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Original Contribution

Childhood Cod Liver Oil Consumption and Bone Mineral Density in a Population-based Cohort of Peri- and Postmenopausal Women

The Nord-Trøndelag Health Study

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Use of cod liver oil, which is rich in vitamins A and D, is traditionally recommended during the fall and winter months as a protective measure against vitamin D deficiency in several countries. It is not known whether childhood cod liver oil intake is related to variations in bone mineral density (BMD) or fractures in adult life. In 2001, a total of 3,052 Norway women aged 50–70 years had forearm BMD measured in a substudy of the population-based Nord-Trøndelag Health Study. Women reporting no childhood cod liver oil intake had statistically significantly higher BMD than those with any ingestion of cod liver oil. The odds ratio for low BMD (>1 standard deviation below age-specific mean) in women reporting cod liver oil intake throughout the year as compared with women with no intake was 2.3 (95% confidence interval: 1.4, 3.9), adjusted for body mass index, smoking, menopausal status, estrogen use, and current milk consumption. There were indications of a negative dose-response effect of childhood cod liver oil intake on bone. Although the vitamin A content of commercial cod liver oil was recently reduced by 75% in Norway, the past high concentration remains a possible explanation for the observed negative association between childhood cod liver oil intake and forearm BMD.

bone density; cod liver oil; densitometry; menopause; public health; vitamin A; vitamin D; women

Abbreviations: BMD, bone mineral density; HUNT, Nord-Trøndelag Health Study.

Use of cod liver oil during the fall and winter is a traditional and important source of vitamin D in Nordic countries. The high amounts of omega-3 fatty acids in cod liver oil also protect against cardiovascular disease. Thus, regular intake of cod liver oil is recommended for several purposes. Since the 1920s, health authorities in several countries have recommended a daily spoonful (5 ml) of cod liver oil during the autumn and winter months as a measure of protection against rickets and vitamin D deficiency (1). In Norway, until a few years ago, only butter and margarine were fortified with vitamin D, whereas current fortification measures also involve one type of low-fat milk. Despite no skin synthesis of vitamin D during 3–6 months of the year (2), the vitamin D status of the Norwegian population is similar to or even better than that of populations further south in Europe (3). Nevertheless, dependent on sun exposure and latitude, moderate hypovitaminosis D (25-hydroxyvitamin D level < 37.5 nmol/liter) is rather prevalent (4, 5).

The concentration of other fat-soluble vitamins such as vitamin A (only retinol) is also high in the cod liver. Until 1999, 5 ml of cod liver oil in commercial use in Norway contained 1,000 μg of vitamin A (3,300 IU) and 10 μg of vitamin D (40 IU). Because of reports of detrimental effects of excessive vitamin A intake on bone remodeling and a possible association with fractures (6, 7), the vitamin A content of cod liver oil was gradually reduced by 75 percent

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between 1999 and 2002, to a current amount of 250 μg/5 ml (825 IU). For women above age 60 years, recommended daily intakes of vitamins D and A are currently 10 μg and 700 μg (40 IU and 2,310 IU), respectively (8), which are similar to recommendations in other countries. The traditional Nordic diet is also rich in other sources of vitamin A, such as dairy products and fatty fish. It has been shown that vitamin A intake in Scandinavia is up to six times higher than intakes in Southern Europe (9), and it is postulated that this partly explains the high fracture rates in Scandinavia in comparison with other countries (6).

The purpose of this study was to investigate whether retrospective self-reports of cod liver oil intake in childhood would reflect variations in bone mineral density (BMD) among midlife women in the county of Nord-Trøndelag. Because of the area's geographic location between 63°N and 65°N, the "vitamin D winter" lasts from about mid-October to March (2), and thus vitamin D supplementation is highly recommended.

MATERIALS AND METHODS

The Nord-Trøndelag Health Study (HUNT) is a multipurpose health survey focusing on the total population over age 19 years, virtually all Caucasians, in the rural county of Nord-Trøndelag in central Norway (10). Two main rounds of data collection have taken place, the first in 1984–1986 (HUNT I) and the second in 1995–1997 (HUNT II) (11). On both occasions, overall participation rates have been satisfactory (88.1 percent in HUNT I and 71.2 percent in HUNT II) (10). Forearm BMD measurements were included as one of the physical examinations for preplanned subsets of the population in HUNT II. In 2001, a follow-up study with new forearm BMD measurements was performed in a subset of HUNT II participants, aiming specifically at peri- and postmenopausal women. This study was mainly based on data from the 2001 survey, as the question on cod liver oil intake in childhood was only asked during that survey.

