

n-3 Fatty acids and cardiovascular disease risk factors among the Inuit of Nunavik¹⁻³

Eric Dewailly, Carole Blanchet, Simone Lemieux, Louise Sauvé, Suzanne Gingras, Pierre Ayotte, and Bruce John Holub

ABSTRACT

Background: Inuit traditionally consume large amounts of marine foods rich in n-3 fatty acids. Evidence exists that n-3 fatty acids have beneficial effects on key risk factors for cardiovascular disease.

Objective: Our goal was to verify the relation between plasma phospholipid concentrations of the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and various cardiovascular disease risk factors among the Inuit of Nunavik, Canada.

Design: The study population consisted of 426 Inuit aged 18-74 y who participated in a 1992 health survey. Data were obtained through home interviews and clinical visits. Plasma samples were analyzed for phospholipid fatty acid composition.

Results: Expressed as the percentage of total fatty acids, geometric mean concentrations of EPA, DHA, and their combination in plasma phospholipids were 1.99%, 4.52%, and 6.83%, respectively. n-3 Fatty acids were positively associated with HDL-cholesterol concentrations and inversely associated with triacylglycerol concentrations and the ratio of total to HDL cholesterol. In contrast, concentrations of total cholesterol, LDL cholesterol, and plasma glucose increased as n-3 fatty acid concentrations increased. There were no significant associations between n-3 fatty acids and diastolic and systolic blood pressure and plasma insulin.

Conclusions: Consumption of marine products, the main source of EPA and DHA, appears to beneficially affect some cardiovascular disease risk factors. The traditional Inuit diet, which is rich in n-3 fatty acids, is probably responsible for the low mortality rate from ischemic heart disease in this population. *Am J Clin Nutr* 2001;74:464-73.

KEY WORDS n-3 Fatty acids, eicosapentaenoic acid, docosahexaenoic acid, fish intake, cardiovascular disease, risk factor, cholesterol, LDL, HDL, triacylglycerol, blood pressure, glucose, insulin, Natives, Inuit

INTRODUCTION

Diets rich in fish and marine mammals have been linked to a lower incidence of thrombotic disease in Greenland and Japan (1, 2). Dietary fish and marine oils are rich in eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3), which are long-chain polyunsaturated fatty acids of the n-3 series. n-3 Fatty acids favorably affect risk factors impli-

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cated in the pathogenesis of atherosclerotic and thrombotic diseases (3-6). Epidemiologic evidence also exists for an inverse relation between fish consumption and death from ischemic heart disease (IHD) (7-12). Higher concentrations of EPA and DHA in plasma and serum phospholipids are inversely correlated with cardiovascular disease (CVD) and IHD (13, 14).

Located in a vast territory of $\approx 563\,515$ km² north of the 55th parallel, the Inuit population of Nunavik (northern Quebec) is estimated at 8970 persons and is distributed among 14 coastal villages (15). Compared with the rest of Canada, the Inuit population is very young. In 1991, 40% of the Inuit were ≤ 15 y of age and 2% were ≥ 65 y, compared with 20% and 11%, respectively, of the remaining Canadian population (16). Inuit are confronted with challenging environmental conditions such as extreme cold; historically, the abundance of arctic fauna has supported the survival of this population. The traditional diet consists primarily of marine mammals [white whale (beluga) and seal], fish, and caribou, which are eaten fresh (raw or cooked) or dried, with use of the skin, blubber, liver, and fat in different meals.

In 1992 daily intakes of n-3 fatty acids from traditional food, especially fish, marine mammals, and piscivorous wild-fowl, were high among Inuit persons compared with intakes by other populations (2, 17, 18). However, strong evidence exists of a decrease in traditional food consumption by the Inuit, primarily from 1950 to 1970, when Inuit populations settled into permanent communities and market foods became increasingly available (18, 19). In several native populations, a shift away from traditional lifestyles and diets is associated with an increased prevalence of risk factors for CVD, such as high blood pressure, elevated blood lipids, diabetes, and obe-

¹From the Public Health Research Unit, CHUL Research Center, Centre Hospitalier Universitaire de Quebec, Ste-Foy, Canada; the Departments of Social and Preventive Medicine and of Food Sciences and Nutrition, Laval University, Ste-Foy, Canada; and the Department of Human Biology and Nutritional Sciences, the University of Guelph, Guelph, Canada.

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³Address reprint requests to E Dewailly, Laval University Medical Research Center, 2400 d'Estimauville, Beauport, Quebec G1E 7G9, Canada. E-mail: eric.dewailly@crchul.ulaval.ca.

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sity (20–23). Additionally, evidence points to increasing rates of death from IHD and stroke among native populations. In this study, we examined the n-3 fatty acid status of a representative sample of Nunavik Inuit and verified the relation between plasma phospholipid concentrations of n-3 fatty acids and various CVD risk factors.

SUBJECTS AND METHODS

Study design

In 1992 Santé Québec, an organization of the Quebec Health and Social Services Ministry, conducted a health survey among the Inuit population of Nunavik as part of the federal-provincial Canadian Heart Health Initiative. The primary objective of the survey was to collect relevant information on the physical, social, and psychosocial health of the Inuit population (24). This information was gathered in several stages. First, face-to-face interviews were conducted at each participant's home to administer a lifestyle questionnaire. Among the same participants, a clinical session was conducted in the village health clinic to obtain physiologic and anthropometric measurements. Finally, a face-to-face interview was conducted by a nurse to collect 24-h recalls of dietary intake. A food-frequency questionnaire was administered only to women who were neither pregnant nor breast-feeding. Stored plasma samples were used to measure the fatty acid composition of plasma phospholipids. Samples were stored at -80°C for ≤ 4 mo. Our team was responsible for analyzing the fatty acids and contaminants in the blood samples. Information on demographic characteristics, the prevalence of CVD risk factors, and food intake was obtained from the Santé Québec data files.

