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Review

Health and ecological implications of fish consumption: A deeper insight

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Abstract. Many studies suggest that fish consumption could be protective for health, but epidemiological studies on different dietary patterns show that fish-eaters have a higher cardiometabolic risk when compared to people relying on a plant-based diet not including fish.

The benefit of fish consumption was related to its content of omega-3 long chain polyunsaturated fatty acids (LC-PUFAs), but toxic chemicals released into environment like heavy metals and several industrial by-products, because of their lipophilic properties, concentrate in fish fatty tissues, the same containing LC-PUFAs. Furthermore, the continuous increase in demand for fish is progressively damaging the marine biodiversity, and the volume of the fishing catch, the latter lower than the demand, made it necessary to resort to fish farming. Although meat, dairy and fish products represent dietary sources of PCBs, the latter represent the main source in human diet (respectively 9%, 19% and 67%). Methyl-mercury's main source also seems to be fish products. Fish farming products are safer for methyl-mercury residue but other substances could be found in higher concentrations than fish caught. Moreover, ecological impact could be detrimental. From this point of view, a reassessment of the health risk-benefit ratio and sustainability of fish consumption is warranted.

Keywords: Fish, pollutants, methyl-mercury, omega-3 fatty acids, PCBs

1. Introduction

Many studies suggest that fish consumption could be protective for cardiovascular health in the context of an omnivorous diet. Accordingly, evidence coming from epidemiological studies on different dietary patterns shows that people that eat fish, but not meat (fish-eaters) benefit from lower cardiometabolic risk when compared to people who also consume meat. Nevertheless, fish-eaters have a higher risk for these risk factors when compared to people that rely on a plant-based diet, avoiding not only meat, but fish as well (Table 1). Plant-based diets

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Table 1

Results of studies on different dietary patterns

	Non-vegetarian	Fish eaters	LOV	Vegan
BMI (kg/m^2, $M \pm$ SD) [12][a]	28.8 ± 6.3	26.3 ± 5.2	25.7 ± 5.1	23.6 ± 4.4
DM prevalence (%) [12][b]	7.6	4.8	3.2	2.9
DM risk (OR, 95% CI) [14][c]	1	0.79 (0.58–1.09)	0.62 (0.5–0.76)	0.38 (0.24–0.62)
Total Cholesterol (mmol/dl)	M 5.23 (5.09–5.37)	M 5.08 (4.94–5.22)	M 4.88 (4.74–5.02)	M 4.47 (4.34–4.61)
(M, 95% CI), (Males, Females) [4][d]	F 5.03 (4.92–5.13)	F 4.87 (4.77–4.97)	F 4.76 (4.66–4.86)	F 4.48 (4.38–4.58)

[a]Adjusted for age, sex, ethnicity, education, income, physical activity, television watching, sleep habits, alcohol use, and BMI; $p = 0.0001$. [b]Unadjusted prevalence of type 2 diabetes according to diet; $p < 0.0001$. [c]Adjusted for age, gender, BMI, lifestyle, sleep habits, physical activity, alcohol use, ethnicity, income, and education. Type-1 diabetes were excluded; $p < 0.05$. [d]The model included age (continuous), alcohol (continuous), physical activity (categorical) and BMI (continuous) as covariates; $p < 0.001$.

Table 2

Results of studies on vegetarians and non-vegetarians on cardiovascular risk

	Non-vegetarians	Vegetarians (LOV, Vegan)
Hypertension (OR, 95%CI) [15][a]	1	0.57 (0.36–0.92) LOV 0.37 (0.19–0.74) vegan
IHD risk (death and hospitalization) (HR, 95%CI) [7][b]	1	0.68 (0.58–0.81)
Metabolic syndrome (OR, 95%CI) [16][c]	1	0.44 (0.30–0.64)

