# US Family Physicians Overestimate Personal $\omega$ -3 Fatty Acid Biomarker Status: Associations with Fatty Fish and $\omega$ -3 Supplement Intake

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#### Abstract

**Background:** The health benefits of  $\omega$ -3 (n–3) fatty acids are well established. Only a small percentage of Americans consume the recommended amounts of fatty fish, the main dietary source of  $\omega$ -3 fatty acids, and most have low  $\omega$ -3 fatty acid blood concentrations.

**Objective:** We aimed to measure biomarkers of long-chain  $\omega$ -3 fatty acid (EPA and DHA) status among family physicians, and determine whether having their  $\omega$ -3 status tested would influence attitudes and patient recommendations.

**Methods:** Family physicians attending a medical conference (n = 340) completed an  $\omega$ -3 intake survey and had a finger stick blood sample taken.  $\omega$ -3 Index, percentage of  $\omega$ -6 (%n–6) in highly unsaturated fatty acids (HUFAs), and EPA:arachidonic acid (AA) ratio were calculated from whole blood fatty acid profiles. Post-conference, a subsample of participants (n = 100) responded to a survey regarding attitudes and recommendations about  $\omega$ -3s.

**Results:** Average age (mean  $\pm$  SEM) of participants was 48.0  $\pm$  0.7 y and 59% were women. Average  $\omega$ -3 Index was 5.2%  $\pm$  0.1%, %n–6 in HUFA was 75%  $\pm$  0.4%, and EPA:AA ratio was 0.076  $\pm$  0.004. 57% of family physicians reported consuming <2 servings/wk of fatty fish, and 78% reported using  $\omega$ -3 supplements  $\leq$ 1/wk. Although 51% believed  $\omega$ -3 status was in a desirable range, only 5% had an  $\omega$ -3 Index  $\geq$ 8%. Biomarkers of  $\omega$ -3 status were significantly associated with fatty fish intake and supplement use, and were correlated (R<sup>2</sup> ranging from 0.59 to 0.77). Physicians who had  $\omega$ -3 status tested (n = 65) were more likely to agree with statements affirming the health benefits of  $\omega$ -3 fatty acids and more willing to recommend  $\omega$ -3 fatty acids to their patients (P = 0.004).

**Conclusions:** Blood concentrations of  $\omega$ -3 fatty acids in family physicians were below recommendations, and were associated with fatty fish intake and  $\omega$ -3 supplement use. There was a discrepancy between perceived and actual  $\omega$ -3 status. Increased awareness of personal  $\omega$ -3 status among physicians may facilitate patient communication and recommendations about  $\omega$ -3 fatty acid intake. This trial was registered at clinicaltrials.gov as, NCT03056898. *Curr Dev Nutr* 2018;2:nzx007.

# Introduction

As of 2017, it is estimated that 92.1 million adults living in the United States have  $\geq 1$  form of cardiovascular disease (CVD). By 2030, 43.9% of adults are expected to have some form of CVD, incurring an estimated \$1.2 trillion (2012 US \$) in total direct and indirect healthcare costs (1). Lifestyle factors, including nutrient intake, dietary patterns, and physical activity, are important in CVD prevention and treatment through effects on modifiable risk factors (2). Long-chain  $\omega$ -3 PUFAs, specifically EPA (C20:5n–3) and DHA (C22:6n–3), have an established role in supporting cardiovascular health (3, 4). Adequate Intakes have been set for  $\alpha$ -linolenic acid (ALA, C18:3n–3) because it is an essential fatty acid precursor for EPA and DHA (5, 6). However, the rates of desaturation and elongation of ALA to EPA, and subsequently



**Keywords:** omega-3 status, physicians, eicosapentaenoic acid, EPA, docosahexaenoic acid, DHA, fatty fish intake, omega-3 supplement use

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Supplemental Materials 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/cdn/. Address correspondence to NVM (e-mail: nathan.matusheski@dsm.com).

Abbreviations used: AA, arachidonic acid; CHD, coronary heart disease; CVD, cardiovascular disease; HUFA, highly unsaturated long-chain fatty acids; %-6, percentage of  $\omega$ -6 fatty acids. to DHA, are low (7, 8) and have been found to be affected by diet, sex, and genotype (8, 9). As such, consumption of dietary or supplemental sources of EPA and DHA remains the most effective way to increase the concentrations of these fatty acids in the human bloodstream (10).