Study population

The target population of the survey comprised all permanent residents of Nunavik aged 18–74 y, excluding households consisting of only non-Inuit persons and persons not related to an Inuit and excluding institutionalized persons (24). The population was stratified according to the 14 villages and the sample was stratified by village, with the quasiproportional representation of the member of households in each stratum. The Quebec Bureau of Statistics chose a design that would afford an acceptable degree of precision for any prevalence $\geq 10\%$ for all communities combined. Of the household respondents, 492 participants underwent the clinical measurements and blood tests. Of these 492 Inuit, 66 did not fast for ≥ 12 h before blood sampling and were therefore excluded. The study protocol was approved by the Ethics Committee of Maisonneuve-Rosemont Hospital (Montreal).

Plasma lipids, glucose, and insulin

Concentrations of plasma total cholesterol, triacylglycerols, LDL cholesterol, and HDL cholesterol were analyzed according to the methods of the Lipid Research Clinics (25). Cholesterol and triacylglycerol concentrations were measured in plasma and in lipoprotein fractions with use of an Auto-Analyzer II (Technicon Instruments Corporation, Tarrytown, NY). The HDL fraction was obtained after precipitation of LDL in the infranant fluid with heparin and manganese chloride. Plasma glucose was measured enzymatically and fasting insulin concentrations were measured with a commercial double-antibody radioimmunoassay (LINCO Research, St Louis) that showed little cross-reactivity ($<0.2\%$) with human proinsulin and for which CVs were $\leq 5.5\%$ (26).

Plasma phospholipid fatty acids

To measure the fatty acid composition of plasma phospholipids, 200- μL plasma samples were extracted after the addition of chloroform:methanol (2:1, by vol) in the presence of a known amount of internal standard (diheptadecanoyl phospholipid) (27). The total phospholipid was isolated from the lipid extract by thin-layer chromatography with heptane:isopropyl ether:acetic acid (60:40:3, by vol) as the developing solvent. After transmethylation with boron trifluoride:methanol, the fatty acid profile was determined by capillary gas-liquid chromatography. Fatty acid concentrations in plasma phospholipids were expressed as percentages of the total area of all fatty acid peaks from 14:0 to 24:1. In this study, plasma phospholipid concentrations of fatty acids correspond to relative percentages of total fatty acids by weight.

Blood pressure

Four blood pressure measurements were taken by a trained survey nurse according to the recommendations of the Consensus Conference on the Management of Mild Hypertension in Canada (28). Standard mercury sphygmomanometers, 38-cm (15-in) stethoscopes, and appropriately sized cuffs were used. Pressure readings were taken at the beginning and at the end of both the home interviews and the clinical visits. These values are reported as the arithmetic mean of the 4 readings.

Lifestyle assessment and anthropometry

Lifestyle habits (alcohol consumption, smoking status, etc) were assessed by questionnaire during a face-to-face interview. Height, weight, and waist and hip girth were measured during the clinical session. Waist girth was measured by positioning the measuring tape horizontally at the level of noticeable waist narrowing and recording the circumference to the nearest centimeter. The mean (\pm SD) body mass index (BMI; in kg/m^2) of the subjects was 26.7 ± 4.9 , their mean waist girth was 86.0 ± 13.1 cm, and the correlation coefficient between these 2 indexes was 0.88 ($P = 0.0001$). In this study, the accumulation of adipose tissue in the abdominal area as measured by waist girth was used to measure abdominal obesity (29–31). A waist girth ≥ 100 cm for subjects aged <40 y and ≥ 90 cm for subjects aged ≥ 40 y was defined as abdominal obesity (32).

Dietary assessment

Data on fish and marine mammal intake were obtained with use of a 24-h dietary recall and a food-frequency questionnaire administered by a nurse (18). The 24-h dietary recall assessed the amounts of marine foods consumed by the Inuit community (men and women) the day before the survey. The food-frequency questionnaire was administered to 226 women and measured their consumption of traditional and market foodstuffs. *Traditional food* referred to 23 food items (including several parts of marine mammals such as meat, fat, skin, and liver) derived from fishing and hunting; frequency of consumption was recorded for all 4 seasons. A specific question regarding the monthly frequency of consumption of seal meat was asked of all study participants (men and women). The n-3 fatty acid content of traditional foods eaten most often by the Inuit population was determined in a previous study (19, 33).

