Serum phospholipid n−3 long-chain polyunsaturated fatty acids and physical and mental health in a population-based survey of New Zealand adolescents and adults[1–3]

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ABSTRACT

Background: Evidence from observational studies suggests that there is an association between n−3 long-chain polyunsaturated fatty acids and depression; however, this association has yet to be examined in a population-based study.

Objective: The objective was to assess whether n−3 long-chain polyunsaturated fatty acids in serum phospholipids are associated with mental and physical well-being.

Design: The fatty acid composition of serum phospholipids was measured in 2416 New Zealanders aged ≥15 y who took part in the 1997 National Nutrition Survey. The mental and physical component scores were assessed by using the short-form 36 health questionnaire.

Results: After adjustment for a number of covariates, there was a significant positive trend in self-reported physical well-being across the quintiles of eicosapentaenoic acid (*P* for trend = 0.009) and the ratio of eicosapentaenoic to arachidonic acid (*P* for trend = 0.012). The differences in the physical component score between the first and fifth quintiles were 2.4 and 2.5 points, respectively. The results showed that neither the proportion of eicosapentaenoic acid nor that of docosahexaenoic acid was associated with the mental component score; however, there was a significant positive trend in mental well-being across the quintiles of the ratio of eicosapentaenoic to arachidonic acid (*P* for trend = 0.044).

Conclusion: The results from this population-based survey of New Zealanders suggest a strong and consistent association between eicosapentaenoic acid in serum phospholipids and self-reported physical well-being; the association with mental well-being is less compelling. *Am J Clin Nutr* 2007;86:1278–85.

KEY WORDS Mental health, n−3 fatty acids, quality of life, nutrition surveys, New Zealanders

INTRODUCTION

Over the past century, the lifetime risk of depression has increased worldwide (1, 2). By the year 2030, the World Health Organization estimates that unipolar depressive disorders will rank second in the leading causes of disability-adjusted life years (3). Therefore, identification of modifiable risk factors is an important element of reducing disease burden. There has been considerable effort in recent times to determine whether diet plays an important role, and some evidence indicates that a low intake of n−3 long-chain polyunsaturated fatty acids is a contributing factor in the etiology of depressive illness (4, 5).

There are several biologically plausible mechanisms underlying the association between depression and the 2 major n−3 long-chain polyunsaturated fatty acids, eicosapentaenoic (20:5n−3) and docosahexaenoic (22:6n−3) acids (6, 7). Although the results of most observational studies support an association between eicosapentaenoic and docosahexaenoic acids and depression (8–13), findings from placebo-controlled intervention trials have not been consistent in showing an alleviation of depressive symptoms after supplementation with n−3 long-chain polyunsaturated fatty acids in participants with depressive disorders (14). Furthermore, because the majority of the observational studies conducted have focused on persons with depression, the extent to which n−3 long-chain polyunsaturated fatty acids influence the mental well-being of the general population has not been well described.

The short-form 36 (SF-36) is a quality-of-life questionnaire that has been used in many studies to assess the self-reported physical and mental well-being of large groups of people (15). Although the SF-36 is not a tool used to diagnose depression, the mental and physical component scores are generally lower in those with a clinical diagnosis of depression (16–18), and scores increase in response to standard treatments for depression (19, 20).

The objective of this study was to assess the association between the proportion of n−3 long-chain polyunsaturated fatty acids in serum phospholipids, as biomarkers of dietary intake, and the mental and physical component scores in a population-based survey of New Zealand adolescents and adults.

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SUBJECTS AND METHODS

Subjects

The sample from the 1997 National Nutrition Survey (NNS97) was drawn from the 1996-1997 New Zealand Health Survey (NZHS), a population-based survey that assessed the health status and use of health services in noninstitutionalized New Zealand adolescents and adults aged ≥15 y. A more detailed description of the methods from the NNS97 was published elsewhere (21–24). Fourteen ethics committees throughout New Zealand approved the survey, and all participants or the legal guardian of those aged <18 y provided written informed consent. The procedures followed were in accordance with the ethical standards of the New Zealand Health Research Council.

Methods

Data for the NZHS were collected from October 1996 to October 1997. During a face-to-face interview, participants completed a questionnaire that was designed to assess health status, health risk behaviors, the use of health services, and demographic and socioeconomic circumstances. Ethnicity was self-reported and categorized into 3 groups: New Zealand Maori, Pacific Island People, and New Zealand European and other (NZEO). Age was self-reported and categorized into 5 groups: 15–19, 19–24, 25–44, 45–64, and ≥65 y. Marital status was classified as "married/living as married;" "previously married" for those who had been divorced, separated, or widowed; and "never married" for those who had not been married or living as married. Labor force status was categorized as "employed" (full or part-time), "unemployed" for those who did not have a job but who were actively seeking employment, and "not in the labor force" for those who did not have a job and were not currently seeking employment. Socioeconomic status was assessed on the basis of education, family income, and the NZDep96. The NZDep96 is an area-based level of deprivation and has a scale of 1–4 (one being the least deprived). Education was categorized as "no qualification," "school qualification only or postschool qualification only," or "school and postschool qualification." Family income was classified as an annual family income of "loss/zero–$20 000", "$20 001-$30 000," "$30 001–50 000," and ">$50 000." Smoking status was obtained from 3 questions relating to smoking behavior, and the participants were categorized as "never," "former," and "current" smokers. A set of questions relating to shortness of breath, asthma attacks, and use of asthma medication identified individuals with asthma. Participants were asked whether they had ever received a diagnosis of diabetes (type I or type II) from a doctor and were categorized accordingly. Participants were asked whether they had ever taken or were currently taking blood pressure medication and were categorized as "currently," "formerly," or "never." Participants were categorized by dwelling as follows: "major urban," "secondary urban," "minor urban," or "rural" (25).

