Vital Choice
SEAFOOD

WHITE PAPER

Long Chain Omega-3 Fatty Acids In Human Health

The Vital Roles of Eicosapentaenoic, Docosahexaenoic and Alpha-Linolenic Acids (EPA, DHA, and ALA)

A VITAL CHOICE WHITE PAPER
Long Chain Omega-3 Fatty Acids In Human Health

(Last updated December 27, 2010)

Click underlined topics to jump down to each

Contents

Introduction

The overwhelming majority of scientific evidence indicates that people whose diets contain ample amounts of long-chain "marine" omega-3 fatty acids (EPA and DHA) – whether obtained from fish or fish oil capsules – enjoy reduced risks of heart disease, sudden cardiac death, stroke, depression, anxiety, and macular degeneration.

However, omega-3s of all kinds (fish-derived and plant-derived) have become very scarce in the diets consumed in America and many other countries.

In addition, the proportion of omega-3s to omega-6 fatty acids in modern diets is radically lower than it was over millions of years of evolutionary history.

This White Paper presents a summary of the scientific evidence concerning the effects of omega-3 fatty acids and the omega-3/omega-6 intake ratio on heart health, mental health, child development, cancer, diabetes, inflammation, and other health concerns.

Essential fatty acids (EFAs) in brief

To survive and thrive, humans need to consume two kinds of nutritionally essential fatty acids: omega-3 and omega-6.

While these fatty acids constitute essential structural and functional components of our cells, and regulate many critical aspects of metabolism and immunity, they cannot be synthesized in our bodies and must be obtained from our diets.

Omega-3 EFAs

Omega-3 EFAs are found in two places:

- Leafy green vegetables and certain seeds and oils.
- Fish, shellfish, zooplankton, and aquatic plants (algae, plankton, seaweed).

Only fish, shellfish, zooplankton, and aquatic plants contain the long-chain or "marine" omega-3 fatty acids the human body actually uses:

- Omega-3 DHA is an essential component of all cell membranes. DHA is also the dominant fatty acid in human brains, and is essential to proper brain and eye functioning and to regulation of metabolic rate. (DHA stands for docosahexaenoic acid.)
- Omega-3 EPA is found in all cell membranes, and is needed to make critical inflammation-moderating messenger chemicals called eicosanoids. (EPA stands for eicosapentaenoic acid.)

Plant foods contain a "short-chain" omega-3 fatty acid called alpha-linolenic acid (ALA), whose primary purpose in the body is to provide the raw material with which to make the long-chain, "marine" omega-3s essential to good health.

When you see reports about the benefits of omega-3s, these almost invariably refer to the results of studies using one or both of the long-chain marine omega-3s (DHA and EPA).

Researchers employ the long-chain "marine" omega-3s in biomedical studies because these omega-3s yield much stronger effects in much smaller amounts, compared with plant-derived omega-3s (i.e., ALA).

The very small amount of omega-3 ALA found in most Americans' diets comes from seed oils like soy and canola, which contain far higher levels of omega-6 fatty acids.

The best common food sources of dietary ALA are green leafy vegetables (e.g., spinach, kale, lettuces). Flaxseed, flax oil, hemp seeds, and hemp oil are the richest food sources of ALA, and therefore constitute the best supplemental sources of ALA.

The human body converts from two to 15 percent of dietary ALA into DHA and EPA. Nonetheless, people can survive and thrive if they consume enough plant-derived ALA.

In contrast people can survive and thrive entirely without ALA if they consume fish or fish oil supplements, which are naturally rich in DHA and EPA.

Omega-6 EFAs

Linoleic acid (LA) is a short-chain omega-6 fatty acid that the body uses to make arachidonic acid (AA), a long-chain omega-6 fatty acid which, like omega-3 DHA, is an essential constituent of our cell membranes.

Most dietary LA comes from grains, seeds, and vegetables, while meats such as chicken, beef, pork, and lamb contain both LA and AA.

What do EFAs do in the body?

Essential fatty acids play key structural and functional roles in cell membranes, affecting their fluidity, flexibility, permeability and the activity of critical membrane-bound enzymes. DHA is selectively incorporated into cell membranes in the retina of the eye and into postsynaptic neuronal cell membranes, which suggests it plays important roles in vision and nervous system function.

Omega-6 and omega-3 EFAs also affect the expression of a number of genes, including those involved with fatty acid metabolism and inflammation. They do this by interacting with cellular compounds called “transcription factors”, including Nf-kappa-b, AP-1, peroxisome proliferator-activated receptors (PPARs), and liver X receptors (LXRs).

Omega-3 and omega-6 EFAs also influence the production of ephemeral, hormone-like compounds known as eicosanoids or autocoids, which include prostaglandins, thromboxanes, and leukotrienes. These potent chemical messengers influence key body functions, including blood pressure, blood clotting, inflammation, and immune function.

In response to injury, infection, or large amounts of dietary sugars, the body will initiate an inflammatory response that begins when enzymes known as cyclooxygenases and lipoxygenases act on omega-6 AA and omega-3 EPA in cell membranes to form eicosanoids (prostaglandins, thromboxanes, and leukotrienes).

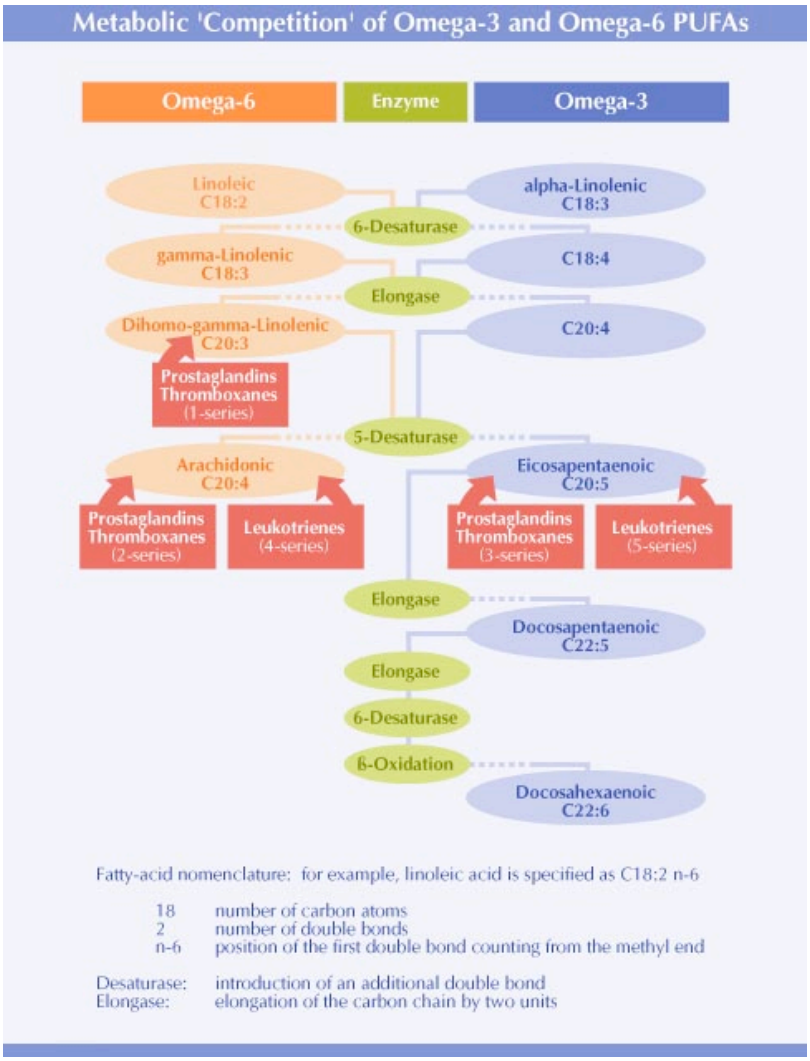
However, in contrast to the eicosanoids derived from EPA, which moderate inflammation, eicosanoids derived from AA tend to induce strong, persistent inflammation, blood vessel constriction, and coagulation.

The cell membranes of people who consume typical Western diets are excessively high in omega-6 AA relative to the amount of omega-3 EPA. This imbalance results in the preferential formation of pro-inflammatory eicosanoids derived from AA.

The chronic, low-level inflammation produced by diets high in omega-6 EFAs promotes cardiovascular disease and cancer and is associated with Alzheimer’s disease.

Increasing one’s dietary intake of omega-3s increases the EPA content of your cell membranes, resulting in higher proportions of eicosanoids that moderate inflammation.

Thanks to their specific effects on gene expression and eicosanoids, omega-3s tend to decrease inflammation and the risk or severity of cardiovascular disease, diabetes, autoimmune diseases, and certain cancers, while omega-6s tend to increase the risk and severity of these conditions.



Graphic courtesy www.fatsoflife.com

The extreme EFA imbalance in Western diets

Paleoanthropologists believe that, compared with modern diets, the diets of hominids and early humans were much higher in omega-3s and much lower in omega-6s. Constant exposure to this fatty acid intake ratio exerted a critical evolutionary influence on the characteristics and nutritional requirements of present-day human bodies and brains.

However, humans' food consumption pattern began to change with advent of agriculture (cereal grains like wheat) some 10,000 years ago, and these changes started to accelerate rapidly in the mid-1800s as processed foods became widely available.

One of the most important human dietary changes brought about by agriculture and processed foods was the shift away from foods relatively high omega-3s – leafy greens, wild game, and pasture-grazed animals – in favor of foods high in omega-6 fatty acids, such as seed oils, grains, and grain-fed livestock.

This imbalance results in a very high proportion of omega-6 to omega-3 fats, relative to the near-equal proportions that humans consumed throughout the vast majority of evolutionary history.

This historically recent imbalance in EFA intake is extreme. While research indicates that the body functions best when people consume two to four parts omega-6 EFAs to each part omega-3 EFA, the average American's diet contains from 10 to 40 times more omega-6 EFAs than omega-3 EFAs.

The fact that most Americans and Europeans consume about 10 times more omega-6 fat in relation to omega-3s explains why government health authorities on both sides of the Atlantic recommend that their citizens increase dietary intake of omega-3s.

(These authorities should, but rarely do, recommend that people also reduce their intake of omega-6s.)

The enormous excess of omega-6s in the diets of developed countries accounts for the beneficial effect seen in population surveys and controlled studies when people consume less omega-6s and ample amounts of fish or supplemental omega-3s.

In other words, while most people in developed countries would benefit from increased intake of omega-3s, experts believe that much benefit would also accrue from a sharp decrease intake of omega-6s.

Because omega-6 EFAs are so abundant in the cooking oils, meats, poultry, and processed or prepared foods that dominate most modern diets it is easier to redress the imbalance by increasing omega-3 intake than by drastically reducing omega-6 intake.

Accordingly, it makes good sense to increase intake of both types of omega-3s – from plants and fish – even though the plant form is less useful to the body. Small amounts of short-chain omega-3s (ALA) are found in all leafy green plants, including dark cooking greens such as spinach, collards, kale, and the like.

In addition, some brands of eggs are high in omega-3 DHA, thanks to chicken feed that's high in fish meal and/or plant sources of omega-3s. And some brands of yogurt, cereal, waffles, and other packaged foods are fortified with omega-3 ALA, usually via addition of flaxseed (or its oil), which is the seed highest in this fatty acid.

Back to top

Cardiovascular (Heart/Artery) Health

There is an overwhelming amount of scientific support for the idea that long-chain marine omega-3s (EPA and DHA) provide cardiovascular benefits.

Health authorities in the US, UK, Europe, and Japan agree that people with higher than average intakes of omega-3s enjoy significantly reduced risks of stroke and cardiac death.

The American Heart Association recommends that people eat fish, particularly oily fish, at least twice a week. For adults diagnosed with coronary heart disease, the Heart

Association (AHA) recommends consuming one gram (1,000 mg) of omega-3 fatty acids per day from fish and/or supplemental fish oil.

The AHA's guidance is echoed by the U.S. Food and Drug Administration (FDA) and the Agency for Healthcare Research and Quality (AHRQ), whose independent reviews of the available evidence led both agencies to conclude that the long-chain "marine" omega-3s from fish and fish oil (EPA and DHA) offer unique cardiovascular benefits not available from the short-chain omega-3 fatty acid found in selected plant foods (alpha-linolenic acid or ALA).

As the authors of the March, 2004 AHRQ review reported, "Overall, consumption of omega-3 fatty acids, whether from fish or from supplements, reduces all-cause mortality and improves various CVD outcomes. The evidence for benefit from ALA [i.e., plant-derived omega-3] supplements is sparse and inconclusive."

The FDA has permitted use of a qualified health claim on the labels of foods and dietary supplements containing EPA and DHA:
"Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease." (Note: The FDA health claim cannot be used on foods or supplements containing only short-chain omega-3s from plant foods such as flaxseed.)

Survivors of a heart attack who consume as little as one gram of omega-3s per day have half the mortality from heart disease. Rates of heart disease are extremely low in Japan, Iceland, and other countries where diets are very high in fish.

In addition, the results of recent evidence reviews indicate that marine omega-3s rival the benefits of statin drugs when it comes to reducing the risk of heart attack, even though omega-3s do not lower cholesterol levels substantially.

These findings support the increasingly influential hypothesis that one's overall cholesterol level may not be the most critical factor in the onset of cardiovascular disease or the risk of heart attack. (People's relative proportions of LDL and HDL cholesterol seem more important than their total cholesterol levels.)

According to the most recent evidence review conducted by scientists affiliated with the American Heart Association, marine omega-3s can decrease the risk of cardiovascular disease and resulting heart attacks and strokes in several ways:

- Prevent arrhythmias (irregular heartbeats) that can lead to sudden cardiac death. (See our discussion of congestive heart failure and implanted cardiac defibrillators, below.)
- Decrease the risk of clotting (thrombosis) that can lead to a heart attack or ischemic stroke. Ischemic strokes, which constitute three out of four strokes in the US, result from insufficient blood flow to an area of the brain and typically occur when an artery supplying the brain becomes constricted or blocked by a clot.
- Reduce blood levels of triglycerides (fats).
- Slow the growth of arterial plaques.
- Improve the function of the endothelial cells that line the arteries.
- Lower blood pressure modestly.

- Decrease inflammation in blood and artery walls.

Omega-3s in Congestive Heart Failure and Defibrillator Patients

Congestive heart failure (CHF) is the condition in which the heart is too weak to pump blood effectively to the rest of the body.

CHF is characterized by reduced blood and oxygen supply to heart muscles, usually caused by narrowing of coronary arteries from atherosclerosis (build up of sticky, fatty, unstable "plaque" in artery walls): a condition called ischemic heart disease.

There is preliminary clinical evidence that omega-3s from fish oil can help reverse the dangerous weight loss – called cardiac cachexia – that often occurs in advanced congestive heart failure (CHF), and reduce blood levels of pro-inflammatory, cachexia-promoting immune-system chemicals (cytokines) found in CHF patients.

The results of some of the extant studies testing omega-3 supplements in people with implanted cardioverter defibrillators (ICDs) have raised hypothetical concerns about contraindications for omega-3s in patients with CHF and/or ICDs.

Some, but not all such studies detected a trend toward an increased risk of ventricular arrhythmias – although not an increased risk of death – in patients taking fish oil.

People with CHF have dangerously few functional heart cells, which are starved for blood flow, which makes them "hyper-excitable" and prone to trigger the arrhythmias that cause most cases of sudden cardiac death.

Omega-3s selectively quiet hyper-excitable cells, bringing anti-arrhythmia benefits to most heart patients … and to the many outwardly healthy people who die from unexpected arrhythmias daily.

The hypothetical risk to people with congestive heart failure and/or implanted cardiac defibrillators stems from the possibility that dietary omega-3s could suppress pumping action in the hyper-excitable cells that account for an unusually large proportion of their blood-pumping power.

