

NFI *CENTRO STUDI DELL'ALIMENTAZIONE*
NUTRITION FOUNDATION OF ITALY

Scientific Dossier on the Health Benefits of Fish Consumption

*From international food research, an up-to-date picture of
the latest and most significant
scientific evidence*

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Scientific Dossier on the Health Benefits of Fish Consumption

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SCIENTIFIC DOSSIER ON THE HEALTH BENEFITS OF FISH CONSUMPTION

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INTRODUCTION

by Andrea Poli, scientific director of the Nutrition Foundation of Italy

The association between fish consumption and the reduction in cardiovascular risk has attracted researchers' attention since the Seventies of the past century, when the first studies conducted on Inuit Eskimos documented the reduced incidence of heart attacks in these populations, their greater tendency to bleed on wounding and their low blood pressure. This is how this line of research began and it later led to a definition of the physiological effects and protective role of omega 3 polyunsaturated fatty acids. These fatty acids, whose cardioprotective effect is now universally accepted, are now also being investigated for a rich and promising series of effects of a different nature, that concern cognitive function, mood and a wide range of metabolic disorders.

Over the past few years, however, attention has returned from the nutrient (the omega 3 fatty acids) to the food (fish), thus enabling us to define the contribution of other aspects of the composition of fish (such as the rich protein content and the presence of some minerals) that contribute to the favourable effects it has on human health.

The fact that, in the Western world, fish often means canned fish is often neglected. Canned tuna, mackerel, salmon and sardines enter our homes and appear our tables, with most of their nutritional characteristics in safely preserving and controlled quality containers that help us all, even those who live far away from the sea, to reach the optimum levels of fish intake for our health.

This short monograph is dedicated to fish, in all the forms in which it is eaten, in the hope that it may help to explain to people how and why regular consumption of this food is so important for all of us.

FISH AND HEALTH: NEW AND CONSOLIDATED INFORMATION FROM SCIENTIFIC LITERATURE AND EPIDEMIOLOGICAL OBSERVATIONS

Positive effects on the cardiovascular system

The benefits that eating fish has on health in general, and in particular against chronic degenerative diseases such as cardiovascular disease, are now widely recognized.

The first observations, made in the Seventies, on the low prevalence of death due to heart attack in the inhabitants of Greenland associated with their high fish consumption were confirmed by the results of later studies, which conclusively demonstrated that **1-2 servings of fish a week may have a major protective effect on the heart and blood vessels**. In particular, fish consumption has been correlated with a reduction in the death rate due to severe ventricular arrhythmia (sudden death), heart attack, atrial fibrillation and cardiac decompensation, but also death due to an extremely invalidating disease of our societies, ischemic stroke.

The protective effect is observed even at moderate levels of consumption: a diet that includes at least 30 g of fish a day already significantly reduces the risk of developing cardiovascular disease; in particular, every increase of about 20 g of fish a day would reduce the risk of death due to cardiovascular disease by 7% in persons who only eat fish occasionally (*Mozaffarian, 2006*).

These observations become even more important if you think that cardiovascular disease represents the first cause of death both in Italy and in the European Union, where it is responsible for about 40% of deaths (ISTAT, 2008, Eurostat 2010).

Even if the physiological effects at the origin of these benefits have not been entirely clarified, **the benefits of fish are attributed mainly to its content of long-chain omega 3 polyunsaturated fatty acids, EPA and DHA, of which fish represents the main source in food for man**.

The positive effects of fish on the cardiovascular system have also been confirmed by analysis of the results of several prospective studies and randomized clinical trials, which show, comparing groups of persons who eat fish only occasionally with those with a moderate fish intake (equivalent to 250-500 mg a day of EPA plus DHA and thus about 1-2 servings a week), that the latter have a 25% lower risk of cardiovascular events. If fish

consumption is increased further, no additional benefit seems to be obtained. In fact, a combined assessment of the data available shows that, while up to 250 mg of omega 3 a day (about two servings of fish a week) the risk of fatal coronary events is reduced by about 15% every extra 100 mg eaten (for a total reduction of 36% with the maximum amount considered, that is 250 mg/day), for high levels of consumption, the risk remains substantially unchanged. Even among the Japanese, the population with one of the highest levels of fish consumption, cardiovascular system protection follows the same “plateau” trend (larger quantities do not correspond to greater benefits) but seems to reach maximum protection for larger quantities of fish consumed, equivalent to 900 mg a day of EPA plus DHA (about 5 servings of fish a week); protection is not increased any further by larger intakes of these fatty acids.

