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# Highly purified eicosapentaenoic acid and docosahexaenoic acid in humans have similar triacylglycerol-lowering effects but divergent effects on serum fatty acids[1–3]

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**ABSTRACT** To compare the effects of highly purified ethyl ester concentrates of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) on serum lipids, apolipoproteins, and serum phospholipid fatty acids in humans, we conducted a double-blind, placebo-controlled, parallel design intervention study. Healthy nonsmoking men ($n$ = 234) aged 36–56 y were randomly assigned to dietary supplementation with 3.8 g EPA/d, 3.6 g DHA/d, or 4.0 g corn oil/d (placebo) for 7 wk. Serum triacylglycerols decreased 26% ($P < 0.0001$) in the DHA group and 21% ($P = 0.0001$) in the EPA group compared with the corn oil group. Although not significant, net decreases in serum triacylglycerols were consistently greater in the DHA group across all quartiles of baseline triacylglycerol concentrations. Serum high-density-lipoprotein cholesterol increased 0.06 mmol/L ($P = 0.0002$) in the DHA group. In the EPA group, serum total cholesterol decreased 0.15 mmol/L ($P = 0.02$) and apolipoprotein A-I decreased 0.04 g/L ($P = 0.0003$). In the DHA group, serum phospholipid DHA increased by 69% and EPA increased by 29%, indicating retroconversion of DHA to EPA. In the EPA group, serum phospholipid EPA increased by 297% whereas DHA decreased by 15%, suggesting that EPA is not elongated to DHA in humans. The serum phospholipid ratio of n−3 to n−6 fatty acids increased in both groups, whereas the relative changes in n−6 fatty acids suggested possible alterations in liver desaturation activity in the DHA group. We conclude that both DHA and EPA decrease serum triacylglycerols, but have differential effects on lipoprotein and fatty acid metabolism in humans. *Am J Clin Nutr* 1997;66:649–59.

**KEY WORDS** Fatty acids, n−3 fatty acids, eicosapentaenoic acid, docosahexaenoic acid, triacylglycerols, phospholipids, randomized controlled trials

## INTRODUCTION

Accumulating evidence indicates that fish oil, rich in eicosapentaenoic acid (EPA; 20:5n−3) and docosahexaenoic acid (DHA; 22:6n−3) of the n−3 family, can modify a variety of cellular processes associated with lipid metabolism, atherosclerosis, hypertension, thrombosis, and inflammation (1). The amount and the ratio of DHA to EPA in different marine sources vary considerably (1, 2). Earlier studies of n−3 fatty acid supplementation in humans used oils varying in dosage form, total dose of fatty acids, and relative content of DHA and EPA. Examination of these data shows that the most consistent effect of n−3 fatty acids on cardiovascular disease risk factors is a reduction in serum triacylglycerol concentration, whereas reported effects on other variables are less consistent (3–5). It is possible that the inconsistencies derive from chance findings in small-scale studies or differences in study design. However, they may also be attributed to varying metabolic effects of DHA and EPA.

Animal studies showed that EPA and DHA accumulate in different compartments in the body and thus may be subject to differences in both metabolism and effects (6–8). DHA selectively attenuated expression of proatherogenic and proinflammatory proteins in human endothelial cells, suggesting a beneficial effect of DHA on atherosclerosis (9), whereas EPA may be a more potent platelet inhibitor than DHA (10, 11). In vitro studies indicate that EPA and DHA have different effects on triacylglycerol synthesis (12), and it was suggested that EPA is primarily responsible for the hypotriacylglycerolemic effect of n−3 fatty acids both in rats (13) and humans (14). The extent to which these reports can be generalized is constrained by limitations in study design, however. Knowledge of the specific effects of EPA and DHA is needed to target n−3 supplements for specific effects. Long-term studies with adequate sample size comparing the biological effects of pure DHA and EPA in human volunteers have not been reported (10, 14–16). We therefore conducted a double-blind, randomized, placebo-controlled, parallel design intervention study to evaluate effects of dietary supplementation with highly purified EPA or DHA on serum lipids, apolipoproteins, and serum phospholipid fatty acid composition.