Data analysis

All statistics presented in this paper were obtained from weighted data to reestablish the equiprobability of an individual



TABLE 1
Relative concentrations of fatty acids in plasma phospholipids in the Inuit of Nunavik¹

Fatty acids	Arithmetic $\bar{x} \pm SE$	Geometric \bar{x}	95% CI	Minimum	Maximum
<i>% by wt of total fatty acids</i>					
PUFA					
n-3 Series					
Total ²	9.71 \pm 0.23	8.63	(8.23, 9.04)	2.41	29.51
EPA	3.01 \pm 0.13	1.99	(1.81, 2.18)	0.09	17.27
DHA	4.95 \pm 0.10	4.52	(4.33, 4.71)	0.39	11.88
EPA+DHA	7.95 \pm 0.21	6.83	(6.46, 7.21)	0.58	26.50
n-6 Series					
Total ³	28.45 \pm 0.23	28.04	(27.57, 28.51)	13.12	41.12
AA	6.22 \pm 0.09	5.97	(5.80, 6.14)	1.82	14.85
Total PUFA, n-3 + n-6 series	38.16 \pm 0.13	38.06	(37.80, 38.33)	25.99	48.64
n-3:n-6	0.38 \pm 0.01	0.31	(0.29, 0.33)	0.06	2.25
EPA:AA	0.51 \pm 0.02	0.33	(0.30, 0.37)	0.01	4.77
MUFA ⁴	18.21 \pm 0.13	18.03	(17.79, 18.27)	11.98	29.70
SFA ⁵	43.63 \pm 0.15	43.52	(43.23, 43.82)	27.44	58.02
P:S	0.88 \pm 0.01	0.87	(0.86, 0.89)	0.45	1.77

¹PUFA, polyunsaturated fatty acids; EPA, eicosapentaenoic acid (20:5n-3); DHA, docosahexaenoic acid (22:6n-3); AA, arachidonic acid (20:4n-6); MUFA, monounsaturated fatty acids; SFA, saturated fatty acids; P:S, ratio of PUFA to SFA.

²18:3 + 18:4 + 20:3 + 20:4 + 20:5 + 22:5 + 22:6.

³18:2 + 18:3 + 20:2 + 20:3 + 20:4 + 22:2 + 22:4 + 22:5.

⁴14:1 + 16:1 + 18:1 + 20:1 + 22:1 + 24:1.

⁵14:0 + 16:0 + 17:0 + 18:0 + 20:0 + 22:0 + 24:0.

being selected for the sample and to take into account nonresponse by age and sex. To this end, each respondent was given a value (weight) corresponding to the number of subjects he or she represented in the Nunavik population. Thus, all results presented in this paper were weighted and are representative of the entire Nunavik adult population (24). Crude *n* values are presented for information only.

In the statistical analysis we sought to first to describe the plasma phospholipid concentrations of n-3 fatty acids. Plasma and serum phospholipid fatty acid profiles are recognized as useful biomarkers for EPA and DHA status and intake (3, 34). Subjects were grouped according to biological and lifestyle factors. The statistical distribution of plasma fatty acid concentrations was first checked and was found to be skewed. Therefore, the geometric mean was used as the measure of central tendency for fatty acid concentrations. Arithmetic means were also calculated to facilitate comparisons with other surveys. Results also include 95% CIs of geometric means.

Analysis of variance (ANOVA) on the logarithm of plasma fatty acid concentrations was used to determine effect comparisons among groups. Mean daily intakes of traditional foods and of n-3 fatty acids and mean values of CVD risk factors were calculated according to age and sex. The potential interaction effect of age and sex was checked by using a two-factor ANOVA with an interaction term. The associations between the plasma phospholipid concentrations of n-3 fatty acids, particularly of EPA and DHA, and values for cardiovascular disease risk factors were assessed by use of multiple linear regression analysis. The potential interaction effect of age and sex was also checked in the regression models. Regression analyses were conducted with data from subjects who were not taking prescribed drugs for hypercholesterolemia, high blood pressure, or diabetes. Adjustments were made for potential confounding effects of age, sex, waist girth, smoking, and alcohol intake. Covariance analysis was used to calculate mean concentrations of HDL and triacyl-

glycerols according to quintiles of EPA+DHA concentrations in plasma phospholipids. Covariance analysis was performed to control for the same confounding variables as described above and excluded the same subjects. A test for trends was performed across quintiles. All statistical analyses were performed with the SAS software package [version 6.12; SAS Institute Inc, Cary, NC (35)] and statistical significance was set at $\alpha = 0.05$.

RESULTS

The study population consisted of 426 Inuit aged 18-74 y, of whom 179 were men (mean age: 38.7 y) and 247 were women (mean age: 37.8 y). The fatty acid composition in the plasma phospholipids of the study population is shown in **Table 1**. The geometric mean concentrations of EPA, DHA, and their combination (EPA+DHA) were 1.99%, 4.52%, and 6.83% by wt, respectively. Nearly 25% and 66%, respectively, of the Inuit had plasma concentrations of EPA and DHA >5.0% by wt (data not shown). EPA+DHA accounted for 80% of total n-3 fatty acids and 10% of the Inuit had EPA+DHA concentrations as high as 15.0% by wt. The geometric mean concentration of total n-6 fatty acids was 28.04% by wt and arachidonic acid (AA) accounted for 21% of n-6 fatty acids. Concentrations of total n-3 and n-6 fatty acids were inversely correlated ($r = -0.81$, $P \leq 0.0001$). The ratios of EPA to AA and of n-3 to n-6 fatty acids were 0.33 and 0.31, respectively, and 20% of the Inuit had an EPA:AA >1.0. Monounsaturated and saturated fatty acids in plasma phospholipids were 18.03% and 43.52% by wt of total fatty acids, respectively. The ratio of polyunsaturated to saturated fatty acids was 0.87, and 10% of the Inuit had a ratio >1.0.