However, this concern may be exaggerated, given the positive outcomes of other studies that examined the effects of supplemental omega-3s in patients with ICDs.

In addition, the preponderance of research suggests that the ability of omega-3s to reduce risk of sudden cardiac death extends to the four groups for which this hypothetical concern has been expressed:

- Patients with ischemic heart disease:
- Patients with congestive heart failure.
- Patients with implanted cardioverter defibrillators.
- Patients who are susceptible to heart arrhythmias.

And, significantly – given the difficulty of verifying the reported diets of participants in epidemiological studies, and the compliance of participants in clinical trials – the anti-arrhythmia effects associated with fish and fish oil have been confirmed in studies that

verified the level of omega-3 fatty acid intake by measuring plasma phospholipid fatty acid content.

Omega-3s, inflammation and heart disease

The anti-inflammatory effects of omega-3s may play a greater role in heart health than previously thought. In 2005, results from the ongoing ATTICA study in Athens, Greece provided the first direct evidence showing that omega-3s reduce the kinds of inflammation increasingly accepted as key risk factors for heart attack.

About 90 percent of the ATTICA study participants reported eating fish at least once a month. Compared with those who ate little fish, the participants who ate the most fish – about 10.5 ounces per week – had much lower levels of five key markers of inflammation:

- C-reactive protein (33 percent lower)
- Interleukin-6 (33 percent lower)
- Tumor necrosis factor-alpha (21 percent lower)
- Serum amyloid A (28 percent lower)
- White blood cells (4 percent lower).

The Greek researchers, who were careful to adjust for any other factors that might reduce inflammation, also found significantly lower levels of these inflammation markers in participants who ate between five and ten ounces of fish per week.

As the scientific team concluded, "Fish consumption was independently associated with lower inflammatory markers levels, among healthy adults. The strength and consistency of this finding has implications for public health and should be explored further."

Lead author Antonis Zampelas, Ph.D., added that the results indicate that omega-3 supplements should be comparably beneficial: "… the amount of omega-3 fatty acids seems to play a role in the reduction of inflammatory markers levels … omega-3 fatty acid intake in the level of 0.6 grams [600 mg] per day could be [beneficial] to other populations …"

American Heart Association Summary of Recommendations for Omega-3 Fatty Acid Intake

Patients without documented coronary heart disease (CHD):

- Eat a variety of (preferably fatty) fish at least twice a week.
- Include oils and foods rich in alpha-linolenic acid (flaxseed, canola and soybean oils; flaxseed and walnuts).

Patients with documented CHD:

- Consume about 1 g of EPA+DHA per day, preferably from fatty fish. EPA+DHA supplements could be considered in consultation with the physician.

Patients who need to lower triglycerides:

- 2 to 4 grams of EPA+DHA per day provided as capsules under a physician's care.

Patients taking more than 3 grams of omega-3 fatty acids from supplements should do so only under a physician's care. High intakes could cause excessive bleeding in some people.

Evidence from prospective secondary prevention studies suggests that taking EPA+DHA ranging from 0.5 to 1.8 grams per day (either as fatty fish or supplements) significantly reduces deaths from heart disease and all causes. For alpha-linolenic acid, a total intake of 1.5–3 grams per day seems beneficial.

Increasing omega-3 fatty acid intake through foods is preferable. However, coronary artery disease patients may not be able to get enough omega-3 by diet alone. These people may want to talk to their doctor about taking a supplement. Supplements also could help people with high triglycerides, who need even larger doses. The availability of high-quality omega-3 fatty acid supplements, free of contaminants, is an important prerequisite to their use.

Back to top

Alzheimer's Disease and other Dementias

The results of a number of large studies suggest that people who consume fish once per week or more enjoy a substantially reduced risk of Alzheimer's disease, compared with those who rarely or never eat fish, and that people whose blood is high in DHA enjoy significantly reduced rates of Alzheimer's disease and other forms of dementia.

The mechanism by which omega-3s might reduce these risks is suggested by new research from the Massachusetts Institute of Technology, where researchers found that omega-3s increase the growth of synaptical connections between the brain cells of rodents.

Back to top

Mental Health and Performance

In recent years, the results of population, clinical, and laboratory studies have demonstrated a range of likely positive mental health and performance effects associated with increased intake of omega-3s:

Substantial Evidence of Benefit

- Reduce the risk and severity of depression.
- Enhance mood and brain speed in healthy people.
- Extend periods of remission in bi-polar disorder.
- Reduce anger and hostility in alcoholics, cocaine addicts, troubled adolescents, and violence-prone prisoners.

Preliminary, Mixed or Weak Evidence of Benefit

- Reduce the risk and severity of post-partum depression.
- Enhance conventional medical treatment of schizophrenia.
- Reduce the risk and severity of social anxiety disorder.
- Reduce frequency and severity of seizures in epileptics.

Omega-3s for Depression and Mood Disorders

Among all mental conditions studied, the strongest evidence of benefit from higher intake of omega-3s relates to prevention of depression and other mood disorders.

The authors of a recent evidence review (Freeman MP et al 2006) concluded that the preponderance of evidence from two sources -- epidemiologic (population/diet) studies and from studies comparing people's tissue levels of marine omega-3s (EPA and DHA) with their mental health status ("compositional" studies) -- indicate that higher intake of omega-3s reduces the risk of depression.

These authors – who included leading psychiatric clinicians and researchers at America's National Institutes of Health -- noted that prior meta-analyses of randomized controlled trials demonstrate that omega-3s produce statistically significant benefits in regular (unipolar) and bipolar depression.

However, the authors of another review, published simultaneously (Appleton KM et al 2006), found the evidence from clinical trials too weak to support a firm conclusion. But compared with the relative abundance of evidence from epidemiologic studies, there is much less evidence available from clinical trials, and the results are difficult to pool for analysis due to differences in the doses and specific omega-3s (DHA, EPA, or both) used.

The authors of a third review of the available evidence, published the same year (Sontrop J, Campbell MK 2006), made these relevant comments:
"The relationship between omega-3s and depression is biologically plausible and is consistent across study designs, study groups, and diverse populations, which increases the likelihood of a causal relationship."
"It remains unclear whether omega-3 supplementation is effective independently of antidepressant treatment, for depressed patients in general, or only those with abnormally low concentrations of … [omega-3s]."

Back to top

Child Development
Because DHA forms an integral part of cell membranes in the brain and in the retina of the eye it is considered important to optimal child development.

This hypothesis is borne out by the generally positive results of studies designed to examine the effects of increased omega-3 intake by mothers and infants on mental and vision development.

Specifically, the majority of studies suggest that increased omega-3 intake by mothers and infants can enhance growing children's intelligence, attention, hand-eye coordination, and even their risk of developing high blood pressure in adulthood.

The last trimester of pregnancy is a critical period for the accumulation of DHA in the brain and retina, so preterm infants are particularly prone to suffer the adverse effects of insufficient DHA. Human milk contains DHA in addition to EPA and the plant-derived omega-3 ALA. Still, until recently, ALA was the only omega-3 fatty acid added to conventional infant formulas.

Although preterm infants can synthesize DHA from ALA, they generally cannot make enough to prevent declines in blood and cellular DHA concentrations. Accordingly, preterm infant formulas typically contain added DHA.

Infant formulas enriched with DHA are also commercially available for full-term infants, although the results of randomized controlled trials of these formulas on visual acuity and development in term infants have, like those conducted in preterm infants, have been mixed.

Since DHA appears to be critical to visual and neurological development, most expert observers consider it prudent to give non-breastfed infants formula enriched with DHA to ensure optimal visual and neurological development.

Mothers are the sole source of omega-3s for fetuses and exclusively breast-fed infants, and preliminary findings suggest that mothers who take supplemental omega-3s may reduce their risk of premature delivery and increase their length of gestation significantly.

Fish Intake by Pregnant or Nursing Mothers

A series of evidence reviews conducted in recent years indicate that the rewards of eating fish during pregnancy and nursing outweigh any mercury-related risks to fetuses and infants.

For example, analysis of data from a study of almost 9,000 British families found "… no evidence to lend support to the warnings of the US [fish-and-mercury] advisory that pregnant women should limit their seafood consumption", and reported that "… children of mothers who ate small amounts of seafood were more likely to have suboptimum neuron-developmental outcomes than children of mothers who ate more seafood." (Hibbeln JR et al 2007)

The findings of five Harvard-led dietary fish risk/reward analyses found that fears among the general public created by government mercury warnings directed to expectant/nursing mothers may cause many other women – and many men – to cut fish intake.

These were the Harvard teams' basic findings:

- Government advisories warning women of childbearing age about mercury exposure appear likely to lead the general public to cut fish consumption, with a resulting loss of substantial omega-3-related preventive health benefits"
- If pregnant women decrease their fish consumption by 17 percent – as they did in response to the government's 2001 mercury advisory – the loss of omega-3 fatty acids during pregnancy would cut the nutritional benefit to infants of eating fish by 80 percent. (In other words, that 17 percent reduction in fish intake had an impact on their infants far greater than one would expect.)

In the best study of its kind, US researchers found no evidence of harm in children in the Seychelles Islands, where mothers and children eat more than 10 times as much fish as Americans. (On average, the ocean species the islanders consume contain the same amounts of mercury as the species most commonly consumed in the US.) University of Rochester researchers followed more than 600 children from birth through age 15, finding no evidence of harm, and the study continues.

In 2007, a group of 14 professors of obstetrics and nutrition (the Maternal Nutrition Group) examined the evidence and urged women to eat at least 12 ounces of fish per day.

This conclusion was based in part on the results of a study conducted in 2007 at the Medical University of South Carolina (MUSC), which indicate that awareness of the FDA/EPA fish-intake advisory for pregnant and nursing women caused 56 percent of pregnant women to lower their fish consumption to levels well below the beneficial minimums.

Pregnant and nursing women should favor the species lowest in mercury and highest in omega-3s (e.g., Sardines, Sablefish, wild Salmon, low-weight, troll caught Tuna), or take supplemental fish oil. They are advised to avoid four species that are high in mercury: swordfish, shark, king mackerel, and tilefish.

Back to top

Attention-Deficit Disorders and Social/Cognitive Development
A growing body of evidence – including landmark results of a series of findings from the Oxford-Durham project in England – indicates that increased intake of fish or supplemental omega-3s can alleviate the symptoms of attention-deficit and developmental coordination disorders.

And, intriguingly, there is recent evidence that a shift in the fat composition of the diets of "normal" school-aged children – toward fish fats and away from animal and plant fats – may enhance their psychosocial and cognitive functioning; i.e., their interactions with others and their thinking capacity and speed.

Back to top

Cancer
The evidence that marine omega-3s can slow cancer growth substantially – and that high intake of omega-6 EFAs promotes cancer growth substantially – is growing fast.

It includes epidemiological studies – in which researchers seek statistical correlations between diet and cancer rates – as well as basic research in human and animal cancer cells (*in vitro* studies) and animal studies (*in vivo* studies).

Likely explanations for the anti-cancer impact of dietary omega-3s include damping of inflammation (a cause and growth promoter of common cancers), increased propensity of cancer cells to commit "suicide" (via apoptosis or necrosis), and modulation of estrogen signaling with regard to breast cancer.

When added to breast, prostate, and colon cancer cell lines cultured outside the body, omega-3s inhibit reproduction or multiplication of cancer cells (i.e., "proliferation"); and promote apoptosis (programmed cell death), and inhibit proliferation in human colorectal mucosa.

The results of animal studies indicate that omega-3s decrease the occurrence and progression of breast, prostate, and intestinal tumors.

In the few human epidemiologic (case-control and cohort) studies where fish consumption among subjects was relatively high, researchers have found significant inverse relationships between fish or omega-3 intake and the risk of breast, prostate, or

colorectal cancer, and several types of cancer affecting white blood cells, including leukemia, multiple myeloma, and non-Hodgkin lymphoma. In particular, EPA promotes apoptosis in lymphoma cells in which the enzyme acyl-CoA synthetase (ACS) is expressed to high degree.

Interestingly, people whose jobs require the handling of fish appear to enjoy a reduced risk of leukemia and lymphoma, while people in occupations associated with beef cattle – whose fat is high in omega-6 EFAs – suffer an increased risk for developing leukemia and lymphoma.

Studies that measure tissue concentrations of EPA and DHA and dietary omega-6 to omega-3 fatty acid ratios – as opposed to dietary intake of fish – would provide better guidance regarding omega-3 intake and human cancer risk.

A large body of literature (of varying quality) suggests that omega-3 dietary enrichment may help inhibit or prevent tumor growth.

In January of 2006, the U.S. Agency for Healthcare Research and Quality (AHRQ) issued their review of the evidence, which included four conservative conclusions:

- "In a large body of literature spanning many countries and cohorts with different demographic characteristics, the evidence does not suggest a significant association between omega-3 fatty acids and cancer incidence.
- "In a small body of literature, there is no significant association between omega-3 fatty acids and clinical outcomes after tumor surgery.
- "Although the combination of omega-3 fatty acids, arginine, and RNA are associated with a reduced risk of postoperative complications and reduced length of hospital stay, it is not possible to ascertain whether these effects are due to omega-3 fatty acids, arginine, RNA, or a combination of these.
- "A large body of literature (of varying quality) suggests that omega-3 dietary enrichment may help inhibit or prevent tumor growth in some animal models; the quality of the review articles is not, however, sufficient to permit drawing strong conclusions."

Adjunct cancer therapy

Evidence from animal studies indicates that supplemental omega-3s can improve the efficacy of toxic cancer drugs such as doxorubicin, epirubicin, CPT-11, 5-fluorouracil, as well as the efficacy of tamoxifen and radiation therapy. And preliminary clinical research results indicate that omega-3 fatty acids can constitute a meaningful, if not equivalent, alternative therapy for the small minority of patients unable to withstand radiation or chemotherapy.

Omega-3s also appear to improve quality of life for people with cancer, in part by combating cancer-associated appetite loss, physical wasting, and malnutrition. However, the evidence is mixed.

Back to top

Diabetes

People who eat a lot of fish – like the Japanese, Icelanders, and Greenland's Inuit Eskimos – enjoy lower rates of diabetes. While there is no proof that diets high in fish or marine omega-3s can prevent or treat diabetes, there is ample evidence that diets high

in fish or supplemental omega-3s can improve key cardiovascular functions and reduce key risk factors for heart disease.

Heart disease is one of the most threatening "side effects" of diabetes, and this is why the ADA recommends two to three servings of fish per week – advice that echoes similar guidelines published by the American Heart Association. Eating fish frequently appears to be safe and beneficial for diabetics, and some studies indicate that dietary fish may protect against the development of impaired glucose tolerance – an early warning sign of diabetes.

There is some evidence that fish oil or supplemental omega-3s (specifically, the EPA found only in fish oil) may help prevent some of the adverse effects of diabetes, from oxidation, inflammation, and hypertension to kidney, nerve, and blood-vessel damage.

For example, the authors of two relevant studies on the effects of marine omega-3s (EPA and DHA) in diabetes came to these conclusions:

- "… [omega-3 EPA] has significant beneficial effects on diabetic neuropathy and serum lipids as well as other diabetic complications such as nephropathy and macroangiopathy."
- "Supplementation with omega-3 fatty acids has beneficial effects on serum [blood] triglycerides, HDL-cholesterol, lipid peroxidation and antioxidant enzymes, which may lead to decreased rate of occurrence of vascular complications in diabetes."

NOTE: Supplemental omega-3s do not appear to increase insulin sensitivity, and have worsened diabetics' blood sugar control initially in some, but not all studies. This effect seems to be a temporary, self-correcting phenomenon, but diabetics should monitor their blood sugar closely when first taking omega-3 supplements.

