Obesity Facts
The European Journal of Obesity

Original Article

Obes Facts 2011;4:312–318
DOI: 10.1159/000330710

Published online: August 1, 2011

Plasma Phospholipid Long-Chain n-3 Polyunsaturated Fatty Acids and Body Weight Change

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Keywords
Body weight · Cohort study · n-3 fatty acids · Omega-3 fatty acids · Weight change

Summary
Objective: We investigated the association between the proportion of long-chain n-3 polyunsaturated fatty acids (PUFA) in plasma phospholipids from blood samples drawn at enrollment and subsequent change in body weight. Sex, age, and BMI were considered as potential effect modifiers. **Method:** A total of 1,998 women and men participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) were followed for a median of 4.9 years. The associations between the proportion of plasma phospholipid long-chain n-3 PUFA and change in weight were investigated using mixed-effect linear regression. **Results:** The proportion of long-chain n-3 PUFA was not associated with change in weight. Among all participants, the 1-year weight change was –0.7 g per 1% point higher long-chain n-3 PUFA level (95% confidence interval: –20.7 to 19.3). The results when stratified by sex, age, or BMI groups were not systematically different. **Conclusion:** The results of this study suggest that the proportion of long-chain n-3 PUFA in plasma phospholipids is not associated with subsequent change in body weight within the range of exposure in the general population.

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Introduction

Although obesity is known to be a disorder of energy balance, an understanding of its causes and treatment remains elusive. Studies in rodents show that adding the long-chain n-3 polyunsaturated fatty acids (PUFA), eicosapentaenoic acid (EPA, C20:5n-3) and docosahexaenoic acid (DHA, C22:6n-3), to a rodent diet reduces body fat mass and prevents development of obesity [1]. These beneficial effects of long-chain n-3 PUFA on body fat mass have been related to alterations of gene expression that increase fat oxidation and energy expenditure and reduce fat deposition [1].

Fish consumption is the major dietary source of long-chain n-3 PUFA. No epidemiological studies have investigated the association between fish consumption and body weight. One study, however, investigated the association between fish consumption and subsequent change in waist circumference [2]. In that study no substantial associations were found. Biologically, however, it may not be the dietary intake of long-chain n-3 PUFA that is the relevant exposure in studies of body weight and fat distribution but the endogenous exposure. The proportion of long-chain n-3 PUFA in plasma phospholipids is an objective measure of the endogenous exposure, reflecting habitual dietary intake of long-chain n-3 PUFA (weeks to months) and the fatty acid metabolism [3, 4]. In a case-control study by Karlsson et al. [5], the proportion of DHA, but not EPA, in plasma phospholipids was significantly lower in obese female adolescents compared with lean age-matched females. Among male adolescents, the proportion of DHA was also lower in obese compared with lean male adolescents, although not statistically significant; there was no difference in the proportions of EPA [5].

We investigated the association between the proportion of long-chain n-3 PUFA in plasma phospholipids and subsequent change in body weight. Based on previous findings, we hypothesized that the level of plasma phospholipid long-chain n-3 PUFA is inversely associated with change in body weight. We used data from the European Prospective Investigation into Cancer and Nutrition (EPIC). Sex, age, and BMI were considered as potential effect modifiers.

Material and Methods

Study Population

This study is a part of the Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of Home and Obesity (PANACEA) project, which aims at studying determinants of body weight and subsequent changes in weight in Europe using data from the EPIC. The EPIC population includes 521,448 participants recruited in 23 centers located in 10 European countries: Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden, and UK [6, 7]. At enrollment, which took place between 1992 and 2000, information on habitual diet, sociodemographic and lifestyle characteristics, and anthropometry was collected. Blood samples of ≥30 ml were drawn and stored at 5–10 °C protected from light and transported to local laboratories for processing and aliquoting. The only exceptions were the Oxford center (UK), where blood samples were collected from a network of general practitioners and transported to a central laboratory by post, and the Danish and Swedish centers where blood samples were aliquoted within 1 h of drawing. The blood samples were aliquoted into 0.5 ml plastic straws (plasma, serum, erythrocytes, and buffy coat for DNA) and stored in liquid nitrogen at –196 °C. The only exceptions were the Danish and Swedish centers where samples were aliquoted into tubes and stored in nitrogen vapor at –150 °C and in freezers at –70 °C, respectively. Follow-up information on anthropometry was collected 2.7–9.9 years (80% central range) after initial enrollment.