Summarized in **Table 2** is the relation between relative concentrations of n-3 fatty acids and characteristics of the Inuit population. Concentrations of EPA, DHA, and EPA+DHA and the ratios of EPA to AA and of n-3 to n-6 fatty acids varied significantly according to sex, with Inuit women having higher



TABLE 2

Relative concentrations of n-3 fatty acids in plasma phospholipids according to characteristics of the Inuit population¹

Potential confounding variables	EPA	DHA	EPA+DHA	EPA:AA	n-3:n-6
	<i>% by wt of total fatty acids</i>				
Sex					
Men (n = 179)	1.80 ± 0.19	4.12 ± 0.15	6.19 ± 0.32	0.29 ± 0.03	0.28 ± 0.02
Women (n = 247)	2.20 ± 0.17	4.97 ± 0.13	7.55 ± 0.27	0.38 ± 0.03	0.35 ± 0.02
P	0.03	0.0001	0.0003	0.0003	0.0003
Age					
18-39 y (n = 254)	1.50 ± 0.12	4.03 ± 0.11	5.76 ± 0.21	0.25 ± 0.02	0.25 ± 0.01
≥40 y (n = 172)	3.58 ± 0.23	5.77 ± 0.15	9.79 ± 0.35	0.59 ± 0.04	0.48 ± 0.02
P	0.0001	0.0001	0.0001	0.0001	0.0001
Waist girth					
Normal (n = 283)	1.83 ± 0.15	4.32 ± 0.11	6.46 ± 0.23	0.31 ± 0.03	0.29 ± 0.01
Elevated (n = 121)	2.68 ± 0.28	5.17 ± 0.21	8.22 ± 0.46	0.42 ± 0.05	0.40 ± 0.03
P	0.0007	0.0004	0.0002	0.01	0.0001
Smoking status					
Smoker (n = 248)	2.14 ± 0.16	4.58 ± 0.12	7.03 ± 0.26	0.36 ± 0.03	0.31 ± 0.02
Nonsmoker (n = 130)	2.01 ± 0.26	4.59 ± 0.19	6.92 ± 0.42	0.33 ± 0.04	0.32 ± 0.03
P	0.53	0.96	0.79	0.79	0.95
Alcohol intake					
None (n = 139)	2.41 ± 0.27	5.07 ± 0.18	7.89 ± 0.42	0.41 ± 0.05	0.36 ± 0.03
1-4 drinks/d (n = 61)	1.64 ± 0.34	4.23 ± 0.25	6.20 ± 0.53	0.29 ± 0.06	0.27 ± 0.03
≥5 drinks/d (n = 127)	2.04 ± 0.18	4.28 ± 0.15	6.58 ± 0.30	0.32 ± 0.03	0.29 ± 0.02
P	0.03	0.001	0.004	0.02	0.004
Medication for CVD problems					
Yes (n = 24)	2.82 ± 0.56	5.75 ± 0.39	8.98 ± 0.88	0.47 ± 0.08	0.43 ± 0.05
No (n = 402)	1.95 ± 0.13	4.47 ± 0.10	6.74 ± 0.21	0.33 ± 0.02	0.30 ± 0.01
P	0.11	0.02	0.03	0.12	0.02

¹Geometric $\bar{x} \pm$ SE. EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; AA, arachidonic acid; CVD, cardiovascular disease. P by one-way ANOVA.

values than Inuit men. About 38% of the Inuit women had concentrations of EPA+DHA as high as 10.0% by wt; only 27% of the Inuit men had concentrations this high ($P < 0.001$; data not shown). Concentrations of n-3 fatty acids increased significantly with age, as did the ratios of EPA to AA and of n-3 to n-6 fatty acids. Concentrations of EPA $\geq 5.0\%$ by wt or of DHA $\geq 5.0\%$ by wt were observed mainly among Inuit aged ≥ 40 y (data not shown). About 85% of Inuit aged 18-39 y had total n-6 fatty acid concentrations $>25.0\%$ by wt, whereas this concentration was reached by only 48% of Inuit aged >40 y (data not shown). Subjects with high waist girths had higher concentrations of n-3 fatty acids than did subjects with normal waist girths. n-3 Fatty acid concentrations did not vary significantly according to smoking status, but alcohol abstainers had higher concentrations of EPA, DHA, and EPA+DHA and higher ratios of EPA to AA and of n-3 to n-6 than did subjects who consumed ≥ 1 alcoholic drink/d. Higher concentrations of DHA and EPA+DHA and a higher ratio of n-3 to n-6 fatty acids were observed in Inuit who used medications for hypercholesterolemia, high blood pressure, and diabetes than in nonusers.

Forty-one percent of the Inuit reported having eaten traditional foods the day before the survey. Mean traditional food consumption of marine origin was 131.2 g (Table 3). Quantitatively, the most popular traditional foods consumed by the Inuit were mattak (white whale skin), red char (arctic char), ringed seal meat, lake trout, and lake whitefish (data not shown). According to the 24-h dietary recall, mean intakes of EPA, DHA, and EPA+DHA from traditional foods were 1020.7, 1093.9, and 2114.6 mg, respectively. The maximum daily intake of EPA+DHA was 34.8 g. n-3 Fatty acid intakes increased signifi-

cantly with age but did not vary according to sex. There was no interaction effect of age and sex when daily intakes were compared. Data from the food-frequency questionnaire completed by the Inuit women showed that mean annual daily intakes of EPA, DHA, and EPA+DHA were 576.8, 715.9, and 1292.7 mg, respectively. n-3 Fatty acid intakes were significantly higher among Inuit women aged ≥ 40 y than among women aged 18-39 y.

