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.

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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

work in animal and human studies suggests that the dietary linoleic acid:ALA ratio and dose response to ALA may also be important with regard to the relation between ALA intake and long-chain n−3 PUFA status (4–7).

Although further explanations for mechanisms to explain the findings in our observational study are of interest, this should not distract from the fact that substantial differences between intakes and status of long-chain n−3 PUFAs were found within our study in the different diet-habit groups, and the proportion of circulating long-chain n−3 PUFAs was higher in non-fish-eaters than would be expected given intake: intake of total n−3 PUFAs in meat-eaters was 72% of that in fish-eaters and in vegetarians was 70%, whereas the status of meat-eaters was only 92% and of vegetarians was 87% of that of fish-eaters. (For intakes of EPA and DHA, meat-eaters consumed only 12% of that of fish-eaters and vegetarians consumed only 5%.) Our study is also the largest to date to show such detailed population differences in habitual intake and status, particularly for ALA intake.

Unresolved questions are, first, whether the lower long-chain n−3 PUFA status in non-fish-eating vegetarians and meat-eaters observed in this and other studies is of clinical importance and, second, what conditions induce optimum conversion of ALA to long-chain n−3 PUFAs in non-fish-eating populations. To answer these questions, further carefully controlled human intervention studies are needed to measure the relation between intake of ALA and long-chain n−3 PUFA status in those with vegan and vegetarian eating patterns that also take into account the background dietary composition, dose response, age, and body weight and that are of sufficient size and duration to answer these important questions.

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Heritability of serum vitamin D concentrations: twin studies

Dear Sir:

It was with interest that we read the article by Karohl et al (1), which uses a classical twin study design. Serum 25-hydroxyvitamin D [25(OH)D] concentrations were examined in American adult twins to estimate the genetic contribution in determining circulating 25(OH)D concentrations. The difference in correlation of a given phenotype within monozygotic compared with dizygotic twin pairs, or the intraclass correlation (ICC), provides insight into the relative contributions of genetic factors to the phenotype (2). Structural equation modeling and other methods are used to estimate heritability or the proportion of phenotypic variation that is attributable to genetics (2). Elucidating the genetic components involved in regulating 25(OH)D status is a valuable pursuit given the known associations of suboptimal vitamin D status and a wide range of diseases.

Karohl et al (1) reported ICCs for wintertime serum 25(OH)D of $r = 0.69$ for monozygotic twin pairs and $r = 0.29$ for dizygotic twin pairs in a total of 100 twin pairs. Results from a 2008 twin study in the Journal (3) showed ICCs for winter serum 25(OH)D of $r = 0.71$ for monozygotic twin pairs and $r = 0.32$ for dizygotic twin pairs in 99 twin pairs. In the study by Karohl et al, the proportion of trait variation attributable to genetic factors (heritability) was 0.70, which was very similar to the estimate of 0.77 in the study by Orton et al. Only wintertime 25(OH)D concentrations were examined by Orton et al because of the known seasonal fluctuation and highly dominant environmental influence during summer. Given the similarity in subject material, approach, and findings, we find it surprising that the authors did not acknowledge the Orton et al article. Given that it was published in the Journal <2 y ago, we feel it would have been appropriate to mention that the findings confirm those published by Orton et al.

Furthermore, in the Discussion, Karohl et al (1) consider vitamin D metabolic pathway gene candidates potentially responsible for the observed heritability. However, a key step was overlooked. The 1-α hydroxylase enzyme (CYP27B1) is responsible for the rate-limiting conversion of 25(OH)D to the active vitamin D metabolite and is involved in regulatory feedback loops. The study by Orton et al (3)