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## SUBJECTS AND METHODS

### Subjects and experimental design

In 1986–1987, 21 826 subjects, 81.3% of the men aged 20–61 y old and the women aged 20–56 y old living in the municipality of Tromsø, participated in a health survey (visit 1) (17). All subjects completed a questionnaire about previous disease, use of drugs, and diet and smoking habits, and their height, weight, blood pressure, and nonfasting serum lipid concentrations were measured. Four hundred seven men between the ages of 35 and 55 were selected according to the following criteria: they reported being healthy nonsmokers, did not use nonprescribed or prescribed drugs, and consumed less than four fish dishes per week in their usual diet. They also had serum cholesterol concentrations < 8.0 mmol/L, diastolic blood pressure < 95 mm Hg, and systolic blood pressure < 160 mm Hg. These men were then asked in 1993 to undergo a clinical examination that included a complete medical history, physical examination, and laboratory tests.

Among the 349 men who responded to the invitation, 251 subjects filled the above-mentioned criteria and were recruited into the present study. They had no cardiovascular, liver, or renal disease; bleeding disorder; diabetes mellitus; psychopathologic disease; alcoholism; or other disease that can influence blood pressure, lipid metabolism, or hemostasis. They were not consuming special diets and did not expect to change their diet or lifestyle during the study period. Their mean (± SD) age was 44 ± 5 y (range: 36–56). The study was approved by the regional board of research ethics, and each subject gave informed consent.

The study was performed according to Good Clinical Practice requirements (18). It began with a 4-mo run-in period during which subjects were asked to continue their usual diet and living habits and during which their blood pressure and fasting serum lipid concentrations were measured on two occasions (visit 2 and visit 3). Each subject's average intake of nutrients was calculated on a fourth visit. At the beginning of the run-in period and throughout the study, participants were instructed not to ingest cod liver oil or other fish-oil supplements.

For entry into the intervention phase of the study, a subject's mean serum triacylglycerol concentration during the run-in period had to be < 5.0 mmol/L and mean serum cholesterol concentration < 9.5 mmol/L. Among the 251 subjects, 2 were smokers, 2 had serum glucose or triacylglycerol concentrations above the inclusion criteria, 2 used cardiovascular drugs, 1 consumed more than three fish dishes per week, and 10 dropped out during the run-in period for personal reasons. Thus, 234 men entered the double-blind, parallel group intervention trial, which lasted for 7 wk. Computer-generated random numbers were used to assign the participants to either 4.0 g 95% ethyl ester EPA/d, 4.0 g 90% ethyl ester DHA/d, or 4.0 g corn oil/d. The dietary supplements were administered in indistinguishable soft gelatin capsules that each contained 1.0 g oil and 4–6 IU vitamin E as an antioxidant (**Table 1**). Each individual was asked to ingest two capsules in the morning and two capsules at night. The dietary supplements were manufactured by Pronova Biocare AS, Oslo.

Participants were examined after an overnight fast between 0800 and 1130 on two separate occasions separated by an interval of 3–5 d, both at baseline (visits 5 and 6) and after 7 wk of supplementation (visits 7 and 8). At each visit blood pressure was measured and blood samples were collected. Participants were asked to abstain from alcohol and strenuous exercise for 48 h before the visit. A telephone interview was performed in the middle of the intervention period to monitor study compliance, side effects, and intercurrent disease. Compliance was assessed by counting leftover capsules and was calculated as the percentage of the prescribed capsules taken. We also measured serum phospholipid fatty acid concentrations at baseline and at the end of intervention.

**TABLE 1**
Composition of dietary supplements[1]

| Constituent | DHA | EPA | Corn oil |
|---|---|---|---|
| 22:6n−3 Ethyl ester (mg) | 889 | 12 | 0 |
| 20:5n−3 Ethyl ester (mg) | 18 | 941 | 0 |
| 18:2n−6 (mg) | 0 | 0 | 559 |
| 18:1n−9 (mg) | 0 | 0 | 259 |
| Vitamin E (IU) | 4–6 | 4–6 | 3.7 |
| *p*-Anisidine value | <35 | <35 | — |
| Peroxide value (mmol/g) | <0.01 | <0.01 | — |

[1] Dietary supplements were given in indistinguishable, oblong, soft gelatin capsules of 1.4 g average weight. DHA, docosahexaenoic acid supplement; EPA, eicosapentaenoic acid supplement.

