, lifestyle, health status and use of drugs were assessed using questionnaires, and BMD measurements were undertaken. The supplementation group received daily cholecalciferol 20 µg (800 IU)+ Ca 1000 mg via prescription, while the control group received neither supplementation nor placebo. A total of 593 participants completed the study. Of them, 544 women underwent BMD measurements at the femoral neck and 480 women at the lumbar spine. Additionally, an FFQ was distributed at the follow-up examination. However, not all women were willing to complete the FFQ. This left a total of 341 women who underwent both baseline and 3-year BMD measurements and returned the FFQ. Thereof, fifteen women were excluded because of implausible energy intake (>14644 kJ (>3500 kcal)) and twenty-six were excluded due to incomplete data, leaving 300 women to be included in the final analysis (Fig. 1).

Questionnaires

The OSTPRE-FPS questionnaire (lifestyle questionnaire) was used to collect information on lifestyle, health status and medications at baseline and alcohol consumption at baseline and follow-up. Although it has not been validated to measure alcohol consumption, it was successfully used to demonstrate the association between alcohol intake and spinal BMD in an earlier study(3). In the lifestyle questionnaire, participants were asked questions about age, current and past hormone therapy (HT), current smoking status, mobility, diseases and medications, and use of non-prescribed Ca and/or vitamin D supplements. Non-prescribed Ca and/or vitamin D supplements included those available over the counter, which were consumed in addition to the prescribed Ca and vitamin D intervention of the trial. The mean duration of HT use in years (10.9 years) was substituted for fifty participants who reported that they had used HT but did not remember its exact duration. Criteria for restricted mobility were: (i) not able to walk more than 1km; (ii) not able to walk more than 100 m; (iii) only able to move indoors; and (iv) immobile. To assess alcohol consumption, participants were asked to quantify their intake of beer/cider (bottles), wine (glasses) or spirits/strong alcohol (portions) during the last 4 weeks. A 'drink' referred to a bottle of beer/cider, a glass of wine or one portion of spirits/strong alcohol. In Finland, the average portion size for a bottle of beer/cider is 330 ml, for a glass of wine is 120 ml and for a shot of spirits/strong alcohol 40 ml.

The FFQ assessed the usual dietary intake at follow-up. Participants were asked to report their usual consumption of beer/cider (1 bottle = 330 ml), red or white wine (120 ml) or spirits (40 ml) by selecting one of nine frequency categories: 'never or very seldom', '1–3 times per month', 'once per week', '2–4 times per week', '5–6 times per week', 'once per day', '2–3 times per day', '4–5 times

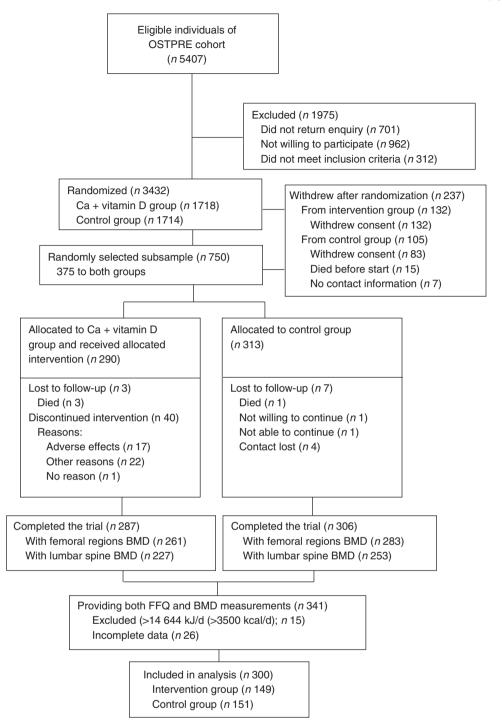


Fig. 1 Flowchart of the subsample of the Kuopio Osteoporosis Risk Factor and Prevention – Fracture Prevention Study (OSTPRE-FPS) trial (BMD, bone mineral density)

per day' or 'more than 5 times per day'. For analysis, average alcohol intakes per week were calculated. Total dietary intakes of energy, protein, K, Ca and vitamin D, out of all questioned food items, were computed. These are considered potential confounders and were therefore used as covariates in the statistical models. The FFQ was validated with food records for energy and nutrient

intakes, and agreement between the two measurement tools was moderate⁽³⁵⁾.

Anthropometric measurements

Weight of the participant was measured with a digital calibrated scale (Philips, type HF 351/00) and height with a calibrated wall meter during the baseline research visit.