[a]Adjusted for age, and gender. Hypertension defined as average systolic blood pressure >139 mmHg or average diastolic blood pressure >89 mmHg or taking antihypertensive medications; $p = 0.02$(LOV) and $p = 0.005$(vegan). [b]Stratified by sex, method of recruitment, and region of residence and adjusted for age, smoking, alcohol, physical activity, educational level, and Townsend Deprivation Index and the use of oral contraceptives or hormone therapy for menopause in women; $p < 0.001$. [c]Adjusted for sex, ethnicity, smoking, alcohol intake, physical activity, and dietary energy intake; $p < 0.001$.

are also shown to be protective on ischemic heart disease (IHD) risk and on the risk for hypertension (Table 2) [1–16].

The two main causes of death in Western countries - cardiovascular disease (CVD) and cancer - are associated with the protective effect of higher consumption of plant foods, and simultaneous lower animal food intakes, particularly of red meat and its derivatives (meat processed by smoking, salting and the addition of chemicals), but also with some special attention to their cooking methods [17–20].

The role of fish products in the diet remains a matter of debate, still unresolved. The beneficial effects of the consumption of fish and its derivatives, as an alternative to meat consumption, represent part of the historical background in epidemiology, starting with the *Seven Country Study* by Dr. *Ancel Keys* [21], which enshrined the Mediterranean diet for its superior health implications, especially to CVD [22–24].

The benefit of fish consumption was related to its content in long chain polyunsaturated fatty acids (LC-PUFAs, eicosapentaenoic acid, EPA and docosahexaenoic acid, DHA), which is higher in large fish of the cold waters (i.e. salmon) and in bluefish. In today’s globalized world, however, the fish market has undergone processes of intensification that caused an impact on volume of the fishing catch and the quantity of farmed fish [25]. The continuous increase in demand for fish is progressively damaging the marine biodiversity and the volume of fish catches -lower than the demand-, making it necessary to resort to fish farming [25].

While both phenomena (intensive fishing and farming), have a strong ecological impact, fish farming, in addition, could lead to effects that nullify the coveted benefit of fish consumption. There is strong evidence that put the focus not only on the real content in polyunsaturated and saturated fatty acids in farmed fish, but also on the process of accumulation in the fish's flesh of pollutants coming from industrial wastes.

2. Aims and scopes

Nutritional epidemiology showed that adding fish to a plant-based regimen (i.e., vegetarian) could add no further protection, and could even be harmful. Based on these data, we tried to investigate which components in fish could explain this effect.

To this aim, we reviewed the literature reporting this kind of information, regardless of the indication and conclusion, when proposed, on the health effect of fish contained in the same papers. Our scope was to identify, when possible, data on harmful components of fish which could be responsible for the observed higher risk for some diseases in fish-eating people, in comparison to non-fish-eating subjects, and to clarify these aspects from an ecologic and health-related point of view.

3. Background

3.1. Recommendation on Polyunsaturated Fatty Acid Intake from Fish

International institutions have maintained a proactive behavior for a long time, suggesting a weekly consumption of fish beyond the usual two servings, with particular emphasis on the consumption of species rich in omega-3 LC-PUFAs (EPA and DHA). While in the past the recommendations provided a minimum consumption limit to follow [26], today the approach has changed, becoming precautionary, in consideration of the possible health adverse effects of marine foods, especially in certain stages of the human lifecycle. The *European Commission* suggests not to exceed with the servings of shark, marlin, swordfish and pike in some population subgroups (pregnant and breastfeeding women, women of childbearing age, and young children), which should limit their maximum consumption to one small portion of 100 grams per week. Because of their higher cardiovascular risk, elderly individuals may be also counted among these vulnerable individuals.

