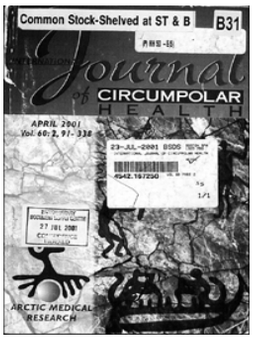

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COD LIVER OIL CONSUMPTION, SMOKING, AND CORONARY HEART DISEASE MORTALITY: THREE COUNTIES, NORWAY

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ABSTRACT

It has been hypothesized that omega-3 fatty acid consumption may lessen the adverse effect of smoking on coronary heart disease (CHD) risk. Thus, we explored whether cod liver oil consumption was protective of coronary heart disease in a cohort of men and women participating in a cardiovascular disease screening in Norway. The study population was aged 35-54 at the time of the baseline screening conducted by the National Health Screening Service of Norway in 1977-1983. Of 56,718 age-eligible men and women, 52,138 participated, of whom 42,612 (82%) completed a dietary questionnaire. Cod liver oil use was reported by 12.5%. At baseline, cod liver oil users had lower triglycerides, adjusting for age, body mass index, time since last meal and income ($p \leq .05$). As of December 1992, 639 and 118 CHD deaths were observed among the men and women, respectively. Overall, we observed no effect of cod liver oil consumption reported at baseline and CHD mortality in Cox Proportional Hazards analyses [Hazard Ratio (HR) = 1.0 (0.8 – 1.3)]. In analyses, stratified by smoking status, never smokers and current smokers showed non-significant beneficial associations between cod liver oil use and CHD mortality (HR = 0.7, 95% CI=0.4 – 1.5; and HR=0.8, 95% CI=0.6 – 1.2, respectively). However, among former smokers a non-significant excess risk of CHD mortality was associated with cod liver oil use (HR= 1.6, 95% CI= 0.9 – 2.6). Smokers, regardless of their cod liver oil use were at a substantially higher risk for CHD mortality relative to non-smokers. Omega-3 fatty acid supplementation, as practiced in this cohort, provided no significant benefits to CHD risk among study participants. *(Int J Circumpolar Health 2001;60: 143-149)*

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It has been hypothesized that omega-3 fatty acid consumption may lessen the adverse effect of smoking on coronary heart disease risk (1). Smoking is associated with elevated

triglycerides and a modest reduction in high-density lipoproteins (HDL), while omega-3 fatty acids lower triglycerides and slightly increase HDL-cholesterol (2-4). In addition, smoking increases, while omega-3 fatty acids decrease plasma fibrinogen (5-6). Omega-3 fatty acids also have effects opposite to those of smoking on plasma and whole blood viscosity, platelet aggregability, vasoconstriction, and the fibrillation threshold. (1,6-7). Thus, it is biologically plausible that a diet high in omega-3 fatty acids may reduce the adverse effect of smoking on CHD risk. In the Honolulu Heart Study, CHD mortality and incidence increased with the number of cigarettes smoked among those with a low fish intake, but not among those with a high fish intake (8). We explored whether supplementing a diet with cod liver oil was protective of coronary heart disease in Norway, where a proportion of the population routinely consumes cod liver oil as a dietary supplement.

METHODS

The study population is a cohort of Norwegian residents living in three counties: Finnmark, Sogn og Fjordane, and Oppland. The residents were recruited to participate in the second cardiovascular disease and risk factors screening survey conducted, between 1977 and 1983, by the National Health Screening Service of Norway. All Finnmark residents aged 35-52 in 1977 (i.e., born 1925-1942); all Sogn and Fjordane residents aged 40-54 in 1980 (i.e., born 1926-1940); and all Oppland residents aged 40-54 in 1981 (i.e., born 1927-1941) were invited to attend the cardiovascular screening. Of 56,718 age-eligible men and women, 52,138 (91.9%) participated in the survey, of whom 42,612 (82%) had completed a dietary questionnaire.