BMI (kg/m²) was computed by dividing the weight (in kilograms) by the square of height (in metres).

Measurements of bone mineral density

BMD measurements were performed at the lumbar spine (L2–L4) and left femoral neck with dual-energy X-ray absorptiometry (DXA; Lunar DPX, Madison, WI, USA) at baseline and year 3 examinations. The quality control of the DXA measurements was run daily. The *in vitro* long-term reproducibility (CV) for the total femur region was 0·3%. Measurements were carried out by following the guidelines of the instrument's manufacturer. The technical quality of each DXA measurement and analysis was carefully checked and those with measurement errors were not included in the statistical analyses⁽³⁶⁾.

Statistical analyses

Average alcohol consumption derived from the lifestyle questionnaires or the FFO was divided into four categories: no use; <1 drink/week; 1–3 drinks/week; and >3 drinks/ week. These cut-offs produced categories with sufficient numbers of participants to be able to generate more stable estimates. Since the number of participants in the highest category was relatively small, more detailed analysis to detect potential differences between moderate v. heavy drinkers was not possible due to limited statistical power. Associations between alcohol intake and other variables potentially affecting BMD were analysed using one-way ANOVA for continuous variables and the χ^2 test for categorical variables. These potential confounders were identified through literature review. Linear mixed-effects modelling was used to examine the relationship between alcohol consumption (added as the mean of two measurement time points using the lifestyle questionnaire, or added as one measurement time point at year 3 using the FFO) and BMD changes over time (added as a time-varying covariate with two measurement time points). No significant changes in alcohol consumption were found and therefore alcohol was entered into the model as the mean of baseline and follow-up. The possibility of an interaction between alcohol intake and the effect of the vitamin D and Ca intervention (study group) on BMD was also tested using the likelihood ratio test, and showed no significance. Therefore, results are presented for all women.

Models were run unadjusted in the first step (accounting for study group only; Model 1); then run adjusted for confounding factors assessed at baseline including age (years), BMI (kg/m²), whether a current smoker (yes/no), HT use current or past (yes/no), duration of HT use (years), use of non-prescribed Ca and vitamin D supplement in addition to intervention (yes/no), study group (intervention/control), restricted mobility (yes/no), disease or medication decreasing BMD (yes/no; Model 2); and finally dietary factors including total energy intake (kJ/d), dietary protein intake (g/d), dietary K intake (mg/d), dietary Ca intake (mg/d) and dietary vitamin D (μg/d) were added to the list of covariates

(Model 3). The diseases potentially affecting bone metabolism included hyperthyroidism, disease of the parathyroid gland, chronic liver disease, chronic intestinal disease, coeliac disease, ventricle operation, chronic nephropathy, arthritis, osteoporosis and lactose intolerance. Medications affecting bone metabolism included loop-diuretics, insulin, anti-epileptics, glucocorticoids and cancer chemotherapy. Results are shown as estimated marginal means. Analyses were conducted separately for alcohol consumption from the lifestyle questionnaire and for alcohol consumption from the FFQ. Statistical analyses were carried out with the statistical software packages SPSS for Windows version 15·0 (SPSS Inc.) and STATA version 9·0 (StataCorp). The level of significance was set at 0·05.

Results

Generally, alcohol consumption among the elderly women was low. The majority of the women were non-drinkers (lifestyle questionnaire $(n\ 118)$, $39\cdot9\%$; FFQ $(n\ 169)$, $56\cdot3\%$) or consumed <1 drink/week (lifestyle questionnaire $(n\ 103)$, $34\cdot8\%$; FFQ $(n\ 69)$, $23\cdot0\%$). A total of $18\cdot9\%$ of women based on the lifestyle questionnaire $(n\ 56)$ and $11\cdot0\%$ of women based on the FFQ $(n\ 33)$ reported intake of 1–3 drinks/week. Only a very few participants consumed >3 drinks/week (lifestyle questionnaire $(n\ 19)$, $6\cdot4\%$; FFQ $(n\ 29)$, $9\cdot7\%$).

Mean alcohol intake measured by the lifestyle questionnaire at baseline and follow-up was 0.82 drinks/week, which was slightly lower than the mean alcohol intake that was obtained from the FFQ (0.93 drinks/week) at the follow-up measurement (Table 1). The mean BMD at the lumbar spine was increased at follow-up ($1.097\,\mathrm{g/cm^3}$) compared with baseline ($1.087\,\mathrm{g/cm^3}$). About half of the women ($54.5\,\%$) currently used or had used HT at some time in their life. Only $4.8\,\%$ of the women were current smokers.