The *European Commission* also suggests limiting the number of tuna servings to no more than two per week, provided that other types of fish are not consumed [27]. Even the *Italian Ministry of Health* recommends that pregnant women limit to no more than 100 grams per week the consumption of large predatory fish, and to no more than two servings of tuna per week [28]. The FDA (*Food and Drug Administration*) and U.S. EPA (*United States Environmental Protection Agency*) suggest that subjects belonging to vulnerable groups avoid the consumption of fish species and shellfish, whose flesh can contain high levels of mercury, namely swordfish, mackerel and tilefish. Amateur fishing catch should be checked according to the recommendations of local authorities, when available [29]. The EFSA (*European Food Safety Agency*), in its report, states that high fish and seafood consumers may even exceed 6 times the acceptable weekly intake of mercury, and recommends that vulnerable groups avoid eating large fish like tuna and swordfish.

3.2. European safety limits

In Europe, fish flesh - in particular tuna, swordfish, cod, whiting and pike, along with hake in children - has been recognized as a major source of exposure to methyl-mercury for all ages [30]. The *European Commission* set 1 ppm (1 mg/kg) as a safety limit for mercury content in fish [31]. A study from 2002 showed that such levels were exceeded by 61.1% to 78.6% of bluefin and white (albacore) tuna, caught in the Mediterranean Sea [32]. Even if the recommendations have been adapted for the mercury levels, they have not yet taken into account the other harmful pollutants, not even the cumulative effect that the many different substances and their congeners may exert [33–35].

3.3. The role of polyunsaturated fatty acids

By now, it has been widely shown that certain polyunsaturated fatty acids (PUFAs) are essential, because the animal body is not able to synthesize *de novo* such nutrients. Even the enzymatic pathways leading to the transformation of PUFAs from plant precursors to long chain polyunsaturated fatty acids (LC-PUFAs), may be insufficient in humans as in other mammals, birds and fish [36, 37].

The debate on the necessity to consume fish, as a source of omega-3 LC-PUFAs, in the form of EPA and DHA, is primarily related to this enzymatic ability, which, however, under certain conditions may be unable to produce adequate amounts of LC-PUFAs from a diet containing only the essential precursors from plant-based foods [38]. It was postulated that the use of fish products or their derivatives may instead be able to provide direct sources of LC-PUFAs, deriving from the progressive concentration of these nutrients along the various levels of the food chain, starting from the algae.

Because of LC-PUFAs low stability to high temperatures and their susceptibility to peroxidation, there are some possible implication in cooking methods and use of different sea-food. Safety and bioavailability of beneficial substances could be not so obvious [39].

3.4. Evidence from plant-based diets

Although the above discussed theory is richly supported in the literature, some evidence supports an alternative point of view: although blood LC-PUFAs levels in subjects not eating fish, like vegans, are lower than those of omnivores, they are permanently higher than the theoretical expected values, without specific supplementation [40]. It is worthy of note that in population studies, vegans showed the lowest risk of diabetes [14], the lowest levels of total cholesterol and systolic and diastolic blood pressure, and the lowest rates of overweight and hypertension [4, 12, 41] among all of the dietary groups: lacto-ovo-vegetarians, vegans, meat-eaters and fish-eaters; moreover, vegetarians as a whole group exhibit a lower risk for IHD and Metabolic Syndrome in comparison to non-vegetarians [7, 16], suggesting the presence of health-protective substances in their diet, besides fish.

The requirements for direct sources of LC-PUFAs are conditioned by the inhibitory influence of Linoleic Acid (dietary omega-6, typically abundant in vegan diets) on the endogenous synthesis of LC-PUFAs starting from Alpha Linolenic Acid (ALA) [42–44]. Furthermore, an increased intake of trans fatty acids, typical in Western diets, may inhibit the enzymes acting on the conversion of ALA precursor to LC-PUFAs. Even energy/nutritional deficits - calcium, copper, zinc, magnesium, biotin, pyridoxine and protein - can affect the conversion, exerting an inhibitory effect [45, 46].