The screening procedures were nearly identical to those of the first cardiovascular screening (9-10). All eligible residents received a letter of invitation and questionnaire by mail. The questionnaire included items on smoking, dietary habits, and health history, including diabetes and cardiovascular disease or symptoms of angina pectoris and intermittent claudication. The dietary questions included whether cod liver oil was consumed on a usual weekly basis and the number of fish dinners consumed in a typical week. However, the type of fish consumed and the amount and frequency of cod liver oil use was not specified. Blood pressure was measured twice with a mercury sphygmomanometer and the resting (sec-

ond) blood pressure measurements were used in the analyses. Height and weight was measured and body mass index calculated (BMI: kg/m^2). A non-fasting blood sample was taken and serum analyzed for cholesterol and triglycerides. Total cholesterol and triglycerides were analyzed at the Central Laboratory, Ullevål Hospital, Oslo, which changed their laboratory procedures from a non-enzymatic to an enzymatic method in 1978 (11). Thus, total cholesterol and triglycerides measured in Finnmark were corrected to ensure comparability in values. Information on education and income was obtained by a census conducted in 1980 that was linked to the screening population by an 11-digit personal identifier.

FOLLOW-UP IDENTIFICATION OF MORTALITY AND CAUSE OF DEATH

The mortality and emigration experience of the cohort as of Dec. 31, 1992 was determined by linkage to the Norwegian Register of Deaths and Statistics Norway. The International Classification of Diseases and Causes of Death (ICD) 8th revision was used for deaths through 1985, and the 9th revision for deaths between 1986 and 1992. Coronary heart disease deaths were determined by codes 410-411,412.0-412.3, 413 for the 8th revision, and by codes 410-413,414.0-414.1,414.3,414.9 for the 9th revision (12, 13).

STATISTICAL METHODS

The baseline characteristics associated with cod liver oil use was examined: chi-square (χ^2) tests for differences in proportions and t-tests for differences in means. Analysis of variance (general linear models) was used to calculate adjusted mean serum triglycerides, total cholesterol, and systolic and diastolic blood pressure in models adjusting for covariates. Mortality rates were based upon person-years of follow-up from the date of screening until the date of death, emigration, or censoring on December 31, 1992, which ever came first. Age-adjusted rates were calculated separately for men and women using the direct method with the percent distribution of person-years by age group (< 45, 45-49, and ≥ 50 years of age) as the weighting factor.

Adjusted hazard rate ratios (HR) were obtained by Cox proportional hazards analyses conducted separately for men and women. As the results were similar for men and women,

final modelling was conducted on all participants, adjusting for gender. Also, because mortality rates differ by county, we conducted the analyses separately by county to examine consistency in the results. As the direction and magnitude of findings were similar, we combined the 3 counties in one analyses. Those with a history of myocardial infarction or angina pectoris at baseline were excluded from the prospective analyses. SPSS Version 8.0 was used for all analyses presented.

RESULTS

Baseline Evaluation

A total of 2,569 men (12%), and 2,774 women (13%) reported taking cod liver oil on a usual weekly basis. For both men and women, cod liver oil users were better educated, had a higher income, were less likely to be obese and to smoke, and were slightly younger than non-users (Table I, p-values $\leq .05$). Cod liver oil users were also more likely to report eating fish for dinner more than twice a week on a usual basis. Cod liver oil users were slightly less likely to have a history of CHD than non-users, findings which were significant among men (p-value, $\leq .05$).

For men and women smokers and non-smokers, cod liver oil users had lower mean serum triglycerides than nonusers at the baseline examination after adjusting for age, time since last meal, body mass index, and income level (Table II).

Among men, no differences in total cholesterol, or in sys-

Table I. Baseline Characteristics of Usual Weekly Cod Liver Oil Consumption, three counties, Norway (N= 42,612).