At the end of the interview, participants filled out a general health questionnaire that included the SF-36, which is comprised of 36 items used to assess the self-reported physical and mental well-being of respondents over the past 4 wk. The 36 items were grouped into 8 scales that measure different physical (physical functioning, role limitations due to physical health, bodily pain, and general health) and mental (mental health, role limitations due to emotional health, vitality, and social functioning) aspects of health. The 8 scales were then standardized and aggregated by factor analysis to form a physical component score and a mental component score with a mean of 50 and an SD of 10. The factor analysis used in 9 other Western countries (15) was modified to incorporate the different concepts of physical and mental health and well-being for Maori and Pacific people (26), and the reliability and validity of the SF-36 in New Zealanders was reported elsewhere (27). The self-administered general health questionnaire also included 10 questions that make up the Alcohol Use Disorders Identification Test (AUDIT), which was designed to assess alcohol consumption and drinking behavior over the past year. The values from AUDIT were categorized into "abstainers" (those who had not had a drink containing alcohol over the past year), "moderate drinkers" (those who had a score >0 but <8 out of a possible total of 40), and "potential hazardous drinkers" (those with a score ≥8) (25).

The NNS97 took place over a 12-mo period from December 1996 to November 1997. During the home visit, height and weight were measured according to standard techniques; Quetelet's body mass index (BMI; in kg/m^2) was calculated. Ethnic-specific BMI cutoffs were used to classify individuals into the BMI categories. For NZEO, those with a BMI ≤24.9 were categorized into the normal BMI category, between 25.0 and 29.9 (inclusive) into the overweight category, and ≥30.0 into the obese category. For NZ Maori and Pacific people, the cutoffs were <25.9 for a normal BMI between 26.0 and 31.9 (inclusive) for the overweight category and those with a BMI ≥ 32.0 were categorized as obese (28). Blood was drawn from the participants from an antecubital vein into vacuum-evacuated tubes with no anticoagulant. Participants were not required to fast. The tubes were centrifuged at 1650 × *g* for 15 min at 4 °C, and the serum was portioned into cryovials for storage at −80 °C. The date of the blood sample collection was grouped into the seasons as follows: "summer" (December 22 to March 21), "autumn" (March 22 to June 21), "winter" (June 22 to September 21), and "spring" (September 22 to December 21) (22).

Detailed methods of the fatty acid analysis were published elsewhere (24, 29). In brief, lipids were extracted from 400 μL serum according to the method of Bligh and Dyer (30). Serum phospholipid was isolated by using thin-layer chromatography, and fatty acids were analyzed by using a DB-225 narrow-bore column (30 m × 0.25 mm ID; film thickness: 0.25 μm; Agilent, Palo Alto, CA) on a HP-6890 gas chromatograph with flame ionization detection (Agilent). The CVs for the eicosapentaenoic, arachidonic (20:4n−6), docosapentaenoic (22:5n−3), and docosahexaenoic acids in serum phospholipids were 14%, 11%, 12%, and 13%, respectively.

All statistical analyses were carried out on SAS version 9.1.2 by using the survey commands when appropriate to control for the survey design of the study. In the preplanned analysis, we used multiple linear regression to examine the relation between serum eicosapentaenoic acid, docosahexaenoic acid, the ratio of eicosapentaenoic to arachidonic acids and the sum of eicosapentaenoic, docosapentaenoic, and docosahexaenoic acids (total n−3 long-chain polyunsaturated fatty acids) with the mental and physical component scores. The characteristics and mental and physical component scores of participants by quintiles of n−3 polyunsaturated fatty acids; eicosapentaenoic acid, docosahexaenoic acid, the ratio of eicosapentaenoic to arachidonic acids, and total n−3 long-chain polyunsaturated fatty acids in serum phospholipids were calculated. The associations for the covariates across the quintiles of fatty acids were tested by using

TABLE 1
Characteristics of the participants[1]

