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- > Tips for Older Supplement Users (FDA)
- > Human Performance Resource Center: Dietary Supplements (DoD)
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- > Información en español

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- > FDA: Consumer Updates on Dietary Supplements
- > FDA: Warnings and Safety Information
- > FDA: How to Spot Health Fraud
- > FTC: Drugs & Dietary Supplements
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Nutrient Recommendations

- > Dietary Reference Intake (DRI) Reports and Tables
- > Online DRI Tool
- > Daily Value (DV) Tables

Omega-3 Fatty Acids and Health

Fact Sheet for Health Professionals

About the reports

This document summarizes the results of eight evidence-based reviews on the effects of omega-3 fatty acids from food or dietary-supplement sources for the prevention and treatment of several diseases. These reviews were prepared under contract to the Agency for Healthcare Research and Quality (AHRQ). All reviews were sponsored and funded by the Office of Dietary Supplements (ODS) of the National Institutes of Health, U.S. Department of Health and Human Services. Five reports were published in March 2004 and 3 additional reports were published in February 2005, all of which are available in their entirety and summary form on the ODS web site (ods.od.nih.gov) and the AHRQ web site (www.ahrq.gov).

Table of Contents

- [About the reports](#)
- [Summary of key findings](#)
- [Background information about omega-3 and omega-6 fatty acids & their known functions](#)
- [Products available](#)
- [Omega-3 fatty acids for cardiovascular health and disease](#)
- [Omega-3 fatty acids for asthma](#)
- [Omega-3 fatty acids for other diseases](#)
- [Omega-3 fatty acids and cognitive function, dementia, and neurological diseases](#)
- [Omega-3 fatty acids for organ transplantation](#)
- [Safety aspects of omega-3 fatty acids](#)
- [References](#)
- [Disclaimer](#)

University of Ottawa, Canada (Ottawa EPC) [5], and the Southern California/RAND Evidence-based Practice Center in Los Angeles (RAND EPC) [6,7].

Summary of key findings

- The polyunsaturated fatty acids alpha-linolenic acid (ALA) and linoleic acid (LA) must come from the diet because they cannot be made by the body. ALA, an omega-3 fatty acid, is converted in the body to the fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). LA, an omega-6 fatty acid, is converted to the fatty acid arachidonic acid (AA).
- Most American diets provide more than 10 times as much omega-6 than omega-3 fatty acids. There is general agreement that individuals should consume more omega-3 and less omega-6 fatty acids to promote good health. Good sources of ALA are leafy green vegetables, nuts, and vegetable oils such as canola, soy, and especially flaxseed. Good sources of EPA and DHA are fish and organ meats. LA is found in many foods, including meat, vegetable oils (e.g.,

Three reports focus on cardiovascular disease (CVD), including the effects of omega-3 fatty acids on cardiac electrophysiology and arrhythmia (the heart's beating rate and disorders of its rhythm), cardiovascular risk factors such as blood pressure, and intermediate markers of disease such as heart rate variability [1-3]. One report focuses on omega-3 fatty acids and asthma. Another report addresses the effects of omega-3 fatty acids on type II diabetes and the metabolic syndrome, inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and osteoporosis [5]. Another report addresses the effects of omega-3 fatty acids on cognitive function in normal aging, the incidence and treatment of dementia, the incidence of Parkinson's disease and cerebral palsy in infants, and clinical outcomes in progressive multiple sclerosis [6]. Another report evaluates whether omega-3 fatty acids improve the outcomes of patients undergoing organ transplantation [7]. These reports were prepared by the Tufts-New England Medical Center Evidence-based Practice Center (Tufts EPC) [1,2,3,4], the University of Ottawa Evidence-based Practice Center at the

safflower, sunflower, corn, soy), and processed foods made with these oils.