Among women born in 1931–1950 (age range, 50–70 years), 4,436 were invited to undergo densitometry measurements, and 3,052 (68.8 percent) participated. The women completed a single-sheet questionnaire with questions on general health, lifestyle, menopausal status, estrogen use, and other questions related to bone health, such as current and childhood cod liver oil intakes, weight at age 20 years, and nutritional status. The participants were requested to fill out the questionnaire at home and bring it to the physical examination. The examination involved height and weight measurements in addition to forearm densitometry. Weight (in kg) and height (in cm) were measured while participants stood in light clothing and without shoes.

Bone mineral density

BMD (in g/cm^2) was measured at the distal forearm and the ultradistal radius of the nondominant arm by means of three different single-energy x-ray bone densitometers (DTX 100; Osteometer MediTech, Inc., Hawthorne, California). Daily calibration of the densitometers was performed with an equipment-specific phantom. The quality assessments and densitometry procedures have been described in detail previously (12, 13).

Analysis

Childhood cod liver oil intake was measured by posing the question, "When growing up, did you consume cod liver oil on a daily basis?" There were four possible responses: never, irregularly, during the fall and winter, and throughout the year. Current cod liver oil intake was measured by posing the question, "During the last year, did you regularly take cod liver oil?" This should have been answered as yes or no. Other variables were recalled childhood milk consumption (0–<1, 1–2, 3–4, 5–6, or >6 glasses/day), current milk consumption (0, <1, 1–2, or ≥3 glasses/day), recalled weight at age 20 years, history of smoking (never, prior, current), age at menarche, age at menopause, and estrogen use (never, ever). Women who had not menstruated within the 12 months prior to the examination were defined as menopausal. Body mass index was calculated as weight (in kg) divided by height squared (in m^2).

Differences in BMD according to category of cod liver oil intake were tested by Student's t test and in general linear models adjusting for age, body mass index, and smoking. The odds ratio for low BMD was calculated by logistic regression in bivariate and multivariate models with childhood cod liver oil intake in categories, adjusting for body mass index, current milk consumption, current cod liver oil intake, smoking, menopausal status, and estrogen use. Low BMD at both the distal and ultradistal sites was defined as a z score less than -1, that is, a BMD greater than one standard deviation below the age-specific mean BMD derived from this population. Childhood milk and current cod liver oil intakes did not contribute at a statistically significant level in the models. Possible interactions were tested, such as the interaction between current and childhood cod liver oil intakes. All statistical tests were two-sided, and the analyses were carried out with SPSS, version 14.0 (SPSS, Inc., Chicago, Illinois).

Ethics

The HUNT study was approved by the Regional Committee of Medical Research Ethics and the Norwegian Data Inspectorate. All participants signed an informed consent document. This study was approved by the HUNT review board.

RESULTS

Childhood cod liver oil intake was reported by more than 90 percent of the 2,854 women who answered the question (94 percent), most frequently during the fall and winter (table 1). Current cod liver oil intake was reported by almost 60 percent of the women. Distal forearm BMD was statistically significantly lower among women reporting ever taking cod liver oil in childhood as compared with women with no childhood intake, both before and after adjustment for age and body mass index (0.426 g/cm^2 vs. 0.435 g/cm^2;

TABLE 1. Characteristics (mean values and 95% confidence intervals) of 3,052 women aged 50–70 years by recalled and current cod liver oil intake at the 2001 follow-up of the second Nord-Trøndelag Health Study, Norway, 1995–1997