Back to top

Inflammatory Diseases (rheumatoid arthritis, IBS/Crohn's, asthma, etc.)
Autoimmune diseases such as type 1 diabetes, lupus and rheumatoid arthritis have long defied attempts to explain why the immune system stops regulating itself and begins attacking the body's own tissues, with inflammation serving as a primary self-damaging weapon.

Early in 2007, a team of scientists from the Whitehead Institute and the Dana Farber Cancer Institute identified a key gene regulator called Foxp3. When it goes awry, the body no longer makes working versions of regulatory T cells – the cells that normally keep the body's immune system in check. This finding may hasten efforts to find effective new therapies for autoimmune diseases.

The effect of fish oil on the various inflammatory auto-immune disorders depends on the specific mechanisms of the disorder as well as the dose and duration of supplemental omega-3s. Outcomes also depend on the balance between omega-3 and omega-6 fatty acids, the relative proportion of EPA and DHA, and dietary intake of vitamin E, which can counter the anti-inflammatory effects of omega-3s.

Fish oil is only mildly effective in damping acute, extreme inflammation. Some animal studies show success in acute inflammation, but these used very high doses that may be unsustainable for humans.

In chronic inflammatory disorders where fish oil has shown benefit, it took several weeks for positive results to appear. Still, the mild anti-inflammatory effects of supplemental omega-3s – likely related to reduced production of pro-inflammatory cytokines – has lead to substantial improvement of symptoms in some seriously ill patients.

Research indicates that fish oil supplementation seems especially effective in disorders involving inappropriate activation of the immune system. Fish oil has only a mild effect on the episodes of extreme inflammation that occur periodically in diseases such as rheumatoid arthritis, SLE (lupus) and Crohn's disease, but some studies indicate that fish oil could prevent relapses.

In diseases where the inflammation is mild, such as IgA nephropathy, studies show that fish oil may slow or even prevent progression of the disease.

High intakes levels of long-chain omega-3s from fish oil inhibits a wide range of immune functions implicated in certain auto-immune disorders. These include antigen presentation, expression of adhesion molecules, Th1 and Th2 responses, production of pro-inflammatory cytokines and eicosanoids, and promoting apoptosis (suicide) among lymphocytes (white blood cells of the immune system).

Interestingly, vitamin E exerts critical influences over the interactions of long-chain omega-3s with immune functions, often reversing the effects of fish oil. Thus, it may be counterproductive to take supplemental vitamin E with fish oil when treating inflammatory conditions.

Animal experiments indicate that omega-6 and omega-3 fatty acids display varying effects in two classes of auto-immune disease:

- Auto-antibody-mediated diseases: Diets low in fat, deficient in essential fatty acids, or high in omega-3s from fish oil increase survival and reduce disease severity. Diets high in fat and omega-6 LA increase disease severity.
- T cell-mediated diseases: Diets deficient in essential fatty acids or supplemented with in omega-3s from fish oil promote disease, whereas diets high in omega-6 LA prevent these or reduce their severity.
- T cell- and antibody-mediated autoimmune disease: Metabolites of omega-6 LA are protective.

Both types of long-chain polyunsaturated fatty acids – omega-6 and omega-3 – can be helpful in treating human autoimmune-inflammatory disorders, but the precise mechanisms by which these fatty acids exert their clinical effects are not well understood. The view that all omega-6 fatty acids are pro-inflammatory is inaccurate, in part, and their essential regulatory role in the immune system is more important than often appreciated. The issue is that the American diet contains an overabundance of omega-6 fatty acids, largely from vegetable oils and grain-fed meat and poultry.

Omega-3 EFAs have been tested, with mixed results, in diseases characterized by chronic inflammation, such as rheumatoid arthritis (RA), inflammatory bowel and Crohn's disease, psoriasis, eczema, hay fever, and asthma.

Rheumatoid arthritis: The results of several controlled clinical trials indicate that supplemental fish oil decreases joint tenderness and reduces the requirement for anti-inflammatory medication in rheumatoid arthritis patients. The available laboratory evidence indicates that omega-3s reduce the inflammation characteristic of RA, which causes pain and damage to joint tissues, and that EPA may be more important than DHA in reducing inflammatory markers of the disease.

Inflammatory bowel disease: While clinical trials of omega-3s have not produced significant alleviation of symptoms, some Crohn's disease patients taking fish oil supplements have remained in remission longer than those taking placebo pills.

Asthma: Omega-3 supplements have decreased the production of inflammatory chemicals in asthmatic patients, and there is some evidence that children of mothers with higher omega-3 intake, and children with higher tissue levels of omega-3s, enjoy a reduced risk of asthma.
There is also some clinical evidence that omega-3s can alleviate symptoms. However, two systematic reviews of randomized controlled trials of long-chain omega-3 fatty acid supplementation in asthmatic adults and children found that while omega-3 supplements can positive effects of on pulmonary function tests, asthmatic symptoms, medication use, and bronchial hyper-reactivity, these results are not consistent across all studies.

Psoriasis and Eczema: The results of clinical studies testing the effects of omega-3s in patients with psoriasis or eczema preclude unambiguously positive conclusions. As the authors of a recent review put it, "… the results of studies evaluating the therapeutic benefit of dietary fish oil have been conflicting and not clearly dose-dependent."
Trials in which people took fish oil capsules produced mixed, generally minor benefits. But the results were far better in trials that involved intravenous omega-3s. While these highly positive results exhibit the strong anti-inflammatory effects of high doses of omega-3s, it is not very practical or cost-effective for patients to get them this way on an ongoing basis.
The results of a crossover clinical trial in which patients alternated eating oily fish or white fish showed that the oily fish produced modest improvements. These results suggest that substances in oily fish or undistilled fish oils (probably phospholipids) may enhance the efficacy of omega-3s, compared with the isolated omega-3s used in virtually all trials.
The reasons why supplemental omega-3s exhibit mixed results may relate to the differences among inflammatory auto-immune disorders, in terms of the precise parts of the immune system affected.
In addition, the results of animal studies indicate that the effect of dietary fatty acids on autoimmune diseases depends on both the type of autoimmune disorder and the amounts and relative proportions of fatty acids consumed.

Back to top

Seizure disorders

The positive results of most of several animal studies, and of a small clinical trial, offer preliminary evidence that increased omega-3 intake may reduce the frequency and strength of epileptic seizures.

It is believed that omega-3s may yield these benefits by the same mechanism of some anti-seizure drugs, which reduce the "excitability" of cell membranes in the brain's hippocampus region. This mechanism is similar to the one through which dietary omega-3s are proven to reduce the risk of cardiac arrhythmias.

Back to top

Safety Considerations
While omega-3s are proven to protect against heart attacks and strokes, they may be inadvisable in certain circumstances. The American Heart Association offers this guidance: "Patients taking more than 3 grams of omega-3 fatty acids from supplements should do so only under a physician's care. High intakes could cause excessive bleeding in some people."

However, doses as high as 8 grams of omega 3 fatty acids per day (contained in from 10 grams to 27 grams of fish oil) show virtually no significant adverse effects.

As the author of a recent review notes, "It has been suggested that the potential anti-thrombosis [anti-clotting] effect of fish oils may theoretically increase the risk for bleeding, which may be a safety concern for individual patients. However, clinical trial evidence has not supported increased bleeding with omega-3 fatty acid intake, even when combined with other agents that might also increase bleeding (such as aspirin and warfarin)." (Bays HE 2007)

The most common side effects from fish oil consumption are complaints of fish-flavored burps, which can be reduced by taking the capsules in the middle of a meal, and by taking lemon-flavored oil. As with other dietary oils, gastrointestinal complaints including loose stools have been reported from people taking relatively high doses, albeit rarely.

Check with your doctor before taking omega-3 fish oil supplements if you meet any of these criteria:

- Taking blood-thinning drugs, including warfarin (coumadin) or aspirin, ibuprofen (Advil), naproxen (Aleve), and other anti-inflammatory pain relievers, including COX-2 inhibitors (e.g., Vioxx, Celebrex). There has never been a reported case of clinical bleeding attributed to fish oil consumption, even during surgery, but people with bleeding disorders and those taking blood thinners or anticoagulants should consult their physician before taking omega-3 supplements.
- Diagnosed with a serious cardiovascular condition – especially a diagnosis of angina or an irregular heartbeat that involves use of an implantable cardioverter defibrillator (ICD). While omega-3s generally reduce the risk of arrhythmias, they may raise the risk of arrhythmias in people with ICDs.
- Diagnosed with type II diabetes. Omega-3 supplements appear to improve the health prospects of type II diabetics, but they can worsen blood sugar control temporarily in diabetics who have never taken them. This effect usually fades within a few days or weeks. Type II diabetics who have never taken omega-3

supplements should start with a relatively low dose (e.g., 150 mg per day) and increase it gradually to the amounts indicated under “Intake Recommendations”, below.

Back to top

Intake Recommendations
The American Heart Association recommends that people eat fish, particularly oily fish, at least twice a week, and that adults diagnosed with coronary heart disease consume one gram (1,000 mg) of omega-3 fatty acids per day from fish and/or supplemental fish oil.

However, this leaves open the question of daily intake recommendations for healthy people. It seems sensible to consider following the intake recommendations of the two scientific bodies with the greatest expertise in this area: the US Institute of Medicine (IOM) and the International Society for the Study of Fatty Acids and Lipids (ISSFAL).

- ISSFAL recommends that adults consume 660 mg of omega-3s per day.
- IOM recommends that men consume 400 mg of omega-3s per day, and that women consume 260 mg per day.

Each 1000 mg capsule of Vital Choice Sockeye Salmon Oil provides about 160 mg of the two key omega-3s (90 mg EPA and 70 mg DHA), so you would need to take two to four capsules per day to meet the IOM and ISSFAL guidelines, as follows.

- To meet ISSFAL’s optimal daily intake level (660 mg), MEN and WOMEN should take *four capsules* of our sockeye oil per day.
- To meet the IOM’s adequate daily intake level (400 mg), MEN should take *three capsules* of our sockeye oil per day.
- To meet the IOM’s adequate daily intake level (260 mg), WOMEN should take *two capsules* of our sockeye oil per day.
- To meet the American Heart Association recommendation for adults diagnosed with coronary heart disease (1,000 mg), MEN and WOMEN should take *six to seven capsules* of our sockeye oil per day.

Back to top

Best Omega-3 Sources*
Wild Salmon
Sardines
Cold water Tuna (e.g., Pacific albacore)
Sablefish
Herring
Mackerel
Pacific Oysters and Scallops

Sources to Avoid
Shark*
Swordfish*
King Mackerel*
Tilefish*
Farmed Salmon***

*Minimal content of mercury and other contaminants; sustainably harvested
**Relatively high in mercury
***Farmed Salmon are high in omega-3s, but are also high in competing omega-6 fatty acids and tend to be high in persistent organic pollutants (PCBs, dioxins)

Further Reading
"Vital Choices" Newsletter Archive: http://www.vitalchoice.com/newsletter_index.cfm
(Enter a term related to your interest, such as "diabetes", in the Search box on the archive page.)
VitalChoice.com Health Benefits page: http://www.vitalchoice.com/health.cfm
National Institutes of Health -- Essential Fatty Acid information at http://efaeducation.nih.gov

Back to top

References

Essential fatty acids (EFAs) in brief

- American Heart Association. Fish and Omega-3 Fatty Acids. Accessed June 12, 2006 at http://www.americanheart.org/presenter.jhtml?identifier=4632.
- Burdge G. Alpha-linolenic acid metabolism in men and women: nutritional and biological implications. Curr Opin Clin Nutr Metab Care. 2004;7(2):137-144.
- Burdge GC, Calder PC. Conversion of alpha-linolenic acid to longer-chain polyunsaturated fatty acids in human adults. Reprod Nutr Dev. 2005 Sep-Oct;45(5):581-97. Review.
- Burdge GC, Finnegan YE, Minihane AM, Williams CM, Wootton SA. Effect of altered dietary n-3 fatty acid intake upon plasma lipid fatty acid composition, conversion of [13C]alpha-linolenic acid to longer-chain fatty acids and partitioning towards beta-oxidation in older men. Br J Nutr. 2003 Aug;90(2):311-21.
- Burdge GC, Jones AE, Wootton SA. Eicosapentaenoic and docosapentaenoic acids are the principal products of alpha-linolenic acid metabolism in young men. Br J Nutr. 2002;88(4):355-364.
- Burdge GC, Wootton SA. Conversion of alpha-linolenic acid to eicosapentaenoic, docosapentaenoic and docosahexaenoic acids in young women. Br J Nutr. 2002;88(4):411-420.
- Calder PC. Dietary modification of inflammation with lipids. Proc Nutr Soc. 2002;61(3):345-358. (PubMed)
- Cunnane SC. Problems with essential fatty acids: time for a new paradigm? Prog Lipid Res. 2003;42(6):544-568.
- Gerster H. Can adults adequately convert alpha-linolenic acid (18:3n-3) to eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3)? Int J Vitam Nutr Res. 1998;68(3):159-73. Review.
- Giltay EJ, Gooren LJ, Toorians AW, Katan MB, Zock PL. Docosahexaenoic acid concentrations are higher in women than in men because of estrogenic effects. Am J Clin Nutr. 2004;80(5):1167-1174.
- Hamazaki T, Okuyama H. The Japan Society for Lipid Nutrition recommends to reduce the intake of linoleic acid. A review and critique of the scientific evidence. World Rev Nutr Diet. 2003;92:109-32. Review.

- Lichtenstein AH, Jones PJ. Lipids: absorption and transport. In: Bowman BA, Russel RM, eds. Present Knowledge in Nutrition. 8th ed. Washington, D. C.: ILSI Press; 2001:93-103
- Muskiet FA, Fokkema MR, Schaafsma A, Boersma ER, Crawford MA. Is docosahexaenoic acid (DHA) essential? Lessons from DHA status regulation, our ancient diet, epidemiology and randomized controlled trials. J Nutr. 2004;134(1):183-186.
- Nakamura MT, Nara TY. Structure, function, and dietary regulation of delta6, delta5, and delta9 desaturases. Annu Rev Nutr. 2004;24:345-376.
- Price PT, Nelson CM, Clarke SD. Omega-3 polyunsaturated fatty acid regulation of gene expression. Curr Opin Lipidol. 2000;11(1):3-7. (PubMed)
- Rodriguez-Cruz M, Tovar AR, del Prado M, Torres N. [Molecular mechanisms of action and health benefits of polyunsaturated fatty acids] Rev Invest Clin. 2005 May-Jun;57(3):457-72. Review. Spanish.
- Sampath H, Ntambi JM. Polyunsaturated fatty acid regulation of gene expression. Nutr Rev. 2004;62(9):333-339.
- Shahidi F, Miraliakbari H. Omega-3 fatty acids in health and disease: part 2--health effects of omega-3 fatty acids in autoimmune diseases, mental health, and gene expression. J Med Food. 2005 Summer;8(2):133-48. Review.
- Simopoulos AP, Leaf A, Salem N, Jr. Workshop statement on the essentiality of and recommended dietary intakes for Omega-6 and Omega-3 fatty acids. Prostaglandins Leukot Essent Fatty Acids. 2000;63(3):119-121.
- Stillwell W, Wassall SR. Docosahexaenoic acid: membrane properties of a unique fatty acid. Chem Phys Lipids. 2003;126(1):1-27.
- Williams CM, Burdge G. Long-chain n-3 PUFA: plant v. marine sources. Proc Nutr Soc. 2006 Feb;65(1):42-50. Review.
- Zampelas A, Paschos G, Rallidis L, Yiannakouris N. Linoleic acid to alpha-linolenic acid ratio. From clinical trials to inflammatory markers of coronary artery disease. World Rev Nutr Diet. 2003;92:92-108. Review.