We examined the relation between concentrations of total n-3 fatty acids and the ratio of EPA to AA in plasma phospholipids and the frequency of seal meat consumption (Figure 1). In all the Inuit, as the frequency of seal meat consumption increased, the concentrations of total n-3 fatty acids and the EPA:AA increased ($P = 0.0001$).

For subsequent analyses, 20 of the 426 subjects were excluded because they reported taking medication related to CVD. In these analyses, mean concentrations of total and LDL cholesterol did not vary according to sex but increased significantly with age (Table 4). The mean HDL-cholesterol concentration was higher in women than in men and increased with age. In contrast, the ratio of total to HDL cholesterol was higher in men than in women and did not vary according to age. Mean concentrations of triacylglycerols did not vary according to sex or age. Both systolic and diastolic blood pressures were higher in men than in women and increased with age. Mean concentrations of glucose and insulin did not vary according to sex and only glucose concentrations increased significantly with age. When comparing mean values of CVD risk factors among groups, an interaction effect of age and sex was found for HDL, the ratio of total to HDL cholesterol, systolic blood pressure, and insulin.



TABLE 3Daily intakes of marine foods, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) in the Inuit population, by sex and age¹

Daily intakes	24-h Dietary recall				Food-frequency questionnaire (women only)			
	Men (n = 179)	Women (n = 247)	18–39 y (n = 254)	≥40 y (n = 172)	All (n = 426)	18–39 y (n = 128)	≥40 y (n = 98)	All (n = 226)
Traditional foods (g)	142.6 ± 18.3	119.6 ± 12.3	92.1 ± 11.7	205.6 ± 19.8 ²	131.2 ± 10.7	157.6 ± 14.4	175.5 ± 13.3	163.2 ± 10.0
EPA (mg)	1046.7 ± 190.8	994.4 ± 124.4	793.8 ± 128.6	1453.4 ± 198.1 ³	1020.7 ± 110.1	550.2 ± 75.6	635.3 ± 54.1	576.8 ± 48.7 ⁴
DHA (mg)	1149.2 ± 199.0	1038.0 ± 129.4	832.4 ± 130.6	1592.5 ± 211.5 ⁵	1093.9 ± 114.7	689.9 ± 109.8	773.3 ± 75.2	715.9 ± 70.1 ⁶
EPA+DHA (mg)	2196.0 ± 388.5	2031.4 ± 253.2	1626.1 ± 258.7	3045.9 ± 408.0 ⁵	2114.6 ± 224.2	1240.1 ± 184.1	1408.6 ± 127.8	1292.7 ± 117.9 ⁶

¹ Arithmetic $\bar{x} \pm SE$.^{2,3,5} Significantly different from 18–39 y (two-factor ANOVA): ² $P \leq 0.0001$, ³ $P \leq 0.05$, ⁵ $P \leq 0.01$.^{4,6} Significantly different from 18–39 y (one-way ANOVA): ⁴ $P \leq 0.05$, ⁶ $P \leq 0.01$.

Shown in **Table 5** are the regression coefficients (β values) from the multiple linear regression analysis with CVD risk factor values as the dependant variables and relative concentrations of n–3 fatty acids in plasma phospholipids as the predictor variable. n–3 Fatty acid concentrations were positively associated with concentrations of total, LDL, and HDL cholesterol. EPA and the ratio of EPA to AA were negatively associated with the ratio of total to HDL cholesterol. All n–3 fatty acids showed negative associations with triacylglycerol concentrations, except for DHA, for which no significant association was found. n–3 Fatty acids were not associated with diastolic or systolic blood pressures. All n–3 fatty acids were positively associated with plasma glucose. n–3 Fatty acids, especially EPA and the ratio of EPA to AA, tended to be inversely associated with plasma insulin, but this relation was not significant. No modification effect was found for age and sex on the observed associations when these relations were verified through regression analysis.

Covariance analysis was conducted to examine mean concentrations of HDL and triacylglycerols according to quintiles of EPA+DHA concentrations in plasma phospholipids. The mean concentration of HDL varied significantly according to quintiles of EPA+DHA and reached as high as 1.70 mmol/L at quintile 5 (**Figure 2**). The mean concentration of triacylglycerols also varied according to quintiles of EPA+DHA and was significantly lower in quintile 5 than in the lowest quintiles (**Figure 3**).

DISCUSSION

The plasma phospholipids of the Nunavik Inuit, who traditionally consume large amounts of marine foods, contained relatively high concentrations of n–3 fatty acids. Older Inuit had higher concentrations of n–3 fatty acids than did younger Inuit, reflecting their higher intakes of marine foods. This last observation is consistent with previous studies conducted in northern native populations (36–41). Modifications in the Inuit diet, including reductions in marine product consumption, have taken place over the past decades, especially in younger Inuit. This decline in marine food consumption is attributable in part to the greater availability of market foods in communities (19). However, n–3 fatty acid intakes among the Inuit are high compared with intakes of other populations (17). The results of a recent study suggest that traditional food consumption has not varied greatly since 1992 and that the greatest sources of n–3 fatty acids (eg, marine mammals and fish) in the Inuit diet remain popular in Nunavik today (42).