	NZHS (n = 7862)	NNS97 (n = 4636)	NNS97		P[2]
			PL fatty acid (n = 2416)	No PL fatty acid (n = 2220)	
Percentage of original NZHS cohort (%)	—	59	31		
Sex [n (%)]					
Male	3258 (41)	1927 (42)	1079 (45)	848 (38)	<0.001
Female	4604 (59)	2709 (58)	1337 (55)	1372 (62)	
Age category [n (%)]					
15–18 y	405 (5)	246 (5)	104 (4)	142 (6)	<0.001
19–24 y	645 (8)	354 (8)	183 (8)	171 (7)	
25–44 y	3221 (41)	1964 (42)	1073 (44)	891 (37)	
45–64 y	2063 (26)	1255 (27)	667 (28)	588 (24)	
≥65 y	1528 (19)	817 (18)	389 (16)	428 (19)	
Ethnicity [n (%)]					
NZEO	5896 (75)	3626 (78)	1940 (80)	1686 (76)	0.004
NZ Maori	1321 (17)	703 (15)	345 (14)	358 (16)	
Pacific	646 (8)	307 (7)	131 (5)	176 (8)	
Smoking category [n (%)]					
Never or not specified	3529 (45)	2108 (45)	1065 (44)	1043 (47)	0.136
Current	2280 (29)	1258 (27)	677 (28)	593 (27)	
Former	2053 (26)	1270 (27)	674 (28)	584 (26)	
Marital status [n (%)]					
Married or living as married	4188 (53)	2600 (56)	1427 (59)	1199 (54)	<0.001
Separated divorced or widowed	1757 (22)	964 (21)	468 (19)	496 (22)	
Never married or not specified	1917 (24)	1072 (23)	521 (22)	525 (24)	
Family income [n (%)]					
Loss or 0–$20 000	—	1247 (27)	637 (26)	610 (27)	0.001
$20 001–30 000	—	689 (15)	362 (15)	327 (15)	
$30 001–50 000	—	932 (20)	516 (21)	416 (19)	
>$50 000	—	1108 (24)	608 (25)	500 (23)	
Not specified	—	660 (14)	293 (12)	367 (17)	
Mental Component Score	50.0 ± 10.0[3]	50.1 ± 9.8	50.1 ± 9.8	50.2 ± 9.7	0.930
Physical Component Score	50.0 ± 10.0	50.1 ± 9.7	50.2 ± 9.6	50.0 ± 9.8	0.389

[1] NZHS, 1996–1997 New Zealand Health Survey; NNS97, 1997 National Nutrition Survey; PL, phospholipid; NZEO, New Zealand European and other.
[2] Represents the difference between NNS97 participants with a PL fatty acid value (n = 2416) and those without a value (n = 2220). The differences were tested by using chi-square tests for categorical variables and t tests for continuous variables.
[3] $\bar{x}$ ± SEM (all such values).

chi-square tests. In the fully adjusted model, the covariates age category, sex, BMI category, season of blood collection, urban or rural dwelling, socioeconomic status (NZDep96, family income, and education), marital status, employment, smoking status, diabetes, asthma, use of blood pressure medication, and AUDIT category were treated as indicator variables in the model to calculate adjusted mental and physical component scores for the quintiles of serum fatty acids. Interactions between sex and age category with the other categorical variables were also tested in the models and were included if $P < 0.05$. The partially adjusted regression model included all covariates except the presence of illness (diabetes, asthma, or use of blood pressure medication). A level of significance of $P < 0.05$ was chosen to be statistically significant. Linear prediction was used to calculate the multivariate-adjusted values of the mental and physical component scores for the quintiles of the two n−3 long-chain polyunsaturated fatty acids, the ratio of eicosapentaenoic to arachidonic acids, and the sum of the n−3 long-chain polyunsaturated fatty acids.

RESULTS

When calculating the mental and physical component scores, the use of ethnic-specific or nonspecific factor analysis (26) had no bearing on the association between the fatty acid composition of serum phospholipids and the scores; therefore, results from the ethnic-specific factor analysis are reported.

The fatty acid composition of serum phospholipids was completed for 2416 of the 3223 serum samples collected in the NNS97. The distributions of sex, age, ethnicity, marital status, and family income for participants in the NNS97 who had a phospholipid fatty acid measurement (n = 2416) were significantly different from the participants who did not have a measurement (n = 2220); the latter included those who did not provide a blood sample (n = 1413) (**Table 1**). There were no significant differences in the distributions of smoking or the mean mental and physical component scores.