According to their alcohol consumption categories assessed through the lifestyle questionnaire at baseline and follow-up, women in the higher categories of alcohol intake were more likely to be smokers (Table 2).

Alcohol use was significantly associated with BMD (Tables 3 and 4). Using the FFQ, women in the highest category of alcohol intake had significantly higher BMD than non-consumers at both measurement sites (Table 3). At the femoral neck, the P value for the unadjusted model was 0·020 (Model 1). The strongest association between alcohol intake and BMD was observed after adjustment for both lifestyle and dietary factors (P=0·014). In this model, women consuming >3 alcoholic drinks/week had 12·0% higher BMD values than abstainers (Model 3). Similar results were found for the lumbar spine, where the association between alcohol intake and BMD was strongest in the unadjusted model (P=0·002; Model 1). After adjustment for lifestyle and dietary factors, women

Table 1 Characteristics of the study participants: elderly Finnish women (*n* 300), Kuopio Osteoporosis Risk Factor and Prevention – Fracture Prevention Study (OSTPRE-FPS)

Characteristic	Mean or %	SD
Baseline (February 2003–May 2004)		
Age (years; <i>n</i> 298)	67.8	1.8
BMI (kg/m ² ; <i>n</i> 298)	28.4	4.3
Current or past HT use (%; n 279)	54∙5	_
Duration of HT use (years; n 153)	11.3	5.9
Non-prescribed use of Ca and vitamin D supplements (%; n 298)	13.8	_
Current smoking (%; n 293)	4.8	_
Restricted mobility (%; n 292)	6.2	_
Disease or medication decreasing BMD (%; n 298)	31.8	_
Follow-up (January 2006–May 2007)		
Total energy intake (kJ/d; n 300)	8979	2297
Total energy intake (kcal/d; n 300)	2146	549
Dietary protein intake (g/d; n 300)	90.7	27.3
Dietary Ca intake (mg/d; n 300)	1324	502
Dietary vitamin D intake (μg/d; n 300)	10.0	4.8
Dietary K intake (mg/d; n 300)	4777	1301
Total alcohol intake (drinks/week)		
Lifestyle questionnaire (average of baseline and follow-up; n 296)	0.82	1.30
FFQ (follow-up; n 300)	0.93	1.87
BMD (g/cm ³)		
Femoral neck		
Baseline (<i>n</i> 292)	0.866	0.127
Follow-up (n 291)	0.852	0.121
Lumbar spine		
Baseline (<i>n</i> 252)	1.087	0.184
Follow-up (n 247)	1.097	0.181
Study group (%)		
Intervention	49.7	_
Control	50.3	_

HT, hormone therapy; BMD, bone mineral density.

in the highest category of alcohol intake had 9.2% higher BMD compared with non-users (P = 0.006; Model 3).

Using the lifestyle questionnaire to assess alcohol intake, significant associations between alcohol intake and BMD at both bone sites were found in unadjusted and adjusted models (Table 4). At the femoral neck, the P value in the unadjusted model was 0.008 (Model 1). Women who consumed any amount of alcohol (from <1 to >3 drinks/week) had significantly higher BMD than women who abstained from alcohol after adjustment for lifestyle and dietary factors (Model 3). Women drinking >3 alcoholic drinks/week had 7.7% higher BMD than non-drinkers after adjustment for both lifestyle and dietary factors (P = 0.025; Model 3). Analysis at the lumbar spine showed that women consuming 1-3 and >3 alcoholic drinks/week had significantly higher BMD than non-drinkers in the unadjusted model (P = 0.008and P = 0.039, respectively; Model 1). After adjustment for lifestyle and dietary factors, only women drinking 1-3 alcoholic drinks/week had significantly higher BMD (6.4%) than abstainers (P = 0.019; Model 3).

Discussion

The findings of the present study suggest that low alcohol consumption may be beneficially related to bone health

in elderly women. Depending on the alcohol assessment method, alcohol consumption of >3 drinks/week (FFQ) or 1-3 and >3 drinks/week (lifestyle questionnaire) was positively associated with BMD at the femoral neck and lumbar spine. All associations between alcohol use and BMD at both measurement sites remained significant after adjustment for lifestyle and dietary factors (Model 3). Depending on measurement site, dietary factors, including total energy intake and dietary intakes of protein, Ca, vitamin D and K, strengthened or attenuated the association between alcohol and BMD. The latter have been identified as the most evident dietary factors affecting BMD in the literature (37-41) and were therefore added to the analysis. These findings suggest that low alcohol consumption has an independent effect on BMD. However, other dietary issues and many other factors contribute to bone health.