- EPA and DHA are metabolized through the same biochemical pathways as AA. EPA and AA are precursors for hormone-like agents known as eicosanoids. It is not known whether a desirable ratio of omega-6 to omega-3 fatty acids exists or to what extent high intakes of omega-6 fatty acids interfere with any benefits of omega-3 fatty acid consumption.
- Impact on cardiovascular disease: According to both primary and secondary prevention studies, consumption of omega-3 fatty acids, fish, and fish oil reduces all-cause mortality and various CVD outcomes such as sudden death, cardiac death, and myocardial infarction. The evidence is strongest for fish and fish oil supplements.
- Impact on heart function: Animal and isolated organ/cell culture studies demonstrate that omega-3 fatty acids affect cellular functions involved in ensuring a normal heart rate and coronary blood flow.
- Impact on CVD risk factors: Fish oils can lower blood triglyceride levels in a dose-dependent manner. Fish oils have a very small beneficial effect on blood pressure and possible beneficial effects on coronary artery restenosis after angioplasty and exercise capacity in patients with coronary atherosclerosis.
- Impact on asthma: No conclusions could be drawn about the value of omega-3 fatty acid supplements in the prevention or treatment of asthma for adults or children other than the fact that they have an acceptable safety profile.
- Impact on other conditions: Omega-3 fatty acids can reduce joint tenderness and need for corticosteroid drugs in rheumatoid arthritis. Data are insufficient to support conclusions about the effects of omega-3 fatty acids on inflammatory bowel disease, renal disease, systemic lupus erythematosus, bone density, and diabetes.
- Impact on cognitive function: The quantity and strength of evidence is inadequate to conclude that omega-3 fatty acids protect cognitive function with aging or the incidence or clinical progression of dementia (including Alzheimer's disease), multiple sclerosis, and other neurological diseases.
- Impact on organ transplantation: No conclusive evidence suggests specific benefits of omega-3 fatty acid supplementation on any outcome in any form of organ transplantation. However, available studies are small, have methodological problems, and may not fully apply to current transplantation procedures.
- Safety: Adverse events related to consumption of fish-oil or ALA supplements are generally minor and typically gastrointestinal in nature (such as diarrhea). They can usually be eliminated by reducing the dose or discontinuing the supplement.
- Conclusion: The health effects of omega-3 fatty acids require further investigation. Each report provides recommendations on specific research needs and how to improve the quality of future studies.

Background information about omega-3 and omega-6 fatty acids & their known functions

There are two major classes of polyunsaturated fatty acids (PUFAs) -- the omega-3 and the omega-6 fatty acids -- distinguished by their chemical structure. Only the fatty acids alpha-linolenic acid (ALA) and linoleic acid (LA) must come from the diet because they cannot be made by the body. ALA, an omega-3 fatty acid, is converted in the body to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA also occur naturally in some foods. LA, an omega-6 fatty acid, is converted in the body to arachidonic acid (AA). Both EPA and DHA are metabolized through the same biochemical pathways as AA. Studies show that omega-3 fatty acids in general decrease triglyceride and very-low-density lipoprotein blood levels in hyperlipidemic individuals but may increase or have no effect on low-density lipoprotein (LDL) levels.

Both AA and EPA are further metabolized to produce hormone-like agents called eicosanoids, which include prostaglandins, thromboxanes, and leukotrienes. Eicosanoids regulate fundamental physiological processes such as cell division and growth, blood clotting, muscle activity, secretion of digestive juices and hormones, and movement of substances like calcium into and out of cells. However, AA and EPA lead to the production of different subgroups of eicosanoids with sometimes opposing effects. Eicosanoids formed from AA (particularly the series-2 prostaglandins and series-4 leukotrienes) are released in the body in response to injury, infection, stress, or certain diseases. They increase platelet aggregation and enhance vasoconstriction and the synthesis of substances involved with the inflammatory process. Eicosanoids derived from EPA (particularly the series-3 prostaglandins), in contrast, decrease excessive series-2 prostaglandin production. As a result, adequate production of EPA-derived series-3 prostaglandins may help protect individuals against heart attacks and strokes as well as certain inflammatory diseases such as arthritis, systemic lupus erythematosus, and asthma.