Regular fish consumption also has a positive effect on the risk of developing type 2 diabetes, which is associated with a series of complications of a varying nature (cardiovascular events, severe visual damage and even blindness, renal insufficiency, etc.) and the frequency is increasing all over the world. According to the 2008 Istat – Italian Statistics Institute - yearly report, the prevalence of this disease, which strikes 4.8% of Italians (5.2% of women and 4.4% of men) increases with age, reaching 18.8% of individuals aged 75 years and over. An analysis of the results of the EPIC- Norfolk (European Prospective Investigation of Cancer) study confirms the fact that **one serving of fish a week (both fatty and lean) significantly reduces the risk of developing this disease.**

Considering the role of omega 3 fatty acids in these protective effects, it has been hypothesized that the benefits observed for the consumption of fish are associated above all with the consumption of fatty fish, such as salmon, herring and mackerel, which are very rich in omega 3 fatty acids (*Mozaffarian, 2006*). It should however be considered that **lean fish, such as tuna**, is the kind of fish most widely consumed in the western world, and represents 60-80% of total fish consumption; as a result, **although it has lower concentrations of EPA and DHA per serving, it provides most of the total omega 3 fatty acid intake of the population at large** (*Amiano, 2001*).

Improvement in Mood

Several years ago emerged the initial data indicating an inverse correlation between the habit of eating fish regularly and the probability of developing depression, a disease which, according to the WHO, is one of the principal causes of invalidity in the world. A comparative assessment of the frequency of depression in France, Germany, United States, Canada, New Zealand, Korea, Porto Rico, Taiwan and Japan indicates that in Japan, the country with the highest fish consumption, the prevalence of major depression is about 50 times less than in other countries such as Germany, New Zealand and Canada, where the low fish consumption is associated with a larger number of diagnoses (*Hibbeln, 1998*). Within the Japanese population, a study conducted in the nineties demonstrated that the risk of developing suicidal tendencies was reduced among individuals who eat one serving of fish a day compared those who ate less (*Hirayama, 1990*).

More recently, in Finland, depression and suicidal tendencies were correlated with the composition of the diet of 3,000 adults: even after the statistical data correction for the confusing factors (age, sex, marital status, education, economic and professional status, smoking, alcohol consumption, coffee and physical exercise) cases of depression and suicide attempts were both significantly less frequent (-37% and -43%, respectively, on average) among individuals who eat fish frequently (*Tanskanen, 2001*).

A more stable mood is reflected in psychophysical well-being not only in terms of depression. According to data collected in an observational study conducted in New Zealand, the number of weekly servings of fish consumed is directly correlated with mental health to a statistically significant degree (*Silvers & Scott, 2002*).

Reduction in the Risk of Dementia

The protective effects of fish seem also to extend to the cognitive functions of the brain. **In a French population of elderly patients, the consumption of a single serving of fish per week seemed to reduce the risk of developing dementia**, Alzheimer's disease in particular, for up to 7 years after the start of the study (*Barberger-Gateau 2002*). The results obtained from the Chicago Health and Aging Project, a population study on risk factors for Alzheimer's disease, confirm that the **regular weekly consumption of fish reduces the risk of developing this disease by about 60%**

with respect to individuals who only eat it occasionally (*Morris, 2003*).

The cognitive decline associated with old age is slowed down by fish consumption, as is confirmed by a more recent study conducted on 210 individuals aged between 70 and 89 years: a quantity of this food equivalent to about 400 mg a day of EPA+DHA (more or less 2 servings of fatty fish or 5 of lean fish a week) delays cognitive decline by 5 years (*van Gelder, 2007*).