Cod liver oil intake	No. of women	%	Age (years)	95% CI*	Distal forearm BMD* (g/cm^2)	95% CI	Ultradistal radius BMD (g/cm^2)	95% CI	Body mass index†	95% CI	Weight (kg) at age 20 years	95% CI
Childhood‡												
Never	267	9.4	59.7	59.2, 60.3	0.435	0.428, 0.442	0.335	0.328, 0.342	28.5	27.8, 29.1	60.1	58.9, 61.2
Irregularly	695	24.4	59.7	59.4, 60.1	0.424	0.420, 0.429	0.328	0.323, 0.333	27.5	27.2, 27.9	59.3	58.7, 59.9
Fall and winter	1,655	58.0	59.2	59.0, 59.4	0.428	0.425, 0.431	0.330	0.327, 0.333	27.1	26.9, 27.3	58.9	58.5, 59.3
Whole year	237	8.3	59.4	58.9, 60.0	0.420	0.412, 0.429	0.323	0.315, 0.330	27.2	26.5, 27.8	59.2	58.2, 60.2
Current‡												
No	1,254	42.1	59.0	58.8, 59.3	0.428	0.425, 0.432	0.329	0.326, 0.333	27.7	27.4, 28.0	59.3	58.8, 59.8
Yes	1,727	57.9	59.6	59.4, 59.8	0.425	0.422, 0.428	0.328	0.325, 0.331	27.0	26.8, 27.2	58.8	58.5, 59.2
Total		100.0	59.4	59.3, 59.6	0.426	0.424, 0.429	0.329	0.327, 0.331	27.3	27.2, 27.5	59.1	58.8, 59.4

* CI, confidence interval; BMD, bone mineral density.

† Weight (kg)/height $(m)^2$.

‡ A total of 2,854 (93.5%) and 2,981 (97.7%) women answered the questions on childhood and current cod liver oil intake, respectively.

$p = 0.018$). In addition, when measured at the ultradistal site, the age- and body mass index-adjusted mean BMD was lower in women reporting ever taking cod liver oil in childhood than in those without such intake, but not at a statistically significant level (0.329 g/cm^2 vs. 0.335 g/cm^2; $p = 0.11$). There was no association between current cod liver oil intake and BMD ($p = 0.3$) (table 1). Women reporting cod liver oil intake, either in childhood or currently, reported lower body weight at age 20 years and lower current body mass index than the women who had not taken cod liver oil (table 1).

In logistic regression analysis, we found an increasing odds ratio for a low age-specific BMD (defined as a z score less than -1 standard deviation) with increasing regularity of childhood cod liver oil intake (table 2). This negative relation was observed in both the bivariate and multivariate models at both the distal (table 2) and ultradistal (table 3) sites. Among the women who recalled taking cod liver oil throughout the year, the odds ratio for low BMD at the distal forearm was more than doubled in comparison with women who reported no cod liver oil intake. No statistically significant interaction between current and childhood cod liver oil intakes ($p = 0.18$) was found. A positive correlation between current milk consumption and childhood cod liver oil intake was observed, and current milk consumption was a statistically significant positive predictor of BMD in the multivariate analyses. This was not observed for recalled childhood milk intake. No statistically significant interactions between these factors were observed.

Among the 1,254 women (42.1 percent) who reported no current cod liver oil consumption, defined as consumption during the preceding year, the odds ratio for low BMD at the distal forearm among women who recalled taking childhood cod liver oil throughout the whole year was almost three times higher than that of women who possibly had never taken cod liver oil. This relation remained after adjustment for significant covariates (table 4). A strong statistical trend toward an increasing odds ratio for low BMD with increasing regularity of childhood cod liver oil intake was found (χ^2 for trend = 8.94, $p < 0.003$) (table 4). The same pattern was found for the ultradistal radius (data not shown). This could indicate a negative dose-response relation between childhood cod liver oil and forearm BMD.

DISCUSSION

In this population-based study of peri- and postmenopausal Norwegian women aged 50–70 years, we found a strong and negative association between self-reported frequency of childhood cod liver oil intake and current forearm BMD. This unexpected result is paradoxical, considering the good bone health intentions behind the long-standing cod liver oil recommendations.