To study proportions of fatty acids in plasma phospholipids and associations with dietary intakes, 16 geographical regions were designated by grouping some of the 23 centers: Aarhus and Copenhagen (Denmark); northeast France; Heidelberg (southwest Germany); Potsdam (east Germany); Greece; Florence (central Italy); Naples and Ragusa (southern Italy); Turin and Varese (northern Italy); Bilthoven and Utrecht (The Netherlands); Asturias, Navarre, and San Sebastian (northern Spain); Granada (southern Spain); Murcia (southeastern Spain); Malmö (southern Sweden); Umeå (northern Sweden); Cambridge (UK); and Oxford (UK) [8]. Except for France, where only women were enrolled, 100 women and 100 men from each of the 16 regions were randomly selected to participate in the biomarker study, which resulted in a total of 3,100 persons. Selection was stratified by four age groups (45–49, 50–54, 55–59, and 60–64 years) with an equal number of women and men in each group. As far as possible, equal numbers of persons were selected for each season in which the blood samples were collected. Only persons for whom information on dietary intake was obtained were included (n = 3,089). Laboratory results for plasma phospholipid analyses were available for 3,009 persons. No data for Norway are included in the study as Norway joined the EPIC after selection of participants for the biomarker study.

The exclusion criteria for this study were length of follow-up equals to 0, extreme reported energy intake (<1% and >99% percentile of the ratio of reported energy intake to estimated energy requirement), missing information on weight or height, extreme anthropometric measurements (height <130 cm, BMI <16 kg/m^2, waist circumference <40 or >160 cm, waist circumference <60 cm if BMI >25 kg/m^2, or average weight change >5 kg/year during the observation period), missing information on lifestyle (tobacco or alcohol consumption), pregnancy, and chronic disease (prevalent diabetes, cancer, or cardiovascular disease) at enrollment. The final population consisted of 1,998 persons (54% women).

Plasma Phospholipid Analyses

Samples of the same sex and age category were ordered randomly within analysis batches. Each batch included one sample from each participating center and one sample from a standard pool for quality control (injected twice at the middle and end of each series). Fatty acid composition in plasma phospholipids was analyzed as described by Saadatian-Elahi et al. [8]. Briefly, phospholipids were purified by adsorption chromatography on silica tubes and trans-methylated at room temperature. The percentage composition of 22 individual fatty acids with a chain length between 14 and 22 carbons was determined by gas chromatography (a 30-meter capillary column, i.d. 0.32 mm) with helium as a carrier gas. Analytic quality control was carried out by the daily use of the standard quality control plasma (n = 137) and by analyzing the fatty acid composition of 10 aliquots of the standard quality control plasma during the same day. The between-day coefficient of variation (CV) was 3.86% for EPA, 4.70% for docosapentaenoic acid (DPA, C22:5n-3), and 4.55% for DHA. The within-day CV was 4.18% for EPA, 3.05% for DPA, and 1.36% for DHA. For this study we used the proportion of total long-chain n-3 PUFA defined as the sum of the proportions of EPA, DPA and DHA, and the proportions of the individual long-chain n-3 PUFA.

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Data on Anthropometry and Lifestyle Factors

At enrollment, height and weight were measured by trained staff by standardized methods in all centers, except in the French and Oxford (UK) centers where information on anthropometry was collected through standardized questionnaires [9]. Height and weight were measured without shoes. Height was measured to the nearest 0.1, 0.5, or 1.0 cm, and weight was measured to the nearest 0.1 or 0.5 kg depending on center [9]. Weight was adjusted to reduce heterogeneity due to protocol differences in clothing worn during measurement (light underwear, light clothing, or normal clothing). For participants in light clothing the adjustment was –1.0 kg and for participants in normal clothing –1.5 kg [9, 10]. In the Oxford center, self-reported values were corrected using prediction equations [11].

At follow-up, information on weight was collected through standardized questionnaires in all centers, except in the Bilthoven (The Netherlands) and Cambridge (UK) centers. In the Bilthoven center, weight was measured by trained staff for 57 persons (Doetinchem), and self-reported values were collected from 56 persons (Amsterdam/Maastricht). In the Cambridge center, weight was measured by trained staff as previously described [12]. Weight was adjusted to reduce heterogeneity due to protocol differences in clothing worn during measurement as described above. No follow-up data were available from Ragusa and Turin centers in Italy. The outcome measure was defined as weight at follow-up minus weight at enrollment and expressed as average 1-year change in weight. BMI was calculated as weight in kilograms divided by height in meters squared.