Cardiovascular (Heart) health

- Aizer A, Gaziano M, MansonJE, Buring JE, Albert CM. Relationship between fish consumption and the development of atrial fibrillation in men. Oral Abstract Sessions AB03, Abstract AB03-2, presented at the 27th annual meeting of the Heart Rhythm Society, Thursday, May 18, 2006, Boston, USA.
- Albert CM, Campos H, Stampfer MJ, Ridker PM, Manson JE, Willett WC, Ma J. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. N Engl J Med. 2002 Apr 11;346(15):1113-8.
- American Heart Association. Fish and Omega-3 Fatty Acids. Accessed June 12, 2006 at http://www.americanheart.org/presenter.jhtml?identifier=4632.
- Anti-inflammatory Effect May Help Explain Fish Benefit: Best results seen among people who ate more than half a pound of fish each week. Accessed online July 8, 2005 at http://www.acc.org/media/releases/highlights/2005/july05/fish.htm
- Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC. Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States. BMJ. 1996;313(7049):84-90.
- Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol. 1998;81(4A):7B-12B.
- Balk E, Chung M, Lichtenstein A, et al. Effects of omega-3 fatty acids on cardiovascular risk factors and intermediate markers of cardiovascular disease. Evid Rep Technol Assess (Summ). 2004(93):1-6.
- Bemelmans WJ, Lefrandt JD, Feskens EJ, et al. Increased alpha-linolenic acid intake lowers C-reactive protein, but has no effect on markers of atherosclerosis. Eur J Clin Nutr. 2004;58(7):1083-1089.
- Bucher HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. Am J Med. 2002 Mar;112(4):298-304.
- Burr ML, Ashfield-Watt PA, Dunstan FD, Fehily AM, Breay P, Ashton T, Zotos PC, Haboubi NA, Elwood PC. Lack of benefit of dietary advice to men with angina: results of a controlled trial. Eur J Clin Nutr. 2003 Feb;57(2):193-200.
- Burr ML, Fehily AM, Gilbert JF, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). Lancet. 1989;2(8666):757-761.
- Calo L, Bianconi L, Colivicchi F, Lamberti F, Loricchio ML, de Ruvo E, Meo A, Pandozi C, Staibano M, Santini M. N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. J Am Coll Cardiol. 2005 May 17;45(10):1723-8.
- Daviglus ML, Stamler J, Orencia AJ, et al. Fish consumption and the 30-year risk of fatal myocardial infarction. N Engl J Med. 1997;336(15):1046-1053.
- Dayton S, Pearce ML, Goldman H, et al. Controlled trial of a diet high in unsaturated fat for prevention of atherosclerotic complications. Lancet. 1968;2(7577):1060-1062.
- de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation. 1999;99(6):779-785.
- Dolecek TA. Epidemiological evidence of relationships between dietary polyunsaturated fatty acids and mortality in the multiple risk factor intervention trial. Proc Soc Exp Biol Med. 1992;200(2):177-182.
- Frantz ID, Jr., Dawson EA, Ashman PL, et al. Test of effect of lipid lowering by diet on cardiovascular risk. The Minnesota Coronary Survey. Arteriosclerosis. 1989;9(1):129-135.
- Frost L, Vestergaard P. n-3 Fatty acids consumed from fish and risk of atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study. Am J Clin Nutr. 2005 Jan;81(1):50-4.

- Gillum RF, Mussolino ME, Madans JH. The relationship between fish consumption and stroke incidence. The NHANES I Epidemiologic Follow-up Study (National Health and Nutrition Examination Survey). Arch Intern Med. 1996;156(5):537-542.
- Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet. 1999;354(9177):447-455.
- Guallar E, Hennekens CH, Sacks FM, Willett WC, Stampfer MJ. A prospective study of plasma fish oil levels and incidence of myocardial infarction in U.S. male physicians. J Am Coll Cardiol. 1995 Feb;25(2):387-94.
- Harris WS. n-3 fatty acids and serum lipoproteins: human studies. Am J Clin Nutr. 1997;65(5 Suppl):1645S-1654S.
- He K, Rimm EB, Merchant A, et al. Fish consumption and risk of stroke in men. JAMA. 2002;288(24):3130-3136.
- Hooper L, Thompson RL, Harrison RA, Summerbell CD, Moore H, Worthington HV, Durrington PN, Ness AR, Capps NE, Davey Smith G, Riemersma RA, Ebrahim SB. Risks and benefits of omega 3 fats for mortality, cardiovascular disease, and cancer: systematic review. BMJ, doi:10.1136/bmj.38755.366331.2F (published 24 March 2006)
- Hooper L, Thompson RL, Harrison RA, Summerbell CD, Moore H, Worthington HV, Durrington PN, Ness AR, Capps NE, Davey Smith G, Riemersma RA, Ebrahim SB. Omega 3 fatty acids for prevention and treatment of cardiovascular disease. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD003177. Review.
- Hu FB, Bronner L, Willett WC, et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. JAMA. 2002;287(14):1815-1821.
- Hu FB, Stampfer MJ, Manson JE, et al. Dietary intake of alpha-linolenic acid and risk of fatal ischemic heart disease among women. Am J Clin Nutr. 1999;69(5):890-897.
- Iso H, Rexrode KM, Stampfer MJ, et al. Intake of fish and omega-3 fatty acids and risk of stroke in women. JAMA. 2001;285(3):304-312.
- Keli SO, Feskens EJ, Kromhout D. Fish consumption and risk of stroke. The Zutphen Study. Stroke. 1994;25(2):328-332.
- Kris-Etherton PM, Harris WS, Appel LJ. Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. Arterioscler Thromb Vasc Biol. 2003;23(2):151-152.
- Kris-Etherton PM, Hecker KD, Binkoski AE. Polyunsaturated fatty acids and cardiovascular health. Nutr Rev. 2004;62(11):414-426.
- Kromhout D, Bosschieter EB, de Lezenne Coulander C. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. N Engl J Med. 1985;312(19):1205-1209.
- Kromhout D, Feskens EJ, Bowles CH. The protective effect of a small amount of fish on coronary heart disease mortality in an elderly population. Int J Epidemiol. 1995;24(2):340-345. Dolecek TA, Granditis G. Dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial (MRFIT). World Rev Nutr Diet. 1991;66:205-216.
- Lands WE. Primary prevention in cardiovascular disease: moving out of the shadows of the truth about death. Nutr Metab Cardiovasc Dis. 2003 Jun;13(3):154-64. Review.
- Leaf A, Xiao YF, Kang JX, Billman GE. Prevention of sudden cardiac death by n-3 polyunsaturated fatty acids. Pharmacol Ther. 2003;98(3):355-377. Albert CM, Hennekens CH, O'Donnell CJ, et al. Fish consumption and risk of sudden cardiac death. JAMA. 1998;279(1):23-28.
- Lemaitre RN, King IB, Mozaffarian D, Kuller LH, Tracy RP, Siscovick DS. n-3 Polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study. Am J Clin Nutr. 2003 Feb;77(2):319-25.
- Leng GC, Lee AJ, Fowkes FG, et al. Randomized controlled trial of gamma-linolenic acid and eicosapentaenoic acid in peripheral arterial disease. Clinical Nutrition 1998. 17(6):265-271. (PubMed)
- Leren P. The Oslo diet-heart study. Eleven-year report. Circulation. 1970;42(5):935-942.
- Marchioli R, Barzi F, Bomba E, et al. Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione. Circulation. 2002;105(16):1897-1903.
- Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. Arterioscler Thromb. 1992;12(8):911-919.
- Miettinen M, Turpeinen O, Karvonen MJ, Pekkarinen M, Paavilainen E, Elosuo R. Dietary prevention of coronary heart disease in women: the Finnish mental hospital study. Int J Epidemiol. 1983;12(1):17-25.
- Morris MC, Manson JE, Rosner B, Buring JE, Willett WC, Hennekens CH. Fish consumption and cardiovascular disease in the physicians' health study: a prospective study. Am J Epidemiol. 1995;142(2):166-175.
- Mozaffarian D, Ascherio A, Hu FB, et al. Interplay between different polyunsaturated fatty acids and risk of coronary heart disease in men. Circulation. 2005;111(2):157-164.
- Mozaffarian D, Bryson CL, Lemaitre RN, Burke GL, Siscovick DS. Fish intake and risk of incident heart failure. J Am Coll Cardiol. 2005 Jun 21;45(12):2015-21.
- Mozaffarian D, Geelen A, Brouwer IA, Geleijnse JM, Zock PL, Katan MB. Effect of fish oil on heart rate in humans. A meta-analysis of randomized controlled trials. Circulation 2005;112:1945-1952.
- 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.
- Mozaffarian D, Longstreth WT Jr, Lemaitre RN, Manolio TA, Kuller LH, Burke GL, Siscovick DS. Fish consumption and stroke risk in elderly individuals: the cardiovascular health study. Arch Intern Med. 2005 Jan 24;165(2):200-6. Erratum in: Arch Intern Med. 2005 Mar 28;165(6):683.

- Mozaffarian D, Psaty BM, Rimm EB, Lemaitre RN, Burke GL, Lyles MF, Lefkowitz D, Siscovick DS. Fish intake and risk of incident atrial fibrillation. Circulation. 2004 Jul 27;110(4):368-73. Epub 2004 Jul 19.
- Mozaffarian D. Does alpha-linolenic acid intake reduce the risk of coronary heart disease? A review of the evidence. Altern Ther Health Med. 2005;11(3):24-30.
- Nilsen DW, Albrektsen G, Landmark K, et al. Effects of a high-dose concentrate of n-3 fatty acids or corn oil introduced early after an acute myocardial infarction on serum triacylglycerol and HDL cholesterol. Am J Clin Nutr 2001. 74(1):50-56. (PubMed)
- Nilsen DW, Albrektsen G, Landmark K, Moen S, Aarsland T, Woie L. Effects of a high-dose concentrate of n-3 fatty acids or corn oil introduced early after an acute myocardial infarction on serum triacylglycerol and HDL cholesterol. Am J Clin Nutr. 2001;74(1):50-56.
- Oh K, Hu FB, Manson JE, Stampfer MJ, Willett WC. Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the nurses' health study. Am J Epidemiol. 2005;161(7):672-679.
- O'Keefe JH Jr, Abuissa H, Sastre A, Steinhaus DM, Harris WS. Effects of omega-3 fatty acids on resting heart rate, heart rate recovery after exercise, and heart rate variability in men with healed myocardial infarctions and depressed ejection fractions. Am J Cardiol. 2006 Apr 15;97(8):1127-30. Epub 2006 Mar 3. Oomen CM, Ocke MC, Feskens EJ, Kok FJ, Kromhout D. alpha-Linolenic acid intake is not beneficially associated with 10-y risk of coronary artery disease incidence: the Zutphen Elderly Study. Am J Clin Nutr. 2001;74(4):457-463.
- Orencia AJ, Daviglus ML, Dyer AR, Shekelle RB, Stamler J. Fish consumption and stroke in men. 30-year findings of the Chicago Western Electric Study. Stroke. 1996;27(2):204-209.
- Pietinen P, Ascherio A, Korhonen P, et al. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Am J Epidemiol. 1997;145(10):876-887.
- Rallidis LS, Paschos G, Liakos GK, Velissaridou AH, Anastasiadis G, Zampelas A. Dietary alpha-linolenic acid decreases C-reactive protein, serum amyloid A and interleukin-6 in dyslipidaemic patients. Atherosclerosis. 2003;167(2):237-242.
- Sacks FM, Katan M. Randomized clinical trials on the effects of dietary fat and carbohydrate on plasma lipoproteins and cardiovascular disease. Am J Med. 2002;113 Suppl 9B:13S-24S.
- Sacks FM, Stone PH, Gibson CM, Silverman DI, Rosner B, Pasternak RC. Controlled trial of fish oil for regression of human coronary atherosclerosis. HARP Research Group. J Am Coll Cardiol. 1995;25(7):1492-1498.
- Schmier JK, Rachman NJ, Halpern MT. The cost-effectiveness of omega-3 supplements for prevention of secondary coronary events. Manag Care. 2006 Apr;15(4):43-50.
- Shekelle RB, Shryock AM, Paul O, et al. Diet, serum cholesterol, and death from coronary heart disease. The Western Electric study. N Engl J Med. 1981;304(2):65-70.
- Simon JA, Hodgkins ML, Browner WS, Neuhaus JM, Bernert JT Jr, Hulley SB. Serum fatty acids and the risk of coronary heart disease. Am J Epidemiol. 1995 Sep 1;142(5):469-76.
- Singh RB, Niaz MA, Sharma JP, Kumar R, Rastogi V, Moshiri M. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian experiment of infarct survival--4. Cardiovasc Drugs Ther. 1997;11(3):485-491.
- Siscovick DS, Raghunathan TE, King I, Weinmann S, Wicklund KG, Albright J, Bovbjerg V, Arbogast P, Smith H, Kushi LH, et al. Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. JAMA. 1995 Nov 1;274(17):1363-7.
- Turpeinen O, Karvonen MJ, Pekkarinen M, Miettinen M, Elosuo R, Paavilainen E. Dietary prevention of coronary heart disease: the Finnish Mental Hospital Study. Int J Epidemiol. 1979;8(2):99-118.
- von Schacky C, Angerer P, Kothny W, Theisen K, Mudra H. The effect of dietary omega-3 fatty acids on coronary atherosclerosis. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 1999;130(7):554-562.
- Wang C, Chung M, Balk E, Kupelnick B, DeVine D, Lawrence A, et al. Effects of omega-3 fatty acids on cardiovascular disease. Rockville,MD, USA: Agency for Healthcare Researchand Quality, 2004. Evidence Report/Technology Assessment 94. Accessed online March 26, 2006 at www.ncbi.nlm.nih.gov/books/bv.fcgi?rid = hstat1a.chapter.38290.
- Yuan JM, Ross RK, Gao YT, Yu MC. Fish and shellfish consumption in relation to death from myocardial infarction among men in Shanghai, China. Am J Epidemiol. 2001;154(9):809-816.
- Zampelas A, Panagiotakos DB, Pitsavos C, Das UN, Chrysohoou C, Skoumas Y, Stefanadis C. Fish Consumption Among Healthy Adults Is Associated With Decreased Levels of Inflammatory Markers Related to Cardiovascular Disease The ATTICA Study. J Am Coll Cardiol. 2005 Jul 5;46(1):120-4.
- Zhao G, Etherton TD, Martin KR, West SG, Gillies PJ, Kris-Etherton PM. Dietary alpha-linolenic acid reduces inflammatory and lipid cardiovascular risk factors in hypercholesterolemic men and women. J Nutr. 2004;134(11):2991-2997.

Alzheimer's disease and other dementias

- 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.
- Schaefer EJ, et al.Plasma Phosphatidylcholine (PC) Docosahexaenoic Acid (DHA), Fish Intake and Risk of Dementia. American Heart Association Scientific Sessions 2003. November 9-12 2003, Orlando Florida. Moderated Poster Sessions, APS.94.4M. Novel Environmental, Personal and Pharmacologic Risk Factors.
- Calon F, Lim GP, Yang F, Morihara T, Teter B, Ubeda O, Rostaing P, Triller A, Salem N Jr, Ashe KH, Frautschy SA, Cole GM. Docosahexaenoic acid protects from dendritic pathology in an Alzheimer's disease mouse model. Neuron. 2004 Sep 2;43(5):633-45.

- Fackelmann K. “Fishing for answers to Alzheimer's.” USA TODAY, http://www.usatoday.com/news/health/2004-11-16-fish-alzheimers_x.htm. Accessed 11/16/04.
- Kalmijn S, Launer LJ, Ott A, Witteman JC, Hofman A, Breteler MM. Dietary fat intake and the risk of incident dementia in the Rotterdam Study. Ann Neurol. 1997 Nov;42(5):776-82.
- Lichtenstein AH. Dietary fat and cardiovascular disease risk: quantity or quality? J Womens Health (Larchmt). 2003 Mar;12(2):109-14. Review.
- Ludwig DS. Diet and development of the insulin resistance syndrome. Asia Pac J Clin Nutr. 2003;12 Suppl:S4.
- Wijendran V, Hayes KC. Dietary n-6 and n-3 fatty acid balance and cardiovascular health. Annu Rev Nutr. 2004;24:597-615. Review.