The mean fatty acid composition of serum phospholipids for 2416 participants in the NNS97 is shown in **Table 2**. When participants were categorized by quintile of increasing

TABLE 2
Fatty acid composition of serum phospholipids for participants in the 1997 National Nutrition Survey (n = 2416)

Fatty acid	Value
	mol %
14:0	0.53 ± 0.01
15:0	0.30 ± 0.00
16:0	31.83 ± 0.09
16:1	0.83 ± 0.01
18:0	14.45 ± 0.07
18:1	9.97 ± 0.05
18:2n−6	19.03 ± 0.11
18:3n−3	0.25 ± 0.00
20:3n−6	2.64 ± 0.02
20:4n−6	7.18 ± 0.04
20:5n−3	1.02 ± 0.01
22:4n−6	0.47 ± 0.01
22:5n−6	0.48 ± 0.01
22:5n−3	0.90 ± 0.01
22:6n−3	2.64 ± 0.02
24:0	1.30 ± 0.01
24:1	1.73 ± 0.01

proportion of eicosapentaenoic acid in serum phospholipids, those in the highest quintile were older and there were significant positive associations across the quintiles for the proportion of individuals in the highest socioeconomic status category and married individuals (**Table 3**). There were significant inverse associations for the proportion of women, asthmatics and those who had visited a mental health professional in the past 4 wk across the quintiles of eicosapentaenoic acid. In the unadjusted analysis, those in the highest quintile of eicosapentaenoic acid had a mental component score 2.6 points higher than the lowest quintile and the difference in the physical component score between the highest and lowest quintile was 2.8 points. After adjusting for confounding variables, the positive trend for the mental component score across the quintiles of eicosapentaenoic acid was no longer statistically significant either after partial or full adjustment. The positive trend across the quintiles of eicosapentaenoic acid for the physical component score remained significant after adjustment, with a difference between the highest and the lowest quintile of 2.4 points after partial as well as full adjustment.

Individuals categorized into the highest quintile of docosahexaenoic acid in serum phospholipid were almost 6 y older than those in the lowest quintile, and there was a higher proportion of women and married individuals (**Table 4**). There was a significant inverse association for the proportion of hazardous drinkers across the quintiles of docosahexaenoic acid. There was no significant trends across the quintiles of docosahexaenoic acid for the mental or physical component scores in either the unadjusted, the partially or fully adjusted models.

The characteristics of participants by the quintile of eicosapentaenoic/arachidonic acid ratio in serum phospholipid are shown in **Table 5**. Across the quintiles, age increased, as did the proportion of individuals in the highest socioeconomic status category and those who are married. The proportion of women, asthmatics, and individuals seeing a mental health professional all decreased. In the unadjusted analysis, there was a significant

TABLE 3
Characteristics of the participants in the 1997 National Nutrition Survey by quintile of eicosapentaenoic acid in serum phospholipid[1]

	Quintile					
	1 (n = 475)	2 (n = 475)	3 (n = 475)	4 (n = 475)	5 (n = 475)	P
Phospholipid eicosapentaenoic acid (mol%)[2]	0.47 ± 0.01 (0.07–0.63)	0.74 ± 0.00 (0.63–0.84)	0.94 ± 0.00 (0.84–1.04)	1.17 ± 0.00 (1.04–1.33)	1.78 ± 0.03 (1.33–6.84)	
Females (%)[2]	54.6 ± 3.2	48.4 ± 3.1	48.5 ± 2.9	44.9 ± 3.0	40.2 ± 2.8	0.0210
Highest category of SES (%)[2,3]	27.3 ± 3.1	36.3 ± 3.0	41.5 ± 3.1	30.9 ± 2.8	32.0 ± 3.2	0.0088
Married or living as married (%)[2]	57.0 ± 3.2	57.2 ± 3.0	68.9 ± 2.8	70.5 ± 2.7	69.1 ± 2.9	<0.0001
Never smoked (%)[2]	49.6 ± 3.0	53.3 ± 3.0	48.9 ± 3.0	48.3 ± 3.3	44.8 ± 3.2	0.1122
Asthmatic (%)[2]	19.7 ± 2.4	21.1 ± 2.5	12.7 ± 1.9	13.2 ± 1.8	16.1 ± 2.1	0.0136
Hazardous drinker (%)[2,4]	17.4 ± 2.3	19.4 ± 2.7	17.6 ± 2.6	18.6 ± 2.7	17.4 ± 2.6	0.8642
Seeing a mental health professional (%)[2,5]	4.3 ± 1.9	1.6 ± 0.6	1.3 ± 0.6	0.8 ± 0.4	1.4 ± 0.6	0.0083
Age (y)[2]	38.6 ± 1.0	38.1 ± 1.0	40.5 ± 0.9	45.0 ± 1.0	47.5 ± 1.1	<0.0001
Mental component score[2]						
Unadjusted	49.1 ± 0.7	49.6 ± 0.6	51.3 ± 0.5	50.7 ± 0.6	51.7 ± 0.5	0.006
Partially adjusted[6]	46.5 ± 2.8	46.3 ± 2.8	47.7 ± 2.8	47.2 ± 2.8	48.1 ± 2.8	0.085
Fully adjusted[7]	48.1 ± 2.6	48.1 ± 2.6	49.1 ± 2.6	48.6 ± 2.6	49.6 ± 2.6	0.211
Physical component score[2]						
Unadjusted	48.9 ± 0.7	50.1 ± 0.5	51.5 ± 0.5	50.8 ± 0.5	51.7 ± 0.5	0.008
Partially adjusted[6]	49.2 ± 2.3	49.4 ± 2.2	50.9 ± 2.2	50.6 ± 2.2	51.6 ± 2.3	0.003
Fully adjusted[7]	50.0 ± 2.1	50.5 ± 2.1	51.5 ± 2.1	51.3 ± 2.1	52.4 ± 2.1	0.009

