publication, which obviously reports results from the same study (2), the authors state that they evaluated dietary habits by using a special, repeatable, interviewer-administered semiquantitative food-frequency questionnaire that they developed in their institution, and they quote 2 articles (3, 4) that refer to their CARDIO2000 study. Earlier articles on the CARDIO2000 study (5, 6), however, quote the use of a questionnaire developed by our research team (7).

Other issues aside, the dietary assessment tool is a key element in nutritional epidemiologic studies. Different instruments have different strengths and limitations, and proper documentation of the tools used is essential for the correct interpretation of the results reported. Conflicting references to different questionnaires should not be acceptable.

For the readership of the Journal to fully evaluate the implications of the article, the validation information should be provided or appropriately referenced and an explanation for the conflicting references regarding the dietary questionnaire used should be given.

The questionnaire used in reference 7 represents the work of the author.

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Reply to D Trichopoulos

Dear Sir:

Regarding the letter by Trichopoulos, we would like to clearly state that in our work published in the Journal in 2010 we used a semiquantitative food-frequency questionnaire (FFQ) that was briefly presented in our articles and was not the FFQ implied in the letter. Regarding its history, our FFQ was initially developed in the late 1990s to assess dietary habits of cardiac patients (who participated in the CARDIO2000 study) and included dietary behaviors and food items that are commonly consumed in our population. This FFQ was then extended, validated (1), and used in the present study in acute coronary patients. The sequence of the citations mentioned in the aforementioned letter, none of which were presented in our article, refers to articles that discuss (among several other issues) food habits and behaviors in relation to clinical conditions in the Greek population as well as dietary assessment methods, which were also discussed in our articles. Needless to say that none of the articles mentioned in the letter presented any FFQ nor can it be concluded that they were used as a reference for an FFQ in our studies. Therefore, there is no any inconsistency in our articles.

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Polyunsaturated fatty acid intakes and α-linolenic acid metabolism

Dear Sir:

Maintaining adequate concentrations of the n−3 polyunsaturated fatty acids (PUFAs) eicosapentaenoic (EPA) and docosahexaenoic (DHA) acid in cell membranes is important for optimal tissue function. These fatty acids may be obtained from the diet, principally from oily fish, or by desaturation and elongation of α-linolenic acid (ALA). Metabolic and dietary supplementation studies have shown that conversion of ALA to EPA and DHA is limited in humans (1). However, women of reproductive age are able to synthesize more EPA and DHA, and have higher DHA status than do men (2, 3). Such differences are under endocrine control such that DHA status can be modified in men and women by sex hormone therapy (4, 5). Sex differences in DHA status have

also been found in rats and were associated with differential expression of Δ^6 and Δ^5 desaturases (6, 7).

In the November issue of the Journal, Welch et al (8) describe the effect of differences in dietary n−3 PUFA intake on concentrations of ALA, EPA, docosapentaenoic acid (DPA), and DHA in plasma phospholipids in men and women. They showed higher concentrations of EPA + DPA + DHA compared with ALA in women than in men regardless of dietary n−3 PUFA intake. This is consistent with previous findings that have shown higher EPA and DHA status and greater ALA conversion in women than in men (1). However, the terminology used to describe the relative amounts of ALA to its longer-chain metabolites throughout the article seems likely to mislead readers in regard to the interpretation of the data. The phrase used is "precursor:product ratio," whereas the data are presented as product:precursor. For example, in the title of Table 6 precursor:product ratio is referred to as the ratio of EPA + DPA + DHA to ALA (product:precursor), which is incorrect. The importance of this error is that summarizing the findings as a higher precursor:product ratio in women than in men suggests that the ability of women to convert ALA to longer-chain metabolites is less than in men, although the data show the opposite. Granted, the authors interpret their data as higher conversion in women, but this adds to the confusion.

Welsh et al (8) found significant differences in the product:precursor ratio between dietary groups in both sexes, such that the lowest ratio was in fish eaters and the highest in vegans. If it is assumed that the proportions of n−3 PUFA in plasma phospholipids reflect to some extent capacity for ALA conversion, then Welsh's findings suggest that conversion of ALA to its longer-chain metabolites was inhibited by greater intakes of EPA, DPA, and DHA. Pawlosky et al (9) have shown previously in a mixed group of men and women by kinetic modeling of the metabolism of deuterated n−3 PUFA that consumption of a fish-based diet inhibited conversion of DPA to DHA. Furthermore, consuming a fish-based diet had little effect on conversion of DPA to DHA in men but reduced DHA synthesis by >50% in women (10). Pawlosky et al's findings suggest that the reactions that convert DPA to DHA are sensitive to dietary intakes of n−3 PUFA. Furthermore, these metabolic processes appear to show differential sensitivity to n−3 PUFA intakes between men and women. The findings of Welch et al are in direct agreement with those of Pawlosky et al, but unfortunately the earlier studies are not referred to in Welch's article.

In summary, the findings of Welch et al (8) make a significant contribution to understanding how n−3 PUFA metabolism is modulated in humans by diet and sex. However, the article is weakened by confusing presentation of the observations and by not citing data published previously that would have increased the impact of the research by providing a mechanistic framework for interpreting the findings.

The author did not declare any conflicts of interest.

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Reply to GC Burdge

Dear Sir:

We thank Burdge for his careful reading of our article. Our study had 3 purposes: *1*) to assess detailed n−3 (omega-3) polyunsaturated fatty acid (PUFA) intakes and food sources (plant, marine, and others) in dietary-habit groups representative of eating habits within the UK population (of 14,442 fish-eaters and non-fish-eating groups of meat-eaters, vegetarians, or vegans), *2*) to describe the n−3 PUFA status in these groups, and *3*), to statistically model whether increased estimated conversion of dietary α-linolenic acid (ALA) to plasma long-chain n−3 PUFAs [eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA)] might occur in non-fish-eaters compared with fish-eaters (1). Burdge's comments on the third aspect of this article have been helpful, in particular, noting that the term *precursor-product ratio* should more correctly read *product-precursor ratio* (although the ratio and the data are correctly referred to throughout the article). An erratum has been issued.

In addition to the factors that might influence conversion of ALA to long-chain n−3 PUFAs that were adjusted for in our article (sex, linoleic acid, age, smoking habit, and body size), it was also helpful for Burdge to note that one carefully controlled metabolic study in 10 men and women suggests a further mechanistic reason for our findings of differences in statistically estimated conversion between dietary-habit groups (2). Increasing intake of EPA and DHA by 0.5g/d resulted in a reduction in the efficiency of the biosynthetic processes from DPA to DHA by 46%, suggesting potentially greater competitive inhibition of desaturase expression or activity in people who consume more long-chain n−3 PUFAs (2). In a further subanalysis of their data, Pawlowsky et al (3) also found that sex was important. However, besides this mechanism, other more recent