	MEN* (N=21,418) Weekly Cod Liver Oil		WOMEN* (N=21,194) Weekly Cod Liver Oil	
Characteristic	Yes (n=2,569)	No (n=18,849)	Yes (n=2,774)	No (n=18,420)
Mean Age in years (SD)	45.9 (5.0)	46.1 (4.9)*	45.9 (5.2)	46.2 (4.9)*
% Current Smoking	36.7	47.5*	28.2	34.9*
% Body Mass Index (kg/m^2) > 27	20.3	28.3*	17.8	26.0*
% Income in highest quartile	29.1	24.5*	27.5	24.6*
% ≥ 11 years education	27.9	17.2*	18.1	9.6*
% Fish dinner > than twice a week	36.5	30.3*	41.4	32.2*
% History of CHD +	2.0	2.8*	0.8	1.1

* $p \leq .05$ for differences in means or proportions.

+ CHD defined as myocardial infarction or angina pectoris.

tolic or diastolic blood pressure levels were observed by cod liver oil use (Table II). For women, cod liver oil use was associated with slightly higher total cholesterol levels and slightly lower systolic and diastolic blood pressure levels in analyses adjusting for age, BMI, and income (p-value $\leq .05$).

Mortality Follow-up

As of December 1992, a total of 639 CHD deaths were observed among men, 132 of whom had a history of CHD at baseline, and 118 CHD deaths were observed among women, of whom 17 had a history of CHD at baseline. In multivariate Cox proportional hazards analyses, excluding all study participants with a history of CHD at baseline (n=810), we observed no overall effect of cod liver oil consumption on CHD mortality (HR=1.0, 95% CI=0.8 – 1.3). In analyses stratified by smoking status, current smokers reporting usual weekly cod liver oil consumption at baseline had a non-significant 20% reduction in CHD mortality relative to smokers not reporting cod liver oil use (HR=0.8, 95% CI=0.6-1.2) (Table III). When compared to the referent group of never smokers not reporting cod liver oil use, smokers taking cod liver oil had a HR of CHD of 2.5 (95% CI=1.6-3.5), while smokers not taking cod liver oil had a HR of 3.1 (95% CI= 2.5 – 3.6). All multivariate analyses were adjusted for age, gender, systolic blood pressure, non-fasting serum total cholesterol and triglycerides, income, body mass index, and county of residence.

Table II. Adjusted Means and Standard Errors (S.E.) of Non-fasting Serum Triglycerides+, Total Cholesterol+ (mmol/l), and Systolic and Diastolic Blood Pressure++ by Smoking and Usual Weekly Cod Liver Oil Use At A Baseline ScreeningThree Counties, Norway (N=42,612)

	Smokers (N=9,297) Weekly Cod Liver Oil Use		Non-Smokers (10,979) Weekly Cod Liver Oil Use	
	Yes	No	Yes	No
	Mean (S.E.)	Mean (S.E)	Mean (S.E.)	Mean (S.E.)
MEN	(n=943)	(n=8,948)	(n=1,626)	(n=9,901)
Triglycerides *	2.10 (.03)	2.23 (.01)	1.98 (.03)	2.11 (.01)
Total Cholesterol	6.45 (.03)	6.43 (.01)	6.22 (.02)	6.20 (.01)
Systolic BP	137.0 (.35)	137.2 (.17)	137.0 (.33)	137.2 (.16)
Diastolic BP	86.7 (.22)	87.9 (.11)	87.5 (.21)	87.8 (.10)
WOMEN	(n= 783)	(n=6,429)	(n=1,991)	(n=11,991)
Triglycerides *	1.61 (.02)	1.68 (.01)	1.35 (.02)	1.42 (.01)
Total Cholesterol *	6.57 (.03)	6.46 (.01)	6.26 (.02)	6.12 (.01)
Systolic BP *	131.9 (.38)	133.0 (.21)	132.5 (.34)	133.6 (.16)
Diastolic BP *	83.1 (.22)	83.5 (.12)	83.5 (.19)	83.9 (.09)

+Adjusted for age, time since last meal, body mass index, and income.
++Adjusted for age, body mass index, and income.
*p-value $\leq .05$ for differences in means by cod liver oil use.