Although earlier observations suggested a potential protective effect of moderate alcohol consumption on BMD at the femoral neck and/or lumbar spine in postmenopausal women (10-12,14-16,18,20-23), highest BMD values were mostly found in women who consumed at least one drink daily. Among a group of peri- and postmenopausal women, alcohol consumption (mean intake of consumers was 125 g/week) was a positive predictor for spine BMD⁽³⁾. The women participating in the present study consumed at most 1–3 drinks/week or >3 drinks/week, respectively,

Table 2 Characteristics of the study participants according to alcohol intake assessed using the lifestyle questionnaire: elderly Finnish women (n 300), Kuopio Osteoporosis Risk Factor and Prevention – Fracture Prevention Study (OSTPRE-FPS)

					Alcoh	Alcohol intake (drinks/week	drinks	/week)					
		No use			\ \			1–3			>3		
	и	Mean or %	SD	и	Mean or %	SD	и	Mean or %	SD	и	Mean or %	SD	P for difference*
Age (years)	117	2.79	1.9	102	0.89	1.7	99	6.79	1.9	19	9.29	1.8	0.424
BMI (kg/m²)	117	28.9	4.3	102	27.9	4.2	26	28·1	4.0	19	27.4	4.4	0.276
Current or past HT use (%)	108	49.5	ı	94	51.1	I	22	63.6	ı	19	73.7	I	0.103
Duration of HT use (years)	53	10.4	5.3	49	11.9	5.9	35	11.4	7.1	14	12.9	5.4	0.458
Non-prescribed use of Ca and vitamin D supplements (%)	117	11:1	ı	102	15.7	I	26	14.3	ı	19	21.1	ı	0.605
Current smoking status (%)	116	5.6	I	66	2.0	ı	22	12.7	ı	19	10.5	I	0.008
Restricted mobility (%)	114	9.6	ı	100	2.0	1	26	3.6	ı	19	0	I	0.214
Disease or medication decreasing BMD (%)	117	32.0	I	102	25.5	I	26	37.5	I	19	26·3	I	0.315
Dietary intake													
Energy (kJ/d)	118	0006	2322	103	8874	2247	26	9176	2339	6	8807	2343	0.863
Energy (kcal/d)	118	2151	222	103	2121	537	26	2193	229	19	2105	260	0.863
Protein (g/d)	118	90.3	26.5	103	88.5	25.9	26	95.3	31.2	19	91.4	27.0	0.516
Ca (mg/d)	118	1344	203	103	1278	42.2	26	1341	528	19	1357	778	0.760
Vitamin D (µg/d)	118	9.6	5.5	103	10.0	3.9	26	10.9	5.2	19	10.7	4.4	0.421
K (mg/d)	118	4813	1379	103	4731	1199	26	4893	1362	19	4527	1240	0.717

HT, hormone therapy; BMD, bone mineral density. *The difference between continuous variables using ANOVA.

which corresponds to weekly alcohol intake of 10–30 g or more. Laitinen *et al.*⁽¹¹⁾ and Rapuri *et al.*⁽¹⁸⁾ have previously reported a beneficial effect of low alcohol consumption on BMD. Laitinen *et al.*⁽¹¹⁾ found higher BMD for postmenopausal women consuming 11–77 g alcohol/week than for abstainers at all measurement sites (femoral neck, Ward's triangle, trochanter and lumbar spine). Similar results were found in the study conducted by Rapuri *et al.*⁽¹⁸⁾ where women with an alcohol consumption of 28.7-57.2 g/week had the highest lumbar spine, total body and mid-radius BMD compared with non-users. Therefore, alcohol consumption may already be beneficial for bone health at lower doses than previously assumed.