The omega-3 fatty acid DHA, while not involved in eicosanoid formation, is the major polyunsaturated fatty acid found in the brain and is important for brain development and function. Synapses are rich in DHA, which suggests that this fatty acid is involved in signal transmission along neurons. DHA is also required to produce one member of a family of compounds called resolvins that participate in the body's response to inflammation in the brain. The DHA-derived resolvin in particular helps to reduce

inflammation brought about by ischemic insults (reductions in blood flow). (EPA also helps to temper inflammatory responses by decreasing production of proinflammatory compounds such as cytokines.)

Most American diets provide at least 10 times more omega-6 than omega-3 fatty acids. There is now general scientific agreement that individuals should consume more omega-3 and fewer omega-6 fatty acids for good health. It is not known, however, whether a desirable ratio of omega-6 to omega-3 fatty acids exists for the diet or to what extent high intakes of omega-6 fatty acids interfere with any benefits of omega-3 fatty acid consumption. Tufts EPC investigators reviewed the Third National Health and Nutrition Examination Survey (NHANES III; 1988-1994) database to examine intakes of omega-3 fatty acids in the United States. They found that men consumed significantly less ALA than women, adults consumed more than children, and those with a history of CVD consumed less than those without CVD (when energy intake was taken into account in the analysis). On any given day, only 25% of the population reported consuming any EPA or DHA. Average daily intakes were 14 g LA, 1.33 g ALA, 0.04 g EPA, and 0.07 g DHA.

ALA is present in leafy green vegetables, nuts, vegetable oils such as canola and soy, and especially in flaxseed and flaxseed oil. Good sources of EPA and DHA are fish (both finfish and shellfish and their oils and eggs) and organ meats. LA is found in many foods consumed by Americans, including meat, vegetable oils (e.g., safflower, sunflower, corn, soy), and processed foods made with these oils. The Institute of Medicine has established Adequate Intakes for ALA and LA (1.1-1.6 g/day and 11-17 g/day, respectively, for adults) but not for EPA and DHA.

Products available

Omega-3 fatty acids are found in a variety of dietary supplements. For example, products containing flaxseed oil provide ALA, fish-oil supplements provide EPA and DHA, and algal oils provide a vegetarian source of DHA.

Omega-3 fatty acids for cardiovascular health and disease [1-3]

Epidemiological studies first published in the late 1970s noted relatively low cardiovascular mortality in populations such as Eskimos with high fish consumption. The apparent health benefits of fish are explained, at least in part, by the EPA and DHA they contain. Since these early studies, hundreds of observational and clinical trials have been conducted to evaluate the effects of EPA and DHA from marine sources and ALA from plant sources on CVD and its many risk factors and intermediate markers and to understand the potential benefits of increased intakes of omega-3 fatty acids.

The three reports by the Tufts EPC focused on different areas of research concerning this relationship between omega-3 fatty acids and cardiovascular health and disease and involved systematic reviews of the available scientific-medical literature. The first report focused on whole animal and isolated organ and cell culture studies to assess the effects of omega-3 fatty acids on arrhythmogenic mechanisms and outcomes. The second assessed the effects of EPA, DHA, and ALA on various CVD risk factors and intermediate markers of CVD in healthy people and people with dyslipidemia, diabetes, or known CVD. The third reviewed experimental and observational studies that investigated the effect of dietary or supplemental omega-3 fatty acids on specific clinical CVD outcomes (e.g., myocardial infarction and stroke) and whether these substances can play a role in the primary or secondary prevention of these outcomes.

Animal and isolated organ/cell culture studies [1]

A systematic review and screening of the literature identified 86 studies that met inclusion criteria and provided appropriate data. Of the 26 studies on living animals, a meta-analysis of 13 studies (with rats and monkeys) that compared the antiarrhythmic effects of ALA or fish oil with omega-6 fatty acids showed that fish-oil supplements (but not ALA) significantly reduced risk of death, ventricular tachycardia, and ventricular fibrillation. Since the majority of these studies were conducted by one research group, studies need to be repeated in other laboratories to confirm these results.

Another 60 studies evaluated the effects of omega-3 fatty acids on isolated organs and cell cultures. Seven of them reported that EPA and DHA (and in one instance ALA) protected against spontaneous or induced arrhythmias in both rat and guinea pig models. In the presence of various arrhythmogenic agents and across the species studied, omega-3 fatty acids consistently decreased the contraction rate and thereby had a protective effect compared with other substances, including placebos, but studies that did not administer an arrhythmogenic agent showed inconsistent results.