A recent meta-analysis of 19 prospective cohort studies from 16 countries found a significant relation between fatal coronary heart disease (CHD) and long-chain  $\omega$ -3 status, with each standard deviation increase in EPA, DHA, or docosapentaenoic acid associated with an approximate 9% reduction in fatal CHD (11). In another publication, a meta-analysis of 16 prospective cohort studies found that higher EPA and DHA intake from foods and supplements was associated with an 18% reduction in risk for any cardiovascular event, and a meta-analysis of randomized controlled trials identified a significant risk reduction in CHD following EPA and DHA supplementation among higher-risk populations including those with elevated triglyceride (>150 mg/dL) or LDL cholesterol concentrations (>130 mg/dL; 12). A recent metaanalysis of 14 randomized controlled trials including 71,899 subjects taking EPA and DHA supplements for  $\geq 6$  mo noted a modest reduction in cardiac death (13). A science advisory from the American Heart Association recently confirmed that there is a low risk of major adverse effects, including bleeding, and that  $\omega$ -3 supplementation is reasonable for 1) secondary prevention of CHD and sudden cardiac death in patients with prevalent CHD, and 2) secondary prevention of outcomes in patients with heart failure (4). For the general population, authoritative bodies continue to recommend consumption of EPA and DHA from  $\geq 2$ servings fatty fish/wk (14-17). Despite these recommendations, most Americans continue to have low fish intake (18, 19), and as a result do not have blood concentrations of EPA and DHA associated with cardioprotection (20-22).

Physicians and other healthcare providers are a leading source of information about  $\omega$ -3 fatty acids and other nutrients (23, 24). However, research suggests that US medical schools do not provide adequate nutrition education training (25, 26). Therefore, it is possible that many physicians lack a comprehensive view of the research on  $\omega$ -3s and of the importance of fatty fish and  $\omega$ -3 consumption for general and cardiovascular health. Likewise, they may not consume adequate amounts of  $\omega$ -3 fatty acids in their own diets as a result.

Various biomarkers have been reported for the measurement of  $\omega$ -3 status. The  $\omega$ -3 Index is commonly used, and quantifies the concentration of EPA and DHA as a proportion of total erythrocyte fatty acids. A cardioprotective range of  $\geq$ 8% has been suggested by Harris and von Schacky (20, 27). Another approach quantifies the relative proportions of  $\omega$ -3 and  $\omega$ -6 fatty acids within the pool of long-chain highly unsaturated fatty acids (HUFAs). HUFAs are defined as fatty acids with  $\geq$ 20 carbons (20 or 22) and  $\geq$ 3 (4, 5, or 6) carbon-carbon double bonds. This biomarker has been presented as either percentage of n-3 or percentage of n-6 (%n-6) in HUFAs, which are reciprocals and thus have an inverse relation (28). In our research, we express this biomarker as %n−6 in HUFAs. A cardioprotective range of <50% n−6 in HUFAs has been suggested based on estimation of tissue HUFA concentrations and relation with CHD mortality using ecologic data from 38 countries (29). An even more specific marker quantifies the ratio of EPA to arachidonic acid (AA) 30). An EPA:AA ratio of >0.3 has been suggested as a cardioprotective range because a ratio <0.3 has been found to be predictive of cardiovascular events due to peripheral artery disease (31) and highrisk plaque (32). While each of these biomarkers expresses  $\omega$ -3 status differently, it seems likely that they would respond similarly to  $\omega$ -3 intake. However, only in rare instances have these biomarkers been compared within the biological specimens of the same subject population.

We hypothesized that  $\omega$ -3 status among healthcare practitioners, assessed with different biomarkers, would be below previously suggested cardioprotective ranges, and would be related to fatty fish and  $\omega$ -3 supplement intake. We also hypothesized that attitudes toward patient communication and recommendations for  $\omega$ -3s would vary depending upon their willingness to have their  $\omega$ -3 concentrations tested.

### Methods

# ω-3 Status Assessment

Attendees of an annual medical conference who visited a DSM exhibitor booth and had their badges scanned (n = 479) were asked to volunteer in a research study to learn their  $\omega$ -3 Index. Of the 387 individuals who agreed to participate, professional affiliations were indicated as family physician (n = 340), internal medicine (n = 1), physician assistant (n = 1), nurse practitioner (n = 8), other (n = 36), or left blank (n = 1). Because of the low numbers of individuals in the nurse practitioner, physician assistant, and internal medicine categories, and uncertainty about other affiliations, only family physicians' (n = 340) data were analyzed. All participants signed an informed consent form (New England IRB #20160824, Jul 20, 2016; see Supplemental Material 1), completed a survey of dietary fatty fish intake and  $\omega$ -3 supplement use (see Supplemental Material 2), and were asked whether they thought that their  $\omega$ -3 status would be in a desirable range. Sample collection and fatty acid analysis were conducted in collaboration with OmegaQuant, LLC (Sioux Falls, SD) using a dried whole-blood spot as previously described by Harris and colleagues (33-36). A whole blood sample (finger stick) was taken by a certified professional (InHouse Physicians, St. Charles, IL) and spotted onto a filter paper sample collection card pre-treated with a multi-component antioxidant cocktail. Blood samples, informed consent forms, and dietary surveys were shipped to OmegaQuant, LLC for fatty acid analysis, data collation, and anonymization. Erythrocyte  $\omega$ -3 Index was calculated from whole blood fatty acid concentrations using a previously described conversion equation (35). The complete