### Clinical and laboratory measurements

Height was measured during the run-in period and weight was measured at baseline and after the intervention period on an electronic scale with subjects wearing light clothing and no shoes. Before the intervention each subject's habitual nutrient intake was assessed during a 1-h interview by a certified clinical nutritionist using the dietary history method. Food models and containers were used to estimate quantities. Dietary constituents were calculated from standard food tables that also cover individual fatty acids by using a specially designed computer program (19–22). Each subject completed a self-administered questionnaire at baseline and during the last week of the intervention to monitor food habits and physical activity during the intervention. Participants were asked how many times they ate fish or meat for dinner and how many units of alcohol they consumed during the past week (one unit of alcohol equals 9 g). Those who reported being physically active four or more times weekly for ≥ 20 min, leading to sweating or shortness of breath, were categorized as active; those reporting 1–3 times weekly were categorized as moderately active; and those reporting 0 times weekly were categorized as sedentary.

Blood samples were drawn from an antecubital vein into an evacuated tube system using minimal stasis. Serum was prepared by clotting whole blood in a glass tube (Becton Dickinson, Meylan Cedex, France) at room temperature for 1 h and then centrifuging the sample at 2000 × *g* for 15 min at 22 °C. One-milliliter aliquots of serum were transferred into sterile 2-mL cryovials (Corning, Park Ridge, IL), flushed with nitrogen, and stored at −70 °C. Blood for plasma preparation was collected into vacutainers (Becton Dickinson) containing 0.129 mol sodium citrate/L (blood:anticoagulant = 10:1). Plasma was prepared by centrifugation at 2000 × *g* for 15 min at 22 °C, transferred into sterile cryovials in aliquots of 1 mL,

flushed with nitrogen, and stored at −70 °C. All blood samples were analyzed after completion of the intervention period and before the randomization code was broken.

Serum lipids were analyzed on a Hitachi 737 Automatic Analyzer (Boehringer Mannheim, Mannheim, Germany) with reagents from the manufacturer. Total cholesterol was measured with an enzymatic colorimetric method (CHOD-PAP) and high-density-lipoprotein (HDL) cholesterol was assayed by the same procedure after precipitation of lower-density lipoproteins with heparin and manganese chloride. Serum triacylglycerol concentrations were determined with an enzymatic colorimetric test (GPO-PAP). Low-density-lipoprotein (LDL) cholesterol was calculated according to the Friedewald formula (23). Apolipoprotein A-I and apolipoprotein B-1 were measured immunochemically by rate nephelometry using the Array Protein System from Beckman Instruments Inc (Brea, CA).

Fatty acids were measured by extracting total lipids from 500 μL serum according to Folch et al (24), with phosphatidylcholine diheptadecanoyl added as an internal standard (P-5014; Sigma Chemical Company, St Louis), chloroform:methanol (2:1, by vol) as a solvent, and butylated hydroxytoluene (75 mg/L) as an antioxidant. Total phospholipids were separated by solid-phase extraction with $NH_2$ columns (size 3 cc; Analytiche Bond Elut LRC; Varian, Harbour City, CA) (25), followed by transmethylation with boron trifluoride, extraction into hexane, and evaporation to dryness. The fatty acid methyl esters were dissolved in hexane and analyzed by gas-liquid chromatography (Shimadzu GC-14 A; Shimadzu Corporation, Kyoto, Japan) fitted with a capillary column (CP-Sil 88; length: 50 m, internal diameter: 0.25 mm) obtained from Chrompack Inc (Raritan, NJ). Retention times and response factors for each fatty acid were determined using standards obtained from Nu-Chek Prep (Elysian, MN). The results were integrated on a Shimadzu C-R4A integrator. Fatty acid concentrations are reported as μmol fatty acid/L serum.