Although **the protective effects of fish against neurodegenerative diseases are generally attributed to DHA**, whose intake in the diet increases the levels of neuroprotective factors in the brain (*Cole, 2010*), more recent observations underline the **importance, in prevention, also of other components of fish, such as selenium**, which performs a fundamental role in cerebral function (*Berr, 2009*).

Positive role in reducing the onset of allergic diseases

A series of studies on the diet of infants after weaning **have suggested that eating fish in early childhood may be effective in preventing allergic diseases**. Recent studies show that the late introduction of some solid foods in the child's diet (such as eggs and fish), which was generally recommended up to a few years ago, could actually increase the risk of allergies (*Nwaru 2010*). Two servings of fish a month, from weaning to the end of the first year of life, apparently reduce the risk of developing above all allergic rhinitis, but also asthma and eczema, in individuals with no hereditary predisposition for these diseases (*Kull 2006*). According to a recent Swedish observation on the spread of non-topical eczema, which, in Sweden, strikes one child in 5 during the first year of life, this condition is largely determined by hereditary factors, but its frequency is reduced by eating fish during the first 9 months of life (*Alm, 2009*).

Adults may also benefit from the positive effect against allergies; inverse dose-response correlations between fish consumption (and, even more so, between levels of omega 3 intake) and the prevalence of allergic rhinitis have been recorded in Japanese women (*Miyake, 2007*) and German women (*Schnappinger 2009*).

Body weight control

It has been demonstrated that fish consumption can modulate both the levels of insulin on an empty stomach (influencing what is known as "insulin resistance"), and the plasma concentrations of leptin and ghrelin, two of the hormones involved in the mechanisms that regulate the appetite and satiety (*Ramel 2009 a*). In confirmation of this, the effect of lean fish on weight loss in overweight young individuals and obese adults has recently been described. **Regular lean fish consumption** (three or five weekly 150 g servings of cod), **within the scope of a low-calorie diet, significantly increased the amount of weight lost**, compared to the same diet with no fish, in a randomized, controlled operational study on overweight and obese individuals (*Ramel 2009 b*). This observation suggests that other lean fish, such as tuna, may be used effectively in weight loss diets.

COMPONENTS OF FISH AND RELATED BENEFITS

Omega 3 fatty acids

The lipid component of fish is rich in omega 3 polyunsaturated fatty acids and above all in the long-chain polyunsaturated fatty acids EPA and DHA, present at high concentrations exclusively in this food (*Arino, 2005*). The levels of the two fatty acids vary considerably, both between different species of fish and within the same species according to the type of feed and breeding. They are not synthesized directly by the fish but by single-celled algae, eaten by marine animals within the food chain (*Arterburn, 2006*). Freezing and cooking result in a minimum loss of omega 3 fatty acids, while frying at high temperatures and poor preservation (in conditions that cause it to oxidise and thus turn rancid) may lead to a significant loss of these compounds.

The intake of EPA and DHA (or their plasma levels, now measurable by specific methods) is inversely correlated with the incidence of degenerative disease such as cardiovascular, neurodegenerative and immune diseases. In general, it has been demonstrated that omega 3 fatty acid intake reduces the levels of triglycerides in circulation and platelet aggregation, and stabilizes the hearth rhythm, an important parameter in individuals who have already suffered coronary events (*Harris, 2009*). In addition, **DHA is the main polyunsaturated fatty acid in the human brain and the retina's rod cells, and is indispensable for the development of the brain and retina of the foetus during pregnancy, and the psychomotor and visual development of the infant during its first few months of life** (*Innis 2008*). In fact, this fatty acid is present at high concentrations in human milk but not (for example) in cow's milk (*Koletzko, 2001*).

The typical western diet provides relatively limited quantities of omega 3, probably unsuitable to protect the body against chronic degenerative diseases. **According to the results of an Italian study (*Tavani, 2003*), about 80% of the population fails to reach the daily intake of EPA and DHA recommended by the international guidelines** (250-500 mg a day). This deficiency has in part been held responsible for the growing number of cases of chronic diseases in our society. According to the indications

given by the American Cardiology Society, the general population should eat two servings of fish a week to avoid developing cardiovascular disease (*Kris-Etherton 2002*).