3.5. Enzymatic activities

In the *EPIC-Norfolk* cohort [47], despite the absence in the diet of direct food sources (foods or supplements containing LC-PUFAs), LC-PUFAs plasma levels were higher than the expected value, especially in vegans and women. Despite the limitations of this research, because of its small sample size, it is possible to hypothesize that reduced dietary intakes can be compensated by a greater activation of the enzymatic pathway leading to PUFAs endogenous synthesis. The existence of a self-regulation mechanism might be the result of evolutionary factors, which have enabled our species to cope with different dietary situations: due to geographical and social causes, in fact, some individuals may be unable to consume foods rich in LC-PUFAs.

Even the well documented gender differences [36, 48–52] could be the result of a homeostatic regulation focused on satisfying the increased requirements associated with procreation, and the need to provide more substrate for the formation of fetal nervous system. The buildup, during the third trimester, of a fetal adipose layer rich in DHA and the process of placental biomagnification of LC-PUFAs, suggest the existence of different physiological adaptations to cope with the increased needs [53, 54]. The amount of dietary PUFAs used for energy production (beta-oxidation) rather than maturation (elongation and desaturation) is consistently higher in men, indicating a gender difference in metabolic management of these important nutrients [55]. The role of hormonal factors is suggested by an increased conversion activity found in women using oral contraceptives; however, it is possible that the increase in LC-PUFAs can derive, at least in part, from a mobilization of woman's fat storages, especially during pregnancy [55–58].

3.6. CVD Prevention and Treatment

All omega-3 PUFAs, both in the form of ALA and its long chain products (EPA and DHA), have proven to be effective in CVD prevention and treatment [59, 60].

On the contrary, the treatment of acute heart attacks with EPA and DHA was shown to be more effective than the treatment with ALA [61]. LC-PUFAs from algae origin have proved as effective as marine products in reducing risk factors [62].

However, there is currently no evidence that preformed LC-PUFAs of marine origin are more effective than their plant precursor (ALA) in the prevention of coronary heart disease. In the *Seven Country Study*, the inverse relationship between fish consumption and mortality from coronary heart disease lost significance after adjustment for confounding factors such as consumption of saturated fatty acids, cigarette smoking, and flavonoids [63]. Other studies, such as the *EURAMIC Study*, failed to demonstrate a protective effect of the consumption of DHA in relation to CVD [64].

Prospective studies conducted on vegetarians also showed that vegetarian diets, typically characterized by high consumption of plant foods and reduced intake of saturated fats, could confer greater protection against CVD, without the inclusion of fish [7, 65].

Therefore, no convincing evidence on the benefits of consuming fish in a plant-based diet is actually available: on the contrary, research on vegetarians allow us to hypothesize that fish consumption could exert a negative effect on health, mainly through toxic mechanisms, although less negative than meat consumption.

4. Pollutants contained in fishery products

4.1. POPs

Tetrachlorodibenzo-dioxin, polychlorinated dibenzodioxins, polycyclic aromatic hydrocarbons, polychlorinated biphenyls (PCBs), polychlorinated dibenzofurans, polychlorinated naphthalenes, dichlorodiphenyltrichloroethane, polybrominated biphenyl ethers, organochlorine pesticides and other industrial products, listed among the dioxin-like polyhalogenated heterocyclic compounds and its congeners, were found in higher concentrations in farmed specimens than in wild ones [66, 67].

These lipophilic compounds can accumulate in the fatty tissues, along the trophic levels of the food chain, until they reach the highest concentrations in the oldest and biggest fish. Although meat, dairy and fish products represent dietary sources of PCBs, the latter represent the main source in human diet (respectively 9%, 19% and 67%) [68].

In living animal bodies, these substances do not have specific disposal systems, and thus they have been called *persistent organic pollutants* (POPs).