Information on sociodemographic (sex, age, menopausal status, and highest educational level achieved) and lifestyle (tobacco consumption and physical activity) characteristics was collected through standardized questionnaires at enrollment. A four-level physical activity index (inactive, moderately inactive, moderately active, and active) was derived by combining occupational and leisure time physical activity over the past year [13].

Statistical Analyses

Median and 80% central range for age, BMI, and proportions of plasma phospholipid long-chain n-3 PUFA at enrollment and annual weight change were calculated.

The associations between the proportion of plasma phospholipid long-chain n-3 PUFA (%) and 1-year change in weight (g) were investigated using mixed-effect linear regression with random effects on intercept taking into account the clustering of the data within geographical regions nested within countries. Exposure and outcome variables were modeled as continuous variables. Analyses were carried out among all participants and separately for women and men.

Two models were used. Model 1 included country, geographical region, and the proportion of plasma phospholipid long-chain n-3 PUFA. EPA, DPA, and DHA were analyzed in mutually adjusted models. Model 2 equals model 1 plus adjusting for suggested risk factors of development of obesity: sex (all participants only), age, BMI at enrollment, menopausal status (pre-, peri-, and post-menopausal, women only), highest educational level achieved (none, primary school, technical or professional school, other secondary school, university or higher education, and not specified), smoking status (never, former, current, and unknown), and physical activity level (inactive, moderately inactive, moderately active, and active). Adjustment of continuous variables was done using restricted cubic spline regression. For categorical variables, missing values were treated as a separate category. By stratifying the data, possible effect modification by sex, age (classified as age at enrollment of <60 and ≥60 years), and BMI (classified as BMI at enrollment of 18.5 to <25 kg/m^2, 25 to <30 kg/m^2, and ≥30 kg/m^2) was investigated. We tested the associations for the proportions of long-chain n-3 PUFA for non-linearity in restricted cubic spline regression models. No violations were detected. In addition, we used categorical analysis to investigate the association between the proportion of plasma phospholipid long-chain n-3 PUFA and subsequent weight change comparing the highest versus the lowest quintile of exposures to maximize the exposure contrast.

Data analyses were performed using Stata statistical software, release 10.1 (Stata Corporation, College Station, TX, USA).

Results

Characteristics of the study population are shown in table 1. The median age was 54 years (80% central range: 47–62 years) among women and 54 years (80% central range: 47–62 years) among men; the median BMI was 25 kg/m^2 (80% central range: 21–32 kg/m^2) among women and 26 kg/m^2 (80% central range: 23–31 kg/m^2) among men. The median proportion of total plasma phospholipid long-chain n-3 PUFA was 7.5% (80% central range: 5.1–11.0%) among women and 7.1% (80% central range 4.6–10.3%) among men. The median follow-up time was 5.0 years (80% central range: 2.5–9.9 years) among women and 4.9 years (80% central range: 2.7–9.9 years) among men, and the median annual weight change was 87 g (80% central range: –1,077 to 1,115 g) among women and 62 g (80% central range: –1,072 to 1,153 g) among men.

Table 2 shows the associations between the proportions of plasma phospholipid long-chain n-3 PUFA and subsequent changes in weight among all participants and separately among women and men. Neither the proportion of total long-chain n-3 PUFA nor the proportions of EPA, DPA, or DHA were consistently or significantly associated with changes in weight. Among all participants, the annual weight change was –0.7 g per 1% point higher total long-chain n-3 PUFA level (95% confidence interval (CI): –20.7 to 19.3 g), –22.7 g per 1% point higher EPA level (95% CI: –85.1 to 39.8 g), 16.8 g per 1% point higher DPA level (95% CI: –200.4 to 233.9 g), and 10.5 g per 1% point higher DHA level (95% CI: –28.6 to 49.6 g). The results when stratified by sex were not systematically different; neither were the results when stratified by age (online supplementary table 1, available at *http://content.karger.com/ProdukteDB/produkte.asp?doi=330710*) or by BMI (online supplementary table 2, available at *http://content.karger.com/ProdukteDB/produkte.asp?doi=330710*). Also in the categorical analyses comparing the weight change among persons in the highest versus the lowest quintile of exposure, no systematic or significant differences were found (data not shown).

