in other populations and with improved methods of dietary assessment, including objective biomarkers of fish intake such as marine-derived fatty acids, vitamin D and toxins, where appropriate” (1).

We were also careful not to make direct comparisons between the effect sizes for fatty fish and total fish and offered the effect of long-chain omega-3 (n–3) PUFAs as one plausible hypothesis, emphasizing that this needs further testing in future studies. We note that different studies have found differing results for the association with types of fish intake, as we recently reported in a systematic review (2), and such differences are likely explained at least in part by geographic location (including different cooking methods) as shown by meta-analyses reported by 3 independent groups (2–4). With regard to the potential role of contaminants, as well as that of the vitamin D content of fish, which was mentioned by Liu, we discussed these issues in our original article and submit that much more research is needed to tease out the effects and potential interactions among the different possible mechanisms that might be at play in any observed association between fish intake and the risk of type 2 diabetes.

As we discussed, some of our observed effects of an inverse association between fatty fish intake and type 2 diabetes could be the result of confounding by healthier lifestyles among those who consume greater amounts of fatty fish. To overcome this, as far as is possible in epidemiologic research, we adjusted for factors that could be potential confounders, including lifestyle and dietary and socioeconomic factors. We discussed specifically in our strengths and limitations section that despite such comprehensive adjustment we were unable to rule out the potential effects of measurement error and residual confounding, which are virtually universal in nutritional epidemiology. As suggested by Liu, we repeated the analysis examining the distribution of baseline characteristics by fatty fish intake status (intake quartiles). Our original analysis did this by using quartiles of combined fish and shellfish intake, which was shown in our article’s Table 1. This reanalysis showed no difference to the reported HRs. Finally, with regard to Liu’s suggestion to examine the effect of weight change and cut-off, we adjusted for this where appropriate (5). We were also careful not to make direct comparisons between the effect sizes for fatty fish and total fish and offered the effect of long-chain omega-3 (n–3) PUFAs as one plausible hypothesis, emphasizing that this needs further testing in future studies. We discussed specifically in our strengths and limitations section that despite such comprehensive adjustment we were unable to rule out the potential effects of measurement error and residual confounding, which are virtually universal in nutritional epidemiology. As suggested by Liu, we repeated the analysis examining the distribution of baseline characteristics by fatty fish intake status (intake quartiles). Our original analysis did this by using quartiles of combined fish and shellfish intake, which was shown in our article’s Table 1. This reanalysis showed no difference to the reported HRs. Finally, with regard to Liu’s suggestion to examine the effect of weight change and cut-off, we adjusted for this where appropriate (5).

Far more work is still needed to resolve the nature of the association between fish intake and the risk of diabetes. We believe that our study is a step in the right direction, with great heterogeneity in exposure across high- and low-fish-consuming populations.

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REFERENCES


Dietary acid load and risk of hypertension

Dear Sir:

In a recent issue of the Journal, Engberink et al (1) reported on the prospective association between 2 different measures of dietary acid load and hypertension risk during a 6-y follow-up. Unlike 2 other observational studies published so far on the association between dietary acidity and blood pressure or hypertension incidence (2, 3), Engberink et al found no increase in hypertension risk with a higher dietary potential renal acid load (PRAL). According to the authors, these divergent findings might be explained by the relatively more alkalizing diet of the investigated Dutch population (1). We agree with the authors that in healthy adults already consuming a rather alkalizing diet, a further reduction in dietary PRAL might not provide additional benefit with regard to hypertension prevention. However, we suggest that differences in the measurement of dietary intake might also partly explain the dissimilar findings between the 2 recent articles (2, 3) and the study by Engberink et al (1). A single food-frequency questionnaire (FFQ) administered at baseline might possibly miss some of the subtle changes in hypertension risk induced by a long-term higher dietary acid load. Actually, the overall accuracy of the measurement of food intake via FFQ has substantial limitations (4), and diet-disease associations that are detectable when diet is assessed by food records are not necessarily observed when dietary intake data are based on an FFQ (5).

Major dietary components that determine the daily proton load are protein and potassium: a higher sulfate production originating from protein metabolism contributes to the daily acid load and a higher potassium intake (eg, from a diet high in fruit and vegetables) contributes to the daily alkali load. In the Dutch population studied by Engberink et al (1), protein intake increased with higher dietary acid load as expected, whereas potassium intake did not differ between tertiles of PRAL and fruit intake varied only weakly and nonlinearly with dietary acidity. In addition, magnesium intake, which contributes to a lower dietary acidity, increased with increasing PRAL tertiles in the Rotterdam Study (1).

These findings contrast with the highly significant lower potassium, magnesium, and fruit and vegetable intakes in the highest PRAL quintiles observed in the study of Murakami et al (2), which used a diet history questionnaire, and with other findings of lower potassium intakes at higher PRALs with the use of either FFQs (6) or 24-h urine samples (7) for PRAL determination. We also observed clearly lower potassium and fruit and vegetable intakes (calculated...
Dear Sir:

We thank Krupp et al for their response to our article on dietary acid load and hypertension in older Dutch adults (1). In contrast to 2 recently published observational studies that showed positive associations of dietary acid load with either blood pressure (2) or incident hypertension (3), we found no increase in hypertension risk with a higher potential renal acid load (PRAL) in the diet (1). Krupp et al raised concerns about the validity of our dietary data and suggest that, from multiple 3-d weighed dietary records, at higher dietary acid loads in a recent analysis (8), which showed a direct prospective association between dietary PRAL during puberty and indexes of liver fat accumulation in young women (Figure 1 in reference 8). Potassium and fruit and vegetable intakes not shown in the original publication are provided in Figure 1 shown here.

The addressed inconsistencies with regard to dietary mineral intake and PRAL indicate that the FFQ used by Engberink et al (1) may possibly not be fully appropriate for the intended purpose. In the prospective study by Zhang et al (3), which reported a positive association between higher estimates of diet-dependent acid load and an increased hypertension risk, diet was also assessed by using an FFQ, but several FFQs during follow-up were available for dietary assessment, which probably estimated long-term dietary acid load with a higher stability.

To further clarify whether 1) a different age range in the currently studied cohort (as compared with the 2 recent studies), 2) a more alkalinizing dietary pattern, or 3) a nonoptimal dietary assessment instrument may be primarily responsible for the contrasting study results, it would be helpful if better established dietary determinants of blood pressure (salt, potassium, fruit and vegetables) and their associations with hypertension risk were also shown for the Dutch cohort. Although salt intake estimates based on nutrient database values for sodium are not very reliable, a corresponding positive trend with hypertension risk and/or an inverse association of the latter with potassium or fruit and vegetable intake could support the suitability of the applied FFQ for prospective diet studies on blood pressure–related outcomes. In any case, the observed positive association between baseline systolic blood pressure and baseline PRAL in these ≥55-y-old Dutch adults encourages us to examine corresponding relations in our DONALD (DOortmund Nutritional And Anthropometric Longitudinally Designed) Study children.

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Reply to D Krupp et al

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