[1] SES, socioeconomic status. Values in parentheses are ranges.
[2] Values are $\bar{x}$ ± SEM.
[3] Defined as a family income of ≥$50 000 per annum.
[4] Defined as having a score ≥8 on the AUDIT (Alcohol Use Disorders Identification Test) questionnaire.
[5] Visited a social worker, psychologist, or counselor in the past 4 wk.
[6] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96 (deprivation scale), family income, education, smoking, hazardous drinking, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, and age category × hazardous drinking interactions by using survey linear regression.
[7] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96, family income, education, smoking, hazardous drinking, diabetes, asthma, use of blood pressure medication, sex × NZDep96, sex × education, age category × labor force status, age category × family income, age category × hazardous drinking, age category × diabetes, and age category × asthma interactions by using survey linear regression.

TABLE 4
Characteristics of participants in the 1997 National Nutrition Survey by quintile of docosahexaenoic acid in serum phospholipids[1]

	Quintile					
	1 (n = 475)	2 (n = 475)	3 (n = 475)	4 (n = 475)	5 (n = 475)	P
Phospholipid docosahexaenoic acid (mol%)[2]	1.49 ± 0.02 (0.06–1.93)	2.18 ± 0.01 (1.93–2.40)	2.60 ± 0.01 (2.40–2.81)	3.06 ± 0.01 (2.81–3.35)	3.98 ± 0.03 (3.35–8.02)	
Females (%)[2]	40.6 ± 2.9	47.8 ± 3.1	43.8 ± 3.1	51.9 ± 3.0	53.5 ± 3.1	0.0174
Highest category of SES (%)[2,3]	32.3 ± 3.0	31.9 ± 3.0	37.8 ± 3.1	32.7 ± 2.8	34.1 ± 3.2	0.7504
Married or living as married (%)[2]	57.6 ± 3.1	60.8 ± 2.8	67.9 ± 3.0	66.8 ± 2.6	70.5 ± 2.9	<0.0001
Never smoked (%)[2]	52.5 ± 2.9	46.3 ± 3.0	47.6 ± 3.0	45.6 ± 3.1	53.5 ± 3.0	0.0048
Asthmatic (%)[2]	21.4 ± 2.6	15.4 ± 2.1	14.0 ± 1.9	17.5 ± 2.2	14.3 ± 1.9	0.0820
Hazardous drinker (%)[2,4]	23.5 ± 2.7	22.1 ± 2.8	18.5 ± 2.6	13.6 ± 2.6	11.6 ± 1.8	0.0002
Seeing a mental health professional (%)[2,5]	1.2 ± 0.5	1.6 ± 0.6	3.6 ± 1.7	1.9 ± 0.7	0.9 ± 0.5	0.0961
Age (y)[2]	38.4 ± 1.0	40.7 ± 1.0	41.5 ± 1.0	45.3 ± 1.0	44.3 ± 1.1	<0.0001
Mental component score[2]						
Unadjusted	50.8 ± 0.6	50.4 ± 0.6	51.0 ± 0.6	50.0 ± 0.6	50.3 ± 0.6	0.749
Partially adjusted[6]	47.0 ± 2.8	46.4 ± 2.9	46.8 ± 2.8	45.9 ± 2.9	46.4 ± 2.9	0.635
Fully adjusted[7]	48.8 ± 2.5	48.0 ± 2.6	48.4 ± 2.5	47.7 ± 2.6	47.9 ± 2.7	0.595
Physical component score[2]						
Unadjusted	51.1 ± 0.5	50.9 ± 0.5	51.0 ± 0.6	49.9 ± 0.6	50.1 ± 0.6	0.477
Partially adjusted[6]	50.0 ± 2.2	49.7 ± 2.3	49.9 ± 2.2	48.9 ± 2.4	49.3 ± 2.4	0.635
Fully adjusted[7]	51.0 ± 2.1	50.6 ± 2.1	50.7 ± 2.1	50.0 ± 2.2	50.1 ± 2.3	0.643

[1] SES, socioeconomic status. Values in parentheses are ranges.
[2] Values are $\bar{x}$ ± SEM.
[3] Defined as a family income of ≥$50 000 per annum.
[4] Defined as having a score ≥ 8 on the AUDIT (Alcohol Use Disorders Identification Test) questionnaire.
[5] Visited a social worker, psychologist, or counselor in the past 4 wk.
[6] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96 (deprivation scale), family income, education, smoking, hazardous drinking, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, and age category × hazardous drinking interactions by using survey linear regression.
[7] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96, family income, education, smoking, hazardous drinking, diabetes, asthma, use of blood pressure medication, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, age category × hazardous drinking, age category × diabetes, and age category × asthma interactions by using survey linear regression.