### Statistical analysis

All results are expressed as means ± SDs. On examination of the frequency distributions, all variables except serum triacylglycerol and certain lifestyle factors such as level of physical activity and fish, meat, and alcohol consumption were normally distributed at baseline and at the end of intervention. Serum lipid concentrations at baseline and at the end of the intervention were calculated as the mean of the values obtained at visits 5 and 6 and the mean of the values obtained at visits 7 and 8, respectively. Change was calculated as the value obtained after intervention minus the value obtained at baseline. Percentage change was calculated as the group-wise mean percentage change from baseline. Because of missing values, change could not be calculated for some individuals. Analysis of changes in serum lipids, serum phospholipid 16:1n−7, and sum of serum phospholipid fatty acids are therefore based on 222, 217, and 209 subjects, respectively. Two influencing outlying values were excluded from the analysis of desaturation indexes.

To evaluate within-group change, we used paired *t* tests for normally distributed variables, the Wilcoxon signed-rank test for ordinal and non–normally distributed variables, and the chi-square statistic for categorical variables. One-way analysis of variance was used to evaluate whether change differed between groups; the *F* test was used for normally distributed variables and the Kruskal-Wallis test for ordinal and non–normally distributed variables. Between-group comparisons of change were done by contrasting groups in the SAS general linear model procedure when the overall *F* test was significant at $P < 0.05$ (26). We did not adjust for multiple comparisons (27). Results were considered significant when the two-sided *P* value was < 0.05. Caution should be applied when interpreting *P* values in the present study because three contrasts were tested. When applying the Tukey multiple-comparison procedure (28), the 95% CI included the null value of no effect for those contrasts for which the unadjusted *P* value was > 0.03. Correlations were tested by computing Pearson or Spearman correlation coefficients.

## RESULTS

Three of the 234 subjects who were randomly assigned to a study arm dropped out during the intervention period. One subject in the DHA group was found to have fat intolerance after cholecystectomy, one subject in the EPA group developed diarrhea, and one subject in the corn oil group experienced vertigo and vomiting that was considered unrelated to the dietary supplements. Two individuals in the DHA group, three in the EPA group, and two in the corn oil group were excluded from the analysis. The reasons for exclusions were possible renal disease ($n = 1$), poor compliance with study protocol ($n = 1$), initiation of a vasoactive drug ($n = 1$), cancer surgery ($n = 1$), and change in amount of physical activity during the intervention ($n = 3$). Thus, 224 subjects are included in the present analysis. Mean ages of the subjects were 43 ± 5, 44 ± 5, and 45 ± 6 y and mean body mass indexes (in $kg/m^2$) were 24.9 ± 2.6, 25.6 ± 2.9, and 24.6 ± 2.7 in the DHA, EPA, and corn oil groups, respectively.

There were no significant changes in hematology, blood chemistry (electrolytes, alanine aminotransferase, γ-glutamyl transferase, alkaline phosphatase, albumin, bilirubin, creatinine, and C-reactive protein), serum glucose, or plasma-active renin after dietary intervention with DHA, EPA, or corn oil (data not shown).

### Compliance and side effects

The mean number of days in the study was 49 ± 5, 48 ± 3, and 48 ± 4 d in the DHA, EPA, and corn oil groups, respectively. Percentage compliance was slightly poorer in the DHA group (91 ± 6%) compared with the EPA and corn oil groups (both 94 ± 6%). There were no within-group correlations between compliance and change in serum DHA, EPA, or linoleic acid concentrations.

Side effects were mild and transient and for most individuals faded 1–2 wk after the start of the intervention. Fifty-eight percent of subjects in the DHA group and 57% in the EPA group experienced belching after initiation of the dietary supplements compared with 4% in the corn oil group. A taste of fish oil during the intervention was reported by 67% of subjects in the DHA group, 65% in the EPA group, and 3% in the corn oil group.