Proteins

Unlike its fat content, the protein content of fish is quite constant, varies little between one species and another and does not depend on the seasonal variations due to diet and reproduction cycles. **The fish proteins, rich in essential amino acids, have a high nutritional value**, similar to that of meat proteins and only slightly less than that of egg proteins. **Due to their low collagen content, fish proteins are easy to digest** (the digestibility coefficient is close to 100). One hundred grams of fish provides 15-25% of the total daily protein requirement of a healthy adult, and 70% that of a child.

Not only the fats but also the proteins of fish have been attributed a beneficial effect against cardiovascular disease (*Jaques, 1995*). In fact, it has been demonstrated that in individuals on a diet based on fish, which therefore represents the only source of protein, the circulating levels of HDL lipoproteins that carry the "good cholesterol", increase more than with diets based on milk or soy proteins (*Gascon, 1996*).

The proteins of some fish are also particularly rich in arginine, the amino acid that the body uses to synthesize Nitroxide (NO), responsible for efficient vascular operation and protection of the arterial vessels against atherosclerosis.

Non-proteic nitrogen compounds in fish provide up to 20% of the total nitrogen content of the muscles; so they are present in larger quantities than in meat, in which they do not represent more than 10% of the total nitrogen. **The best known of these compounds is creatine, which plays an important role in the muscle metabolism of fish** and which is not present in crustaceans or molluscs (*Arino, 2005*).

Fish is also rich in nucleotides, very important for energy processes and largely responsible for the flavour of fish, which are used as indicators of freshness. **Some small peptides also have an anti-oxidant effect.**

Vitamins

The vitamin content of fish is somewhat variable, from the quantitative and qualitative points of view, and depends on the type of feed given to the fish.

The fat-soluble levels of vitamin A (retinol) and vitamin D depend on the fatty content of fish. **Low but significant concentrations of vitamin A** are contained in fatty fish such as the **mackerel and salmon, which contain large quantities of vitamin D. One hundred grams of mackerel, for example, provides more than 100% of the recommended daily allowance (RDA) of this vitamin.**

Vitamin E (tocopherol), which, in some species, reaches higher concentrations than in meat, is only partially available as active tocopherol, as it is broken down rapidly to protect the polyunsaturated fatty acids against oxidation.

In general, **fish is considered to represent a medium-high source of water-soluble vitamins, well represented in all types of fish**, except for vitamin C (ascorbic acid), almost completely absent in all species. **The content of vitamin B2 (riboflavin), B6 (pyridoxine), niacin, biotin and B12 (cobalamine) is relatively high**; 100 g of fish may provide up to 38% of the RDA of riboflavin and up to 100% of that of vitamin B12 (*Arino, 2005*).

Minerals

All types of fish have a well-balanced content of most minerals, both macro and oligo elements. In particular, fish contains little sodium, low levels of potassium and low calcium concentrations, which are, in any case, present in this food in larger quantities than in meat. In addition, small fish bones that can be eaten with fresh fish or small fish increase the calcium intake through fish.

Fish is a valid source of magnesium and phosphorus and contributes considerably to the intake of iron, which is present in it at similar concentrations to those observed in meat. It also represents an **excellent source of iodine**, which it gets from plankton (*Arino 2005*).

100 g of fish may therefore provide 50-100% of the daily requirement of magnesium, phosphor, iron, iodine, and very little sodium (the consumption of which, in the western world, is far too high due to the excessive use of salt).

The importance of the selenium present in some fish such as tuna has been underlined by the results of a French study (EVA) conducted on 200 individuals aged over 70 years. An analysis of the blood samples led to the identification of a direct correlation between omega 3 concentrations in red blood cells and selenium levels: both parameters were found to be directly correlated with fish consumption. In particular, the consumption of fish was responsible for 15% of the plasma selenium. According to the authors, benefits of fish consumption for the elderly may depend not only on its fat content but also on its selenium content (Berr, 2009). It has been hypothesized that selenium, which has an antioxidant effect, slows down the aging process (SINU 1996).