positive trend across quintiles of the ratio of eicosapentaenoic to arachidonic acid and mental component score; those in the highest quintile had a mental component score 3.1 points higher than those in the lowest quintile. After partial and full adjustment for confounding variables, there was a significant positive trend across the quintiles; the differences in mental component scores between quintiles 1 and 5 were 2.1 and 2.0 points, respectively. In the unadjusted analysis, there was a positive trend across the quintiles of the ratio of eicosapentaenoic to arachidonic acid for the physical component score, and the difference between the highest and lowest quintile was 2.8 points. After partial and full adjustment for covariates, the trend for the physical component score across the quintiles remained significant. Partial or full adjustment attenuated the association; the difference was 2.5 points.

Across the quintiles of total n−3 long-chain fatty acids, there were significant positive associations for age and the proportion of married participants, and there was a significant inverse association for those who had never smoked (**Table 6**). There were no significant trends across the quintiles of total n−3 long-chain fatty acids in phospholipids for the mental or physical component scores, either before or after adjustment for the covariates.

It made little difference to the association between total n−3 long-chain polyunsaturated fatty acids and the mental and physical component scores if total n−3 long-chain polyunsaturated fatty acids was calculated as a percentage of total fatty acids or as a percentage of total long-chain polyunsaturated fatty acids (data not shown).

DISCUSSION

The results from this population-based survey showed the proportion of eicosapentaenoic acid and the ratio of eicosapentaenoic to arachidonic acid in serum phospholipids were positively associated with self-reported physical well-being, and there was a positive association between the ratio of eicosapentaenoic to arachidonic acid and self-reported mental well-being in New Zealanders. The n−3 long-chain polyunsaturated fatty acid composition of serum phospholipids was used as a predictor of the mental and physical component score rather than reported fish consumption because the biomarkers reflect actual intake of n−3 long chain polyunsaturated fatty acids from fish (31, 32) and other dietary sources such as meat and eggs (33) and other nondietary determinants of n−3 long-chain polyunsaturated fatty acids such as genotype (34). Furthermore, n−3 long-chain polyunsaturated fatty acids in serum phospholipids, although they may not reflect composition in the brain (35), are physically closer to their biological sites of action (6, 36), and therefore are more likely to reflect an association with mental and physical health if one exists.

A difference of 2.4 and 2.5 points in the physical component score between the highest and lowest quintiles of eicosapentaenoic acid and the ratio of eicosapentaenoic to arachidonic acid is equivalent to effect sizes of 0.24 and 0.25, respectively. Effects sizes of this magnitude are generally considered large and of clinical benefit (37). Furthermore, the magnitude of the difference in physical component score compares with that reported

TABLE 5
Characteristics of participants in the 1997 National Nutrition Survey by quintile of ratio of eicosapentaenoic acid (EPA) to arachidonic acid (AA) in serum phospholipids[1]

	Quintile					
	1 (n = 474)	2 (n = 475)	3 (n = 475)	4 (n = 475)	5 (n = 475)	P
Phospholipid EPA:AA ratio[2]	0.07 ± 0.00 (0.02–0.09)	0.11 ± 0.00 (0.09–0.12)	0.13 ± 0.00 (0.12–0.15)	0.16 ± 0.00 (0.15–0.19)	0.26 ± 0.00 (0.19–0.86)	
Females (%)[2]	51.4 ± 3.2	50.7 ± 3.0	50.4 ± 3.1	45.2 ± 3.0	38.6 ± 2.8	0.0152
Highest category of SES (%)[2,3]	29.9 ± 3.2	42.8 ± 2.8	29.4 ± 2.8	34.0 ± 3.1	32.4 ± 3.2	0.0084
Married or living as married (%)[2]	55.2 ± 3.3	63.6 ± 3.0	64.1 ± 2.6	71.8 ± 2.5	69.0 ± 2.9	<0.0001
Never smoked (%)[2]	48.7 ± 3.1	54.5 ± 3.0	48.6 ± 3.0	47.3 ± 3.0	44.9 ± 3.1	0.1411
Asthmatic (%)[2]	22.0 ± 2.7	13.5 ± 1.9	15.7 ± 2.2	14.0 ± 2.1	17.0 ± 2.2	0.0489
Hazardous drinker (%)[2,4]	21.1 ± 2.8	16.6 ± 2.4	17.4 ± 2.2	16.6 ± 2.3	19.2 ± 3.0	0.6930
Seeing a mental health professional (%)[2,5]	4.8 ± 1.9	1.5 ± 0.6	0.7 ± 0.3	0.8 ± 0.4	1.6 ± 0.6	0.0189
Age (y)[2]	37.8 ± 1.0	38.6 ± 0.9	41.9 ± 1.1	44.4 ± 1.0	47.6 ± 1.1	<0.0001
Mental component score[2]						
Unadjusted	48.8 ± 0.7	50.6 ± 0.6	50.4 ± 0.5	50.7 ± 0.5	51.9 ± 0.5	0.008
Partially adjusted[6]	46.5 ± 2.9	46.9 ± 2.9	47.2 ± 2.9	47.3 ± 2.9	48.6 ± 2.9	0.047
Fully adjusted[7]	48.0 ± 2.6	48.2 ± 2.7	48.3 ± 2.6	48.5 ± 2.6	50.0 ± 2.6	0.044
Physical component score[2]						
Unadjusted	48.9 ± 0.7	51.2 ± 0.5	50.5 ± 0.6	50.8 ± 0.5	51.7 ± 0.6	0.015
Partially adjusted[6]	49.2 ± 2.3	50.1 ± 2.4	50.1 ± 2.3	50.4 ± 2.3	51.7 ± 2.4	0.013
Fully adjusted[7]	50.1 ± 2.1	50.8 ± 2.2	50.7 ± 2.1	51.1 ± 2.2	52.6 ± 2.2	0.012