Mental Health

- Aas V, Rokling-Andersen MH, Kase ET, Thoresen GH, Rustan AC. Eicosapentaenoic acid (20:5 n-3) increases fatty acid and glucose uptake in cultured human skeletal muscle cells. J Lipid Res. 2006 Feb;47(2):366-74. Epub 2005 Nov 21.
- Assies J, Lieverse R, Vreken P, Wanders RJ, Dingemans PM, Linszen DH. Significantly reduced docosahexaenoic and docosapentaenoic acid concentrations in erythrocyte membranes from schizophrenic patients compared with a carefully matched control group. Biol Psychiatry. 2001;49(6):510-522.
- Auestad N, Scott DT, Janowsky JS, Jacobsen C, Carroll RE, Montalto MB, Halter R, Qiu W, Jacobs JR, Connor WE, Connor SL, Taylor JA, Neuringer M, Fitzgerald KM, Hall RT. Visual, cognitive, and language assessments at 39 months: a follow-up study of children fed formulas containing long-chain polyunsaturated fatty acids to 1 year of age. Pediatrics. 2003 Sep;112(3 Pt 1):e177-83.
- Buydens L, Branchey M, Roy A. N-3 Polyunsaturated Fatty Acids Decrease Feelings of Anger in a Population of Substance Abusers. Neuropsychopharmacology. , 2005;30(1):S87-S88.
- Buydens-Branchey L, Branchey M, McMakin DL, Hibbeln JR. Polyunsaturated fatty acid status and aggression in cocaine addicts. Drug Alcohol Depend. 2003 Sep 10;71(3):319-23.
- Champeil-Potokar G, Denis I, Goustard-Langelier B, Alessandri JM, Guesnet P, Lavialle M. Astrocytes in culture require docosahexaenoic acid to restore the n-3/n-6 polyunsaturated fatty acid balance in their membrane phospholipids. J Neurosci Res. 2004 Jan 1;75(1):96-106.
- Chiu CC, Huang SY, Su KP. Omega-3 polyunsaturated fatty acids for postpartum depression. Am J Obstet Gynecol. 2004 Feb;190(2):582-3; author reply 583.
- Colin A, Reggers J, Castronovo V, Ansseau M. [Lipids, depression and suicide] Encephale. 2003 Jan-Feb;29(1):49-58. Review. French.
- Colombo J, Kannass KN, Shaddy DJ, Kundurthi S, Maikranz JM, Anderson CJ, Blaga OM, Carlson SE. Maternal DHA and the development of attention in infancy and toddlerhood. Child Dev 2004;75:1254-1267.
- Conklin SM, Harris JI, Manuck SB, Hibbeln JR, Muldoon MF. Plasma fatty acids are associated with normative variation in mood, personality, and behavior. Abstract 1228, American Psychosomatic Society 64th Annual Meeting, March 1-4, 2006, Denver, Colorado. Accessed online March 10, 2006 at http://www.psychosomatic.org/events/AbstractsForJournal06.pdf.
- Cott J, Hibbeln JR. Lack of seasonal mood change in Icelanders. Am J Psychiatry. 2001 Feb;158(2):328.
- Dennis CL. Preventing postpartum depression part I: a review of biological interventions. Can J Psychiatry. 2004 Jul;49(7):467-75. Review.
- Edwards R, Peet M, Shay J, Horrobin D. Omega-3 polyunsaturated fatty acid levels in the diet and in red blood cell membranes of depressed patients. J Affect Disord. 1998 Mar;48(2-3):149-55.
- Emsley R, Myburgh C, Oosthuizen P, van Rensburg SJ. Randomized, placebo-controlled study of ethyl-eicosapentaenoic acid as supplemental treatment in schizophrenia. Am J Psychiatry. 2002;159(9):1596-1598.
- Fenton WS, Dickerson F, Boronow J, Hibbeln JR, Knable M. A placebo-controlled trial of omega-3 fatty acid (ethyl eicosapentaenoic acid) supplementation for residual symptoms and cognitive impairment in schizophrenia. Am J Psychiatry. 2001;158(12):2071-2074.
- Fontani G, Corradeschi F, Felici A, Alfatti F, Migliorini S, Lodi L. Cognitive and physiological effects of omega-3 polyunsaturated fatty acid supplementation in healthy subjects. Eur J Clin Invest 2005;35:691-699.
- Frangou S, Lewis M, McCrone P. Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomised double-blind placebo-controlled study. Br J Psychiatry. 2006 Jan;188:46-50.
- Freeman MP, Hibbeln JR, Wisner KL, Brumbach BH, Watchman M, Gelenberg AJ. Randomized dose-ranging pilot trial of omega-3 fatty acids for postpartum depression. Acta Psychiatr Scand. 2006 Jan;113(1):31-5.
- Freeman MP. -3 fatty acids in psychiatry: a review. Ann Clin Psychiatry. 2000 Sep;12(3):159-65. Review.
- Green P, Hermesh H, Monselise A, Marom S, Presburger G, Weizman A. Red cell membrane omega-3 fatty acids are decreased in nondepressed patients with social anxiety disorder. Eur Neuropsychopharmacol. 2006 Feb;16(2):107-13. Epub 2005 Oct 21.
- Hakkarainen R, Partonen T, Haukka J, Virtamo J, Albanes D, Lonnqvist J: Is low dietary intake of omega-3 fatty acids associated with depression? Am J Psychiatry 2004; 161:567–569.
- Hamazaki T, Sawazaki S, Itomura M, Asaoka E, Nagao Y, Nishimura N, Yazawa K, Kuwamori T, Kobayashi M: The effect of docosahexaenoic acid on aggression in young adults. A placebo-controlled double-blind study. J Clin Invest 1996; 97: 1129-1133.
- Hibbeln JR, Linnoila M, Umhau JC, Rawlings R, George DT, Salem N Jr. Essential fatty acids predict metabolites of serotonin and dopamine in cerebrospinal fluid among healthy control subjects, and early- and late-onset alcoholics. Biol Psychiatry 1998; 44: 235-242.
- Hibbeln JR, Salem N Jr. Dietary polyunsaturated fatty acids and depression: when cholesterol does not satisfy. Am J Clinical Nutr 1995; 62: 1-9.
- Hibbeln JR, Salem N Jr. Risks of cholesterol-lowering therapies. Biol Psychiatry. 1996 Oct 1;40(7):686-7.

- Hibbeln JR, Umhau JC, George DT, Salem N Jr. Do plasma polyunsaturates predict hostility and depression? World Rev Nutr Diet. 1997;82:175-86. Review.
- Hibbeln JR, Umhau JC, Linnoila M, George DT, Ragan PW, Shoaf SE, Vaughan MR, Rawlings R, Salem N Jr. A replication study of violent and nonviolent subjects: cerebrospinal fluid metabolites of serotonin and dopamine are predicted by plasma essential fatty acids. Biol Psychiatry. 1998 Aug 15;44(4):243-9.
- Hibbeln JR. Fish consumption and major depression (letter). Lancet 1998; 351: 1213.
- Hibbeln JR. Seafood consumption and homicide mortality. A cross-national ecological analysis. World Rev Nutr Diet. 2001;88:41-6.
- Hibbeln JR. Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis. J Affect Disord. 2002 May;69(1-3):15-29.
- Hirayama S, Hamazaki T, Terasawa K. Effect of docosahexaenoic acid-containing food administration on symptoms of attention-deficit/hyperactivity disorder - a placebo-controlled double-blind study. Eur J Clin Nutr. 2004 Mar;58(3):467-73.
- Horrobin DF, Manku MS, Hillman H, Iain A, Glen M. Fatty acid levels in the brains of schizophrenics and normal controls. Biol Psychiatry. 1991;30(8):795-805.
- Huan M, Hamazaki K, Sun Y, Itomura M, Liu H, Kang W, Watanabe S, Terasawa K, Hamazaki T. Suicide attempt and n-3 fatty acid levels in red blood cells: a case control study in China. Biol Psychiatry. 2004 Oct 1;56(7):490-6.
- Innis SM. Perinatal biochemistry and physiology of long-chain polyunsaturated fatty acids. J Pediatr 2003; 143(4 suppl):S1-S8Kalmijn S, van Boxtel MP, Ocke M, Verschuren WM, Kromhout D, Launer LJ. Dietary intake of fatty acids and fish in relation to cognitive performance at middle age. Neurology. 2004 Jan 27;62(2):275-80.
- Iribarren C, Markovitz JH, Jacobs DR, Schreiner PJ, Daviglus M, Hibbeln JR. Dietary intake of n-3, n-6 fatty acids and fish: Relationship with hostility in young adults-the CARDIA study. Eur J Clin Nutr. 2004 Jan; 58(1): 24-31.
- Joy CB, Mumby-Croft R, Joy LA. Polyunsaturated fatty acid supplementation for schizophrenia. Cochrane Database Syst Rev. 2003(2):CD001257.
- Laugharne JD, Mellor JE, Peet M. Fatty acids and schizophrenia. Lipids. 1996;31 Suppl:S163-165.
- Llorente AM, Jensen CL, Voigt RG, Fraley JK, Berretta MC, Heird WC. Effect of maternal docosahexaenoic acid supplementation on postpartum depression and information processing. Am J Obstet Gynecol. 2003 May;188(5):1348-53.
- Locke CA, Stoll AL. Omega-3 fatty acids in major depression. World Rev Nutr Diet. 2001;89:173-185.
- Maes M, Christophe A, Delanghe J, Altamura C, Neels H, Meltzer HY. Lowered omega3 polyunsaturated fatty acids in serum phospholipids and cholesteryl esters of depressed patients. Psychiatry Res. 1999;85(3):275-291.
- Maes M, Smith R, Christophe A, Cosyns P, Desnyder R, Meltzer H. Fatty acid composition in major depression: decreased omega 3 fractions in cholesteryl esters and increased C20: 4 omega 6/C20:5 omega 3 ratio in cholesteryl esters and phospholipids. J Affect Disord. 1996 Apr 26;38(1):35-46.
- Mamalakis G, Tornaritis M, Kafatos A. Depression and adipose essential polyunsaturated fatty acids. Prostaglandins Leukot Essent Fatty Acids. 2002;67(5):311-318.
- Marangell LB, Martinez JM, Zboyan HA, Chong H, Puryear LJ. Omega-3 fatty acids for the prevention of postpartum depression: negative data from a preliminary, open-label pilot study. Depress Anxiety. 2004;19(1):20-3.
- Marangell LB, Martinez JM, Zboyan HA, Kertz B, Kim HF, Puryear LJ. A double-blind, placebo-controlled study of the omega-3 fatty acid docosahexaenoic acid in the treatment of major depression. Am J Psychiatry. 2003;160(5):996-998.
- Nemets B, Stahl Z, Belmaker RH. Addition of omega-3 fatty acid to maintenance medication treatment for recurrent unipolar depressive disorder. Am J Psychiatry 2002: 159: 477-479.
- Nemets H, Nemets B, Apter A, Bracha Z, Belmaker RH. Omega-3 treatment of childhood depression: a controlled, double-blind pilot study. Am J Psychiatry. 2006 Jun;163(6):1098-100.
- Noaghiul S, Hibbeln JR. Cross-national comparisons of seafood consumption and rates of bipolar disorders. Am J Psychiatry. 2003;160(12):2222-2227.
- Otto SJ, de Groot RH, Hornstra G. Increased risk of postpartum depressive symptoms is associated with slower normalization after pregnancy of the functional docosahexaenoic acid status. Prostaglandins Leukot Essent Fatty Acids. 2003 Oct;69(4):237-43.
- Parker G, Gibson NA, Brotchie H, Heruc G, Rees AM, Hadzi-Pavlovic D. Omega-3 Fatty acids and mood disorders. Am J Psychiatry. 2006 Jun;163(6):969-78.
- Parker GB, Heruc GA, Hilton TM, Olley A, Brotchie H, Hadzi-Pavlovic D, Friend C, Walsh WF, Stocker R. Low levels of docosahexaenoic acid identified in acute coronary syndrome patients with depression. Psychiatry Res. 2006 Mar 30;141(3):279-86. Epub 2006 Feb 24.
- Peet M, Brind J, Ramchand CN, Shah S, Vankar GK. Two double-blind placebo-controlled pilot studies of eicosapentaenoic acid in the treatment of schizophrenia. Schizophr Res. 2001;49(3):243-251.
- Peet M, Horrobin DF. A dose-ranging exploratory study of the effects of ethyl-eicosapentaenoate in patients with persistent schizophrenic symptoms. J Psychiatr Res. 2002;36(1):7-18.
- Peet M, Horrobin DF. A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. Arch Gen Psychiatry 2002: 59: 913-919.
- Peet M, Murphy B, Shay J, Horrobin D. Depletion of omega-3 fatty acid levels in red blood cell membranes of depressive patients. Biol Psychiatry. 1998;43(5):315-319.