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idence.

For never smokers, a non-significant beneficial effect of cod liver oil consumption was observed, HR of CHD was 0.7 (95% CI=0.4 – 1.5). However, former smokers who reported cod liver oil use had a non-significant excess risk of CHD mortality relative to former smokers not taking cod liver oil (HR=1.6, 95% CI= 0.9 – 2.6). Fish consumption (2 or fewer fish dinners per week vs. more than 2 fish dinners per week) was not related to CHD mortality. We note that in this cohort there was little variation in fish consumption: nearly everyone reported consuming fish at least once a week.

Table III. Coronary Heart Disease (CHD) Mortality Rates and Hazard Ratio (HR) by Usual Weekly Cod Liver Oil Use and Smoking three counties, Norway.

	(no.)	Person years of follow-up	CHD Deaths	Age-Adjusted Rates Men	Women	Adjusted + CHD Mortality HR (95% CI)	Non-Users As Referents within Smoking Categories
Never Smokers							
Cod Liver Oil – No	13,386	161,002	155	9.7	2.3	Referent	Referent
Cod Liver Oil – Yes	2,382	28,975	27	7.4	1.1	0.7 (0.4 – 1.5)	0.7 (0.4 – 1.5)
Former Smokers							
Cod Liver Oil – No	8,063	98,217	79	11.9	0.3	1.1 (0.8 – 1.5)	Referent
Cod Liver Oil – Yes	1,193	14,795	18	15.8	5.5	1.7 (1.0 – 2.9)	1.6 (0.9 – 2.6)
Current Smokers							
Cod Liver Oil – No	15,061	183,029	392	31.2	8.3	3.1 (2.4 – 4.0)	Referent
Cod Liver Oil - Yes	1,693	21,237	34	25.6	5.6	2.5 (1.6 – 3.7)	0.8 (0.6 – 1.2)

+ Adjusted for age, gender, systolic blood pressure, total cholesterol, triglycerides, income (crowns), body mass index, and county of residence.
810 individuals had a history of CHD at baseline and were excluded from the analyses.
Rates per 1,000 person-years of follow-up.

DISCUSSION

The finding that smokers and non-smokers taking cod liver oil had lower triglyceride levels than those not reporting cod liver oil consumption is compatible with the existing literature. Our blood pressure results are also consistent with published studies showing no or modest blood pressure effects associated with omega-3 supplementation (14). The slightly higher total cholesterol levels observed among women may reflect a modest increase in the high-density lipoprotein fraction (4).

Overall, we found no effect of cod liver oil use on CHD morality in our cohort. Given the large sample size, we had a

power of 80% for detecting an overall 25% reduction in CHD mortality among cod liver oil users (at a 90% confidence level, i.e., *alpha*=.10). Stratifying by smoking status, however, considerably reduced our power to detect differences. The non-significant reduction in CHD mortality associated with cod liver oil use among current and never smokers in this study is biologically plausible. However, our findings of a non-significant elevated CHD risk among former smokers reporting cod liver oil consumption at baseline is difficult to explain. As we have no information regarding changes in smoking status or in cod liver oil use over time, the results should be interpreted with caution. Another caveat of our study is that we have no information regarding the dose or frequency of cod liver oil use.

Fish consumption in our data was not associated with CHD mortality. Unfortunately, the type of fish was not specified in the dietary survey. A recent report found that individuals reporting consuming fatty fish had a significantly lower CHD mortality risk compared to those consuming non-fatty fish (14). Many other studies (8, 16-23), but not all studies (24-26) have found beneficial effects of fish consumption on heart disease risk. In summary, smokers (regardless of their cod liver oil use) were at a substantially and statistically significantly higher risk for CHD mortality relative to non-smokers. Omega-3 fatty acid supplementation as practiced in this cohort provided no benefit to CHD risk.

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