Discussion

In this study, the proportion of long-chain n-3 PUFA in plasma phospholipids was not associated with subsequent change in body weight among women and men participating in the EPIC.

Exclusions were primarily due to non-response at follow-up. Non-response may be related to either the exposure to long-chain n-3 PUFA or to the change in weight but most

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Table 1. Characteristics of the study population

Country	n	Age, years	Anthropometry		Plasma phospholipid long-chain n-3 PUFA, % of total fatty acids			
			BMI, kg/m^2	1-year weight change, g	total long-chain n-3 PUFA	EPA	DPA	DHA
Denmark								
Women	81	58 (51, 63)[a]	25 (21, 29)	–98 (–1,133, 785)	9.9 (7.3, 13.9)	2.0 (1.2, 3.6)	1.3 (1.0, 1.5)	6.5 (5.0, 8.9)
Men	76	57 (52, 63)	26 (22, 31)	–235 (–972, 878)	9.0 (6.6, 14.2)	1.8 (1.0, 3.9)	1.2 (1.1, 1.5)	5.8 (4.0, 8.4)
France								
Women	79	50 (45, 59)	23 (19, 27)	266 (–804, 1,865)	9.2 (6.3, 12.1)	1.3 (0.7, 2.3)	1.1 (0.9, 1.5)	6.5 (4.5, 8.5)
Germany								
Heidelberg								
Women	77	54 (47, 62)	25 (22, 31)	–554 (–2,776, 2,056)	6.5 (5.0, 8.7)	1.0 (0.6, 1.7)	1.1 (0.8, 1.4)	4.4 (3.0, 5.9)
Men	80	54 (47, 62)	26 (22, 31)	–482 (–2,200, 1,049)	6.2 (4.5, 8.1)	1.0 (0.6, 1.7)	1.2 (0.9, 1.4.)	3.9 (2.9, 5.2)
Potsdam								
Women	69	54 (46, 63)	25 (21, 30)	229 (–753, 796)	7.0 (5.3, 10.5)	1.1 (0.6, 2.2)	1.1 (0.7, 1.4)	4.8 (3.5, 6.9)
Men	48	55 (47, 63)	27 (24, 30)	45 (–663, 863)	6.7 (5.0, 9.5)	1.1 (0.7, 2.3)	1.1 (0.9, 1.3)	4.4 (3.1, 6.1)
Greece								
Women	76	51 (43, 60)	26 (22, 31)	338 (–249, 1,115)	7.5 (5.9, 9.7)	0.8 (0.4, 1.4)	0.9 (0.6, 1.1)	5.7 (4.4, 7.5)
Men	80	51 (43, 59)	27 (24, 32)	124 (–605, 1,386)	6.9 (5.1, 9.1)	0.9 (0.5, 1.7)	0.8 (0.6, 1.1)	5.2 (3.7, 6.8)
Italy								
Women	128	53 (46, 63)	26 (21, 31)	93 (–500, 890)	6.4 (4.6, 8.6)	0.9 (0.5, 1.5)	0.9 (0.7, 1.2)	4.6 (3.3, 6.3)
Men	107	54 (46, 61)	26 (23, 30)	92 (–313, 740)	5.9 (4.5, 8.1)	0.8 (0.5, 1.5)	0.9 (0.7, 1.2)	4.2 (2.9, 5.8)
The Netherlands								
Amsterdam/Maastricht								
Women	25	48 (46, 57)	25 (20, 29)	284 (–521, 926)	6.9 (5.0, 10.5)	1.0 (0.4, 2.3)	1.1 (0.9, 1.5)	4.6 (3.2, 6.9)
Men	31	53 (47, 58)	25 (22, 31)	116 (–752, 1,214)	5.9 (4.5, 9.3)	1.1 (0.5, 2.3)	1.1 (0.9, 1.5)	4.1 (2.7, 6.2)
Doetinchem								
Women	22	60 (48, 64)	26 (23, 31)	460 (–543, 1,174)	5.9 (4.9, 8.3)	0.9 (0.5, 2.0)	1.2 (0.8, 1.5)	3.8 (3.2, 5.9)
Men	35	58 (48, 64)	25 (22, 29)	445 (–267, 1,453)	6.1 (4.3, 8.0)	0.8 (0.5, 1.6)	1.1 (0.8, 1.4)	4.2 (2.5, 5.6)
Utrecht								
Women	27	57 (51, 63)	24 (20, 30)	373 (–412, 1,796)	6.5 (5.4, 9.2)	0.9 (0.5, 1.3)	1.3 (1.0, 1.5)	4.4 (3.5, 7.2)
Spain								
Women	262	55 (47, 63)	29 (24, 35)	–263 (–1,935, 947)	8.3 (6.2, 11.0)	1.1 (0.6, 2.3)	0.8 (0.6, 1.0)	6.4 (4.8, 8.0)
Men	231	54 (47, 62)	28 (25, 33)	–232 (–1,580, 1,250)	7.8 (5.7, 10.8)	1.1 (0.5, 2.4)	0.8 (0.6, 1.0)	5.8 (4.4, 7.5)
Sweden								
Malmö								
Women	63	54 (47, 63)	24 (19, 31)	202 (–1,077, 817)	8.1 (6.1, 12.3)	1.5 (0.9, 3.0)	1.1 (0.9, 1.4)	5.6 (4.1, 7.5)
Men	78	54 (49, 61)	26 (22, 29)	406 (–451, 1,681)	9.0 (6.6, 12.5)	1.7 (1.0, 3.5)	1.2 (1.0, 1.5)	6.1 (4.4, 8.6)
Umeå								
Women	39	50 (50, 50)	24 (19, 29)	356 (–51, 1,161)	9.2 (6.6, 11.4)	1.5 (1.0, 2.1)	1.3 (1.0, 1.6)	6.2 (4.1, 7.8)
Men	28	50 (50, 51)	25 (23, 28)	350 (–49, 944)	7.7 (5.7, 10.5)	1.4 (0.8, 2.4)	1.3 (1.1, 1.5)	5.1 (3.5, 6.5)