# **TABLE 1** Characteristics of the sample population and responses to survey questions $(n = 340)^{1}$

#### Parameter

340
200 (59%)
$48\pm0.7$
194 (57%)
146 (43%)
265 (78%)
44 (13%)
31 (9%)
173 (51%)

<sup>1</sup>Values are n (%) or means  $\pm$  SEs. serv., servings.

<sup>2</sup>1 participant did not disclose their sex, n = 339.

<sup>3</sup>6 participants did not disclose their age, n = 334.

fatty acid profile of each dried whole blood sample was also obtained and utilized to calculate the %n–6 in HUFA (28, 37) and the EPA:AA ratio (30). One week after the conference, 271 family physicians who visited the DSM booth (regardless of whether they had their  $\omega$ -3 concentrations measured) were randomly invited and offered a \$20 inducement to participate in an anonymous online follow-up survey including questions about their attitudes about and the frequency of their  $\omega$ -3 patient recommendations, and 100 completed the survey. Statistical analyses of anonymized data were conducted with the use of R version 3.4.0 (38). The influence of fatty fish intake and  $\omega$ -3 supplement use on measures of  $\omega$ -3 status was analyzed using 2-factor ANOVA ( $\alpha = 0.05$ ) with Tukey's honestly significant difference test for multiple comparisons. Because of skewness on inspection of the data distribution, EPA:AA ratio was log-transformed prior to statistical analyses. The trial was registered with clinicaltrials.gov, NCT03056898.

# Results

The average age of the family physicians was  $48.0 \pm 0.7$  y (mean  $\pm$  SEM) and 59% were women (**Table 1**). 57% of family physicians reported not consuming the recommended  $\geq 2$  servings fatty fish/wk and 78% reported using an  $\omega$ -3 supplement  $\leq 1$  time/wk. 51% of subjects believed that their  $\omega$ -3 Index would be within a desirable range.

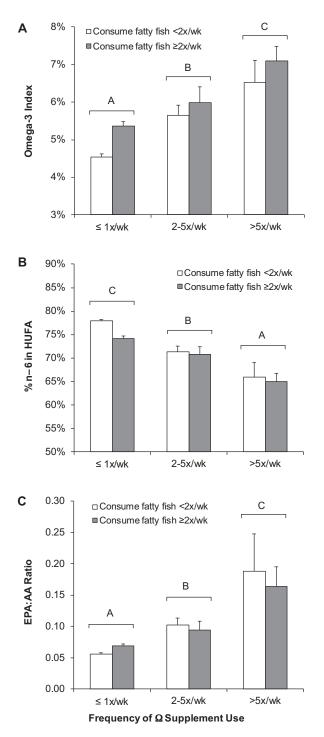
Average whole blood fatty acid concentrations are shown in **Table 2**. Average  $\omega$ -3 Index was 5.2%  $\pm$  0.1%, was positively associated with age (P = 0.001), and did not differ between sexes.  $\omega$ -3 index increased with reported fatty fish consumption (P < 0.0001) and  $\omega$ -3 supplement use (P < 0.0001; **Figure 1**A). There was no significant interaction between fatty fish and supplement consumption. Only 17 subjects (5% of those tested) had  $\omega$ -3 Index values within the suggested cardioprotective range of  $\geq$ 8%. The number of individuals within each

**TABLE 2** Whole blood fatty acid concentrations and quantification of  $\omega$ -3 status within fatty fish and  $\omega$ -3 supplement intake categories<sup>1</sup>