FISH CONSUMPTION IN THE VARIOUS STAGES OF LIFE AND UNDER PARTICULAR CONDITIONS

Childhood

Fish should be included in a varied and balanced diet, on the basis of the considerations made up to now, at all ages (*Meyer, 2009*).

Since weaning, when the omega 3 intake through breast milk ends, **fish represents the only source of these compounds sufficient to guarantee the optimum development of the nervous system and sight** (*Innis, 2008*). In addition, the protein content with a high biological value and its high digestibility make it suitable as early as the age of one year. Some aspects that make it difficult to use in early childhood, such as the presence of fish bones, skin and scales, can be overcome by using sliced fish or preserved products, such as canned tuna and salmon fillets, which have a valid nutritional profile and are easy to eat.

Adulthood

The benefits of fish have also been widely demonstrated during later phases of life such as the menopause and old age.

The positive effects of fish on women's health were investigated above all in a large-scale American study, the Nurses' Health Study, for which about 200,000 nurses were recruited and have been followed for several decades. In this population, those who ate fish even just 1-3 times a month had a 20% higher probability of survival. This benefit was greater for diabetic women and has also been confirmed for young women (*Lopez-Garcia, 2004*).

The benefits of regular fish consumption also appear after the menopause, when the coronary risk increases considerably for the female population (*Bourre, 2007*). In post-menopausal women with coronary artery stenosis, 2 servings of fish a week reduce the progression of atherosclerosis: this effect is more marked among diabetic women (*Erkkila, 2004*).

But the **consumption of saltwater fish** (not freshwater fish, molluscs or crustaceans) **is also directly correlated with bone mass and a reduction in the risk of developing**

osteoporosis (*Chen, 2009*). In addition, regular fish consumption, due above all to the omega 3 fatty acids it contains, seems to reduce the intensity and frequency of hot flushes, which are the most common disorder associated with the menopause (*Lucas, 2009*).

Sport Activities

Regular physical exercise represents an important protective factor against coronary artery disease, hypertension, obesity and diabetes: the same benefits as those attributed to the omega 3 fatty acids in fish. **Both fish consumption and physical exercise increase metabolic efficiency, sensitivity to insulin, the production of NO (nitroxide), the fluidity of the red blood cell membranes, the variability of cardiac rhythm and bone density and reduce the risk of metabolic syndrome and fractures, platelet aggregation and depression.**

In addition, in the athlete, EPA and DHA help to reduce the bronchoconstriction associated with intense physical exercise and to control the inflammation that may result from stress on the muscles and joints (*Simopoulos, 2007*).

METHODS OF PREPARING AND EATING FISH

It has been demonstrated that the methods used to prepare and cook the fish are of fundamental importance to get full benefit from it. A study on the eating habits of about 4,000 Americans aged over 65 years enabled interesting differences to be observed between individuals who ate tuna, baked or grilled fish and those who ate above all fried fish or fish burgers (*Mozaffarian, 2003*). After about nine years of observation, a drastic reduction in the number of deaths due to ischemic heart disease was recorded, (up to 50%, for a consumption of three servings a week), but this reduction was limited to those who ate tuna and grilled or baked fish, not those who ate fried fish. By measuring some haemodynamic parameters, the authors concluded that **the cardiac and vascular function was significantly better for tuna and steamed, baked or grilled fish, while those who ate mainly fried fish presented disorders indicative of a high risk of atherosclerosis** (*Mozaffarian, 2006*). In fact, according to the authors, fried fish has a less favourable fatty acid content, with low levels of omega 3 fatty acids, which are modified further by the oil used to fry the fish; in addition, oil used more than once gradually increases its content of lipid oxidation products and trans fats.