Conclusions cannot be drawn about the biochemical or physiological mechanisms that explain the potential antiarrhythmogenic effects of omega-3 fatty acids. These fatty acids affect cell functions (such as the movement of ions into and out of the cell) that are involved in cardiac electrophysiology to ensure a normal heart rate and coronary blood flow.

Cardiovascular risk factors and intermediate markers of CVD [2]

Many proposed risk factors for and intermediate markers of CVD exist. One report addressed the

many proposed risk factors for, and intermediate markers of, CVD exist. One report addressed the following risk factors and their relationship to omega-3 fatty acids in adults: total, LDL, and high density lipoprotein (HDL) cholesterol; triglycerides; lipoprotein (a); apolipoprotein (apo) A1; apo B; apo B-100 and LDL apo B; systolic and diastolic blood pressure; fasting insulin; C-reactive protein; fibrinogen; blood clotting factors VII, VIII, and von Willebrand factor; and platelet aggregation. The intermediate markers of CVD reviewed were coronary artery restenosis after angioplasty, carotid artery intima-media thickness, exercise tolerance testing, and heart rate variability. The literature review excluded studies of children, studies of daily omega-3 fatty acid intakes greater than 6 g/day, and studies less than 4 weeks long. A total of 123 articles that meet final eligibility criteria were reviewed regarding 23 potential risk factors and intermediate markers of CVD and tissue levels of omega-3 fatty acids. For most outcomes of interest, analysis was confined to the largest randomized trials.

Overall, strong evidence showed that fish-oil supplements had a substantial and beneficial effect on triglycerides that was greater with larger intakes of fish oil; most studies reported a net decrease of about 10-33%. There is also evidence of a very small beneficial effect of fish oils on blood pressure and possible beneficial effects on coronary artery restenosis after angioplasty, exercise capacity in patients with coronary atherosclerosis, and heart rate variability (particularly in patients with recent myocardial infarctions). No consistent beneficial effects were apparent for the other CVD risk factors or intermediate markers analyzed. Regarding concerns that glucose tolerance might be adversely affected by omega-3 fatty acids, there was no consistent evidence of a detrimental effect.

Meta-regression analysis of 50 trials showed that the dose of omega-3 fatty acids consumed was related to changes in EPA and DHA levels -- as plasma or serum phospholipids, platelet phospholipids, or in erythrocyte membranes -- without the influence of other factors. Supplementing the diet with 1-g of EPA and/or DHA resulted in approximately a 1% increase in the level of EPA and DHA and also to increases in granulocyte and monocyte membrane phospholipid levels. Few data are available, however, on how the effect of omega-3 fatty acids on CVD risk factors and intermediate markers differs depending on people's underlying health status and risk of CVD, amount of omega-3 fatty acids consumed, duration of consumption, or source or type of these fatty acids. In particular, the potential effects of ALA are unknown.

Cardiovascular disease [3]

One report examined how dietary or supplemental omega-3 fatty acids affect specific CVD outcomes such as myocardial infarction and stroke and investigated whether these fatty acids can play a role in the primary and secondary prevention of these outcomes. A systematic review of the literature and subsequent screening identified 39 studies that met the investigators' inclusion criteria for reporting mortality or CVD clinical outcomes with a follow-up of at least one year. The primary prevention studies included 22 prospective cohort studies and only one randomized, controlled trial (RCT); they were conducted in countries around the world, most cohorts had several thousand subjects, and studies lasted from 4 to 30 years. The secondary prevention studies, in contrast, consisted of 11 RCTs and one prospective cohort study that reported outcomes on CVD populations; they included over 16,000 patients and lasted from 1.5 to 5 years.