The average alcohol consumption of elderly women in the present study, 0.8-0.9 drinks/week, was relatively low, but comparable to previous estimates found for Finnish elderly (42). Using an FFQ to measure alcohol intake, 37.7% of women aged 65-69 years reported to abstain from alcohol and 35.3% reported to consume less than one alcoholic drink per week (42). The present study found 39.3% of elderly women to abstain from alcohol when using the lifestyle questionnaire and 56.3% when using the FFQ data. Likewise, 34.8% (lifestyle questionnaire) and 23.0% (FFQ) of elderly women consumed less than one alcoholic drink weekly in the present study. It has recently been reported⁽⁴³⁾ that under-reporting of alcohol consumption most likely occurs when data are collected from an FFQ. Additionally, drinking behaviour and beliefs about alcohol differ between cultures and age groups. Studies assessing alcohol use among the elderly (>74 years) in Finland found that alcohol use was less likely to be under-reported if it was in the context of medicinal use⁽⁴⁴⁾. We cannot rule out the possibility that some women may have been misclassified and if so, the association between alcohol intake and BMD would be

In line with the findings from the original OSTPRE-FPS trial⁽³³⁾ where BMD measurements at the lumbar spine had increased after 3 years irrespective of the intervention, results at the lumbar spine were also higher at the follow-up assessment in the present study. This observation has been made in earlier studies^(45,46) and could be explained by age-related degenerative changes, such as osteoarthritis, that have been shown to confound DXA measurements⁽⁴⁷⁾. Since our analysis was adjusted for current and past HT use, duration of HT use and medications affecting BMD, we can rule out the potential impact of these on the BMD increase.

As reported in previous studies (12,14,18,19,21,25) smoking and drinking habits tend to be strongly associated. Although the percentage of smokers in the current study population was low (4.8%), the proportion of smokers was higher among those consuming 1–3 or >3 alcoholic drinks/week than among non-drinkers (12.7% or 10.5% v. 2.6%). Additionally, low body weight or low BMI, which are strong predictors of osteoporotic fractures (148), frequently

Table 3 Estimated marginal means derived from the linear mixed model predicting BMD change over time by category of alcohol intake assessed using the FFQ at follow-up: elderly Finnish women (n 300), Kuopio Osteoporosis Risk Factor and Prevention - Fracture Prevention Study (OSTPRE-FPS)

	Model 1*		N	Model 2t	N	Nodel 3‡
	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI
Femoral neck						_
No use	0.845	0.827, 0.864	0.848	0.830, 0.865	0.847	0.829, 0.865
<1 drinks/week	0.872	0.843, 0.902	0.875	0.848, 0.902	0.874	0.847, 0.901
1-3 drinks/week	0.875	0.833, 0.917	0.879	0.840, 0.918	0.878	0.840, 0.917
>3 drinks/week	0.9038	0.858, 0.948	0.8998	0.858, 0.941	0.9048	0.863, 0.946
Lumbar spine	Ü	,	Ü	•	Ü	,
No use	1.076	1.047, 1.105	1.079	1.051, 1.107	1.080	1.052, 1.108
<1 drinks/week	1.093	1.047, 1.139	1.094	1.051, 1.137	1.093	1.050, 1.136
1-3 drinks/week	1.081	1.014, 1.148	1.089	1.026, 1.152	1.087	1.024, 1.150
>3 drinks/week	1·192§	1.125, 1.261	1·183§	1.119, 1.247	1·179§	1.114, 1.243

BMD, bone mineral density; HT, hormone therapy.

Table 4 Estimated marginal means derived from the linear mixed model predicting BMD change over time by category of alcohol intake assessed using the lifestyle questionnaire at baseline and follow-up (mean): elderly Finnish women (n 300), Kuopio Osteoporosis Risk Factor and Prevention - Fracture Prevention Study (OSTPRE-FPS)

	Model 1*		N	Model 2t	Model 3‡	
	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI
Femoral neck						
No use	0.834	0.812, 0.856	0.835	0.814, 0.857	0.835	0.813, 0.856
<1 drinks/week	0.860	0.836, 0.884	0.870§	0.847, 0.892	0.869§	0.846, 0.891
1-3 drinks/week	0·897§	0.864, 0.929	0⋅889§	0.860, 0.919	0⋅891§	0.861, 0.921
>3 drinks/week	0.9138	0.858, 0.968	0⋅897§	0.848, 0.946	0⋅899§	0.850, 0.948
Lumbar spine	Ü	,	Ü	•	Ü	,
No use	1.071	1.037, 1.105	1.076	1.043, 1.110	1.077	1.044, 1.110
<1 drinks/week	1.068	1.030, 1.106	1.074	1.037, 1.110	1.073	1.036, 1.109
1-3 drinks/week	1.1538	1.103, 1.203	1.1458	1.099, 1.192	1.1468	1.100, 1.192
>3 drinks/week	1⋅164§	1.082, 1.245	1·143ຶ	1.069, 1.217	1·139 ຶ	1.065, 1.212

HT, hormone therapy; BMD, bone mineral density.

occur in alcohol-drinking elderly women (12,14,16,18,20,21,25). However, in our sample there were no statistically significant differences in BMI across the categories of alcohol intake. There seemed to be an association between HT use and alcohol consumption in our study. A total of 73.7% women in the highest category of alcohol intake currently used or had used HT for some time during their life.