In the Inuit women, intakes of marine foods and of n–3 fatty acids measured with use of the food-frequency questionnaire appeared to be lower than those estimated with use of the 24-h dietary recall. Because food-frequency questionnaires are more appropriate for measuring regular intakes (43), it can be assumed that the n–3 fatty acid intakes of the Inuit men may have been overestimated by the 24-h dietary recall method. Indeed, the results

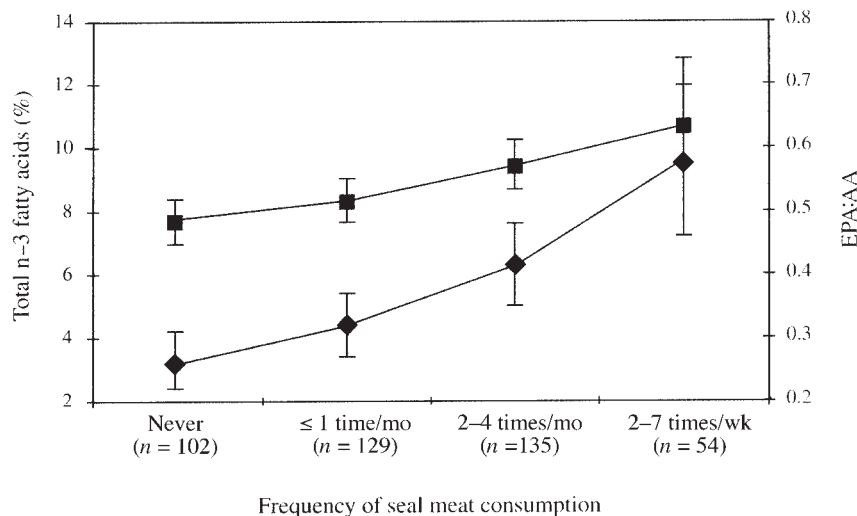


FIGURE 1. Relation between the frequency of seal meat consumption and the mean (and 95% CI) relative concentrations of total n–3 fatty acids (■) and ratio of eicosapentaenoic acid to arachidonic acid (EPA:AA) in plasma phospholipids (◆).

TABLE 4

Values of cardiovascular disease (CVD) risk factors in the Inuit population, by sex and age¹

CVD risk factors	Men (n = 170)	Women (n = 236)	18–39 y (n = 252)	≥40 y (n = 154)	Total (n = 406)	P ² for sex × age
TC (mmol/L)	5.04 ± 0.08	5.10 ± 0.06	4.90 ± 0.06	5.47 ± 0.07 ³	5.07 ± 0.05	0.58
LDL (mmol/L)	3.09 ± 0.07	3.00 ± 0.05	2.94 ± 0.05	3.29 ± 0.07 ⁴	3.04 ± 0.04	0.19
HDL (mmol/L)	1.40 ± 0.03	1.61 ± 0.03 ⁵	1.43 ± 0.03	1.66 ± 0.04 ³	1.50 ± 0.02	0.006
TC:HDL	3.92 ± 0.11	3.40 ± 0.07 ⁵	3.68 ± 0.08	3.63 ± 0.10	3.67 ± 0.06	0.008
Triacylglycerols (mmol/L)	1.22 ± 0.07	1.09 ± 0.03	1.14 ± 0.05	1.20 ± 0.06	1.16 ± 0.04	0.27
SBP (mm Hg)	115.33 ± 0.92	109.80 ± 0.83 ⁵	109.71 ± 0.66	119.35 ± 1.18 ³	112.60 ± 0.63	0.02
DBP (mm Hg)	76.09 ± 0.65	71.37 ± 0.53 ⁵	72.81 ± 0.53	76.00 ± 0.68 ⁴	73.76 ± 0.43	0.79
Glucose (mmol/L)	5.15 ± 0.08	5.12 ± 0.09	4.91 ± 0.04	5.64 ± 0.15 ³	5.14 ± 0.06	0.12
Insulin (pmol/L)	58.32 ± 4.87	59.14 ± 4.44	56.07 ± 3.71	65.01 ± 6.43	58.72 ± 3.27	0.005

¹Arithmetic \bar{x} ± SE. TC, total cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.²Two-factor ANOVA.^{3,4}Significantly different from 18–39 y (two-factor ANOVA); ³P ≤ 0.0001, ⁴P ≤ 0.001.⁵Significantly different from men, P ≤ 0.0001 (two-factor ANOVA).

of a previous study documenting marine mammal consumption among the Inuit of Nunavik indicate that Inuit men and women have similar consumption patterns for traditional foods (44).

Concentrations of EPA, DHA, and total n-3 fatty acids among the Inuit of Nunavik are similar overall to those observed among Alaskan river village Eskimos but are lower than those reported for Igloodik Inuit in Nunavut (Canada) and Alaskan coastal village Eskimos (37, 45). The ratio of n-3 to n-6 fatty acids in the plasma phospholipids of Nunavik Inuit increased with age as shown in previous studies among Alaskan Eskimos, Greenland Inuit, and Inuit of the Nunavut (36, 37, 41, 45). Differences between Arctic regions may be attributed to the different laboratory methods used and also to the territorial availability of fish species; populations in coastal regions consume more marine mammals and fish than do inland populations. Furthermore, traditional food intakes may vary according to the degree of urbanization of Inuit communities (46).

Our results showed a protective effect of n-3 fatty acids on HDL-cholesterol and triacylglycerol concentrations, which are

key risk factors for CVD (47–50). The inverse relation noted between n-3 fatty acid intake and circulating plasma triacylglycerol concentrations is well documented (3). A positive effect of n-3 fatty acids on HDL-cholesterol concentrations has not been consistently found, but is noted mainly when large doses of n-3 fatty acids are used (3, 27, 51). Our study supports these findings. Moreover, although HDL-cholesterol concentrations tend to stabilize or decrease with age (52–54), our results showed that HDL-cholesterol concentrations increased with age among the Inuit. Thus, the elevated intake of n-3 fatty acids in the older Inuit appears to override the effect of age on HDL-cholesterol concentrations.