Overall, evidence from both the primary and secondary prevention studies supports the hypothesis that consumption of omega-3 fatty acids, fish, and fish oil reduces all-cause mortality and various CVD outcomes such as sudden death, cardiac death, and myocardial infarction. The evidence is strongest for fish or fish oil whereas the potential effects of ALA are largely unknown and the relative effects of ALA versus fish oil are not well defined. In the only RCT that directly compared ALA and fish oil, both treatments reduced CVD outcome. No consistent differences in the effects of omega-3 fatty acids on CVD outcomes were found between men and women, largely because the proportion of women in RCTs was small and data from men and women were not analyzed separately to address any differences. Data were also insufficient to determine the optimal quantity and type of omega-3 fatty acids to consume or to identify an optimal ratio of omega-3 to omega-6 fatty acid intake, if one in fact exists.

The lessons to be drawn from all these studies to date regarding use of omega-3 fatty acids for preventing and treating CVD are not completely clear. Because the studies involved a variety of methods of estimating fish or omega-3 fatty acid intake, background diets, background risk for heart disease, settings, and methods for reporting results, the validity of applying the results of studies conducted outside the United States to the U.S. population is uncertain. Furthermore, dietary intervention trials are limited by the multiple and complex dietary changes in the trials that make it difficult to distinguish among components and determine which specific components or combinations of these diets are most beneficial. For example, the different types of fish consumed and the method of food preparation may cause different effects.

Omega-3 fatty acids for asthma [4]

Asthma is a major public health concern for Americans. In 1987 it was hypothesized that the low incidence of asthma among Eskimos resulted from their high intakes of oily fish rich in EPA and DHA. *Recent research suggests that omega-3 fatty acids may affect asthma because their influence on*

Basic research suggests that omega-3 fatty acids may affect asthma because they influence substances that are part of the inflammatory process involved with asthma, such as the series-2 prostaglandin PGE₂.

The Ottawa EPC conducted a comprehensive search of the published and unpublished scientific-medical literature. Its screening process identified 31 reports describing 26 studies. The primary outcome measure evaluated was the forced expiratory volume in one second, considered the best available method to assess pulmonary function. It was not possible to conduct a meta-analysis with the RCTs because of problems and limitations such as flawed designs, missing data, and incompatible study variables; most were small and lacked the ability to detect a statistical difference between the treatments, and inclusion and exclusion criteria were rarely reported.

Conclusions could not be made about the value of omega-3 fatty acid supplements in asthma for adults or children beyond that they have an acceptable safety profile. The evaluation of ten RCTs and nine other studies found the results to be too inconsistent and of limited applicability to larger groups of people to conclude that these supplements are an efficacious adjuvant or monotherapy. In some cases, asthma medications used by the subjects may have prevented the identification of any benefits from the omega-3 supplements. No other characteristics of the treatment (such as the type of fatty acid used, specific source, daily dose, and intervention length) were found to improve respiratory outcomes. As to whether omega-3 fatty acids influence substances that are part of the inflammatory process, such as PGE₂, the 11 relevant studies were insufficient to address this issue because of small sample sizes and differing methodologies.

Whether omega-3 fatty acids are effective in the primary prevention of asthma is unknown. Four observational studies in children support a positive association for dietary patterns that include all fish or oily fish, but a prospective study of adult nurses found no association between asthma onset and dietary fish intake. One RCT is evaluating the relationship in neonates at risk for asthma whose intake of omega-3 fatty acids or placebo was initiated before birth. Its interim results show little benefit from the supplement, though 18 months is probably too early in life to reliably identify asthma.

Omega-3 fatty acids for other diseases [5]

The RAND EPC conducted a comprehensive search of published and unpublished scientific-medical literature on the health effects of omega-3 fatty acids in type II diabetes and metabolic syndrome, inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and bone density/osteoporosis. Only articles that reported the results of RCTs or controlled clinical trials were included except for observational studies of bone mineral status. In all, 83 articles met the inclusion criteria, 82 of which were RCTs. Overall, the data were insufficient to draw conclusions about the value of omega-3 fatty acids for these medical problems with the exception of rheumatoid arthritis.

Type II diabetes and metabolic syndrome

Eighteen of the 34 RCTs whose subjects had type II diabetes or metabolic syndrome provided sufficient statistics to be included in a meta-analysis. The analysis found that omega-3 fatty acids had a favorable effect on triglyceride levels when compared with placebo but had no effect on total, LDL, or HDL cholesterol; fasting blood sugar; or glycosylated hemoglobin. A qualitative analysis of 4 studies concluded that omega-3 fatty acids had no effect on plasma insulin or insulin resistance in subjects with either disorder.