### Diet, body weight, and physical activity

The DHA, EPA, and corn oil groups were well balanced at baseline. Total fat accounted for 30% of energy intake in all

**TABLE 2**
Composition of background diet[1]

| Daily nutrient intake | DHA ($n$ = 72) | EPA ($n$ = 75) | Corn oil ($n$ = 77) |
|---|---|---|---|
| Energy (kJ) | 10 370 ± 2561 | 10 223 ± 2170 | 10 877 ± 2455 |
| Protein (g) | 103 ± 23 | 103 ± 22 | 107 ± 25 |
| Carbohydrate (g) | 335 ± 80 | 324 ± 74 | 349 ± 87 |
| Fiber (g) | 24.1 ± 7.3 | 23.2 ± 6.7 | 25.2 ± 7.7 |
| Alcohol (g) | 5.82 ± 6.28 | 6.39 ± 6.56 | 7.04 ± 7.00 |
| Total fat (g) | 81.2 ± 32.1 | 81.6 ± 23.9 | 85.9 ± 27.0 |
| Cholesterol (mg) | 314 ± 102 | 327 ± 89 | 334 ± 101 |
| Saturated fat (g) | 33.6 ± 12.4 | 34.3 ± 10.9 | 35.4 ± 11.4 |
| Monounsaturated fat (g) | 27.6 ± 11.3 | 28.0 ± 8.7 | 29.6 ± 9.6 |
| Polyunsaturated fat (g) | 13.5 ± 8.4 | 12.7 ± 4.6 | 14.0 ± 6.1 |
| P:S | 0.40 ± 0.15 | 0.39 ± 0.13 | 0.40 ± 0.13 |
| 18:2n−6 (g) | 10.2 ± 7.0 | 9.50 ± 3.70 | 10.7 ± 5.1 |
| 20:5n−3 (g) | 0.18 ± 0.20 | 0.19 ± 0.18 | 0.19 ± 0.21 |
| 22:6n−3 (g) | 0.34 ± 0.32 | 0.35 ± 0.28 | 0.36 ± 0.32 |
| β-Carotene (μg) | 2651 ± 1902 | 2634 ± 1284 | 2749 ± 1905 |
| Retinol (μg) | 1003 ± 955 | 993 ± 717 | 1031 ± 697 |
| Thiamine (mg) | 1.66 ± 0.38 | 1.67 ± 0.35 | 1.76 ± 0.43 |
| Riboflavin (mg) | 2.20 ± 0.70 | 2.29 ± 0.67 | 2.31 ± 0.72 |
| Niacin (mg) | 23.6 ± 4.8 | 23.2 ± 4.8 | 23.8 ± 5.2 |
| Vitamin C (mg) | 90.0 ± 1.6 | 78.6 ± 35.5 | 88.9 ± 45.0 |
| Vitamin D (μg) | 6.08 ± 9.77 | 5.33 ± 4.16 | 5.65 ± 3.81 |
| Vitamin E (mg) | 4.87 ± 1.48 | 4.96 ± 1.34 | 5.33 ± 1.53 |

[1] $\bar{x}$ ± SD. DHA, docosahexaenoic acid group; EPA, eicosapentaenoic acid group; P:S, ratio of polyunsaturated to saturated fatty acids.

groups. Dietary intake of DHA and EPA at baseline accounted for 0.7% of total fat intake. Differences in nutrient intake between the DHA, EPA, and corn oil groups were minor and not significant (**Table 2**). No significantly different within- or between-group changes were found with respect to body weight, physical activity, or food habits during the intervention (**Table 3**). Body weight increased by 0.6 kg in the corn oil group and by 0.7 kg in the DHA and EPA groups. There was a nonsignificant increase in the percentage of participants who reported being sedentary after compared with before the intervention. Alcohol, meat, and fish consumption (dinner meals) increased slightly but not significantly during the intervention. None of the participants reported consuming more than three fish dishes weekly before or during the intervention. There was good agreement between measures of alcohol consumption obtained by the nutritionist during the run-in period and by the self-administered questionnaire at baseline ($r$ = 0.73, $P$ = 0.0001).

### Serum lipids and apolipoproteins

Serum mean (95% CI in parentheses) triacylglycerol concentrations decreased 0.22 mmol/L (0.15, 0.29) in the DHA group and 0.15 mmol/L (0.06, 0.24) in the EPA group (**Table 4**). In the corn oil group serum triacylglycerols increased 0.11 mmol/L (0.03, 0.19). Compared with change for the corn oil group, serum triacylglycerols decreased 26% in the DHA group and 21% in the EPA group. The difference between the DHA and EPA groups was not significant ($P$ = 0.14). However, net decreases in serum triacylglycerols were consistently greater in the DHA group than in the EPA group across quartiles of baseline triacylglycerol concentrations (**Table 5**). In the EPA and DHA groups there were no correlations between changes in individual n−3 fatty acids and changes in serum triacylglycerol concentrations.