In this study, concentrations of EPA+DHA were positively associated with total and LDL cholesterol. The reported effects of n-3 fatty acids on both of these CVD risk factors are inconsistent (3, 55). Fish oil sometimes increases LDL-cholesterol concentrations (56, 57). Although there is still controversy regarding the effects of n-3 fatty acids on the oxidative susceptibility of LDL, n-3 fatty acids may change the composition of

TABLE 5

Regression coefficients from multiple linear regression analysis with values of cardiovascular disease (CVD) risk factors as dependent variables and relative concentrations of fatty acids in plasma phospholipid as predictor variables¹

CVD risk factors	Log EPA	Log DHA	Log EPA+DHA	Log EPA:AA	Log n-3:n-6
TC	0.59 (0.0001)	1.65 (0.0001)	1.22 (0.0001)	0.58 (0.0001)	1.00 (0.0001)
LDL	0.38 (0.005)	1.12 (0.0003)	0.81 (0.0007)	0.40 (0.002)	0.63 (0.003)
HDL	0.29 (0.0001)	0.45 (0.004)	0.48 (0.0001)	0.26 (0.0001)	0.41 (0.0001)
TC:HDL	-0.40 (0.04)	-0.09 (0.85)	-0.50 (0.14)	-0.37 (0.05)	-0.44 (0.14)
Log triacylglycerols	-0.15 (0.0001)	-0.11 (0.12)	-0.19 (0.0003)	-0.11 (0.0002)	-0.15 (0.001)
SBP	-1.55 (0.34)	-1.02 (0.79)	-2.91 (0.32)	-1.54 (0.34)	-2.90 (0.26)
DBP	-0.99 (0.41)	0.51 (0.85)	-1.66 (0.44)	-0.89 (0.45)	-1.78 (0.34)
Glucose	0.41 (0.02)	1.01 (0.01)	0.81 (0.008)	0.97 (0.02)	0.71 (0.008)
Log insulin	-0.08 (0.07)	-0.14 (0.18)	-0.12 (0.13)	-0.08 (0.06)	-0.10 (0.18)

¹P values in parentheses. Each model included age, sex, waist girth, smoking status, and alcohol intake. n = 406. EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; AA, arachidonic acid; TC, total cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

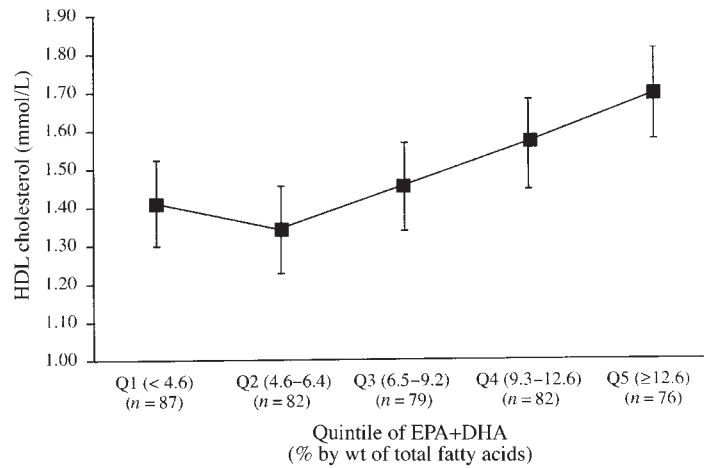


FIGURE 2. Mean (and 95% CI) concentrations of HDL cholesterol according to quintile of eicosapentaenoic plus docosahexaenoic acid (EPA+DHA) concentrations in plasma phospholipids. *P* for trend = 0.0002.

LDL, leading to less atherogenic LDL particles with lower phospholipid and apolipoprotein B concentrations and a higher LDL particle size (58–61). It was also suggested that combining an antioxidant with *n*-3 fatty acids may protect against oxidative stress (57, 61, 62). The results of one study showed that reduced LDL-cholesterol concentrations combined with antioxidant therapy improve impaired endothelium-dependent coronary vasodilatation (63). LDL atherogenicity may be influenced by the presence of antioxidants such as vitamins A and E and perhaps selenium, which inactivate the atherosclerotic properties of LDL (57, 64–66). In the course of the Santé Québec Health Survey, we measured plasma concentrations of selenium in a subsample of 40 Inuit. These subjects had higher selenium concentrations (\bar{x} : 2.0 $\mu\text{mol/L}$) than reported for other general populations (≈ 1 $\mu\text{mol/L}$) (44). White whale skin (mattak) is especially rich in selenium (5.5 $\mu\text{g/g}$) and is consumed by the Inuit in large amounts when it is available (33). Suadicani et al (67) reported an increased risk of IHD in Danes who had serum selenium con-

centrations ≤ 1 $\mu\text{mol/L}$. In a 7-y follow-up study, Salonen (68) found an excess risk of death by coronary disease and CVD and an excess risk of myocardial infarction among subjects with low selenium concentrations. Thus, we can postulate that the paradoxical finding regarding the increase in LDL with increasing *n*-3 fatty acid concentrations in plasma phospholipids may reflect, among the Inuit, an increase in LDL particle size. The antioxidant action of selenium, which enhances the antiatherogenic properties of *n*-3 fatty acids, may also explain the reduced mortality rate from IHD among the Inuit of Nunavik.