4.1.1. Mercury

Methyl-mercury's main source also seems to be fish products [69]. Mercury is a heavy metal that can be produced by human activities such as waste disposal and other industrial processes. Its release into the atmosphere occurs in its inorganic form, and undergoes a conversion cycle to the organic form by microorganisms. While the inorganic form is poorly absorbed, the organic form easily enters tissues to be accumulated, above all in marine organisms [70]. The limited capacity of excretion, and therefore the strong power of biomagnification, causes its accumulation in fish that are most long-living, and at the top of the food chain. The effects for humans of a high mercury exposure can lead to severe neurological damage, such as ataxia, paresthesia, sensory abnormalities, and impaired cognitive and neuromuscular development in utero. The effects of mercury mainly occur through its interaction with enzyme sulfhydryl groups, ion channels, receptors, and antioxidant systems such as selenoproteins [70]. Although these kinds of effects are difficult to verify in experimental conditions, subclinical effects derived by the normal consumption of some fishes, especially during pregnancy, have not yet been exhaustively evaluated.

Toxicant exposure to mercury and other pollutants in humans could be associated with neurodegenerative disorders such as Parkinson's Disease, Azheimer's Disease and dementia [71–73].

The levels of inorganic mercury and methyl-mercury - the most harmful mercury compound that has undergone a process of organication - were found particularly high in selected caught fish species such as shark, swordfish, mackerel, marlin and some varieties of sea bass [30]. Without taking into account other potential dietary sources, by itself the weekly consumption of 140 grams of these species would lead a pregnant woman to exceed by 40% to 90% the levels of methyl-mercury recommended by the *Committee of Toxicity of Chemicals in Food, Consumer Product and the Environment* [74, 75]. The same recommendations should be applied to childbearing women, with particular emphasis if they are planning a pregnancy within the following year, given the persistence of these substances in the body. The question assumes relevance if we consider that in some countries, Italy for instance, the consumption of *squaliformes* is very high, because it is illegally sold as other more prized species on the fish market [76].

4.2. POPs Content in Farmed Fish

Although mercury levels are noteworthy for the caught and not for farmed fish, other substances such as PCBs and dioxins can be found in higher concentrations in some farmed fish [66, 67, 77].

It should be mentioned that the Norwegian salmon from organic farming has the highest toxicity-equivalent values of PCBs, according to the parameters of the *World Health Organization Toxic Equivalency Factor* [78].

The main source of these pollutants seems to derive from the fishery forage system and from the farming method itself, using a high density of individuals per volume unit [79]. The removal of the fatty parts of fish could significantly reduce the intake of these typically lipophilic chemicals, but it is important to remember that the benefit of consuming fish relies on its PUFAs content of fat tissues: so, their removal would nullify any benefit.

Data from aquaculture is derived mainly from salmon species. We can't assert that the same issues about chemical risk could be a matter of concern for other farmed fishes. Salmon remains the major type of fatty fish often indicated as rich in omega-3. We speculate that feeding practices could be the same, hence additional data is needed to clarify this point.

The list of species farmed for commercial purposes is sharply increasing, and their consequent deleterious effects probably will expand. Tuna itself, available on the market, is more and more often a product of breeding, both in fish markets and the canning industry [80]. Despite being among the most consumed fishing products, its concentration of LC-PUFAs is among the lowest, if we exclude other lean fish whose use as food contributes minimally to the assumption of LC-PUFAs [70].

4.3. Exposure from Market Product and Recreational Harvest

The highest contribution of the organic dioxin-like contaminants seems to be referred to sardines, tuna and hake. The species that mainly contribute to human intake of polycyclic aromatic compounds are tuna, hake and shrimp, while shellfish has a greater concentration of these substances. A calculated health endpoint from U.S. EPA's Integrated Risk Information System for pollutants may limit these species to a monthly consumption of half a serving (full meal size of 227 g), based on increase cancer risk level calculated for 70-years exposure [77]. The levels of arsenic and polychlorinated biphenyls in shellfish may exceed the acceptable limits of safety for the risk of cancer as revealed from a study on specimens of shellfish harvested on the north shore of the St. Lawrence River's lower estuary area. The lifetime cancer risk was based on U.S. EPA data, and all four levels of consumption scenarios exceeded the cancer risk limits. Risks for other substances were below upper limits for non-cancer effects, though additional studies are needed to clarify if neutral or additional interaction exists among contaminants [81].