- Pifferi F, Roux F, Langelier B, Alessandri JM, Vancassel S, Jouin M, Lavialle M, Guesnet P. (n-3) polyunsaturated fatty acid deficiency reduces the expression of both isoforms of the brain glucose transporter GLUT1 in rats. J Nutr 2005;135:2241-2246.
- Pouwer F, Nijpels G, Beekman AT, Dekker JM, van Dam RM, Heine RJ, Snoek FJ. Fat food for a bad mood. Could we treat and prevent depression in Type 2 diabetes by means of omega-3 polyunsaturated fatty acids? A review of the evidence. Diabet Med. 2005 Nov;22(11):1465-75. Review.
- Rees AM, Austin MP, Parker G. Role of omega-3 fatty acids as a treatment for depression in the perinatal period. Aust N Z J Psychiatry. 2005 Apr;39(4):274-80. Review.
- Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatrics. 2005 May;115(5):1360-6.
- Richardson AJ, Puri BK. A randomized double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties. Prog Neuropsychopharmacol Biol Psychiatry. 2002 Feb;26(2):233-9.
- Sampalis F, Bunea R, Pelland MF, et al. Evaluation of the effects of Neptune Krill Oil on the management of premenstrual syndrome and dysmenorrhea. Altern Med Rev 2003;8: 171-179.
- Silvers KM, Woolley CC, Hamilton FC, Watts PM, Watson RA. Randomised double-blind placebo-controlled trial of fish oil in the treatment of depression. Prostaglandins Leukot Essent Fatty Acids. 2005;72(3):211-218.
- Sontrop J, Campbell MK. Omega-3 polyunsaturated fatty acids and depression: a review of the evidence and a methodological critique. Prev Med. 2006 Jan;42(1):4-13. Epub 2005 Dec 7. Review.
- Sontrop J, Campbell MK. Omega-3 polyunsaturated fatty acids and depression: a review of the evidence and a methodological critique. Prev Med. 2006 Jan;42(1):4-13. Epub 2005 Dec 7. Review.
- Stevens L, Zhang W, Peck L, Kuczek T, Grevstad N, Mahon A, Zentall SS, Arnold LE, Burgess JR. EFA supplementation in children with inattention, hyperactivity, and other disruptive behaviors. Lipids. 2003 Oct;38(10):1007-21.
- Stoll AL, Severus WE, Freeman MP, Rueter S, Zboyan HA, Diamond E, Cress KK, Marangell LB. Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. Arch Gen Psychiatry. 1999 May;56(5):407-12.
- Su KP, Huang SY, Chiu CC, Shen WW. Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo-controlled trial. Eur Neuropsychopharmacol. 2003 Aug;13(4):267-71. Erratum in: E Neuropsychopharmacol. 2004 Mar;14(2):173.
- Su KP, Huang SY, Chiu CC, Shen WW. Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo-controlled trial. Eur Neuropsychopharmacol. 2003;13(4):267-271.
- Sublette ME, Hibbeln JR, Galfalvy H, Oquendo MA, Mann JJ. Omega-3 polyunsaturated essential Fatty Acid status as a predictor of future suicide risk. Am J Psychiatry. 2006 Jun;163(6):1100-2.
- Tanskanen A, Hibbeln JR, Hintikka J, Haatainen K, Honkalampi K, Viinamaki H. Fish consumption, depression, and suicidality in a general population. Arch Gen Psychiatry. 2001 May;58(5):512-3. No abstract available.
- Tanskanen A, Hibbeln JR, Tuomilehto J, Uutela A, Haukkala A, Viinamaki H, Lehtonen J, Vartiainen E. Fish consumption and depressive symptoms in the general population in Finland. Psychiatr Serv. 2001 Apr;52(4):529-31.
- Tiemeier H, van Tuijl HR, Hofman A, Kiliaan AJ, Breteler MM. Plasma fatty acid composition and depression are associated in the elderly: the Rotterdam Study. Am J Clin Nutr. 2003 Jul;78(1):40-6.
- Timonen M, Horrobin D, Jokelainen J, Laitinen J, Herva A, Räsänen P: Fish consumption and depression: the Northern Finland 1966 birth cohort study. J Affect Disord 2004; 82:447–452
- U. S. Department of Agriculture, Agricultural Research Service. USDA Nutrient Database for Standard Reference, Release 18. 2005. Available at: http://www.nal.usda.gov/fnic/foodcomp.
- Vaddadi KS. The use of gamma-linolenic acid and linoleic acid to differentiate between temporal lobe epilepsy and schizophrenia. Prostaglandins Med. 1981;6(4):375-379.
- Virkkunen ME, Horroboin DF, Jenkins DK, Manku MS: Plasma phospholipid essential fatty acids and prostaglandins in alcoholic, habitually violent and impulsive offenders. Biol Psychiatry 1987; 22: 1087-1096.
- Voigt RG, Llorente AM, Jensen CL, Fraley JK, Berretta MC, Heird WC. A randomized, double-blind, placebo-controlled trial of docosahexaenoic acid supplementation in children with attention-deficit/hyperactivity disorder. J Pediatr. 2001 Aug;139(2):189-96.
- Weidner G, Connor SL, Hollis JF, Connor WE: Improvements in hostility and depression in relation to dietary change and cholesterol lowering. Ann Int Med 1992; 117: 820-823.
- Williams AL, Katz D, Ali A, Girard C, Goodman J, Bell I. Do essential fatty acids have a role in the treatment of depression? J Affect Disord. 2006 Apr 29; [Epub ahead of print]
- Zanarini MC, Frankenburg FR. omega-3 Fatty acid treatment of women with borderline personality disorder: a double-blind, placebo-controlled pilot study. Am J Psychiatry. 2003;160(1):167-169.
- Zimmer L, Vancassel S, Cantagrel S, Breton P, Delamanche S, Guilloteau D, Durand G, Chalon S. The dopamine mesocorticolimbic pathway is affected by deficiency in n-3 polyunsaturated fatty acids. Am J Clin Nutr. 2002 Apr;75(4):662-7.

Child Development

- Auestad N, Halter R, Hall RT, Blatter M, Bogle ML, Burks W, Erickson JR, Fitzgerald KM, Dobson V, Innis SM, Singer LT, Montalto MB, Jacobs JR, Qiu W, Bornstein MH. Growth and development in term infants fed long-chain polyunsaturated fatty acids: a double-masked, randomized, parallel, prospective, multivariate study. Pediatrics. 2001 Aug;108(2):372-81.
- Auestad N, Scott DT, Janowsky JS, Jacobsen C, Carroll RE, Montalto MB, Halter R, Qiu W, Jacobs JR, Connor WE, Connor SL, Taylor JA, Neuringer M, Fitzgerald KM, Hall RT. Visual, cognitive, and language assessments

at 39 months: a follow-up study of children fed formulas containing long-chain polyunsaturated fatty acids to 1 year of age. Pediatrics. 2003 Sep;112(3 Pt 1):e177-83.
- Benolken RM, Anderson RE, Wheeler TG. 1973. Membrane fatty acids associated with the electrical response in visual excitation. Science 182:1253-1254
- Birch EE, Castaneda YS, Wheaton DH, Birch DG, Uauy RD, Hoffman DR. Visual maturation of term infants fed long-chain polyunsaturated fatty acid-supplemented or control formula for 12 mo. Am J Clin Nutr. 2005 Apr;81(4):871-9.
- Carlson SE, et al. 1993a. Visual acuity development in healthy preterm infants: effect of marine-oil supplementation. Am. J. Clin. Nutr. 58:35-42.
- Carlson SE, et al. 1993b. Arachidonic acid status correlates with first year growth in preterm infants. Proc Natl Acad Sci 90:1073-1077.
- Champoux M, et al. 2002. Fatty acid formula supplementation and neuromotor development in rhesus monkey neonates. Pediatr Res 51:273-281.
- Cheruku SR, et al. 2002. Higher maternal plasma docosahexaenoic acid during pregnancy is associated with more mature neonatal sleep-state patterning. Am J Clin Nutr 76:608-613.
- Cohen JT, Bellinger DC, Connor WE, Shaywitz BA. A Quantitative Analysis of Prenatal Intake of n-3 Polyunsaturated Fatty Acids and Cognitive Developmen. Am J Prev Med 2005 Nov;29(4):366.e1-366.e12
- Cohen JT, Bellinger DC, Connor WE, Kris-Etherton PM, Lawrence RS, Savitz DA, Shaywitz BA, Teutsch SM, Gray GM. A Quantitative Risk–Benefit Analysis of Changes in Population Fish Consumption. Am J Prev Med 2005 Nov;29(4):325-334
- Cohen JT, Bellinger DC, Shaywitz BA. A Quantitative Analysis of Prenatal Methyl Mercury Exposure and Cognitive Development. Am J Prev Med 2005 Nov;29(4):353.e1-353.e24
- Colombo J, Kannass KN, Shaddy DJ, Kundurthi S, Maikranz JM, Anderson CJ, Blaga OM, Carlson SE. Maternal DHA and the development of attention in infancy and toddlerhood. Child Dev 2004;75:1254-1267.
- Cunnane SC, et al. 2000. Breast-fed infants achieve a higher rate of brain and whole body docosahexaenoate accumulation than formula-fed infants not consuming dietary docosahexaenoate. Lipids 35:105-111.
- Daniels JL, Longnecker MP, Rowland AS, Golding J; ALSPAC Study Team. University of Bristol Institute of Child Health. Fish intake during pregnancy and early cognitive development of offspring. Epidemiology. 2004 Jul;15(4):394-402.
- Das UN. Hypertension as a low-grade systemic inflammatory condition that has its origins in the perinatal period. J Assoc Physicians India. 2006 Feb;54:133-42.
- Das UN. Long-chain polyunsaturated fatty acids interact with nitric oxide, superoxide anion, and transforming growth factor-beta to prevent human essential hypertension. Eur J Clin Nutr. 2004 Feb;58(2):195-203. Review.
- Fewtrell MS, Morley R, Abbott RA, et al. Double-blind, randomized trial of long-chain polyunsaturated fatty acid supplementation in formula fed to preterm infants. Pediatrics. 2002;110(1 Pt 1):73-82.
- Gibson RA, Chen W, Makrides M. Randomized trials with polyunsaturated fatty acid interventions in preterm and term infants: functional and clinical outcomes. Lipids. 2001;36(9):873-883.
- Gibson RA, Neumann MA, Makrides M. Effect of increasing breast milk docosahexaenoic acid on plasma and erythrocyte phospholipid fatty acids and neural indices of exclusively breast fed infants. Eur J Clin Nutr. 1997 Sep;51(9):578-84.
- Golding J, Pembrey M, Jones RALSPAC Study Team. ALSPAC: the Avon Longitudinal Study of Parents and Children. I. Study methodology. Paediatr Perinat Epidemiol 2001; 15: 74-87.
- Heird WC, Lapillonne A. The role of essential fatty acids in development. Annu Rev Nutr. 2005;25:549-71. Review.
- Heird WC. The role of polyunsaturated fatty acids in term and preterm infants and breastfeeding mothers. Pediatr Clin North Am. 2001 Feb;48(1):173-88. Review.
- Helland IB, Saugstad OD, Smith L, Saarem K, Solvoll K, Ganes T, Drevon CA. Similar effects on infants of n-3 and n-6 fatty acids supplementation to pregnant and lactating women. Pediatrics. 2001 Nov;108(5):E82.
- Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA. Maternal supplementation with very-long-chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. Pediatrics. 2003;111(1):e39-44.
- Hibbeln JR, Davis JM, Steer C, Emmett P, Rogers I, Williams C, Golding J. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. The Lancet 2007; 369:578-585.
- Hoffman DR, Birch EE, Birch DG, Uauy R, Castaneda YS, Lapus MG, Wheaton DH. Impact of early dietary intake and blood lipid composition of long-chain polyunsaturated fatty acids on later visual development. J Pediatr Gastroenterol Nutr. 2000 Nov;31(5):540-53.
- Hoffman DR, Birch EE, Castaneda YS, Fawcett SL, Wheaton DH, Birch DG, Uauy R. Visual function in breast-fed term infants weaned to formula with or without long-chain polyunsaturates at 4 to 6 months: a randomized clinical trial. J Pediatr. 2003 Jun;142(6):669-77.
- Hoffman DR, Theuer RC, Castaneda YS, Wheaton DH, Bosworth RG, O'Connor AR, Morale SE, Wiedemann LE, Birch EE. Maturation of visual acuity is accelerated in breast-fed term infants fed baby food containing DHA-enriched egg yolk. J Nutr. 2004 Sep;134(9):2307-13.
- Jensen CL, Maude M, Anderson RE, Heird WC. Effect of docosahexaenoic acid supplementation of lactating women on the fatty acid composition of breast milk lipids and maternal and infant plasma phospholipids. Am J Clin Nutr. 2000 Jan;71(1 Suppl):292S-9S.
- Jensen CL, Voigt RG, Prager TC, Zou YL, Fraley JK, Rozelle JC, Turcich MR, Llorente AM, Anderson RE, Heird WC. Effects of maternal docosahexaenoic acid intake on visual function and neurodevelopment in breastfed term infants. Am J Clin Nutr. 2005 Jul;82(1):125-32.

- Koo WW. Efficacy and safety of docosahexaenoic acid and arachidonic acid addition to infant formulas: can one buy better vision and intelligence? J Am Coll Nutr. 2003;22(2):101-107.
- Larque E, Demmelmair H, Koletzko B. Perinatal supply and metabolism of long-chain polyunsaturated fatty acids: importance for the early development of the nervous system. Ann N Y Acad Sci. 2002;967:299-310.
- Lauritzen L, Jorgensen MH, Mikkelsen TB, Skovgaard M, Straarup EM, Olsen SF, Hoy CE, Michaelsen KF. Maternal fish oil supplementation in lactation: effect on visual acuity and n-3 fatty acid content of infant erythrocytes. Lipids. 2004 Mar;39(3):195-206.
- Llanos A, Lin Y, Mena P, Salem N Jr, Uauy R. Infants with intrauterine growth restriction have impaired formation of docosahexaenoic acid in early neonatal life: a stable isotope study. Pediatr Res. 2005 Oct;58(4):735-40. Erratum in: Pediatr Res. 2006 May;59(5):746. Li, Yuhong [corrected to Lin, Yuhong].
- Makrides M, Gibson RA. Long-chain polyunsaturated fatty acid requirements during pregnancy and lactation. Am J Clin Nutr. 2000;71(1 Suppl):307S-311S.
- McMichael AJ, Butler CD. Fish, Health, and Sustainability. Am J Prev Med 2005 Nov;29(4):322-323
- O'Connor DL, Hall R, Adamkin D, Auestad N, Castillo M, Connor WE, Connor SL, Fitzgerald K, Groh-Wargo S, Hartmann EE, Jacobs J, Janowsky J, Lucas A, Margeson D, Mena P, Neuringer M, Nesin M, Singer L, Stephenson T, Szabo J, Zemon V; Ross Preterm Lipid Study. Growth and development in preterm infants fed long-chain polyunsaturated fatty acids: a prospective, randomized controlled trial. Pediatrics. 2001 Aug;108(2):359-71.
- Oken E, Kleinman KP, Berland WE, Simon SR, Rich-Edwards JW, Gillman MW. Decline in fish consumption among pregnant women after a national mercury advisory. Obstet Gynecol. 2003 Aug;102(2):346-51.
- Olsen SF, Secher NJ, Tabor A, Weber T, Walker JJ, Gluud C. Randomised clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials In Pregnancy (FOTIP) Team. BJOG. 2000;107(3):382-395.
- Olsen SF, Sorensen JD, Secher NJ, et al. Randomised controlled trial of effect of fish-oil supplementation on pregnancy duration. Lancet. 1992;339(8800):1003-1007.
- Onwude JL, Lilford RJ, Hjartardottir H, Staines A, Tuffnell D. A randomised double blind placebo controlled trial of fish oil in high risk pregnancy. Br J Obstet Gynaecol. 1995;102(2):95-100.
- Rojas CV, Martinez JI, Flores I, Hoffman DR, Uauy R. Gene expression analysis in human fetal retinal explants treated with docosahexaenoic acid. Invest Ophthalmol Vis Sci. 2003 Jul;44(7):3170-7.
- SanGiovanni JP, Parra-Cabrera S, Colditz GA, Berkey CS, Dwyer JT. Meta-analysis of dietary essential fatty acids and long-chain polyunsaturated fatty acids as they relate to visual resolution acuity in healthy preterm infants. Pediatrics. 2000;105(6):1292-1298.
- Simmer K, Patole S. Longchain polyunsaturated fatty acid supplementation in preterm infants. Cochrane Database Syst Rev. 2004(1):CD000375.
- Simmer K. Longchain polyunsaturated fatty acid supplementation in infants born at term. Cochrane Database Syst Rev. 2001(4):CD000376.
- Smuts CM, Huang M, Mundy D, Plasse T, Major S, Carlson SE. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. Obstet Gynecol. 2003;101(3):469-479.
- Teutsch SM, Cohen JT. Health Trade-offs from Policies to Alter Fish Consumption. Am J Prev Med 2005 Nov;29(4):324
- Uauy R, Hoffman DR, Mena P, Llanos A, Birch EE. Term infant studies of DHA and ARA supplementation on neurodevelopment: results of randomized controlled trials. J Pediatr. 2003 Oct;143(4 Suppl):S17-25. Review.
- Uauy R, Hoffman DR, Peirano P, Birch DG, Birch EE. Essential fatty acids in visual and brain development. Lipids. 2001;36(9):885-895.
- Willett WC. Fish: Balancing Health Risks and Benefits. Am J Prev Med 2005 Nov;29(4):320-321
- Wyrwoll CS, Mark PJ, Mori TA, Puddey IB, Waddell BJ. Prevention of programmed hyperleptinemia and hypertension by postnatal dietary omega-3 fatty acids. Endocrinology. 2006 Jan;147(1):599-606. Epub 2005 Oct 6.