Fatty acid	Overall $(n = 340)$	Consume fatty fish <2 times/wk (n = 194)	Consume fatty fish ≥2 times/wk (n = 146)	Take $\omega$ -3 supplements $\leq 1$ time/wk (n = 265)	Take ω-3 supplements 2–5 times/wk (n = 44)	Take ω-3 supplements >5 times/wk (n = 31)
SFAs, %						
C14:0	1.0 ± 0.02	$1.0 \pm 0.03$	1.0 ± 0.04	1.0 ± 0.03	$1.0~\pm~0.07$	1.0 ± 0.06
C16:0	$21.6 \pm 0.09$	$21.6 \pm 0.12$	$21.5 \pm 0.11$	$21.6 \pm 0.10$	$21.5 \pm 0.20$	$21.5 \pm 0.30$
C18:0	$11.2 \pm 0.05$	$11.2 \pm 0.07$	$11.2 \pm 0.08$	11.2 ± 0.06	11.1 ± 0.16	10.9 ± 0.20
C20:0	$0.2 \pm 0.00$	$0.2 \pm 0.00$	$0.2 \pm 0.00$	$0.2 \pm 0.00$	$0.2 \pm 0.01$	$0.2 \pm 0.01$
C22:0	$0.6 \pm 0.01$	$0.5 \pm 0.01$	$0.6 \pm 0.01$	$0.6 \pm 0.01$	$0.5 \pm 0.02$	$0.6 \pm 0.02$
C24:0	$0.7 \pm 0.02$	$0.6 \pm 0.02$	$0.7 \pm 0.02$	$0.7 \pm 0.02$	$0.7 \pm 0.02$	$0.7 \pm 0.02$
Total	$35.2 \pm 0.02$	$35.3 \pm 0.12$	$35.2 \pm 0.13$	$35.3 \pm 0.10$	$35.1 \pm 0.21$	$35.0 \pm 0.34$
MUFAs, %	00.2 ± 0.07	00.0 ± 0.12	00.2 ± 0.10	00.0 ± 0.10	00.1 ± 0.21	00.0 ± 0.01
C16:1–7	0.8 ± 0.02	$0.8 \pm 0.03$	0.8 ± 0.03	0.8 ± 0.03	$0.8 \pm 0.05$	0.9 ± 0.08
C18:1n-9	$19.4 \pm 0.12$	$19.4 \pm 0.16$	$19.3 \pm 0.19$	$19.3 \pm 0.14$	$19.3 \pm 0.37$	19.7 ± 0.49
C20:1n-9	$0.3 \pm 0.00$	$0.3 \pm 0.01$	$0.3 \pm 0.01$	$0.3 \pm 0.01$	$0.2 \pm 0.01$	$0.3 \pm 0.01$
C24:1n-9	$0.6 \pm 0.00$	$0.6 \pm 0.01$	$0.6 \pm 0.01$	$0.6 \pm 0.01$	$0.2 \pm 0.01$ $0.6 \pm 0.05$	$0.5 \pm 0.01$ $0.7 \pm 0.05$
Total	$21.1 \pm 0.13$	$21.1 \pm 0.17$	$21.0 \pm 0.02$	$21.0 \pm 0.02$	$21.0 \pm 0.38$	$21.5 \pm 0.52$
trans Fatty acids, %	21.1 ± 0.15	21.1 ± 0.17	21.0 ± 0.20	21.0 ± 0.14	21.0 ± 0.30	21.3 ± 0.32
C16:1n–7t	$0.1 \pm 0.00$	$0.1 \pm 0.00$	$0.1 \pm 0.00$	$0.1 \pm 0.00$	0.1 ± 0.01	0.1 ± 0.01
C18:1t	$0.1 \pm 0.00$ $0.6 \pm 0.01$	$0.1 \pm 0.00$ $0.6 \pm 0.02$	$0.1 \pm 0.00$ $0.6 \pm 0.02$	$0.1 \pm 0.00$ $0.6 \pm 0.01$	$0.1 \pm 0.01$ $0.6 \pm 0.05$	$0.1 \pm 0.01$ $0.5 \pm 0.03$
C18:2n-6t	$0.3 \pm 0.01$	$0.0 \pm 0.02$ $0.3 \pm 0.01$	$0.0 \pm 0.02$ $0.3 \pm 0.01$	$0.3 \pm 0.01$	$0.3 \pm 0.03$	$0.3 \pm 0.03$ $0.3 \pm 0.02$