The strengths of this study are its population-based design and its rather high participation rate. However, the long period between the childhood cod liver oil exposure and the BMD measurements does raise some concerns. First, we had no data on peak bone mass. If the results indicate a negative influence of cod liver oil on bone formation

TABLE 2. Crude and adjusted odds ratios for low bone mineral density (more than one standard deviation below the age-specific mean (*z* score < -1)) of the distal forearm, as analyzed in bivariate and multivariate models, among 3,052 women aged 50–70 years at the 2001 follow-up of the second Nord-Trøndelag Health Study, Norway, 1995–1997

	Total no. of women	No. with low bone mineral density*	%	Crude OR†	95% CI†	Adjusted‡ OR	95% CI
Cod liver oil intake in childhood§							
Never	267	26	9.7	1.0	Referent	1.0	Referent
Irregular	695	122	17.6	2.0	1.3, 3.1	1.8	1.2, 2.9
Fall and winter	1,655	265	16.0	1.8	1.2, 2.7	1.6	1.1, 2.5
Whole year	237	50	21.1	2.5	1.5, 4.1	2.3	1.4, 3.9
Regular cod liver oil intake in adulthood§							
No	1,254	191	15.2	1.0	Referent		
Yes	1,727	296	17.1	1.2	0.9, 1.4		
Milk consumption in childhood (glasses/day)							
0	215	36	16.7	1.0	Referent		
1–2	672	103	15.3	0.9	0.6, 1.4		
3–4	1,301	214	16.4	1.0	0.7, 1.4		
≥5	594	98	16.5	1.0	0.6, 1.5		
Milk consumption in adulthood (glasses/day)							
0	658	125	19.0	1.0	Referent		
<1	618	97	15.7	0.8	0.6, 1.1		
1–2	1,305	203	15.6	0.8	0.6, 1.0		
≥3	290	42	14.5	0.7	0.5, 1.1		
Smoking							
Never smoker	1,421	190	13.4	1.0	Referent		
Former smoker	853	125	14.7	1.1	0.9, 1.4		
Current smoker	776	184	23.7	2.0	1.6, 2.5		
Menopausal status							
Menopausal	2,883	485	16.8	1.0	Referent		
Perimenopausal¶	62	6	9.7	0.5	0.2, 1.2		
Premenopausal	104	7	6.7	0.4	0.2, 0.8		
Estrogen use							
Never use	1,561	322	20.6	1.0	Referent		
Ever use	1,396	159	11.4	0.5	0.4, 0.6		

* Number with a *z* score < -1.
† OR, odds ratio; CI, confidence interval.
‡ Adjusted for body mass index, current milk consumption, menopausal status, estrogen use, and smoking.
§ A total of 2,854 (93.5%) and 2,981 (97.7%) women answered the questions on childhood and current cod liver oil intake, respectively.
¶ The participant's last menstrual period had occurred less than 12 months previously.

during growth, the current BMD should reflect variations in peak bone mass. Secondly, BMD in peri- and postmenopausal women is a result of both peak bone mass and ensuing bone loss. Other factors not considered in these analyses may have affected bone loss. In order to assess the influence of bone loss, we replaced BMD measured in 2001 with BMD measured 5 years earlier in HUNT II, in otherwise identical models. These analyses revealed the same results (data not shown), suggesting that recent bone loss did not influence the association. Thirdly, we had few data about other factors in childhood and youth that could have influenced peak bone mass, such as health disorders, physical activity, ultraviolet light exposure, and nutritional status. Although recalled childhood milk consumption did not contribute significantly to the analyses, we had no data on general caloric intake. Recalled weight at age 20 years

TABLE 3. Crude and adjusted odds ratios for low bone mineral density (more than one standard deviation below the age-specific mean (*z* score < −1)) of the ultradistal radius, as analyzed in bivariate and multivariate models, among 3,052 women aged 50–70 years at the 2001 follow-up of the second Nord-Trøndelag Health Study, Norway, 1995–1997

Cod liver oil intake in childhood*	Total no. of women	No. with low bone mineral density†	%	Crude OR‡	95% CI‡	Adjusted§ OR	95% CI
Never	267	26	9.7	1.0	Referent	1.0	Referent
Irregular	695	105	15.1	1.7	1.1, 2.6	1.5	1.0, 2.4
Fall and winter	1,655	287	17.3	1.9	1.3, 3.0	1.8	1.2, 2.8
Whole year	237	41	17.3	1.9	1.1, 3.3	1.8	1.0, 3.0

* A total of 2,854 women (93.5%) answered the question on childhood cod liver oil intake.
† Number with a *z* score < −1.
‡ OR, odds ratio; CI, confidence interval.
§ Adjusted for body mass index, current milk consumption, menopausal status, estrogen use, and smoking.

represents an indicator of nutritional state during the achievement of peak bone mass, but it did not explain the association.