ADD, ADHA, and Developmental Disorders

- Auestad N, Scott DT, Janowsky JS, Jacobsen C, Carroll RE, Montalto MB, Halter R, Qiu W, Jacobs JR, Connor WE, Connor SL, Taylor JA, Neuringer M, Fitzgerald KM, Hall RT. Visual, cognitive, and language assessments at 39 months: a follow-up study of children fed formulas containing long-chain polyunsaturated fatty acids to 1 year of age. Pediatrics. 2003 Sep;112(3 Pt 1):e177-83.
- Colombo J, Kannass KN, Shaddy DJ, Kundurthi S, Maikranz JM, Anderson CJ, Blaga OM, Carlson SE. Maternal DHA and the development of attention in infancy and toddlerhood. Child Dev 2004;75:1254-1267.
- Hirayama S, Hamazaki T, Terasawa K. Effect of docosahexaenoic acid-containing food administration on symptoms of attention-deficit/hyperactivity disorder - a placebo-controlled double-blind study. Eur J Clin Nutr. 2004 Mar;58(3):467-73.
- Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatrics. 2005 May;115(5):1360-6.
- Richardson AJ, Puri BK. A randomized double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties. Prog Neuropsychopharmacol Biol Psychiatry. 2002 Feb;26(2):233-9.
- Stevens L, Zhang W, Peck L, Kuczek T, Grevstad N, Mahon A, Zentall SS, Arnold LE, Burgess JR. EFA supplementation in children with inattention, hyperactivity, and other disruptive behaviors. Lipids. 2003 Oct;38(10):1007-21.

- Voigt RG, Llorente AM, Jensen CL, Fraley JK, Berretta MC, Heird WC. A randomized, double-blind, placebo-controlled trial of docosahexaenoic acid supplementation in children with attention-deficit/hyperactivity disorder. J Pediatr. 2001 Aug;139(2):189-96.
- Zampelas A, Panagiotakos DB, Pitsavos C, Das UN, Chrysohoou C, Skoumas Y, Stefanadis C. Fish Consumption Among Healthy Adults Is Associated With Decreased Levels of Inflammatory Markers Related to Cardiovascular Disease The ATTICA Study. J Am Coll Cardiol. 2005 Jul 5;46(1):120-4.
- Zhang J, Hebert JR, Muldoon MF. Dietary fat intake is associated with psychosocial and cognitive functioning of school-aged children in the United States. J Nutr. 2005 Aug;135(8):1967-73.

Cancer

- Adlercreutz H. Phytoestrogens and breast cancer. J Steroid Biochem Mol Biol. 2002 Dec;83(1-5):113-8. Review.
- Agency for Healthcare Research and Quality. Effects of Omega-3 Fatty Acids on Cancer. Accessed June 2, 2006 at http://www.ahcpr.gov/clinic/tp/o3cantp.htm
- Anti M, Armelao F, Marra G, Percesepe A, Bartoli GM, Palozza P, Parrella P, Canetta C, Gentiloni N, De Vitis I, et al. Effects of different doses of fish oil on rectal cell proliferation in patients with sporadic colonic adenomas. Gastroenterology. 1994 Dec;107(6):1709-18.
- Anti M, Marra G, Armelao F, Bartoli GM, Ficarelli R, Percesepe A, De Vitis I, Maria G, Sofo L, Rapaccini GL, et al. Effect of omega-3 fatty acids on rectal mucosal cell proliferation in subjects at risk for colon cancer. Gastroenterology. 1992 Sep;103(3):883-91.
- Astorg P. [Dietary fatty acids and colorectal and prostate cancers: epidemiological studies] Bull Cancer. 2005 Jul;92(7):670-84. Review. French.
- Astorg P. Dietary N-6 and N-3 polyunsaturated fatty acids and prostate cancer risk: a review of epidemiological and experimental evidence. Cancer Causes Control. 2004 May;15(4):367-86. Review.
- Augustsson K, Michaud DS, Rimm EB, Leitzmann MF, Stampfer MJ, Willett WC, Giovannucci E. A prospective study of intake of fish and marine fatty acids and prostate cancer. Cancer Epidemiol Biomarkers Prev. 2003 Jan;12(1):64-7.
- Bagga D, Anders KH, Wang HJ, Glaspy JA. Long-chain n-3-to-n-6 polyunsaturated fatty acid ratios in breast adipose tissue from women with and without breast cancer. Nutr Cancer. 2002;42(2):180-5.
- Bartoli GM, Palozza P, Marra G, Armelao F, Franceschelli P, Luberto C, Sgarlata E, Piccioni E, Anti M. n-3 PUFA and alpha-tocopherol control of tumor cell proliferation. Mol Aspects Med. 1993;14(3):247-52.
- Binukumar B, Mathew A. Dietary fat and risk of breast cancer. World J Surg Oncol. 2005 Jul 18;3:45.
- Bougnoux P, Menanteau J. [Dietary fatty acids and experimental carcinogenesis] Bull Cancer. 2005 Jul;92(7):685-96. Review. French.
- Brown MD, Hart CA, Gazi E, Bagley S, Clarke NW. Promotion of prostatic metastatic migration towards human bone marrow stoma by Omega 6 and its inhibition by Omega 3 PUFAs. Br J Cancer (2006) 94, 842-853. doi:10.1038/sj.bjc.6603030 Published online 7 March 2006
- Campos FG, Logullo Waitzberg AG, Kiss DR, Waitzberg DL, Habr-Gama A, Gama-Rodrigues J. Diet and colorectal cancer: current evidence for etiology and prevention. Nutr Hosp. 2005 Jan-Feb;20(1):18-25. Review.
- Chen HW, Chiang T, Wang CY, Lii CK. Inhibition of tert-butyl hydroperoxide-induced cell membrane bleb formation by alpha-tocopherol and glutathione. Food Chem Toxicol. 2000 Dec;38(12):1089-96.
- Cheng J, Ogawa K, Kuriki K, Yokoyama Y, Kamiya T, Seno K, Okuyama H, Wang J, Luo C, Fujii T, Ichikawa H, Shirai T, Tokudome S. Increased intake of n-3 polyunsaturated fatty acids elevates the level of apoptosis in the normal sigmoid colon of patients polypectomized for adenomas/tumors. Cancer Lett. 2003 Apr 10;193(1):17-24. Erratum in: Cancer Lett. 2004 Mar 18;205(2):227.
- Clark MA, Perks CM, Winters ZE, Holly JM. DNA damage uncouples the mitogenic response to IGF-I in MCF-7 malignant breast cancer cells by switching the roles of PI3 kinase and p21WAF1/Cip1. Int J Cancer. 2005 Sep 10;116(4):506-13.
- Cotroneo MS, Wang J, Fritz WA, Eltoum IE, Lamartiniere CA. Genistein action in the prepubertal mammary gland in a chemoprevention model. Carcinogenesis. 2002 Sep;23(9):1467-74.
- Dai Q, Shu XO, Jin F, Potter JD, Kushi LH, Teas J, Gao YT, Zheng W. Population-based case-control study of soyfood intake and breast cancer risk in Shanghai. Br J Cancer. 2001 Aug 3;85(3):372-8.
- Di Mauro S, Cesario E, Bartolo V, Maglitto D, Nucita R, Di Mauro L. [Nutritional habits and colon-rectal tumours] Minerva Gastroenterol Dietol. 2004 Jun;50(2):135-41. Review. Italian.
- Donaldson MS. Nutrition and cancer: a review of the evidence for an anti-cancer diet. Nutr J. 2004 Oct 20;3:19.
- Eastwood GL. Pharmacologic prevention of colonic neoplasms. Effects of calcium, vitamins, omega fatty acids, and nonsteroidal anti-inflammatory drugs. Dig Dis. 1996 Mar-Apr;14(2):119-28. Review.
- Fernandez-Banares F, Esteve M, Navarro E, Cabre E, Boix J, Abad-Lacruz A, Klaassen J, Planas R, Humbert P, Pastor C, Gassull MA. Changes of the mucosal n3 and n6 fatty acid status occur early in the colorectal adenoma-carcinoma sequence. Gut. 1996 Feb;38(2):254-9.
- Folsom AR, Demissie Z. Fish intake, marine omega-3 fatty acids, and mortality in a cohort of postmenopausal women. Am J Epidemiol. 2004 Nov 15;160(10):1005-10.
- Fritschi L, Ambrosini GL, Kliewer EV, Johnson KC; Canadian Cancer Registries Epidemiologic Research Group. Dietary fish intake and risk of leukaemia, multiple myeloma, and non-Hodgkin lymphoma. Cancer Epidemiol Biomarkers Prev. 2004 Apr;13(4):532-7.
- Fritschi L, Johnson KC, Kliewer EV, Fry R; Canadian Cancer Registries Epidemiology Research Group. Animal-related occupations and the risk of leukemia, myeloma, and non-Hodgkin's lymphoma in Canada. Cancer Causes Control. 2002 Aug;13(6):563-71.
- Gago-Dominguez M, Yuan JM, Sun CL, Lee HP, Yu MC. Opposing effects of dietary n-3 and n-6 fatty acids on mammary carcinogenesis: The Singapore Chinese Health Study. Br J Cancer. 2003 Nov 3;89(9):1686-92.

- Gee JM, Watson M, Matthew JA, Rhodes M, Speakman CJ, Stebbings WS, Johnson IT. Consumption of fish oil leads to prompt incorporation of eicosapentaenoic acid into colonic mucosa of patients prior to surgery for colorectal cancer, but has no detectable effect on epithelial cytokinetics. J Nutr. 1999 Oct;129(10):1862-5.
- Giovannucci E. Modifiable risk factors for colon cancer. Gastroenterol Clin North Am. 2002 Dec;31(4):925-43. Review.
- Goodstine SL, Zheng T, Holford TR, Ward BA, Carter D, Owens PH, Mayne ST. Dietary (n-3)/(n-6) fatty acid ratio: possible relationship to premenopausal but not postmenopausal breast cancer risk in U.S. women. J Nutr. 2003 May;133(5):1409-14.
- Hardman WE, Sun L, Short N, Cameron IL. Dietary omega-3 fatty acids and ionizing irradiation on human breast cancer xenograft growth and angiogenesis. Cancer Cell Int. 2005 Apr 28;5(1):12.
- Hardman WE. (n-3) fatty acids and cancer therapy. J Nutr. 2004 Dec;134(12 Suppl):3427S-3430S. Review.
- Hardman WE. Maternal or offspring consumption of omega 3 fatty acids to prevent breast cancer. Proc Amer Assoc Cancer Res 2005;46:3472.
- Heimli H, Hollung K, Drevon CA. Eicosapentaenoic acid-induced apoptosis depends on acyl CoA-synthetase. Lipids. 2003 Mar;38(3):263-8.
- Hilakivi-Clarke L, Cho E, Cabanes A, DeAssis S, Olivo S, Helferich W, Lippman ME, Clarke R. Dietary modulation of pregnancy estrogen levels and breast cancer risk among female rat offspring. Clin Cancer Res. 2002 Nov;8(11):3601-10.
- Hilakivi-Clarke L. Early life exposure to n-3 polyunsaturated fatty acids, breast cancer risk and the mediating pathways. Georgetown University Lombardi Comprehensive Cancer Center Washington, DC, USA. 2005 WCRF / AICR International Research Conference on Food, Nutrition and Cancer, July 14-15, Washington, D.C.
- Huang YC, Jessup JM, Forse RA, Flickner S, Pleskow D, Anastopoulos HT, Ritter V, Blackburn GL. n-3 fatty acids decrease colonic epithelial cell proliferation in high-risk bowel mucosa. Lipids. 1996 Mar;31 Suppl:S313-7.
- Hughes-Fulford M, Li CF, Boonyaratanakornkit J, Sayya S. Arachidonic Acid Activates Phosphatidylinositol 3-Kinase Signaling and Induces Gene Expression in Prostate Cancer. Cancer Res 66, 1427-1433, February 1, 2006.
- Jakes RW, Duffy SW, Ng FC, Gao F, Ng EH, Seow A, Lee HP, Yu MC. Mammographic parenchymal patterns and self-reported soy intake in Singapore Chinese women. Cancer Epidemiol Biomarkers Prev. 2002 Jul;11(7):608-13.
- Jatoi A. Fish oil, lean tissue, and cancer: is there a role for eicosapentaenoic acid in treating the cancer anorexia/weight loss syndrome? Crit Rev Oncol Hematol. 2005 Jul;55(1):37-43.
- Jho DH, Babcock TA, Tevar R, Helton WS, Espat NJ. Eicosapentaenoic acid supplementation reduces tumor volume and attenuates cachexia in a rat model of progressive non-metastasizing malignancy. JPEN J Parenter Enteral Nutr. 2002 Sep-Oct;26(5):291-7.
- Lamartiniere CA. Genistein chemoprevention of breast cancer: timing and mechanisms of action. University of Alabama at Birmingham, Birmingham, AL, USA. 2005 WCRF / AICR International Research Conference on Food, Nutrition and Cancer, July 14-15, Washington, D.C.
- Lands WEM. Fish, Omega-3, and Health, 2nd Edition. AOCS Press 2005. Champaign, Illinois.
- Larsson SC, Kumlin M, Ingelman-Sundberg M, Wolk A. Dietary long-chain n-3 fatty acids for the prevention of cancer: a review of potential mechanisms. Am J Clin Nutr. 2004 Jun;79(6):935-45. Review.
- Leitzmann MF, Stampfer MJ, Michaud DS, Augustsson K, Colditz GC, Willett WC, Giovannucci EL. Dietary intake of n-3 and n-6 fatty acids and the risk of prostate cancer. Am J Clin Nutr. 2004 Jul;80(1):204-16.
- MacLean CH, Newberry SJ, Mojica WA, Khanna P, Issa AM, Suttorp MJ, Lim YW, Traina SB, Hilton L, Garland R, Morton SC. Effects of omega-3 fatty acids on cancer risk: a systematic review. JAMA. 2006 Jan 25;295(4):403-15. Review.
- Mukherjee S, Conrad SE. c-Myc suppresses p21WAF1/CIP1 expression during estrogen signaling and antiestrogen resistance in human breast cancer cells. J Biol Chem. 2005
- Norat T, Bingham S, Ferrari P, Slimani N, Jenab M, Mazuir M, Overvad K, Olsen A, Tjonneland A, Clavel F, Boutron-Ruault MC, Kesse E, Boeing H, Bergmann MM, Nieters A, Linseisen J, Trichopoulou A, Trichopoulos D, Tountas Y, Berrino F, Palli D, Panico S, Tumino R, Vineis P, Bueno-de-Mesquita HB, Peeters PH, Engeset D, Lund E, Skeie G, Ardanaz E, Gonzalez C, Navarro C, Quiros JR, Sanchez MJ, Berglund G, Mattisson I, Hallmans G, Palmqvist R, Day NE, Khaw KT, Key TJ, San Joaquin M, Hemon B, Saracci R, Kaaks R, Riboli E. Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. J Natl Cancer Inst. 2005 Jun 15;97(12):906-16.
- Olivo SE, Hilakivi-Clarke L. Opposing effects of prepubertal low- and high-fat n-3 polyunsaturated fatty acid diets on rat mammary tumorigenesis. Carcinogenesis. 2005 Sep;26(9):1563-72. Epub 2005 May 11.
- Personal communication with W. Elaine Hardman, Ph.D. January 27, 2006.
- Personal communication with William E. M. Lands, Ph.D. January 27, 2006.
- Rao CV, Hirose Y, Indranie C, Reddy BS. Modulation of experimental colon tumorigenesis by types and amounts of dietary fatty acids. Cancer Res. 2001 Mar 1;61(5):1927-33.
- Rose DP, Connolly JM. Antiangiogenicity of docosahexaenoic acid and its role in the suppression of breast cancer cell growth in nude mice. Int J Oncol. 1999 Nov;15(5):1011-5.
- Rose DP, Connolly JM. Omega-3 fatty acids as cancer chemopreventive agents. Pharmacol Ther. 1999 Sep;83(3):217-44. Review.
- Rose DP, Connolly JM. Omega-3 fatty acids as cancer chemopreventive agents. Pharmacol Ther. 1999 Sep;83(3):217-44. Review
- Rose DP, Connolly JM. Regulation of tumor angiogenesis by dietary fatty acids and eicosanoids. Nutr Cancer. 2000;37(2):119-27. Review.
- Rose DP. Effects of dietary fatty acids on breast and prostate cancers: evidence from in vitro experiments and animal studies. Am J Clin Nutr. 1997 Dec;66(6 Suppl):1513S-1522S. Review.