Total	$1.0 \pm 0.01$	$1.0 \pm 0.01$	$1.0 \pm 0.01$	$1.0 \pm 0.01$	$1.0 \pm 0.02$	$0.3 \pm 0.02$ $0.9 \pm 0.04$
$\omega$ -6 PUFAs, %	$1.0 \pm 0.02$	$1.0 \pm 0.02$	$1.0 \pm 0.02$	$1.0 \pm 0.02$	$1.0 \pm 0.00$	0.7 ± 0.04
C18:2n-6	24.0 ± 0.14	24.1 ± 0.17	23.9 ± 0.24	24.1 ± 0.16	23.9 ± 0.41	23.4 ± 0.52
C18:3n-6	$0.3 \pm 0.01$	$0.3 \pm 0.01$	$0.3 \pm 0.01$	$0.3 \pm 0.01$	$0.3 \pm 0.02$	$0.3 \pm 0.02$
C10:31-0 C20:2n-6	$0.3 \pm 0.01$ $0.3 \pm 0.00$	$0.3 \pm 0.01$ $0.3 \pm 0.00$	$0.3 \pm 0.01$ $0.3 \pm 0.00$	$0.3 \pm 0.01$ $0.3 \pm 0.00$	$0.3 \pm 0.02$ $0.3 \pm 0.01$	$0.3 \pm 0.02$ $0.3 \pm 0.01$
C20:3n-6	$0.3 \pm 0.00$ $1.4 \pm 0.02$	$0.3 \pm 0.00$ $1.5 \pm 0.02$	$0.3 \pm 0.00$ 1.4 ± 0.02	$0.3 \pm 0.00$ 1.4 ± 0.02	$0.3 \pm 0.01$ 1.4 ± 0.04	$1.3 \pm 0.01$
C20:31-6 C20:4n-6	$1.4 \pm 0.02$ 10.0 ± 0.10	$1.3 \pm 0.02$ 10.1 ± 0.13	$9.9 \pm 0.16$	$1.4 \pm 0.02$ 10.2 ± 0.11	$9.8 \pm 0.30$	
						$9.0 \pm 0.41$
C22:4n-6	$1.3 \pm 0.02$	$1.3 \pm 0.02$	$1.2 \pm 0.03$	$1.3 \pm 0.02$	$1.1 \pm 0.05$	$0.9 \pm 0.05$
C22:5n-6	$0.4 \pm 0.04$	$0.4 \pm 0.05$	$0.5 \pm 0.06$	$0.4 \pm 0.04$	$0.4 \pm 0.10$	$0.5 \pm 0.13$
Total	37.7 ± 0.15	37.9 ± 0.21	37.4 ± 0.23	$38.0\pm0.16$	37.1 ± 0.44	35.7 ± 0.62
ω-3 PUFAs, %	0 ( ) 0 01	0 ( ) 0 01		0 ( ) 0 01	0 ( ) 0 0 (	0 (   0 0 (
C18:3n-3	$0.6 \pm 0.01$	$0.6 \pm 0.01$	$0.6 \pm 0.02$	$0.6 \pm 0.01$	$0.6 \pm 0.04$	$0.6 \pm 0.04$
C20:5n-3	$0.7 \pm 0.03$	$0.7 \pm 0.03$	$0.8 \pm 0.04$	$0.6 \pm 0.02$	$0.9 \pm 0.08$	$1.4 \pm 0.15$
C22:5n-3	$1.1 \pm 0.01$	1.0 ± 0.02	1.1 ± 0.02	$1.0 \pm 0.01$	1.2 ± 0.04	$1.3 \pm 0.05$
C22:6n-3	$2.7 \pm 0.05$	$2.4 \pm 0.06$	$3.0 \pm 0.08$	$2.5 \pm 0.05$	$3.0 \pm 0.14$	$3.5 \pm 0.17$
Total	$5.0\pm0.08$	4.7 ± 0.09	$5.4~\pm~0.12$	4.7 ± 0.07	5.7 ± 0.22	$6.8~\pm~0.32$
Biomarkers of $\omega$ -3 status	75	74	70 . 0 /	74		(F ) ( F
%n–6 in HUFA	75 ± 0.4	76 ± 0.5	73 ± 0.6	76 ± 0.3	71 ± 1.0	65 ± 1.7
EPA:AA ratio	0.076 ± 0.004	$0.071 \pm 0.005$	0.084 ± 0.006	$0.061 \pm 0.002$	0.099 ± 0.009	0.174 ± 0.031
$\omega$ -3 Index <sup>2</sup>	$5.2 \pm 0.1$	$4.8 \pm 0.1$	$5.7 \pm 0.1$	$4.9 \pm 0.1$	$5.8 \pm 0.2$	$6.9 \pm 0.3$