Table 1 continued on next page

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Table 1. Continued

Country	n	Age, years	Anthropometry		Plasma phospholipid long-chain n-3 PUFA, % of total fatty acids			
			BMI, kg/m^2	1-year weight change, g	total long-chain n-3 PUFA	EPA	DPA	DHA
UK								
Cambridge								
Women	61	55 (47, 61)	25 (22, 28)	342 (–621, 1,382)	7.9 (6.1, 11.0)	1.4 (0.9, 2.4)	1.2 (1.0, 1.6)	5.4 (3.9, 7.2)
Men	60	55 (46, 63)	24 (21, 28)	473 (–587, 1,904)	7.6 (5.5, 11.2)	1.4 (0.8, 3.3)	1.2 (1.0, 1.6)	5.1 (3.3, 7.0)
Oxford								
Women	67	55 (47, 63)	22 (19, 27)	224 (–597, 1,089)	4.0 (2.8, 6.1)	0.4 (0.2, 0.9)	1.1 (0.7, 1.5)	2.4 (1.5, 3.8)
Men	68	55 (47, 62)	23 (20, 28)	170 (–556, 1,188)	3.9 (2.4, 5.3)	0.5 (0.2, 0.9)	1.1 (0.7, 1.6)	2.1 (1.2, 2.9)
All cohorts								
Women	1,076	54 (47, 62)	25 (21, 32)	87 (–1,077, 1,115)	7.5 (5.1, 11.0)	1.1 (0.5, 2.3)	1.0 (0.7, 1.4)	5.4 (3.3, 7.8)
Men	922	54 (47, 62)	26 (23, 31)	62 (–1,072, 1,153)	7.1 (4.6, 10.3)	1.1 (0.5, 2.3)	1.0 (0.7, 1.4)	5.0 (2.8, 7.0)

[a]Median; 80% central range in parentheses.

likely not to both the exposure to long-chain n-3 PUFA and the change in weight. Thus, selection bias is unlikely to have affected the results. The proportion of long-chain n-3 PUFA in plasma phospholipids is an objective long-term measure of the endogenous exposure, and using data from different populations with different diets allowed us to investigate the association between the proportion of long-chain n-3 PUFA in plasma phospholipids and subsequent change in body weight over a wide range of exposures. At enrollment, weight was measured by trained staff, but at follow-up information on weight was self-reported. However, most likely the reporting of follow-up weight was not related to the exposure to long-chain n-3 PUFA. Thus, in this study information bias is of limited concern. Relevant control for potential confounders did not change the observed associations. Residual confounding is therefore unlikely. However, confounding from other risk factors of development of obesity not taken into account remains a possible explanation for the observed associations. The proportion of long-chain n-3 PUFA in plasma phospholipid level reflects habitual dietary intake and endogenous fatty acid metabolism. We decided not to control for potential confounding from diet as the measures of associations from models including diet would be without clear interpretation.