Serum total cholesterol decreased 0.15 mmol/L ($P < 0.05$) in the EPA group and apolipoprotein A-I decreased 0.04 g/L ($P <$ 0.001, Table 4). These changes differed significantly from both the DHA and the corn oil groups. In the DHA group, HDL cholesterol increased 0.06 mmol/L ($P < 0.001$), differing significantly from both the EPA and corn oil groups. Hence, in both the EPA and DHA groups there was an increase in the ratio of HDL cholesterol to apolipoprotein A-I and a decrease in the ratio of total cholesterol to HDL cholesterol.

### Serum phospholipid fatty acid concentrations

In the total study group ($n$ = 224), the correlations between dietary intake and serum phospholipid concentrations of DHA and EPA at baseline were $r$ = 0.39 and $r$ = 0.35, respectively (both $P$ = 0.0001). The mean of individual ratios of dietary DHA to EPA at baseline was 2.5 ± 1.2, whereas the serum phospholipid ratio of DHA to EPA was 3.8 ± 1.6 ($P$ = 0.0001, for the difference between the ratios), indicating accumulation of DHA relative to EPA in serum phospholipids.

**TABLE 3**
Body weight and lifestyle factors at baseline and change after 7 wk of supplementation with docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), or corn oil[1]

| | DHA ($n$ = 72) | | EPA ($n$ = 75) | | Corn oil ($n$ = 77) | |
|---|---|---|---|---|---|---|
| | Baseline | Change | Baseline | Change | Baseline | Change |
| Body weight (kg) | 80.0 ± 10.0[2] | 0.7 ± 1.2 | 82.6 ± 10.0 | 0.7 ± 1.4 | 79.5 ± 9.4 | 0.6 ± 1.1 |
| Fish consumption (dishes/wk) | 2.10 ± 1.01 | 0.06 ± 1.13 | 2.16 ± 1.05 | 0.16 ± 1.06 | 2.03 ± 1.10 | 0.21 ± 1.29 |
| Meat consumption (dishes/wk) | 2.46 ± 1.31 | 0.24 ± 1.53 | 2.56 ± 1.39 | 0.16 ± 1.23 | 2.93 ± 1.28 | 0.15 ± 2.01 |
| Teetotalers (%) | 4 | 0 | 1 | 0 | 4 | 0 |
| Alcohol consumption (g/wk)[3] | 45.3 ± 44.3 | 0.3 ± 5.1 | 59.6 ± 63.9 | −0.8 ± 6.5 | 55.5 ± 50.8 | 1.5 ± 7.0 |
| Physical activity | | | | | | |
| Sedentary (%) | 22 | 3 | 26 | 1 | 25 | 6 |
| Moderate (%) | 69 | −6 | 59 | −1 | 54 | 1 |
| Active (%) | 9 | 3 | 15 | 0 | 21 | −7 |

[1] There were no significant differences among groups.
[2] $\bar{x}$ ± SD.
[3] Teetotalers were excluded from analysis of alcohol consumption.

**TABLE 4**
Serum lipids and apolipoproteins at baseline and change after 7 wk of supplementation with docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), or corn oil