We found no relation between *n*-3 fatty acids and plasma pressure. Morris et al (69) reported that the hypotensive effect of high doses of fish oil may be strongest in hypertensive subjects and in those with clinical atherosclerotic disease or hypercholesterolemia. Most studies that targeted healthy individuals with no clinical manifestation of hypertension failed to detect a hypotensive effect of *n*-3 fatty acids on blood pressure (69–72). Nearly 6% of the Inuit had high blood pressure, compared with $\approx 14\%$ of

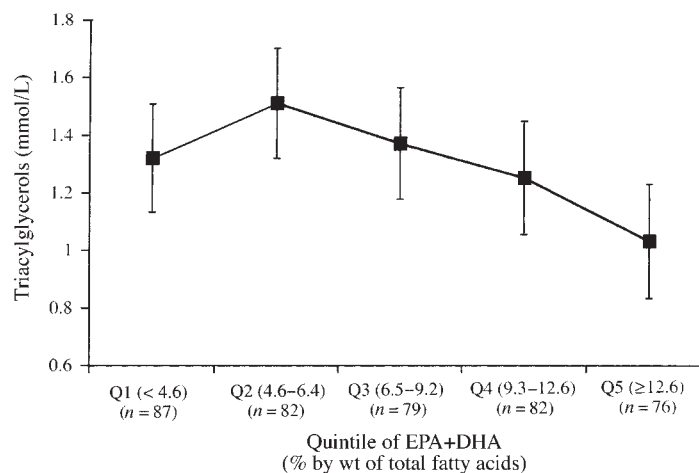



FIGURE 3. Mean (and 95% CI) concentrations of triacylglycerols according to quintile of eicosapentaenoic plus docosahexaenoic acid (EPA+DHA) concentrations in plasma phospholipids. *P* for trend = 0.03.

the general Quebec population during the same period (73). Considering the high prevalence of obesity and cigarette smoking in this population, which are known risk factors for high blood pressure (74, 75), it can be considered that the Inuit diet contributes to the low prevalence of high blood pressure in this population.

The effect of n-3 fatty acids on glycemia, insulinemia, and type 1 and 2 diabetes is not clear (76-78). n-3 Fatty acids may play a role in enhancing glucose metabolism, insulin secretion, and insulin receptor sensitivity (79-81). In this study, n-3 fatty acids were positively associated with plasma glucose, whereas an increase in EPA and the ratio of EPA to AA appeared to be inversely associated with plasma insulin. The prevalence of type 2 diabetes among native populations has been increasing in recent decades (21, 82-84). A sedentary lifestyle, the progressive abandoning of a traditional diet, an increasing intake of energy in the form of carbohydrates, and the high rates of obesity found in this population have favored this emergence (21, 85). Obesity is highly prevalent among the Inuit of Nunavik (86-88). Obese subjects (particularly those with abdominal obesity) are generally characterized by a cluster of metabolic disturbances including glucose intolerance, hyperinsulinemia, hypertriglyceridemia, low HDL-cholesterol concentrations, and an elevated ratio of total to HDL cholesterol (86, 89, 90). Our results agree with these findings (data not shown). Effectively, obese Inuit had higher values for these risk factors than did nonobese Inuit. However, as compared with obese Quebecers, obese Inuit had higher concentrations of n-3 fatty acids and HDL cholesterol and lower concentrations of insulin and triacylglycerols and a lower ratio of total to HDL cholesterol (91). Hence, these results suggest that n-3 fatty acids may attenuate metabolic disorders in obese subjects.

Kromhout et al (9) reported that mortality rates for arterial diseases were $\approx 50\%$ lower among Dutch who consumed ≥ 30 g fish/d than among those who consumed no fish. In 1992-1996, the age-standardized mortality rate (per 100 000 person-years) for IHD [codes 410-414 in the 9th revision of the *International Classification of Diseases* (92)] was 66.3 for the Nunavik Inuit compared with 140.2 for the entire province of Quebec (93). Plasma phospholipid concentrations of EPA and DHA are higher in the Inuit than in Quebecers (geometric mean of EPA+DHA = 1.70; 95% CI: 1.67, 1.72) (91). Marine food intake by the Inuit was 131 g the day before the survey, corresponding to an intake of ≈ 2115 mg EPA+DHA. During the same period, the customary diet of Quebecers included ≈ 13 g fish/d (≈ 170 mg EPA+DHA), close to the mean daily intake in a typical US diet (between 100 and 200 mg) (17, 91, 94). Therefore, the lower IHD mortality rate observed in the Inuit population than in the general Quebec population suggests that the Inuit diet may contribute substantial benefits regarding cardiovascular health.

Despite the high prevalence of obesity and smoking among the Inuit of Nunavik, the mortality rate of IHD is low in this population, most likely because of their traditional diet rich in n-3 fatty acids. Our study showed some benefits of n-3 fatty acids (derived from marine sources) on CVD risk, notably, increased HDL-cholesterol and reduced triacylglycerol concentrations. However, evidence points to decreasing traditional food consumption by younger Inuit. Thus, the promotion of safe nutritional habits among Inuit presents a 2-fold challenge: maintain or increase traditional food use, which confers a comparative advantage to the Inuit population (eg, low IHD mortality rate), and support efforts to increase the use of healthy market foods. 

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