Diabetics also benefit from eating one or more servings of grilled or steamed saltwater fish a week, whether it is lean (like tuna) or fatty (like salmon or mackerel), while the consumption of fried fish brings no benefit whatsoever. In most studies, **canned fish, prepared using modern technology, has a similar nutritional profile to fresh, grilled, steamed or boiled fish.**

SUSTAINABILITY AND SUPPLY OF FISH

In economically developed countries, a greater consumption of fish, which represents the main source of animal proteins for about 2.6 thousand million people is recommended to improve one's health (*Brunner, 2009*). The growing demand for fish products is often seen as a potential risk for the ecosystem, with various species at a risk of extinction. The sustainability problem actually concerns aquaculture and fishing as well as agriculture, forestal resources, water and energy sources. In addition, the benefits associated with fish consumption make it worthwhile to tackle and solve the problem, taking economic and environmental needs into account, by regulating sustainable fishing, trade and aquaculture (*Mozaffarian 2006*).

The seasonal nature of fishing for some species, such as yellowfin tuna, alternating bans with permits in some geographical areas helps to preserve the species. In fact, sustainable aquaculture, adopted for salmon, is used to obtain safe products of an excellent quality from the nutritional and organoleptic points of view.

CONCLUSIONS

In conclusion, a moderate consumption of fish (about two servings a week) is correlated with a clear reduction in the risk of developing a wide range of degenerative diseases of various kinds. Today, it is known that the beneficial effect of eating fish, until the Nineties attributed exclusively to its omega 3 fatty acid content, is actually more complex, and is probably the result of a combination of several aspects concerning the other components of fish, including the high content of proteins of a high quality and with a high satiating power, vitamins, minerals and other nitrogen-based substances, as well as the favourable effects of replacing other compounds (proteins and fatty acids) of animal origin in the diet.

It is thus the consumption of fish, as it is, that represents the nutritional element capable of giving the favourable effects observed in the major observational studies: and the pharmacotherapeutic use of some components of the fish (such as purified omega 3 fatty acids), though it may have a specific indication in well-defined conditions of disease (for example, after a heart attack), certainly cannot take the place of a regular consumption of fish in the population.

The fish eaten the most, such as tuna, thus plays an important role in our health: with a value (such as protection against dementia and some kinds of cancer) that we are only now beginning to comprehend and investigate with rigorous methods.

An intelligent and farsighted use of this essential food resource will also allow future generations to benefit from its irreplaceable protective effects.

REFERENCES

- Alm B, Aberg N, Erdes L, Möllborg P, Pettersson R, Norvenius SG, Goksör E, Wennergren G. Early introduction of fish decreases the risk of eczema in infants. *Arch Dis Child*. 2009 Jan;94(1):11-5.
- Amiano P, Dorransoro M, de Renobales M, Ruiz de Gordoa JC, Irigoien I; EPIC Group of Spain. Very-long-chain omega-3 fatty acids as markers for habitual fish intake in a population consuming mainly lean fish: the EPIC cohort of Gipuzkoa. *European Prospective Investigation into Cancer and Nutrition*. *Eur J Clin Nutr*. 2001 Oct;55(10):827-32.
- Arino A, Beltran J, Herrera A Roncales P. Fish in: *Encyclopedia of Human Nutrition* Elsevier Ltd, 2005.
- Arterburn LM, Hall EB, Oken H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. *Am J Clin Nutr*. 2006, 83:1467S-1476S.
- Berr C, Akbaraly T, Arnaud J, Hininger I, Roussel AM, Barberger Gateau P. Increased selenium intake in elderly high fish consumers may account for health benefits previously ascribed to omega-3 fatty acids. *J Nutr Health Aging*. 2009 Jan;13(1):14-8.
- Bourre JM. Dietary omega-3 fatty acids for women. *Biomed Pharmacother*. 2007 Feb-Apr;61(2-3):105-12.
- Brunner EJ, Jones PJS, Friel S, Bartle. y MFish, human health and marine ecosystem health: policies in collision. *Int J Epidemiol* 2009;38:93–100.
- Chen YM, Ho SC, Lam SS. Higher sea fish intake is associated with greater bone mass and lower osteoporosis risk in postmenopausal Chinese women. *Osteoporos Int*. 2009 Aug 6. [Epub ahead of print].
- Cole GM, Frautschy SA. DHA may prevent age-related dementia. *J Nutr*. 2010 Apr;140(4):869-74.
- Erkkilä AT, Lichtenstein AH, Mozaffarian D, Herrington DM. Fish intake is associated with a reduced progression of coronary artery atherosclerosis in postmenopausal women with coronary artery disease. *Am J Clin Nutr*. 2004 Sep;80(3):626-32.
- Eurostat Public Health 2010.