 $^1$ Values are % total fatty acids or means  $\pm$  SEs. AA, arachidonic acid; HUFA, highly unsaturated fatty acids.

<sup>2</sup>Expressed as  $\omega$ -3 index of erythrocytes, calculated as described by Harris and Polreis (35).



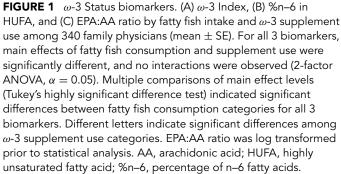


TABLE 3	Number of physicians within each subgroup of
self-repor	ted fatty fish and dietary supplement intake <sup>1</sup>

	Consuming fatty fish ≤1 time/wk	Consuming fatty fish ≥2 times/wk
$\omega$ -3 Supplements $\leq$ 1 time/wk	156 (0.6%)	109 (4.6%)
$\omega$ -3 Supplements 2–5 times/wk	25 (8.0%)	19 (5.3%)
$\omega$ -3 Supplements >5 times/wk	13 (23.1%)	18 (27.8%)

<sup>1</sup>Values are *n* (%). The percentage of each subgroup with the suggested cardioprotective range of  $\omega$ -3 Index  $\geq$ 9% is shown in parentheses. *n* = 340.

fatty fish and supplement use subgroup, and percentage of each subgroup with  $\omega$ -3 Index  $\geq$  8%, are shown in Table 3.

Average %n–6 in HUFA was 75%  $\pm$  0.4% (Table 2), was negatively associated with age (P < 0.0001), and did not differ between sexes (74.5%  $\pm$  0.6% for men and 75.0%  $\pm$  0.5% for women). %n–6 in HUFA decreased with increased reported fatty fish consumption (P < 0.0001) and  $\omega$ -3 supplement use (P < 0.0001; Figure 1B). There was no significant interaction between fatty fish and supplement consumption. Only 2 subjects had %n–6 in HUFA values within the suggested cardioprotective range of <50% (data not shown).

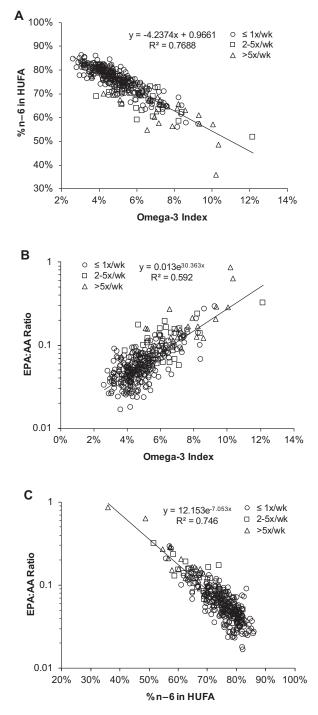
The average EPA:AA ratio was  $0.076 \pm 0.004$  (Table 2), was positively associated with age (P < 0.0001), and did not differ between sexes ( $0.074 \pm 0.005$  for men and  $0.074 \pm 0.003$  for women). The EPA:AA ratio increased with increased reported fatty fish consumption (P = 0.001) and  $\omega$ -3 supplement use (P < 0.0001; Figure 1C). There was no significant interaction between fatty fish and supplement consumption. Only 3 subjects had EPA:AA ratios within the suggested cardioprotective range of >0.3 (data not shown).

Significant relation were observed among the 3 biomarkers of  $\omega$ -3 status that we calculated.  $\omega$ -3 index and %n-6 in HUFAs were inversely related (P < 0.0001) with an unadjusted R<sup>2</sup> of 0.7688 (**Figure 2A**).  $\omega$ -3 index and log EPA:AA ratio were positively related (P < 0.0001) with an unadjusted R<sup>2</sup> of 0.592 (Figure 2B). The %n-6 in HUFAs and log EPA:AA ratio were inversely related (P < 0.0001) with an unadjusted R<sup>2</sup> of 0.746 (Figure 2C).

Responses to the follow-up survey revealed differences in  $\omega$ -3 patient recommendations depending upon whether the physicians had agreed to have their  $\omega$ -3 concentrations tested (**Table 4**). Physicians who had their  $\omega$ -3 status tested were more likely to agree with statements affirming the health benefits of  $\omega$ -3 fatty acids and were more willing to recommend  $\omega$ -3 fatty acids to their patients.