Inflammatory bowel disease (Crohn's disease and ulcerative colitis)

In the 13 studies that reported outcomes in patients with inflammatory bowel disease, omega-3 fatty acids had variable effects on assessment scores (clinical, sigmoidoscopic, and histologic), induced remission, and relapse rates. For ulcerative colitis, omega-3 fatty acids had no effect on the relative risk of relapse in a meta-analysis of three studies. The requirement for corticosteroids among patients receiving omega-3 fatty acids relative to placebo was not significantly reduced in two studies. No studies evaluated the effect of omega-3 fatty acids on the requirements for other immunosuppressive medications.

Rheumatoid arthritis

A meta-analysis of nine studies of patients with rheumatoid arthritis concluded that omega-3 fatty acids had no effect on patients' reports of pain and disease severity, swollen joint count, or erythrocyte sedimentation rate (a measure of disease activity). However, an earlier meta-analysis found that the omega-3 fatty acids produced a statistically significant improvement in tender joint count as compared with placebo. A qualitative analysis of seven studies that assessed the effect of omega-3 fatty acids on anti-inflammatory drug or corticosteroid requirements found that six demonstrated reduced requirements. No studies assessed how the supplements affected requirements for disease-modifying antirheumatic drugs and no studies used a composite score that incorporated both subjective and objective measures of disease activity. Overall, omega-3 fatty acids appear to reduce tender joint counts in individuals with rheumatoid arthritis and may reduce requirements for corticosteroids. The studies do not demonstrate an effect of the supplements on other clinical outcomes.

Renal disease

A qualitative analysis of nine studies assessing the effects of omega-3 fatty acids in renal disease concluded that the supplements had various effects on serum creatinine and creatinine clearance but no effect on the progression to end-stage renal disease. The one study that assessed hemodialysis graft patency found graft patency to be significantly better with fish oil than placebo. No studies assessed whether omega-3 fatty acids altered requirements for corticosteroids.

Systemic lupus erythematosus

A qualitative analysis of the three studies that assessed the effects of omega-3 fatty acids in systemic lupus erythematosus found variable effects on disease activity. No study assessed their effect on damage or patient perceptions of the severity of their disease. Omega-3 fatty acids had no effect on corticosteroid requirements in one study, but no study assessed how these supplements affected requirements for other immunosuppressive drugs. No study used both subjective and objective measures to study disease activity.

Bone density/osteoporosis

A qualitative analysis of five studies described in four reports found variable effects of omega-3 fatty acids on bone density. No studies were identified that assessed their effects on fractures.

Omega-3 fatty acids and cognitive function, dementia, and neurological diseases [6]

Omega-3 fatty acids appear to be important in brain development and function. Their effects on cognitive function in normal aging, incidence and treatment of dementia, incidence of several neurological diseases, and progression of multiple sclerosis were evaluated. A comprehensive search of the published and unpublished scientific-medical literature identified 12 studies that met inclusion criteria.

Cognitive function in normal aging and dementia

In the one cohort study that assessed the effects of omega-3 fatty acids on cognitive function with normal aging, fish consumption was only weakly associated with a reduced risk of cognitive impairment and had no association with cognitive decline over time; omega-3 fatty acid consumption was not associated with either outcome. Three prospective cohort studies evaluated the effects of these compounds on the incidence of dementia. Fish consumption was associated with a significant reduction in the incidence of non-Alzheimer's dementia in only one study. In all three, however, fish consumption was linked to a reduced risk of Alzheimer's dementia but was statistically significant in only one study. Total omega-3 fatty acid consumption and consumption of DHA (but not ALA or EPA) were associated with a significant reduction in the incidence of Alzheimer's disease. In the one RCT that assessed the effects of omega-3 fatty acids for the treatment of dementia, DHA produced a small improvement in scores on a dementia rating scale, but the sample size was small and the study was of poor quality.