| | DHA ($n$ = 72) | | EPA ($n$ = 75) | | Corn oil ($n$ = 77) | | | Contrasts between groups: $P$ | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | Change | Baseline | Change | Baseline | Change | $F$ test: $P$[1] | DHA vs EPA | DHA vs corn oil | EPA vs corn oil |
| Triacylglycerols (mmol/L) | 1.24 ± 0.58[2] | −0.22 ± 0.31[3] | 1.23 ± 0.57 | −0.15 ± 0.40[4] | 1.22 ± 0.55 | 0.11 ± 0.34[4] | 0.0001 | 0.14 | 0.0001 | 0.0001 |
| Total cholesterol (mmol/L) | 6.00 ± 0.95 | 0.03 ± 0.49 | 5.98 ± 0.94 | −0.15 ± 0.55[5] | 6.02 ± 1.08 | 0.10 ± 0.55 | 0.01 | 0.04 | 0.4 | 0.004 |
| LDL cholesterol (mmol/L) | 4.06 ± 0.86 | 0.07 ± 0.46 | 4.06 ± 0.83 | −0.08 ± 0.48 | 4.04 ± 0.98 | 0.06 ± 0.48 | 0.10 | — | — | — |
| HDL cholesterol (mmol/L) | 1.36 ± 0.30 | 0.06 ± 0.13[3] | 1.33 ± 0.31 | 0.01 ± 0.12 | 1.41 ± 0.28 | −0.01 ± 0.11 | 0.001 | 0.009 | 0.0005 | 0.4 |
| Apolipoprotein A-I (g/L) | 1.38 ± 0.21 | 0.02 ± 0.13 | 1.38 ± 0.20 | −0.04 ± 0.10[4] | 1.46 ± 0.23 | 0.00 ± 0.12 | 0.003 | 0.0008 | 0.3 | 0.02 |
| Apolipoprotein B (g/L) | 1.00 ± 0.21 | −0.01 ± 0.11 | 1.01 ± 0.23 | −0.03 ± 0.11[5] | 1.02 ± 0.28 | 0.02 ± 0.11 | 0.05 | — | — | — |
| HDL:apolipoprotein A-I | 0.97 ± 0.14 | 0.04 ± 0.07[3] | 0.96 ± 0.13 | 0.04 ± 0.08[4] | 0.97 ± 0.12 | −0.01 ± 0.06 | 0.0001 | 0.8 | 0.0003 | 0.0001 |
| Total:HDL cholesterol | 4.62 ± 1.19 | −0.19 ± 0.52[4] | 4.70 ± 1.24 | −0.13 ± 0.47[5] | 4.43 ± 1.19 | 0.11 ± 0.62 | 0.002 | 0.4 | 0.0006 | 0.007 |

[1] ANOVA for between-group comparisons of change.
[2] $\bar{x}$ ± SD.
[3–5] One-sample $t$ test of difference between baseline and 7 wk: [4] $P < 0.001$, [4] $P < 0.01$, [5] $P < 0.05$.

**TABLE 5**
Change in serum triacylglycerol concentration in docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and corn oil groups according to quartiles of baseline triacylglycerol concentration

| Baseline triacylglycerol concentration | Change in serum triacylglycerol concentration | | | Estimated n−3 fatty acid effect[1] | |
|---|---|---|---|---|---|
| | DHA ($n$ = 72) | EPA ($n$ = 75) | Corn oil ($n$ = 77) | DHA | EPA |
| | *mmol/L* | | | *mmol/L (%)* | |
| 1st quartile: | | | | | |
| 0.69 (0.34–0.82) mmol/L[2] | 0.00 ± 0.13[3] | 0.03 ± 0.21 | 0.10 ± 0.21 | −0.10 (−14) | −0.07 (−10) |
| 2nd quartile: | | | | | |
| 0.96 (0.83–1.09) mmol/L | −0.14 ± 0.18 | −0.04 ± 0.26 | 0.15 ± 0.28 | −0.29 (−30) | −0.19 (−20) |
| 3rd quartile: | | | | | |
| 1.24 (1.10–1.44) mmol/L | −0.16 ± 0.23 | −0.03 ± 0.34 | 0.14 ± 0.32 | −0.30 (−24) | −0.17 (−14) |
| 4th quartile: | | | | | |
| 2.01 (1.45–3.61) mmol/L | −0.56 ± 0.35 | −0.52 ± 0.46 | 0.03 ± 0.50 | −0.59 (−29) | −0.55 (−27) |

[1] Effect attributable to DHA and EPA; ie, change in DHA group minus change in corn oil group and change in EPA group minus change in corn oil group.
[2] $\tilde{x}$; range in parentheses.
[3] $\bar{x}$ ± SD.

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