Consumers are not yet aware of the fact that almost all of the salmon sold in supermarkets is a farmed product, which contains consistently high pollutant levels, especially if from the European Atlantic area [67]. Its frequent consumption in children younger than 5 years would easily lead to exceeding the tolerable limits proposed by the *World Health Organization*, especially for PCBs [82, 83].

Several research groups argue that the beneficial properties of fish can compensate for, and even overcome, its negative effects, as revealed by epidemiological studies [84]. In the absence of reliable data on the actual levels of pollutants in the single fish products available on the market, it would be prudent to rely on the experimental data provided by the sampling carried out for research purposes.

According to the U.S. EPA, on the basis of these data, the maximum precautionary limit for a European farmed salmon would correspond to a portion of fish every 5 months; it is clear that, following these recommendations, the beneficial effects of LC-PUFAs would be less than marginal, if any.

The most optimistic estimates never allow more than one serving per month (in the case of the consumption of South Pacific fish farming products), which considerably differ from the standard advice for the population, suggesting the consumption of at least two weekly meals with fatty fish (typically salmon) [74].

4.4. Health risks from POPs

POPs represent a great concern for human health because of their effects on the development of cancer and other health conditions, as well as increased cardiovascular risk, hyperlipidemia and type 2 diabetes [85–90]. The half-life of POPs stored in adipose tissue varies greatly, from a few up to tens of years, with greater excretion in pregnant and breastfeeding women, through the placental flow and milk production, respectively [91, 92].

European and international policies are becoming increasingly more attentive towards these potential pollutants in the form of industrial by-products. However, their long persistence in the biosphere is the cause of their presence in the environment and in living bodies, so that the same international organizations that encourage dietary fish consumption now focus concern on their consumption in vulnerable groups, and on the kind of species to be consumed.

Although it has been hypothesized that these pollutants do not represent, to date, a threat that can justify avoiding fish for the general population [93–95], not all potentially harmful substances have been assessed for their health risk [77]. For this reason, it is possible that the sum of the single risks from the various compounds may be underestimated, since the daily tolerable levels for many potentially harmful substances have not yet been established. The detrimental consequences of these substances are mainly related to their carcinogenic effects, which occur through mutations and altered cell signaling, in addition to immunosuppression, allergic events, increased cardiovascular risk, diabetes, cognitive impairment and endocrine dysfunctions [96–98].

The potential risks of following the official recommendations on fish consumption have been stigmatized in 2007 in a review [74], in which it was suggested that recommendations should take into account various factors such as serving size, intake frequency and the balance of health benefit and risk, since seafood is the primary source of exposure to various contaminants, as claimed by the *American Heart Association* [74].

4.5. Health benefits in fish-eaters

While fish consumption may be responsible for cardiovascular risk reduction in individuals who consume meat products, definitive data supporting the benefits on cardiovascular risk of consumption of fish in a plant-based diet are lacking. Moreover, studies that specifically evaluated some health conditions in the dietary group of fish-eaters, found that some risk factors were higher in fish-eaters than in vegetarians (e.g., total cholesterol levels, diabetes incidence and prevalence, and BMI) [4, 5, 12].

Even assuming that it is possible to estimate which is the correct amount of fish that can ideally maximize the health benefit-risk ratio (amount of PUFAs in relation to the concentration of harmful substances, age group, gender etc.), the environmental issues certainly remain open, increasingly worrisome for the ecosystem.

5. Environmental consequences and exploitation of resources

5.1. Fishing and farming sustainability

The fishing catch volume has reached a level of exploitation that represents a high risk for the ocean-dwelling species, suggesting the need to put a limit to the increasing depletion of marine resources [99, 100]. Nevertheless, even aquaculture proposes worrying aspects from an environmental point of view [79, 101].