The principal long-chain n-3 PUFA in the diet are EPA and DHA with fish consumption being the main source. In addition to intake of long-chain n-3 PUFA, EPA can also be synthesized by humans from α-linolenic acid (C18:3n-3) but conversion of α-linolenic acid to EPA appears to be limited [14]. Studies in rodents show that adding long-chain n-3 PUFA to a rodent diet reduces body fat mass and prevents development of obesity [1]. These beneficial effects of long-chain n-3 PUFA on body fat mass have been related to alterations of gene expression that increase fat oxidation and energy expenditure and reduce fat deposition [1]. The lack of an association between the proportion of long-chain n-3 PUFA in plasma phospholipids and body weight in this study is in contrast to previous findings. In a case-control study including 10 obese adolescents and 15 lean aged-matched controls, the proportion of DHA, but not EPA, in plasma phospholipids was significantly lower in obese females compared with lean females [5]. Among males, the proportion of DHA was also lower in obese compared with lean males, although not statistically significant; there was no difference in the proportions of EPA [5]. In a cross-sectional study including 60 normal-weight and 45 overweight adolescents the proportion of plasma DHA, but not EPA, was significantly lower among overweight adolescents as compared with normal-weight adolescents [15]. In another cross-sectional study the proportions of plasma EPA and DHA were significantly inversely associated with BMI and waist circumference among obese adults, but not among normal-weight or overweight adults [16]. However, the interpretation of the findings from that study is not clear as

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Table 2. Association between the proportion of plasma phospholipid long-chain n-3 PUFA (%) and 1-year change in weight (g)

	All participants g/% point		Women g/% point		Men g/% point	
	β	(95% CI)	β	(95% CI)	β	(95% CI)
Total long-chain n-3 PUFA[a]						
Model 1[b]	–0.2	(–20.6, 20.1)	9.9	(–17.2, 37.0)	–18.4	(–48.8, 12.0)
Model 2[c]	–0.7	(–20.7, 19.3)	6.1	(–19.9, 32.1)	–19.9	(–49.4, 9.6)
EPA[a]						
Model 1[b]	–21.2	(–85.0, 42.7)	8.9	(–76.3, 94.0)	–63.4	(–161.6, 34.8)
Model 2[c]	–22.7	(–85.1, 39.8)	8.3	(–74.4, 91.0)	–66.3	(–161.4, 28.7)
DPA[a]						
Model 1[b]	71.0	(–151.0, 293.0)	–31.4	(–337.7, 274.9)	249.9	(–61.2, 561.0)
Model 2[c]	16.8	(–200.4, 233.9)	–45.7	(–344.7, 253.3)	83.6	(–220.2, 387.3)
DHA[a]						
Model 1[b]	5.4	(–33.8, 44.7)	14.0	(–37.9, 65.9)	–18.1	(–79.2, 43.1)
Model 2[c]	10.5	(–28.6, 49.6)	9.2	(–40.4, 58.8)	–2.2	(–61.2, 56.8)

[a]n = 1,998 for all participants; n = 1,076 for women; and n = 922 for men.
[b]From multilevel mixed-effect linear regression with random effects on intercept, taking into account the clustering of the data within geographical regions nested within countries. The proportions of the specific plasma phospholipid long-chain n-3 PUFA were analyzed in mutually adjusted models.
[c]As model 1 plus adjusting for sex (all participants only), age, BMI at enrollment, menopausal status (women only), highest educational level achieved, smoking status, and physical activity level.

analyses were stratified by BMI which was the outcome of the study.