## Discussion

Blood concentrations of  $\omega$ -3 fatty acids among family physicians were below previously suggested cardioprotective ranges. A discrepancy was observed between physicians' perceptions of their own  $\omega$ -3 status and actual tested values. About half of the population thought their  $\omega$ -3 Index would be within a desirable range. However, only 17 individuals (5% of the population) had an  $\omega$ -3 Index  $\geq$ 8%, while only 2 individuals had <50% n–6 in HUFAs and only 3 individuals had an EPA:AA ratio >0.3. This finding suggests that many physicians are unaware of their own  $\omega$ -3 status and how it relates to their daily dietary habits. The observation that only small numbers of individuals met the suggested



**FIGURE 2** Associations of (A)  $\omega$ -3 Index with %n-6 in HUFA; (B)  $\omega$ -3 Index with EPA:AA ratio; and (C) %n-6 in HUFA with EPA:AA ratio. AA, arachidonic acid; HUFA, highly unsaturated fatty acid; %n-6, percentage of n-6 fatty acid.

cardioprotective ranges for each of the 3 biomarkers may indicate that current criteria are too stringent. The suggested cardioprotective ranges for the biomarkers we examined were developed separately by different research groups based upon different population-wide associations or clinical outcomes. Other nutrients are known to be insufficient or deficient in relatively high percentages of the US population, and estimates of deficiency prevalence also depend upon the cutoffs used. For example, estimates of vitamin D inadequacy in the US population vary widely depending upon which serum 25-hydroxyvitamin D cutoff is used (39).

The average  $\omega$ -3 Index in this population of physicians (5.2%) was higher than that of the general US population (typically ranging from 3.2–5.4%, with most studies ranging from 4–5%), but lower than in regions of the world with high fish intakes (21, 22). The association of increased  $\omega$ -3 concentrations with age has been previously observed elsewhere (40). The implications of this association for determining cardioprotective  $\omega$ -3 biomarker ranges may require further research. 43% of physicians reported consuming fatty fish >2 times/wk, which is higher than the general US population (18).

Not surprisingly, fatty fish intake and  $\omega$ -3 supplement use were each independently associated with increased  $\omega$ -3 status, regardless of which biomarker was used.  $\omega$ -3 supplement use was associated with a notably larger magnitude of difference in the  $\omega$ -3 concentrations shown in Figure 1. In addition, a greater proportion of regular supplement users had an  $\omega$ -3 Index within the suggested cardioprotective range (for example,  $\omega$ -3 Index  $\geq$ 8%), regardless of their reported fatty fish consumption (Table 3). Although the number of individuals was small in these categories, this observation seems reasonable, given that  $\omega$ -3 supplementation has been shown to make a significant contribution to the usual intakes of  $\omega$ -3 fatty acids (18) and the effect of EPA and DHA supplementation on  $\omega$ -3 status is well-established (41).

The relation we observed among the  $\omega$ -3 status biomarkers were informative. The  $\omega$ -3 Index is a marker of EPA and DHA enrichment in the erythrocyte and considered a proxy for tissue concentrations (20). The %n-6 in HUFAs provides the proportion of  $\omega$ -6 in the total longchain HUFA pool (including  $\omega$ -3 and  $\omega$ -6 long-chain HUFAs). This information reflects substrate availability for pro-inflammatory (n-6) and anti-inflammatory (n-3) precursors (42). The EPA:AA ratio provides information on 2 key fatty acid substrates (30). Each of these markers have been correlated with clinical outcomes and they are considered to have prognostic implications for assessing cardiovascular risk (20, 29, 31, 32). Mathematically, it is not surprising to observe log-linear relations between the EPA:AA ratio and the other markers that are a proportion of a total, either total fatty acids or total long-chain HUFAs. Each of these biomarkers was similarly associated with fatty fish and  $\omega$ -3 supplement intake and they were consistent with one another. For example, an  $\omega$ -3 Index of  $\geq$ 8% has been suggested as the cardioprotective range, and would equate to about 60% n-6 in HUFAs (Figure 2A) or an EPA:AA ratio of about 0.15 (Figure 2B) in our subject population. 50% n–6 in HUFA would equate to an  $\omega$ -3 Index of ~11–12% (Figure 2A) and an EPA:AA ratio of about 0.3 (Figure 2C). The numerical relation we observed between  $\omega$ -3 Index and %n-6 in HUFAs was similar to that previously described (28). Using these 3 approaches, and the suggested cardioprotective ranges established for each, similar conclusions were derived for this study population. Taken together, a reasonable minimum criterion of  $\omega$ -3 adequacy may fall within an  $\omega$ -3 Index range of 8-12%.

The observation that physicians who had their  $\omega$ -3 concentrations tested were more likely to agree with affirmative statements about  $\omega$ -3s and recommend them to patients suggests that increased awareness of personal  $\omega$ -3 status may be a valuable tool in facilitating patient communication and recommendations about dietary EPA and DHA intake.