Mobility is another factor with positive impact on BMD. All elderly women consuming >3 drinks/week had normal mobility, whereas 9.6% of the abstaining women had restricted mobility. Higher physical activity among alcohol-consuming women was reported by Ganry et al. (17) and Mukamal et al. (21). Alcohol-drinking women participating in the study conducted by Felson et al. (14)

were exercising less than non-drinking women. Based on the findings from this and previous studies, elderly women who drink alcohol seem to have a certain lifestyle pattern. They are more likely to smoke and exercise, have lower BMI and are more likely to use HT than alcoholabstaining elderly women.

The present study sought to investigate the impact of alcohol consumption on BMD at the femoral neck and lumbar spine in a homogeneous study population. There was repeated longitudinal information on alcohol consumption using the lifestyle questionnaire and BMD measurements, and the analytical approach selected allowed the correlation between repeated BMD measurements on the same participants to be taken into account.

^{*}Adjusted for study group (intervention v. control).

⁺Adjusted for age, BMI, HT use, duration of HT use, current smoking, use of Ca and vitamin D supplements, restricted mobility, disease or medication decreasing BMD, study group (intervention v. control).

[‡]Adjusted for age, BMI, HT use, duration of HT use, current smoking, use of Ca and vitamin D supplements, restricted mobility, disease or medication decreasing BMD, study group (intervention v. control), energy intake, dietary protein, dietary Ca, dietary vitamin D, dietary K. The difference between category no use v. other categories is statistically significant at the 0.05 level.

^{*}Adjusted for study group (intervention v. control).
+Adjusted for age, BMI, HT use, duration of HT use, current smoking, use of Ca and vitamin D supplements, restricted mobility, disease or medication decreasing BMD, study group (intervention v. control).

[‡]Adjusted for age, BMI, HT use, duration of HT use, current smoking, use of Ca and vitamin D supplements, restricted mobility, disease or medication decreasing BMD, study group (intervention v. control), energy intake, dietary protein, dietary Ca, dietary vitamin D, dietary K. \$The difference between category no use v. other categories is statistically significant at the 0.05 level.

Strengths of the study also include the ability to control for well-established confounders, including lifestyle factors and dietary factors. However, limitations of our study are also recognized. Although data on alcohol consumption using the lifestyle questionnaire were collected from baseline and 3-year follow-up, the FFQ was distributed only at the follow-up examination. One of the drawbacks was also the relatively small sample size. Since data on dietary intake were available from only about half the women initially enrolled in the trial, we cannot rule out the possibility of attrition bias. However, the women participating in the study showed no differences in terms of main characteristics (age, BMI, HT use, duration of HT use and smoking) compared with those who did not participate. The proportions of women with restricted mobility (9.3%), non-prescribed use of Ca and vitamin D supplements (18.5%) and disease or medication decreasing BMD (41.6%) were higher in non-participating women. The study was part of a nonplacebo-controlled, parallel-group trial, where half of the sample received vitamin D and Ca supplementation. To rule out the possibility of an independent effect between alcohol intake and the Ca and vitamin D intervention (study group) on BMD, its interaction was tested prior to analysis and showed no significance. Additionally, the study group was added as a covariate to all models of analysis.

Ideally, the effect of alcohol consumption on BMD needs to be studied over a long period of time. The follow-up period of our study was 3 years, and therefore cannot fully address this issue. Another limitation was the fact that physical activity was not directly measured. However we did assess mobility, which reflects the ability to perform physical exercise. Also, the possibility of other unmeasured confounding factors cannot be ruled out.

Conclusion

The results from the OSTPRE-FPS cohort suggest that low alcohol intake may exert protective effects on bone health in elderly women. Further studies are needed to confirm these findings.

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were responsible for the original OSTPRE-FPS study design. All of the authors contributed to revising the manuscript and approved the final version. The authors thank Ms Seija Oinonen for technical support.