[1] SES, socioeconomic status. Values in parentheses are ranges.
[2] Values are $\bar{x}$ ± SEM.
[3] Defined as a family income of ≥$50 000 per annum.
[4] Defined as having a score ≥8 on the AUDIT (Alcohol Use Disorders Identification Test) questionnaire.
[5] Visited a social worker, psychologist, or counselor in the past 4 wk.
[6] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96 (deprivation scale), family income, education, smoking, hazardous drinking, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, and age category × hazardous drinking interactions by using survey linear regression.
[7] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96, family income, education, smoking, hazardous drinking, diabetes, asthma, use of blood pressure medication, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, age category × hazardous drinking, age category × diabetes, and age category × asthma interactions by using survey linear regression.

between young and older New Zealand adults. For the entire New Zealand Health Survey, of which the NNS97 population is a subset, the difference in physical component score between the 15–24-y and 25–64-y age groups was 3.0 points for women and 7.4 points for men (27).

The association between the quintiles of eicosapentaenoic acid, the ratio of eicosapentaenoic to arachidonic acid, and better self-reported physical well-being is biologically plausible. The synthesis of the inflammatory series-2 prostaglandins and series-4 leukotrienes from arachidonic acid would be reduced in favor of the less inflammatory series-3 prostaglandins and series-5 leukotrienes synthesized from eicosapentaenoic acid (36). These biochemical changes may lessen the effects of inflammatory conditions such as asthma and rheumatoid arthritis. The results from 2 meta-analyses showed that individuals with rheumatoid arthritis report less joint tenderness after supplementation with fish oil (38, 39). We have no information on the prevalence of rheumatoid arthritis, but individuals with this disease score lower on the physical scales of the SF-36 than do the general population (40).

It is possible that a higher proportion of eicosapentaenoic acid was a proxy for a diet with more fish along with a healthier lifestyle, which in turn was associated with a higher rating of physical health. If this were the case, one would have expected a significant trend in the physical component score across the quintiles of docosahexaenoic acid and total n−3 long-chain polyunsaturated fatty acids, both of which correlate with fish consumption (31). Our results suggest a specific effect of eicosapentaenoic acid on physical well-being. This is consistent with experimental evidence showing that eicosapentaenoic acid is a better inhibitor than is docosahexaenoic acid of the synthesis of series-2 prostaglandins and series-4 leukotrienes from arachidonic acid (41, 42).

We found no evidence of an association between eicosapentaenoic and docosahexaenoic acids and mental well-being. This contrasts with the findings of Silvers and Scott (43), who reported that fish eaters had a mean mental component score that was 8.2 points higher than that of nonfish eaters. These findings are questionable because only 87 of 4644 participants were categorized as nonfish consumers, and there was little adjustment for lifestyle and demographic characteristics that could confound the relation. Our results suggest that the relation between eicosapentaenoic acid and mental well-being, which occurred in the unadjusted analysis, was entirely explained by confounding variables. In other studies, the association between fish intake and depression has been inconsistent (44–48). Results from the only prospective study that assessed the intake of fish or total n−3 fatty acids and the incidence of depression over 9 y showed that there was no association between depressive illness and

TABLE 6
Characteristics of participants in the 1997 National Nutrition Survey by quintile of total n−3 long-chain polyunsaturated fatty acid (LCPUFA) in serum phospholipids[1]