Fence waste from fish farms, including carcasses of fish and trapped marine predators, such as seals, are released in specific landfills, or used as fertilizer or feed. According to estimates of the *Scotland's World Wildlife Fund*, the breeding of 200,000 units of salmon releases in the biosphere nitrogen equivalents similar to the activity of 20,000 human beings, phosphate equivalents similar to 25,000 humans, and fecal residues equivalent to a city of about 65,000 inhabitants. It is estimated that, between 2000 and 2001, salmon aquaculture in North-East Europe (Denmark, Norway, Scotland, Ireland, etc.), produced about 6,600 tons of phosphate and 40,000 tons of nitrogen [102].

The most obvious consequences of this type of pollution concern contamination of the seabed and of the associated benthic species, the contribution to fish and shellfish to antibiotic resistance, and eutrophication of marine areas, which causes toxic algal overproduction. The accumulation of fecal material around the breeding cages threatens the marine biodiversity and creates dead zones under the fences, which inhibit the growth of all forms of life on the seabed [103]. Every year the fish operators are forced to move in different places, in order to prevent the death of the seabed, thus promoting the increase of the contaminated areas. Moreover, the farming of fish is poorly efficient, with mortality rates from 10% to 40%.

5.2. Mortality in aquaculture stock

Despite the continuous effort to remove the dead individuals, the remaining ones can still transmit parasites and diseases to neighboring specimens [104]. Events such as infectious salmon anemia, in 1998/1999, lead to the sacrifice of entire culture tanks for precautionary reasons, leading to the suppression about 8 million fish [105, 106].

Flavobacterium columnare represents one of the most harmful pathogenic bacterial agents as regards the trout, salmon and catfish farming industry [107, 108]. The conditions of forced breeding density, up to 1,000 times the normal natural conditions, promote the transmission of infectious agents among fish, especially in homogeneous systems of subspecies. The high density of individuals causes the weakening of the natural immune defenses of farmed specimens [109, 110]. Moreover, the presence of numerous carcasses facilitates the persistence of saprophyte pathogens and their subsequent transmission. Surprisingly, despite the presence of this microorganism in the cold seas, its expansion mainly derives from the practice of farming [111, 112]. The antibiotic treatments introduced in the last two decades have failed avoid the huge losses of animals caused by the bacterium, despite the increase in the dosages used to treat the infection [113]. It is likely that the conditions themselves offered by the farms have facilitated the selection of resistant strains with increased virulence.

For every 1.9 million global tons of salmon produced and placed on the market, several hundred tons of carcasses (called ≪morts≫) must be disposed of, as a result of high mortality rates. The alternative to the simple accumulation in isolated lands is represented by the use of silos in which chemical agents are applied in order to speed up body decomposition, whose degradation product is reused as garden fertilizer or as feed for other fish farms, mink and as products for domestic pets [102]. The use of more environmentally friendly means of disposal is not covered by the normal practices of the industry, because it would bring down the profits of fish farming [102].

6. Alternative omega-3 sources

Hemp seeds, chia seeds, flax seed and flax seed cold pressed oil are very rich in ALA and could be the best foods to balance polyunsaturated acid from diet [114].

Moreover, algae, which are at the basis of the marine food chain, produce LC-PUFAs. Algal oil, containing DHA, is obtained through the production of biomass under controlled conditions (*Crypthecodinium cohnii*, especially *Schizochytricum* and *Ulkenia*). Algal DHA at the average dose of 1.68 g/day (well above the recommendations) resulted effective in reducing triglyceride levels and increasing HDL and LDL cholesterol (respectively –15%, +8% and +5%), an equivalent effect of 3.25 grams of fish oil, and with a possible net benefit on cardiovascular risk reduction, despite the increase in LDL-cholesterol [115].