- Roynette CE, Calder PC, Dupertuis YM, Pichard C. n-3 polyunsaturated fatty acids and colon cancer prevention. Clin Nutr. 2004 Apr;23(2):139-51. Review.
- Roynette CE, Calder PC, Dupertuis YM, Pichard C. n-3 polyunsaturated fatty acids and colon cancer prevention. Clin Nutr. 2004 Apr;23(2):139-51. Review.
- Stoll BA. N-3 fatty acids and lipid peroxidation in breast cancer inhibition. Br J Nutr. 2002 Mar;87(3):193-8. Review.
- Terry PD, Rohan TE, Wolk A. Intakes of fish and marine fatty acids and the risks of cancers of the breast and prostate and of other hormone-related cancers: a review of the epidemiologic evidence. Am J Clin Nutr. 2003 Mar;77(3):532-43. Review.
- Terry PD, Terry JB, Rohan TE. Long-chain (n-3) fatty acid intake and risk of cancers of the breast and the prostate: recent epidemiological studies, biological mechanisms, and directions for future research. J Nutr. 2004 Dec;134(12 Suppl):3412S-3420S. Review.
- United States Department of Health and Human Services, Centers for Disease Control and Prevention. Colorectal Cancer: The Importance of Prevention and Early Detection. 2004/2005 Fact Sheet. Accessed online Ocotober 1, 2005 at http://www.cdc.gov/cancer/colorctl/about2004.htm
- Winters ZE, Leek RD, Bradburn MJ, Norbury CJ, Harris AL. Cytoplasmic p21WAF1/CIP1 expression is correlated with HER-2/ neu in breast cancer and is an independent predictor of prognosis. Breast Cancer Res. 2003;5(6):R242-9. Epub 2003 Oct 3.
- Wu M, Harvey KA, Ruzmetov N, Welch ZR, Sech L, Jackson K, Stillwell W, Zaloga GP, Siddiqui RA. Omega-3 polyunsaturated fatty acids attenuate breast cancer growth through activation of a neutral sphingomyelinase-mediated pathway. Int J Cancer. 2005 May 17; [Epub ahead of print]
- Yee LD, Young DC, Rosol TJ, Vanbuskirk AM, Clinton SK. Dietary (n-3) polyunsaturated fatty acids inhibit HER-2/neu-induced breast cancer in mice independently of the PPARgamma ligand rosiglitazone. J Nutr. 2005 May;135(5):983-8.

Diabetes

- American Diabetes Association. Good Fats and Bad Fats http://www.diabetes.org/diabetes-cholesterol/faqs-fat.jsp
- American Diabetes Association. National Diabetes Fact Sheet http://www.diabetes.org/diabetes-statistics.jsp
- American Heart Association, Inc. “What is the metabolic syndrome?” http://www.americanheart.org/presenter.jhtml?identifier=534
- Borkman M, Chisholm DJ, Furler SM, Storlien LH, Kraegen EW, Simons LA, Chesterman CN. Effects of fish oil supplementation on glucose and lipid metabolism in NIDDM. Diabetes. 1989 Oct;38(10):1314-9.
- Fasching P, Ratheiser K, Waldhausl W, Rohac M, Osterrode W, Nowotny P, Vierhapper H. Metabolic effects of fish-oil supplementation in patients with impaired glucose tolerance. Diabetes. 1991 May;40(5):583-9.
- Fasching P, Rohac M, Liener K, Schneider B, Nowotny P, Waldhausl W. Fish oil supplementation versus gemfibrozil treatment in hyperlipidemic NIDDM. A randomized crossover study. Horm Metab Res. 1996 May;28(5):230-6.
- Goodfellow J, Bellamy MF, Ramsey MW, Jones CJ, Lewis MJ. Dietary supplementation with marine omega-3 fatty acids improve systemic large artery endothelial function in subjects with hypercholesterolemia. J Am Coll Cardiol. 2000 Feb;35(2):265-70.
- Hendra TJ, Britton ME, Roper DR, Wagaine-Twabwe D, Jeremy JY, Dandona P, Haines AP, Yudkin JS. Effects of fish oil supplements in NIDDM subjects. Controlled study. Diabetes Care. 1990 Aug;13(8):821-9.
- Jain S, Gaiha M, Bhattacharjee J, Anuradha S. Effects of low-dose omega-3 fatty acid substitution in type-2 diabetes mellitus with special reference to oxidative stress--a prospective preliminary study. J Assoc Physicians India. 2002 Aug;50:1028-33.
- Kasim SE. Dietary marine fish oils and insulin action in type 2 diabetes. Ann N Y Acad Sci. 1993 Jun 14;683:250-7. Review.
- Kesavulu MM, Kameswararao B, Apparao Ch, Kumar EG, Harinarayan CV. Effect of omega-3 fatty acids on lipid peroxidation and antioxidant enzyme status in type 2 diabetic patients. Diabetes Metab. 2002 Feb;28(1):20-6.
- Luo J, Rizkalla SW, Vidal H, Oppert JM, Colas C, Boussairi A, Guerre-Millo M, Chapuis AS, Chevalier A, Durand G, Slama G. Moderate intake of n-3 fatty acids for 2 months has no detrimental effect on glucose metabolism and could ameliorate the lipid profile in type 2 diabetic men. Results of a controlled study. Diabetes Care. 1998 May;21(5):717-24.
- MacLean CH, Mojica WA, Morton SC, et al. Effects of Omega-3 Fatty Acids on Lipids and Glycemic Control in Type II Diabetes and the Metabolic Syndrome and on Inflammatory Bowel Disease, Rheumatoid Arthritis, Renal Disease, Systemic Lupus Erythematosus, and Osteoporosis. Summary, Evidence Report/Technology Assessment: Number 89. AHRQ Publication Number 04-E012-1, March 2004. Agency for Healthcare Research and Quality, Rockville, MD. http://www.ahrq.gov/clinic/epcsums/o3lipidsum.htm
- McVeigh GE, Brennan GM, Cohn JN, Finkelstein SM, Hayes RJ, Johnston GD. Fish oil improves arterial compliance in non-insulin-dependent diabetes mellitus. Arterioscler Thromb. 1994 Sep;14(9):1425-9.
- Nosari I, Cortinovis F, Lepore G, Maglio ML, Pagani G. [Use of omega-3 in diabetic patients] Clin Ter. 1994 Mar;144(3):213-21. Review. Italian.
- Okuda Y, Mizutani M, Ogawa M, Sone H, Asano M, Asakura Y, Isaka M, Suzuki S, Kawakami Y, Field JB, Yamashita K. Long-term effects of eicosapentaenoic acid on diabetic peripheral neuropathy and serum lipids in patients with type II diabetes mellitus. J Diabetes Complications. 1996 Sep-Oct;10(5):280-7.
- Pelikanova T, Kohout M, Valek J, Kazdova L, Base J. Metabolic effects of omega-3 fatty acids in type 2 (non-insulin-dependent) diabetic patients. Ann N Y Acad Sci. 1993 Jun 14;683:272-8.

- Prince MJ, Deeg MA. Do n-3 fatty acids improve glucose tolerance and lipemia in diabetics? Curr Opin Lipidol. 1997 Feb;8(1):7-11. Review.
- Rivellese AA, Maffettone A, Iovine C, Di Marino L, Annuzzi G, Mancini M, Riccardi G. Long-term effects of fish oil on insulin resistance and plasma lipoproteins in NIDDM patients with hypertriglyceridemia. Diabetes Care. 1996 Nov;19(11):1207-13.
- Schectman G, Kaul S, Kissebah AH. Effect of fish oil concentrate on lipoprotein composition in NIDDM. Diabetes. 1988 Nov;37(11):1567-73.
- Shimizu H, Ohtani K, Tanaka Y, Sato N, Mori M, Shimomura Y. Long-term effect of eicosapentaenoic acid ethyl (EPA-E) on albuminuria of non-insulin dependent diabetic patients. Diabetes Res Clin Pract. 1995 Apr;28(1):35-40.
- Vessby B, Boberg M. Dietary supplementation with n-3 fatty acids may impair glucose homeostasis in patients with non-insulin-dependent diabetes mellitus. J Intern Med. 1990 Aug;228(2):165-71.
- Woodman RJ, Mori TA, Burke V, Puddey IB, Watts GF, Beilin LJ. Effects of purified eicosapentaenoic and docosahexaenoic acids on glycemic control, blood pressure, and serum lipids in type 2 diabetic patients with treated hypertension. Am J Clin Nutr. 2002 Nov;76(5):1007-15.

Inflammatory diseases

- Adam O. Dietary fatty acids and immune reactions in synovial tissue. Eur J Med Res. 2003 Aug 20;8(8):381-7. Review.
- Aslan A, Triadafilopoulos G. Fish oil fatty acid supplementation in active ulcerative colitis: a double-blind, placebo-controlled, crossover study. Am J Gastroenterol. 1992;87(4):432-437.
- Belluzzi A, Brignola C, Campieri M, Pera A, Boschi S, Miglioli M. Effect of an enteric-coated fish-oil preparation on relapses in Crohn's disease. N Engl J Med. 1996;334(24):1557-1560.
- Berbert AA, Kondo CR, Almendra CL, Matsuo T, Dichi I. Supplementation of fish oil and olive oil in patients with rheumatoid arthritis. Nutrition. 2005 Feb;21(2):131-6.
- Calder PC. N-3 polyunsaturated fatty acids and inflammation: from molecular biology to the clinic. Lipids. 2003 Apr;38(4):343-52. Review.
- Cleland LG, James MJ, Proudman SM. The role of fish oils in the treatment of rheumatoid arthritis. Drugs. 2003;63(9):845-53. Review.
- Fortin PR, Lew RA, Liang MH, et al. Validation of a meta-analysis: the effects of fish oil in rheumatoid arthritis. J Clin Epidemiol. 1995;48(11):1379-1390.
- Hawthorne AB, Daneshmend TK, Hawkey CJ, et al. Treatment of ulcerative colitis with fish oil supplementation: a prospective 12 month randomised controlled trial. Gut. 1992;33(7):922-928.
- Hodge L, Salome CM, Hughes JM, et al. Effect of dietary intake of omega-3 and omega-6 fatty acids on severity of asthma in children. Eur Respir J. 1998;11(2):361-365.
- Kjeldsen-Kragh J, Lund JA, Riise T, et al. Dietary omega-3 fatty acid supplementation and naproxen treatment in patients with rheumatoid arthritis. J Rheumatol. 1992;19(10):1531-1536.
- Kremer JM. n-3 fatty acid supplements in rheumatoid arthritis. Am J Clin Nutr. 2000;71(1 Suppl):349S-351S.
- Lau CS, Morley KD, Belch JJ. Effects of fish oil supplementation on non-steroidal anti-inflammatory drug requirement in patients with mild rheumatoid arthritis--a double-blind placebo controlled study. Br J Rheumatol. 1993;32(11):982-989.
- Loeschke K, Ueberschaer B, Pietsch A, et al. n-3 fatty acids only delay early relapse of ulcerative colitis in remission. Dig Dis Sci. 1996;41(10):2087-2094.
- Lorenz R, Weber PC, Szimnau P, Heldwein W, Strasser T, Loeschke K. Supplementation with n-3 fatty acids from fish oil in chronic inflammatory bowel disease--a randomized, placebo-controlled, double-blind cross-over trial. J Intern Med Suppl. 1989;225(731):225-232.
- Lorenz-Meyer H, Bauer P, Nicolay C, et al. Omega-3 fatty acids and low carbohydrate diet for maintenance of remission in Crohn's disease. A randomized controlled multicenter trial. Study Group Members (German Crohn's Disease Study Group). Scand J Gastroenterol. 1996;31(8):778-785.
- Mickleborough TD, Ionescu AA, Rundell KW. Omega-3 Fatty acids and airway hyperresponsiveness in asthma. J Altern Complement Med. 2004 Dec;10(6):1067-75. Review.
- Mickleborough TD, Rundell KW. Dietary polyunsaturated fatty acids in asthma- and exercise-induced bronchoconstriction. Eur J Clin Nutr. 2005 Dec;59(12):1335-46. Review.
- Mihrshahi S, Peat JK, Webb K, Oddy W, Marks GB, Mellis CM; CAPS Team. Effect of omega-3 fatty acid concentrations in plasma on symptoms of asthma at 18 months of age. Pediatr Allergy Immunol. 2004 Dec;15(6):517-22.
- Mori TA, Beilin LJ. Omega-3 fatty acids and inflammation. Curr Atheroscler Rep. 2004 Nov;6(6):461-7. Review.
- Okamoto M, Mitsunobu F, Ashida K, et al. Effects of dietary supplementation with n-3 fatty acids compared with n-6 fatty acids on bronchial asthma. Intern Med. 2000;39(2):107-111.
- Peat JK, Mihrshahi S, Kemp AS, Marks GB, Tovey ER, Webb K, Mellis CM, Leeder SR. Three-year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. J Allergy Clin Immunol. 2004 Oct;114(4):807-13.
- Remans PH, Sont JK, Wagenaar LW, Wouters-Wesseling W, Zuijderduin WM, Jongma A, Breedveld FC, Van Laar JM. Nutrient supplementation with polyunsaturated fatty acids and micronutrients in rheumatoid arthritis: clinical and biochemical effects. Eur J Clin Nutr. 2004 Jun;58(6):839-45.
- Salam MT, Li Y-F, Langholz B, Gilliland FD. Maternal fish consumption during pregnancy and risk of early childhood asthma. J Asthma 2005;42:513-518.
- Stenson WF, Cort D, Rodgers J, et al. Dietary supplementation with fish oil in ulcerative colitis.Ann Intern Med. 1992;116(8):609-614.

- Sundrarjun T, Komindr S, Archararit N, Dahlan W, Puchaiwatananon O, Angthararak S, Udomsuppayakul U, Chuncharunee S. Effects of n-3 fatty acids on serum interleukin-6, tumour necrosis factor-alpha and soluble tumour necrosis factor receptor p55 in active rheumatoid arthritis. J Int Med Res. 2004 Sep-Oct;32(5):443-54.
- Wong KW. Clinical efficacy of n-3 fatty acid supplementation in patients with asthma. J Am Diet Assoc. 2005 Jan;105(1):98-105. Review.
- Woods RK, Thien FC, Abramson MJ. Dietary marine fatty acids (fish oil) for asthma in adults and children. Cochrane Database Syst Rev. 2002(3):CD001283.

Safety Considerations

- American Heart Association. Fish and Omega-3 Fatty Acids. Accessed June 12, 2006 at http://www.americanheart.org/presenter.jhtml?identifier=4632.

Intake Recommendations

- Gebauer SK, Psota TL, Harris WS, Kris-Etherton PM. n–3 Fatty acid dietary recommendations and food sources to achieve essentiality and cardiovascular benefits. Presented at the symposium "n–3 Fatty Acids: Recommendations for Therapeutics and Prevention," Institute of Human Nutrition, Columbia University, New York, NY, 21 May 2005.
- Gebauer SK, Psota TL, Harris WS, Kris-Etherton PM. Supplement: n–3 Fatty Acids: Recommendations for Therapeutics and Prevention. Am J Clin Nutr, Vol. 83, No. 6, S1526-1535S, June 2006.
- International Society for the Study of Fatty Acids & Lipids. US sets fat intake recommendations. Accessed online May 13, 2006 at http://www.issfal.org.uk/welcome/iss032002.pdf

Information in this document has not been reviewed by the US Food & Drug Administration. It is not meant to substitute for the advice provided by medical professionals, nor is it intended to diagnose, treat, cure or prevent disease.

Document ID: 46E5AF8A-5592-28C037