

## Invited Commentary

# The secret story of fish: decreasing nutritional value due to pollution?

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Fish, especially fatty fish, have long been viewed as a healthy dietary component because of their unique content of long-chain *n*-3 PUFA (*n*-3 fatty acids). An observation in 852 male residents of Zutphen, The Netherlands, aged 40–59 years in 1960 indicated that fish intake was inversely associated with the incidence of CHD over 20 years of follow-up<sup>(1)</sup>. On the other hand, fish may also contain diverse environmental pollutants such as heavy metals and persistent organic pollutants (POP), including organochlorine pesticides, polychlorinated biphenyls (PCB), dioxins, polybrominated diphenylether (PBDE) and perfluorinated compounds (PFCO). Therefore, different studies evaluating potential risks *v.* benefits of fish consumption, especially with respect to CVD, have been performed. Although various results have been reported<sup>(2)</sup>, it has generally been suggested that the benefits of fish eating outweigh the risks<sup>(3)</sup>. Compared with CVD, the situation for diabetes has remained largely unexplored. Recently, several prospective studies have documented that the consumption of fish was associated with a higher later occurrence of type 2 diabetes<sup>(4–6)</sup>, a disease strongly linked to heart disease and stroke, yet that has a much distinct pathophysiology linked to glucose dysregulation and microvascular deterioration. In this issue of the *British Journal of Nutrition*, a meta-analysis performed by Zhou *et al.*<sup>(7)</sup> summarises these<sup>(4–6)</sup> and other studies, concluding that fish and *n*-3 fatty acid consumption is associated with a significantly increased risk of type 2 diabetes. In two other meta-analyses of the same topic and of largely the same data, it has been concluded that there was no benefit from fish intake in terms of reduced diabetes risk<sup>(8,9)</sup>. How can we explain these findings? Have the health effects associated with fish consumption been overestimated?

At an experimental level, several pieces of evidence support the idea that the health effects of fish consumption vary depending on the presence or absence of POP. Rats exposed to contaminated salmon oil (containing background levels of POP) developed metabolic complications linked to type 2 diabetes, whereas animals exposed to decontaminated salmon oil (treated to achieve very low levels of POP) did not show such disturbances<sup>(10)</sup>. Furthermore, mice fed commercially available farmed salmon fillet with common POP levels were found to develop insulin resistance, glucose intolerance, visceral obesity, fatty liver and chronic low-grade inflammation, in contrast to mice fed farmed salmon fillet containing lower levels of POP, which showed a better

metabolic profile<sup>(11)</sup>. In addition, consumption of salmon protein hydrolysate containing less than 0.2% of lipids, and therefore very low concentrations of POP, was found to protect rats against insulin resistance induced by a high-fat diet containing lard and 'corn oil'<sup>(12)</sup>. Taken together, these findings emphasise that background levels of POP, which many people consider to be at safe levels, can completely counteract the potential benefits of *n*-3 fatty acids and other nutrients present in fish, in particular leading to the serious metabolic features which often precede type 2 diabetes. Thus, these animal feeding studies are consistent with the recent human prospective and cross-sectional studies showing an association between type 2 diabetes and POP<sup>(13–15)</sup>.

Previously, Kaushik *et al.*<sup>(5)</sup> reported that, whereas fish and *n*-3 fatty acid intake increases the risk of diabetes, the consumption of *n*-3 fatty acid supplements did not. Interestingly, the oil found in most *n*-3 fatty acid supplements differs considerably from the oil found in fatty fish, in that most lipophilic pollutants such as POP have been extracted through decontamination processes. On the other hand, the oil present in fatty fish has not been decontaminated, and often contains many POP because these pollutants are omnipresent in aquatic environments, making fatty fish one of the most important sources of human exposure to POP<sup>(16)</sup>. Furthermore, the presence of POP in fish, compared with other food products, is still poorly regulated<sup>(17)</sup>. In the European Union, the levels of organochlorine pesticides, PCB and PBDE in fish and seafood are, for instance, still unregulated. Thus, the exposure to POP through fatty fish intake could have contributed to an enhanced risk of diabetes. These findings also pinpoint that the common practice to extrapolate the results obtained with *n*-3-derived supplements to fatty fish, or seafood in general, has probably led to a serious misinterpretation and should be done with extreme caution.

The concentrations and types of POP mixtures may vary substantially in fatty fish depending on the food consumed, the time and the geographic area of the fish<sup>(18,19)</sup>. Similarly, although *n*-3-derived supplements may contain lower levels of POP than fatty fish, the levels of POP in these supplements may fluctuate considerably due to differing methods used by the industry to refine the oil, including activated carbon adsorption, short-path distillation and deodorisation<sup>(20–22)</sup>. This varying quality of fish and *n*-3-derived supplements has probably contributed to the different findings about the

health effects of seafood. In addition, fish oil supplements do not contain the food matrix of the whole fish.

Environmental pollutants present in fish are not the only factors that can affect the health outcomes associated with fish intake. More than half of the total fish for human consumption is provided by aquaculture. Because of the limited natural resource and expensive prices, marine oils used in aquafeeds are often replaced by vegetable oils<sup>(23)</sup>. As a consequence, fish currently sold in supermarkets are, from a nutritional perspective, considerably different from the fish that were available some years ago. Between 2005 and 2009, the ratio of EPA (20:5*n*-3) and DHA (22:6*n*-3) to *n*-6 PUFA has, for instance, decreased by about 50% in farmed Atlantic salmon<sup>(24)</sup>, one of the most consumed fishes worldwide. Thus, to the extent that the particular oils supplied by fish are important in human metabolism, the potential benefits of fish have probably changed throughout the years and decades because fish *per se* has been under continuous nutritional adaptations. In line with this, Kromhout *et al.*<sup>(25)</sup> recently pointed out that the strongest reductions in cardiovascular endpoints associated with the consumption of *n*-3 fatty acids were obtained in the oldest human trials, whereas recent studies did not find such positive effect. There have also been studies reporting that plasma *n*-3 fatty acid concentrations are relatively similar between fish eaters and non-fish eaters<sup>(26,27)</sup>, thereby challenging the idea that fatty fish intake is essential for the supply of *n*-3 fatty acids, at least in populations that do not eat large amounts of fish. It is interesting in this line of thought that both Wallin *et al.*<sup>(8)</sup> and Xun & He<sup>(9)</sup> found inverse relationships of fish intake with diabetes in several studies in China, Japan and Australia. Among other explanations of this geographic interaction, the finding in Asian countries could be indicative of differential distribution of POP by geographic area. We note that this geographic interaction is somewhat sensitive to the specific analysis model, since inverse associations strengthened on re-analysis of the original data by Xun & He<sup>(9)</sup>.

The emerging evidence<sup>(7–9)</sup> suggests that *n*-3 fatty acid and fatty fish intake has no significant benefits on type 2 diabetes, while recent studies find little benefit for CVD, as well<sup>(25)</sup>. This discouraging state of affairs has probably emerged through human intervention in the lives of the fish, both through exposure to a wide variety of chemical contaminants and through substantial alteration in fish composition as fish source has moved from fish caught in the wild to fish farmed for financial profit. These studies may be taken as a warning for the need to maintain stewardship of the land and the sea, as we strive for adequate quality of life in an increasingly populous earth.

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