Gascon A, Jacques H, Moorjani S, Deshaies Y, Brun LD, Julien P. Plasma lipoprotein profile and lipolytic activities in response to the substitution of lean white fish for other animal protein sources in premenopausal women. *Am J Clin Nutr.* 1996 Mar;63(3):315-21.

Harris WS. The omega-3 index: from biomarker to risk marker to risk factor. *Curr Atheroscler Rep.* 2009 Nov;11(6):411-7.

Hibbeln JR. Fish consumption and major depression [letter]. *Lancet.* 1998; 351:1213.

Hirayama T. Life-Style and Mortality: A Large Census-Based Cohort Study in Japan. In: *Contributions to Epidemiology and Biostatistics vol.6* Basel, S. Karger, Basel 1990.

Kris-Etherton PM, Harris WS, Appel LJ; American Heart Association. Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation.* 2002 Nov 19;106(21):2747-57.

Koletzko B, Rodriguez-Palmero M, Demmelmair H, Fidler N, Jensen R, Sauerwald T. Physiological aspects of human milk lipids. *Early Hum Dev.* 2001 Nov;65 Suppl:S3-S18.

Kull I, Bergström A, Lilja G, Pershagen G, Wickman M. Fish consumption during the first year of life and development of allergic diseases during childhood. *Allergy.* 2006 Aug;61(8):1009-15.

Jacques H, Gascon A, Bergeron N, Lavigne C, Hurley C, Deshaies Y, Moorjani S, Julien P. Role of dietary fish protein in the regulation of plasma lipids. *Can J Cardiol.* 1995 Oct;11 Suppl G:63G-71G.

Innis SM. Brain Res. Dietary omega 3 fatty acids and the developing brain. 2008 Oct 27;1237:35-43.

ISTAT Annuario statistico italiano 2008 (2008 Italian Statistics Institute annual report).

Lopez-Garcia E, Schulze MB, Manson JE, Meigs JB, Albert CM, Rifai N, Willett WC, Hu FB. Consumption of (n-3) fatty acids is related to plasma biomarkers of inflammation and endothelial activation in women. *J Nutr.* 2004 Jul;134(7):1806-11.

Lucas M, Asselin G, Mérette C, Poulin MJ, Dodin S. Effects of ethyl-eicosapentaenoic acid omega-3 fatty acid supplementation on hot flashes and quality of life among middle-aged women: a double-blind, placebo-controlled, randomized clinical trial. *Menopause.* 2009 Mar-Apr;16(2):357-66.

Meyer R. Infant feeding in the first year. 2: feeding practices from 6-12 months of life. *J Fam Health Care*. 2009;19(2):47-50.

Miyake Y, Sasaki S, Tanaka K, Ohya Y, Miyamoto S, Matsunaga I, Yoshida T, Hirota Y, Oda H; Osaka Maternal and Child Health Study Group. Fish and fat intake and prevalence of allergic rhinitis in Japanese females: the Osaka Maternal and Child Health Study. *J Am Coll Nutr*. 2007 Jun;26(3):279-87.

Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Wilson RS, Aggarwal N, Schneider J. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. *Arch Neurol*. 2003 Jul;60(7):940-6.

Mozaffarian D, Gottdiener JS, Siscovick DS. Intake of tuna or other broiled or baked fish versus fried fish and cardiac structure, function, and haemodynamics. *Am J Cardiol*. 2006 Jan 15;97(2):216-22.

Mozaffarian D, Lemaitre RN, Kuller LH, Burke GL, Tracy RP, Siscovick DS; Cardiovascular Health Study. Cardiac benefits of fish consumption may depend on the type of fish meal consumed: the Cardiovascular Health Study. *Circulation*. 2003 Mar 18;107(10):1372-7.