References

- Johnell O, Kanis JA, Oden A et al. (2005) Predictive value of BMD for hip and other fractures. J Bone Miner Res 20, 1185–1194.
- Cauley JA, Hochberg MC, Lui LY et al. (2007) Long-term risk of incident vertebral fractures, *JAMA* 19, 2761–2767.
- Kröger H, Tuppurainen M, Honkanen R et al. (1994) Bone mineral density and risk factors for osteoporosis – a population-based study of 1600 perimenopausal women. Calcif Tissue Int 55, 1–7.
- Saville PD (1965) Changes in bone mass with age and alcoholism. J Bone Joint Surg 47-A, 492–499.
- Peris P, Parés A, Guañabenes N et al. (1992) Reduced spinal and femoral bone mass and deranged bone mineral metabolism in chronic alcoholics. Alcohol Alcohol 27, 619–625.
- Sampson HW (1998) Alcohol's harmful effects on bone. Alcohol Health Res World 22, 190–194.
- Klein RF (1997) Alcohol-induced bone disease: impact of ethanol on osteoblast proliferation. *Alcohol Clin Exp Res* 21, 392–399.
- Sampson HW (1997) Alcohol, osteoporosis, and bone regulating hormones. Alcohol Clin Exp Res 21, 400–403.
- Turner RT (2000) Skeletal response to alcohol. Alcohol Clin Exp Res 24, 1693–1701.
- Angus RM, Sambrook PN, Pocock NA et al. (1998) Dietary intake and bone mineral density. Bone Miner 4, 265–277.
- Laitinen K, Välimäki M & Keto P (1991) Bone mineral density measured by dual-energy X-ray absorptiometry in healthy Finnish women. *Calcif Tissue Int* 48, 224–231.
- Holbrook TL & Barrett-Connor E (1993) A prospective study of alcohol consumption and bone mineral density. BMJ 306, 1506–1509.
- Nguyen TV, Kelly PJ, Sambrook PN et al. (1994) Lifestyle factors and bone density in the elderly: implications for osteoporosis prevention. J Bone Miner Res 9, 1339–1346.
- Felson DT, Zhang Y, Hannan MT et al. (1995) Alcohol intake and bone mineral density in elderly men and women. Am J Epidemiol 142, 485–492.
- Orwoll ES, Bauer DC, Vogt TM et al. (1996) Axial bone mass in older women. Ann Intern Med 124, 187–196.
- Feskanich D, Willet W, Stampfer M et al. (1996) Protein consumption and bone fractures in women. Am J Epidemiol 143, 472–479.
- Ganry O, Baudoin C & Fardellone P (2000) Effect of alcohol intake on bone mineral density in elderly women. Am J Epidemiol 151, 773–780.
- Rapuri PB, Gallagher JC, Balhorn KE et al. (2000) Alcohol intake and bone metabolism in elderly women. Am J Clin Nutr 72, 1206–1213.
- Williams FMK, Cherkas LF, Spector TD et al. (2005) The effect of moderate alcohol consumption on bone mineral density: a study of female twins. Ann Rheum Dis 64, 309–310.
- Wosje KS & Kalkwarf HJ (2007) Bone density in relation to alcohol intake among men and women in the United States. Osteoporos Int 18, 391–400.
- Mukamal KJ, Robbins JA, Cauley JA et al. (2007) Alcohol consumption, bone density, and hip fracture among older adults: the Cardiovascular Health Study. Osteoporos Int 18, 593–602.
- Pedrera-Zamorano JD, Lavado-Garcia JM, Roncero-Martin R et al. (2009) Effect of beer drinking on ultrasound bone mass in women. Nutrition 25, 1057–1063.

 Tucker KL, Jugdaohsingh R, Powell JJ et al. (2009) Effects of beer, wine, and liquor intakes on bone mineral density in older men and women. Am J Clin Nutr 89, 1188–1196.