Since the intake of LC-PUFAs could exert beneficial effects on the fetus during pregnancy and on the infant during lactation, it may be also prudent to supplement the mother's diet with algal DHA, regardless of her type of diet, in order to eliminate potentially toxic chemical compounds from her diet. The supplementation by the 18th week of pregnancy up to the 13th post-partum (from the last trimester of pregnancy until the third month of lactation) with 100–200 mg per day of algal DHA can protect the mother against the risk of an eventual body store depletion, and a safe amount of LC-PUFAs for the development of brain and retina can be transferred to the fetus, and after birth to the infant [116–118].

Fatty acids omega-6 and omega-3 compete for the same enzyme system for the production of long chain polyunsaturated fatty acids: so it is advisable to maintain a balance in the dietary n6:n3 ratio of 5:1–10:1 [119], although a research group suggested that the ideal ratio to maximize the conversion can be lower, 2.3:1 [120]. This should also be useful in balancing the effects of the respective eicosanoids, produced by LC-PUFAs through the action of the enzymes lipoxygenase and cyclooxygenase. These indications can be used regardless of the individual eating habits.

7. Conclusions

As often happens in science, it is not easy to extrapolate a final and unique conclusion on a given subject. As for the subject of this review, however, there are strong indications that the consumption of fish is not as sustainable as previously claimed, both from a health and ecological point of view.

Because of the lipophilic properties of the pollutants present in the fish flesh, their concentration increases with the increase of fish fatty tissues: the same tissues that contain LC-PUFAs, whose beneficial effect on health has been hypothesized.

The global demand for seafood is constantly growing, and cannot be met by the fish catch volume: thus, fish farming is increasingly becoming a major source of fish products. In the last decade, the livestock density of farms and their ecological implications have attracted the interest of consumers. This is especially true for systems of farm land, but in the case of aquaculture, these issues are still poorly understood. The disposal of fecal by-product and mortality rates due to low efficiency are among the issues of ecological impact, together with the need for raw materials for fodder and the possible disruption of ecosystems in the areas in which cages livestock are located. Important devastating effects are antibiotic resistance, biodiversity loss and death of the underlying seabed [121].

New U.S. EPA's clarifications recommend not to reduce the intake of fish but to maintain a minimum consumption of two servings per week, by selecting the products with a lower content of methyl-mercury and polycyclic aromatic compounds. This selection is not always feasible and unambiguously definable, because of changes in contaminant levels in the local catch and above all because of the capability of consumers to comply with this recommendation [122, 123].

In 2006, the *Institute of Medicine* recommended to consume two cooked fish servings per week for females who are or may become pregnant or who are breast-feeding, avoiding large predatory fish such as shark, swordfish, tilefish, or king mackerel. The same recommendation is given for children. For healthy adults and adolescents, the consumption of fish may reduce risk for CVD [124]. In 2015 an EFSA scientific opinion stated that when consuming species with high methyl mercury content, only a few numbers of servings can be eaten before reaching the *tolerable weekly intake* which may be attained before the *daily reference value* for LC-PUFAs. It is not possible to make general recommendations on fish consumption and each country needs to consider its own dietary pattern [125].

Also non-fatty freshwater fish could be a high source of mercury possibly linked to myocardial infarction, coronary heart disease and CVD [126].

Fish farming products are safer for methyl-mercury residue but other substances could be found in higher concentrations than fish caught. Moreover, ecological impact could be detrimental.

The use of supplements derived from fish oil has often shown conflicting results regarding their health benefits, and the reason may lie in the degree of contamination and degradation of the raw materials used [127, 128]. The use a product such as algal oil may represent a safe, ethical and ecological alternative to provide preformed LC-PUFAs to diet.

In conclusion, fish consumption appears not to be so safe and healthful, and recommendation that take in account the benefit-cost ratio and sustainability of fish consumption, should be updated. We suggest that a re-assessment of the official recommendations would be a correct and strongly precautionary act.

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Author contributions

All authors contributed equally to this work.

Conflicts of interest

The authors declare no conflict of interest.

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