# **TABLE 4** Attitudes of physicians toward patient $\omega$ -3 recommendations by measurement of $\omega$ -3 status<sup>1</sup>

	Had ω-3 status tested (n = 65)	Did not have ω-3 status tested (n = 35)	P value <sup>2</sup>
As a result of seeing and/or experiencing activities and information on $\omega$ -3 at the conference, to what percentage of your patients would you be willing to recommend increasing intake of $\omega$ -3 fatty acids? <sup>3</sup>	60.3 ± 3.6	41.3 ± 5.2	0.004
Below are some statements that you may or may not agree with. Please indicate your personal agreement with each statement by considering each at face value. We are interested in your initial reactions; there is no right or wrong answer <sup>4</sup>			
I am more educated on the benefits of $\omega$ -3 than in the past	$7.69 \pm 0.22$	$7.37 \pm 0.32$	0.408
l am a strong proponent of $\omega$ -3 fatty acid supplementation	$7.32 \pm 0.27$	6.43 ± 0.37	0.056
I am interested in learning more about how $\omega$ -3s can benefit my patients' health	$7.60 \pm 0.25$	$6.62 \pm 0.38$	0.036
It is a productive use of my time with a patient to talk about $\omega$ -3 supplementation	$7.12 \pm 0.24$	$6.00 \pm 0.39$	0.018
The body needs $\omega$ -3s to function, yet the average American is well below current recommendations	7.75 ± 0.25	7.05 ± 0.31	0.082
Insufficient concentrations of $\omega$ -3 can lead to serious health complications	$7.05 \pm 0.26$	$6.77 \pm 0.35$	0.535
Most of my patients consume enough fatty fish to achieve sufficient concentrations of $\omega$ -3 fatty acid	3.63 ± 0.28	3.60 ± 0.35	0.946
More of my patients are taking $\omega$ -3 supplements than in the past	$6.27 \pm 0.28$	$6.48 \pm 0.38$	0.660
I have the tools (i.e., patient guidelines, materials) to make the best recommendation of $\omega$ -3 supplementation for my patients	6.38 ± 0.22	5.71 ± 0.36	0.117
I am inclined to recommend $\omega$ -3 supplements to more of my patients in the future	$7.85 \pm 0.23$	$6.80\ \pm\ 0.37$	0.020

 $^{2}$ t Test with independent samples, assuming unequal variance.

<sup>3</sup>Percentages.

<sup>4</sup>Statements are scored on a scale of 1–10, where 1 = completely disagree and 10 = completely agree.

This study has several limitations. The population consisted of a cross-sectional convenience sample of physicians visiting an exposition booth with information about  $\omega$ -3 fatty acids. This self-selected group may have had greater interest in consuming or prescribing  $\omega$ -3s than the general physician population, which may have influenced  $\omega$ -3 status and patient recommendations. The analysis of fatty acids in whole blood, as used in this study, may yield slightly different results compared to measurement of erythrocyte fatty acids. However, this relation is wellestablished and a correction factor was applied (35). EPA:AA ratio has been typically measured in the total fatty acids of the serum of fasted patients. Subjects were not fasted in this case, so we were also unable to control for proximate intake of fats. However, EPA and DHA concentrations in the triglyceride fraction of plasma are known to be lower than those of the phospholipid fraction (43), so we may expect slight underestimation of  $\omega$ -3 status in the whole blood in the post-prandial state. That said, fasting has previously been shown not to have a significant impact on measurement of blood concentrations of EPA and DHA (44).

Our findings suggest an opportunity to facilitate physician-patient conversations about dietary  $\omega$ -3 fatty acid intake and health by way of  $\omega$ -3 testing. We found the  $\omega$ -3 status of family physicians to be higher than that of the general US population. Fatty fish consumption has been associated with the proportion of EPA and DHA in blood lipids (45). In this study, self-reported fatty fish intake and  $\omega$ -3 supplement use were significantly associated with all 3 markers. The association was greater for  $\omega$ -3 supplement use and no interaction was observed between fatty fish intake and  $\omega$ -3 supplement use. Physicians who had their  $\omega$ -3 status measured were more likely to agree with statements affirming the health benefits of  $\omega$ -3 fatty acids and were more willing to recommend  $\omega$ -3 fatty acids to their patients. Future research should focus on determining the impact of family physician awareness of their own  $\omega$ -3 status and the subsequent influence it may have on their dietary  $\omega$ -3 intake and patient recommendations. Opportunities exist to improve physician awareness of the importance of dietary  $\omega$ -3 intake, diagnostics, and current authoritative dietary and medical recommendations.

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