Multiple sclerosis and other neurological diseases

Two studies (one cohort and one case control) that assessed the association between omega-3 fatty acid intake and incidence of multiple sclerosis found no significant results. In three studies that evaluated omega-3 fatty acid intake on disease progression, the RCT found no effects on disability or relapse rates, though the two single-arm open-label trials reported a significant reduction in disability (with one also reporting improvement on an index of disease progression).

Regarding other neurological diseases, one cohort study assessed the association between consumption of omega-3 fatty acids (from fish, ALA, EPA, or DHA) and risk for Parkinson's disease but found no significant associations. One case-control study found a significant association between maternal fish consumption at least once weekly throughout pregnancy and a lower risk of cerebral palsy in the offspring.

The quantity and strength of evidence for the effects of omega-3 fatty acids on cognitive function and decline, dementia, and neurological diseases vary greatly. Given the overall small number of studies and generally poor quality of clinical trials, substantive conclusions about the value of these compounds for these conditions cannot be drawn.

Omega-3 fatty acids for organ transplantation [7]

Several laboratory, animal, and human studies suggest that omega-3 fatty acids from fish oil may improve outcomes in organ transplantation (e.g., decrease rejection; reduce hyperlipidemia, hypertension, and blood viscosity; and decrease the toxicity of the immunosuppressive agent cyclosporin A). The Tufts EPC systematically identified studies of human subjects who underwent transplantation and received a quantifiable amount of omega-3 fatty acids. A total of 31 studies were included in the review pertaining to transplantation of the kidney (23), heart (6), liver (1), and bone marrow (1). All but one study used fish-oil supplements at doses ranging from 1.2 to 5.4 g/day EPA plus DHA, though in most the daily dose was 2-3 g.

No conclusive evidence was found suggesting specific benefits of omega-3 fatty acid supplementation on any outcome evaluated in any form of transplantation. The one possible exception was a reduction in triglyceride levels in patients who underwent kidney transplantation, which is consistent with the effects of omega-3 fatty acids for other conditions. The supplements did not cause clinically important interactions with cyclosporin A.

The quantity and quality of the evidence and its applicability to current transplantation procedures were limited. All studies were small and had methodological problems, such as the rigor with which endpoints were defined and measured, and most studies were not recent. Because the technology for transplantation continues to improve, whether fish-oil supplementation is beneficial with current procedures is uncertain. Furthermore, in all studies the supplements were begun after transplantation. Because it may take up to three weeks for omega-3 fatty acids to affect cytokine production, supplementation before the transplants might have influenced the outcomes.

Safety aspects of omega-3 fatty acids [3]

The Tufts EPC reviewed 148 studies to evaluate adverse events-not including fishy aftertaste-from the use of omega-3 fatty acid supplements (typically fish oils). More than half (77) reported that no adverse events had occurred. In total, about 10,000 subjects had taken these supplements in various forms and dosages ranging from 0.3 to 8 g/day for at least one week to more than seven years. Most studies were small, with a few dozen subjects receiving supplements for less than six months.

In general, side effects were minor, primarily gastrointestinal in nature (such as diarrhea), and reported by fewer than 7% of subjects. The supplements were not associated with serious adverse events such as death, life-threatening illness, significant disability, or handicap. Omega-3 fatty acids did not affect the frequency of bleeding events. However, several cases of clinical bleeding in two RCTs were reported where patients also took warfarin or aspirin daily; the bleeding (e.g., at the site of a wound or into the gastrointestinal tract) was typically mild.

The Tufts EPC concluded that adverse events related to consumption of fish-oil or ALA supplements appear to be minor and can be managed by reducing the dose or discontinuing the supplement. It noted, however, that adverse event data are incomplete because many studies did not adequately report this information, especially for subjects who withdrew before study completion.

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Disclaimer

This fact sheet by the Office of Dietary Supplements provides information that should not take the place of medical advice. We encourage you to talk to your health care providers (doctor, registered dietitian, pharmacist, etc.) about your interest in, questions about, or use of dietary supplements and what may be best for your overall health. Any mention in this publication of a specific brand name is not an endorsement of the product.

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