These women grew up during a period of changing living conditions, and among those who experienced World War II, with its associated food rationing, one could have expected a negative effect on bone accrual. To control for this, we performed the analysis after stratifying women into those born before World War II and those born after World War II. The same pattern was found; women who reported no cod liver oil intake had higher BMD.

Some effect due to confounding by indication cannot be excluded; one could hypothesize that cod liver oil was more frequently recommended to weak or malnourished children. However, the relatively small number of women who reported no cod liver oil intake suggests that this does not represent a major bias.

Vitamin supplements other than cod liver oil could possibly have had an influence on bone. The participants were questioned about current intake of vitamin D and multivitamin supplements, but when these factors were added to the logistic regression models, none of them explained the association found between childhood cod liver oil intake and BMD.

As with all self-reported retrospective data, there may have been recall bias. With the culturally positive attitude towards cod liver oil in Norway, childhood intakes may have been overstated. This should only have biased the results if the overstating was more pronounced among women with low BMDs. The participants in the follow-up study had been asked to give the result of their last BMD measurement (*z* score, normal or low, in HUNT II). There was no correlation between recalled BMD level and childhood cod liver oil intake. This indicates that systematic misclassification of childhood cod liver oil intake did not occur.

The HUNT study took place in a rather sparsely populated region in Norway. Because of the need for portable and mobile measuring devices, the decision to measure the forearm, instead of the more often preferred axial or weight-bearing parts of the skeleton, was merely a practical and pragmatic one. It is documented, however, that a one-standard-deviation decrease in forearm BMD is associated with 80–110 percent higher hip fracture risk and 40–50 percent increased risk of fracture at any site (14). Nevertheless, this study did not demonstrate a general negative influence of childhood cod liver oil intake on the skeleton.

To our knowledge, this is the first study showing a relation between childhood consumption of a nutrient particularly

TABLE 4. Adjusted* odds ratio for low bone mineral density (more than one standard deviation below the age-specific mean (*z* score < −1)) of the distal forearm among 1,254 women aged 50–70 years reporting no current cod liver oil intake at the 2001 follow-up of the second Nord-Trøndelag Health Study, Norway, 1995–1997

Cod liver oil intake in childhood†	Total no. of women	No. with low bone mineral density‡	%	Odds ratio§	95% confidence interval
Never	162	14	8.6	1.0	Referent
Irregular	320	46	14.4	1.7	0.9, 3.2
Fall and winter	606	97	16.0	1.8	1.0, 3.4
Whole year	81	19	23.5	2.9	1.3, 6.4

* Adjusted for body mass index, current milk consumption, estrogen use, and smoking.
† Of the 1,254 women reporting no current cod liver oil intake, 1,169 answered the question on childhood cod liver oil intake.
‡ Number with a *z* score < −1.
§ χ^2 for trend = 8.94; $p < 0.003$.

rich in both vitamin A and vitamin D, such as cod liver oil, and BMD several decades later in life. Observational studies comparing vitamin A intake and fracture risk, designed either as nested case-control studies or prospective cohort studies, have yielded various results. Some have shown that high intake and hypervitaminosis A involve increased risk (6, 15–17), whereas others have not revealed any significant association (18–20). Increased fracture risk is demonstrated at low serum concentrations as well (17), indicating an inverse U-shaped association. Such an association with vitamin A has also been found for BMD measured at various skeletal sites (21). Vitamin A has been shown to antagonize the ability of vitamin D to maintain normal serum calcium levels (22, 23). Until recently, one spoonful of cod liver oil surpassed the current recommended vitamin A intake, and added to a diet already rich in vitamin A, the total dosage of vitamin A consumed may have reached a harmful level. The observation of a possible dose-response effect, especially strong among women who reported no current cod liver oil intake, supports a causal relation.

In summary, cod liver oil consumption during growth seems to be negatively related to forearm BMD measured in peri- and postmenopausal women. Although the vitamin A content of cod liver oil for human consumption was recently reduced in Norway, the former high vitamin A concentration may explain this observation. Further studies are needed to determine the optimal intake of vitamin A for BMD and to clarify whether excess levels are related to the high incidence of fragility fractures in Nordic countries.

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