	Quintile					
	1 (n = 475)	2 (n = 475)	3 (n = 475)	4 (n = 475)	5 (n = 475)	P
Phospholipid Σn−3 LCPUFAs (mol%)[2,3]	2.76 ± 0.03 (0.21–3.56)	3.89 ± 0.01 (3.56–4.21)	4.50 ± 0.01 (4.21–4.82)	5.15 ± 0.01 (4.82–5.51)	6.60 ± 0.06 (5.51–15.46)	
Females (%)[3]	46.3 ± 3.0	48.3 ± 3.1	50.4 ± 2.9	46.4 ± 3.0	44.7 ± 2.9	0.7240
Highest category of SES (%)[3,4]	31.6 ± 3.0	33.3 ± 3.2	36.6 ± 2.9	34.8 ± 3.0	32.7 ± 3.1	0.3236
Married or living as married (%)[3]	53.1 ± 3.1	65.8 ± 3.0	63.8 ± 2.9	69.4 ± 2.8	70.9 ± 2.8	<0.0001
Never smoked (%)[3]	54.1 ± 2.9	45.1 ± 3.2	47.2 ± 3.0	46.6 ± 3.1	52.8 ± 3.0	0.0012
Asthmatic (%)[3]	21.4 ± 2.6	15.4 ± 2.0	15.9 ± 2.0	14.6 ± 2.2	15.2 ± 1.8	0.1414
Hazardous drinker (%)[3,5]	21.2 ± 2.5	22.0 ± 3.0	17.1 ± 2.3	15.5 ± 2.9	14.3 ± 2.1	0.0622
Seeing a mental health professional (%)[3,6]	1.5 ± 0.6	3.6 ± 1.7	1.9 ± 0.7	1.8 ± 0.7	0.4 ± 0.2	0.3255
Age (y)[3]	37.9 ± 1.0	39.1 ± 0.9	41.2 ± 0.9	44.9 ± 1.0	46.8 ± 1.1	<0.0001
Mental component score[3]						
Unadjusted	50.2 ± 0.6	50.1 ± 0.6	50.7 ± 0.6	50.7 ± 0.5	50.9 ± 0.6	0.829
Partially adjusted[7]	46.9 ± 2.8	46.6 ± 2.7	46.9 ± 2.8	47.1 ± 2.8	46.9 ± 2.9	0.966
Fully adjusted[8]	48.7 ± 2.6	48.2 ± 2.5	48.5 ± 2.6	48.6 ± 2.6	48.5 ± 2.7	0.968
Physical component score[3]						
Unadjusted	50.3 ± 0.6	50.5 ± 0.6	51.2 ± 0.5	50.5 ± 0.5	50.6 ± 0.6	0.765
Partially adjusted[7]	49.7 ± 2.3	49.5 ± 2.1	50.3 ± 2.3	50.0 ± 2.3	49.9 ± 2.4	0.884
Fully adjusted[8]	50.7 ± 2.2	50.4 ± 2.0	51.2 ± 2.1	50.7 ± 2.2	50.8 ± 2.2	0.867

[1] SES, socioeconomic status. Values in parentheses are ranges.
[2] Total n−3 LCPUFAs is the sum of eicosapentaenoic, docosapentaenoic, and docosahexaenoic acids.
[3] Values are $\bar{x}$ ± SEM.
[4] Defined as a family income of ≥$50,000 per annum.
[5] Defined as having a score ≥8 on the AUDIT (Alcohol Use Disorders Identification Test) questionnaire.
[6] Visited a social worker, psychologist, or counselor in the past 4 wk.
[7] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96 (deprivation scale), family income, education, smoking, hazardous drinking, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, and age category × hazardous drinking interactions by using survey linear regression.
[8] Adjusted for sex, age category, ethnicity, BMI category, season of blood collection, urban or rural dwelling, marital status, labor force status, NZDep96, family income, education, smoking, hazardous drinking, diabetes, asthma, use of blood pressure medication, and sex × NZDep96, sex × education, age category × labor force status, age category × family income, age category × hazardous drinking, age category × diabetes, and age category × asthma interactions by using survey linear regression.

the intake of fish or n−3 fatty acids after adjustment for a number of confounding variables (47).

The only significant positive trend detected for the mental component score was across the quintiles of the ratio of eicosapentaenoic to arachidonic acids. We examined the association between the mental component score and several serum fatty acids; thus, it is possible that the association was due to chance. Moreover, the results from a systematic review showed that participants with depression had little improvement in depressive symptoms after supplementation with n−3 long-chain polyunsaturated fatty acids (14).

The cross-sectional design of our study limited our ability to infer that the association between n−3 long-chain polyunsaturated fatty acids and physical component score is causal. It is possible that a decline in physical well-being leads to a poorer diet, with less fish, and a lower proportion of n−3 long-chain polyunsaturated fatty acids in serum phospholipids. A fatty acid measurement was not completed for every participant in the NNS97. A comparison of the characteristics of participants who did or did not have a fatty acid measurement showed several statistically significant differences. Although the magnitude of the differences were small, it is possible that our results are biased from the general population. A major strength of our study was that the associations between serum phospholipid n−3 long chain polyunsaturated fatty acids were adjusted for the effects of a number of lifestyle variables that influence the mental and physical component scores.

The results from this population-based survey showed that those with a higher proportion of eicosapentaenoic acid and a higher ratio of eicosapentaenoic to arachidonic acid had better self-reported physical health. The association has strong biological plausibility and warrants further investigation. The association between n−3 long-chain polyunsaturated fatty acids and self-reported mental well-being was not as consistent.

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