The potential effects of intake of long-chain n-3 PUFA on body weight have been investigated in clinical trials. These studies, however, generally used combinations of EPA and DHA, which makes it difficult to discern specific effects and related health consequences of the individual long-chain n-3 PUFA. In addition, clinical trials used high pharmacologic doses of long-chain n-3 PUFA to ensure maximal therapeutic effects, but failed to provide information on potential threshold effects, particularly with respect to lower intakes compatible with median intakes in the general population which has been estimated to 0.57 g/day among women and 0.70 g/day among men [17]. In a trial of the effect of including 1.8 g EPA plus DHA per day (EPA/DHA capsules) as part of an ad libitum diet on body composition among 6 healthy young adults, substitution of fish oil for visible fats (butter, olive oil, sunflower oil, and peanut oil) significantly decreased body fat mass [18]. In that study, body fat mass was measured using dual-energy X-ray absorptiometry. Using precise measures of body fat mass may be important to detect an effect. Furthermore, that study showed that substitution of fish oil for visible fat increased basal fat oxidation, suggesting that long-chain n-3 PUFA may to some extent modulate the partitioning of fat between oxidation and deposition. However, a high dose of long-chain n-3 PUFA was used, and potential threshold effects were not investigated. In our study we found no consistent associations between the endogenous exposure to long-chain n-3 PUFA and subsequent change in body weight over the range of exposures observed in the general population. In a randomized trial the effect of including seafood or fish oil as part of an energy-restricted diet on weight loss among 278 young overweight or obese adults was investigated [19]. In that study, the inclusion of either lean fish (0.3 g long-chain n-3 PUFA per day), fatty fish (3.0 g long-chain n-3 PUFA per day), or fish oil capsules (1.5 g long-chain n-3 PUFA per day) resulted in more weight loss than did a control diet without marine food, but among men only. A specific effect of long-chain n-3 PUFA may explain more weight loss of the diets including fatty fish or fish oil but not more weight loss of the diet including lean fish, as the content of long-chain n-3 PUFA was only slightly higher in the diet including lean fish than in the control diet. Thus, the findings from that study suggest that there are components of fish that may improve weight loss beyond long-chain n-3 PUFA.

The association between long-chain n-3 PUFA and body fat mass may depend on the size of the fat mass. The size of the fat mass measured as BMI was considered as a potential effect modifier in this study. Using BMI as a measure of fat mass size may rank the participants according to general obesity [20]. Sex and age were also considered as potential effect modifiers due to sex- and age-related differences in the size of the fat mass. The findings from this study, however, did not suggest systematical differences in the associations across strata of sex, age, or BMI.

In conclusion, the results of this study suggest that the proportion of long-chain n-3 PUFA in plasma phospholipids is not associated with subsequent change in body weight within the range of exposure in the general population.

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Acknowledgements

This work is part of the project Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of Home and Obesity (PANACEA), which is supported by the European Union in the framework of the Public Health Programmme (Contract 2005328). The work was further supported by the European Commission: Public Health and Consumer Protection Directorate 1993–2004; Research Directorate-General 2005; Ligue contre le Cancer, Société 3M, Mutuelle Générale de l'Education Nationale, Institut National de la Santé de la Recherche Médicale (INSERM) (France); German Cancer Aid, German Cancer Research Center, Federal Ministry of Education and Research (Germany); Danish Cancer Society (Denmark); ISCIII (RETICC RD06/0020) of the Spanish Ministry of Health, the participating regional governments and institutions (Spain); Cancer Research UK, Medical Research Council, Stroke Association, British Heart Foundation, Department of Health, Food Standards Agency, The Wellcome Trust (UK); Greek Ministry of Health, Greek Ministry of Education, Hellenic Ministry of Health, Stavros Niarchos Foundation, and the Hellenic Health Foundation (Greece); Italian Association for Research on Cancer, National Research Council (Italy); Dutch Ministry of Public Health, Welfare and Sports, Dutch Ministry of Health, Dutch Prevention Funds, LK Research Funds, Dutch Zorg Onderzoek Nederland (ZON), World Cancer Research Fund (WCRF) (The Netherlands); and Swedish Cancer Society, Swedish Scientific Council, Regional Government of Skane and Västerbotten (Sweden). This work is also part of the project Hepatic and Adipose Tissue and Functions in the Metabolic Syndrome (HEPADIP, *www.hepadip.org*), which is supported by the European Commission as an Integrated Project under the 6th Framework Programme (Contract LSHM-CT-2005-018734) and part of the research program of the Danish Obesity Research Centre (DanORC, *www.danorc.dk*), which is supported by the Danish Council for Strategic Research (Contract 2101-06-0005).

Disclosure Statement

The authors declare no conflict of interest.

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