Nwaru BI, Erkkola M, Ahonen S, Kaila M, Haapala AM, Kronberg-Kippilä C, Salmelin R, Veijola R, Ilonen J, Simell O, Knip M, Virtanen SM. Age at the introduction of solid foods during the first year and allergic sensitization at age 5 years. *Pediatrics*. 2010 Jan;125(1):50-9. Epub 2009 Dec 7.

Ramel A, Jonsdottir MT, Thorsdottir I. Consumption of cod and weight loss in young overweight and obese adults on an energy reduced diet for 8-weeks. *Nutr Metab Cardiovasc Dis*. 2009 Dec;19(10):690-6.

Ramel A, Parra D, Martínéz JA, Kiely M, Thorsdottir I. Effects of seafood consumption and weight loss on fasting leptin and ghrelin concentrations in overweight and obese European young adults. *Eur J Nutr*. 2009 Mar;48(2):107-14.

Schnappinger M, Sausenthaler S, Linseisen J, Hauner H, Heinrich J. Fish consumption, allergic sensitisation and allergic diseases in adults. *Ann Nutr Metab*. 2009;54(1):67-74.

Silvers KM, Scott KM. Fish consumption and self-reported physical and mental health status *Public Health Nutrition* 2002; 5:427-431.

Simopoulos AP Omega-3 fatty acids and athletics *Curr Sports Med Rep* 2007, 6:230–236.

SINU (Società Italiana di Nutrizione Umana) Livelli di assunzione di nutrienti raccomandati per la popolazione italiana (LARN), 1996.

Tanskanen A, Hibbeln JR, Hintikka J, Haatainen K, Honkalampi K, Viinamäki H. Fish consumption, depression, and suicidality in a general population. *Arch Gen Psychiatry*. 2001 May;58(5):512-3.

Tavani A, Pelucchi C, Parpinel M, Negri E, Franceschi S, Levi F, La Vecchia C. N-3 polyunsaturated fatty acid intake and cancer risk in Italy and Switzerland. *Int J. Cancer* 2003, 105:113–116.

van Gelder BM, Tjohuis M, Kalmijn S, Kromhout D. Fish consumption, n-3 fatty acids, and subsequent 5-y cognitive decline in elderly men: the Zutphen Elderly Study. *Am J Clin Nutr*. 2007 Apr;85(4):1142-7.

Virtanen JK, Siscovick DS, Longstreth WT Jr, Kuller LH, Mozaffarian D. Fish consumption and risk of subclinical brain abnormalities on MRI in older adults. *Neurology*. 2008 Aug 5;71(6):439-46.

PROFILE OF THE NUTRITION FOUNDATION OF ITALY

The NFI -- Nutrition Foundation of Italy – Food Study Centre is a non-profit association founded in 1976 with the aim of contributing to the development of scientific research, the exchange of information on diet and nutrition and the promotion of interdisciplinary research in this field by establishing relationships of collaboration with institutional and governmental bodies, universities and industry.

The association intends to:

- Help provide useful dietary information and education to companies operating in the nutritional and health fields, opinion makers and consumers;
- Provide a scientific consulting service to the food, drink and pharmaceutical industry, in the biological-nutritional, toxicological and technological sectors;
- Establish institutional relations and interact with governmental and administrative bodies of the State and the European Union, both nationally and internationally, for the food and drink sector.

by carrying out the following activities:

- Preparing medical and scientific material for printing and the public opinion;
- Setting up and updating an internet site dedicated to the very latest major issues in the field of nutrition (www.nutrition-foundation.it);
- Managing and coordinating research projects on the relationship between diet, food or nutrients and various aspects of human health;
- Organizing conferences and refresher courses both for industry and the scientific community;
- Setting up committees for congresses, publishing periodicals, holding conferences.

For all these activities, NFI will consult an Expert Scientific Committee with recognized competence in the various disciplines involved in the areas of nutrition linked to the food and drink sector.