- Stevenson JC, Lees B, Devenport M et al. (1989)
 Determinants of bone density in normal women: risk
 factors for future osteoporosis? BMJ 298, 924–928.
- Hansen MA, Overgaard K, Riis BJ et al. (1991) Potential risk factors for development of postmenopausal osteoporosis – examined over a 12-year period. Osteoporos Int 1, 95–102.
- Bauer DC, Browner WS, Cauley JA et al. (1993) Factors associated with appendicular bone mass in older women. Ann Intern Med 118, 657–665.
- MacInnis RJ, Cassar C, Nowson CA et al. (2003) Determinants of bone density in 30- to 65-year-old women: a co-twin study. J Bone Miner Res 18, 1650–1656.
- 28. Tivis LJ & Tivis RD (2008) One-per-occasion or less: are moderate-drinking postmenopausal women really healthier than their nondrinking and heavier-drinking peers? *Alcohol Clin Exp Res* **32**, 1670–1680.
- Grainge MJ, Coupland CAC, Cliffe SJ et al. (1998) Cigarette smoking, alcohol and caffeine consumption, and bone mineral density in postmenopausal women. Osteoporos Int 8, 355–363.
- Klatsky AL (2007) Alcohol, cardiovascular diseases and diabetes mellitus. *Pharmacol Res* 55, 237–247.
- Onland-Moret NC, Peeters PHM, van der Schouw YT et al. (2005) Alcohol and endogenous sex steroid levels in postmenopausal women: a cross-sectional study. J Clin Endocrinol Metab 90, 1414–1419.
- Gavaler JS (2005) Should we consider an acceptable drinking level specifically for postmenopausal women? Preliminary findings from the postmenopausal health disparities study. Alcohol Alcohol 40, 469–473.
- Kärkkäinen M, Tuppurainen M, Salovaara K et al. (2010) Effect of calcium and vitamin D supplementation on bone mineral density in women aged 65–71 years: a randomized population-based trial (OSTPRE-FPS). Osteoporos Int 21, 2047–2055.
- Honkanen R, Alhava EM, Saarikoski S et al. (1991) Osteoporosis risk factors in perimenopausal women. Calcif Tissue Int 49, Suppl., S74–S75.
- Erkkilä AT, Järvinen R, Karvonen H et al. (2012) Validation of a semi-quantitative food frequency questionnaire using food records as reference in older women in the Kuopio Fracture Prevention Study (OSTPRE-FPS). Public Health Nutr 15, 635–639.

- Kärkkäinen M, Rikkonen T, Kröger H et al. (2009) Physical tests for patient selection for bone mineral density measurements in postmenopausal women. Bone 44, 660–665.
- 37. Darling A, Millward D, Torgerson D *et al.* (2009) Dietary protein and bone health; a systematic review and meta-analysis. *Am J Clin Nutr* **90**, 1674–1692.
- 38. Tang BMP, Eslick GD, Nowson C *et al.* (2007) Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older. *Lancet* **370**, 657–666.
- 39. Cranney A, Weiler HA, O'Donnell S *et al.* (2008) Summary of evidence-based review on vitamin D efficacy and safety in relation to bone health. *Am J Clin Nutr* **88**, issue 2, 5138–519S.
- 40. Lanham-New SA (2008) The balance of bone health: tipping the scales in favor of potassium-rich, bicarbonate-rich foods. *J Nutr* **138**, issue 1, 1725–1775.
- 41. Zhu K, Devine A & Prentice R (2009) The effects of high potassium consumption on bone mineral density in a prospective cohort study of elderly postmenopausal women. *Osteoporos Int* **20**, 335–340.
- Halme JK, Seppä K, Alho H et al. (2010) Alcohol consumption all-cause mortality among elderly in Finland. Drug Alcohol Depend 106, 212–218.
- MacDonald HM (2009) Alcohol and recommendations for bone health; should we still exercise caution? Am J Clin Nutr 89, 999–1000.
- Aira M, Hartikainen S & Sulkava R (2008) Drinking alcohol for medicinal purposes by people aged older 75: a community-based interview study. Fam Pract 25, 445–449.
- 45. Jones G, Nguyen T, Sambrook P *et al.* (1994) Progressive loss of bone in the femoral neck in elderly people: longitudinal findings from the Dubbo osteoporosis epidemiology study. *BMJ* **309**, 691–695.
- 46. Greenspan SL, Maitland LA, Myers ER *et al.* (1994) Femoral bone loss progresses with age: a longitudinal study in women over age 65. *J Bone Miner Res* **9**, 1959–1965.
- 47. Muraki S, Yamamoto S, Ishibashi H *et al.* (2004) Impact of degenerative spinal disease on bone mineral density of the lumbar spine in elderly women. *Osteoporos Int* **15**, 724–728.
- 48. Ricci TA, Hdeymsfield SB, Pierson RN *et al.* (2001) Moderate energy restriction increases bone resorption in obese postmenopausal women. *Am J Clin Nutr* **73**, 347–352.