Background
Research suggests that not all fats are created equal, particularly when it comes to heart health. In fact, various dietary fats or fatty acids can have different effects on blood lipids associated with coronary heart disease (CHD) such as HDL (“good”) cholesterol, LDL (“bad”) cholesterol, and triglycerides. Trans fatty acids and high amounts of certain saturated fatty acids (SFA) in the diet tend to raise LDL cholesterol levels and increase CHD risk. In the context of moderate fat consumption, diets higher in monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) generally decrease CHD risk because they can lower levels of LDL cholesterol and triglycerides in the blood.\(^1\)

The human body can synthesize SFAs and MUFAs but not all the long-chain PUFAs.\(^1,2\) Therefore, some long-chain PUFAs are also called essential fatty acids (EFA) because it is essential that they be obtained from food.\(^2\) Lack of these EFAs, over a period of time, results in adverse clinical symptoms such as impaired growth, skin lesions, and neurological abnormalities.\(^1,2\) There are two subclasses of long-chain PUFAs: omega-3 (n-3) fatty acids and omega-6 (n-6) fatty acids. Important examples of the omega-3 PUFAs are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). ALA is the precursor to EPA and DHA.\(^\text{1}\) Rich sources of EPA and DHA are fatty fish and fish oils, whereas principal sources of ALA are walnuts and certain vegetable oils, including flaxseed and canola.\(^\text{1}\) Examples of the omega-6 PUFAs include linoleic acid (LA), gamma-linolenic acid (GLA), and arachidonic acid (ARA). LA is found primarily in vegetable and plant oils, such as corn, safflower, soybean, and sunflower. GLA is found mostly in evening primrose oil, borage oil, and black current seed oil. ARA is found in animal products such as meat, poultry, and eggs.\(^\text{1}\)

<table>
<thead>
<tr>
<th>Long-chain PUFAs</th>
<th>Name</th>
<th>Abbr.</th>
<th>Structure</th>
<th>Food Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega-3</td>
<td>alpha-linolenic acid</td>
<td>ALA</td>
<td>18:3n-3</td>
<td>Walnuts, flaxseed oil, and canola oil</td>
</tr>
<tr>
<td></td>
<td>eicosapentaenoic acid</td>
<td>EPA</td>
<td>20:5n-3</td>
<td>Fatty fish and fish oils</td>
</tr>
</tbody>
</table>
Health Effects

Omega-6

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Acronym</th>
<th>Carbon Number</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>linoleic acid</td>
<td>LA</td>
<td>18:2n-6</td>
<td>Corn, safflower, soybean, cottonseed, and sunflower oils</td>
</tr>
<tr>
<td>gamma-linolenic acid</td>
<td>GLA</td>
<td>18:3n-6</td>
<td>Evening primrose oil, borage oil, and black current seed oil</td>
</tr>
<tr>
<td>arachidonic acid</td>
<td>ARA</td>
<td>20:4n-6</td>
<td>Meat, poultry, and eggs</td>
</tr>
</tbody>
</table>

Omega-3

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Acronym</th>
<th>Carbon Number</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>docosahexaenoic acid</td>
<td>DHA</td>
<td>22:6n-3</td>
<td>Fatty fish and fish oils</td>
</tr>
<tr>
<td>DHA</td>
<td></td>
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</tr>
</tbody>
</table>

The role of n-3 fatty acids in growth and development as well as in health and disease—particularly CHD—is currently one of the fastest growing research areas in nutritional science. As a result, knowledge of these essential PUFAs has grown significantly. Benefits from n-3 fatty acids were first noticed in epidemiological studies among Greenland Inuits. The rarity of ischemic heart disease (characterized by narrowed heart arteries) in this Eskimo population was attributed to their traditional, EPA-rich diet of marine animals and fish. Moreover, Eskimo consumption of LA was low compared to the typical Danish diet. This observation has led to several epidemiological and observational studies of men and women, who regularly consume fish, showing similar heart health results.

Cardiovascular benefits from n-3 fatty acid consumption have been documented in several prospective studies and randomized clinical trials. A small clinical trial found that patients who were given fish oil concentrate for two years had lower triglyceride levels and minimal artery blockage when compared to those receiving a placebo. These results showed that consuming n-3 fatty acids daily may reduce the risk of abnormal thickening of arteries due to fatty deposits on arterial inner walls (atherosclerosis). A meta-analysis of studies on diabetes and fish oils found a 30 percent reduction in patient triglyceride levels—particularly among subjects with Type I diabetes. This is noteworthy, considering that the high cardiovascular mortality rate of people with diabetes has been partially attributed to increased triglyceride concentrations in the blood.

Larger trials, such as the GISSI-Prevenzione Trial (Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto miocardico),9 the Lyon Heart Study,10 and the Indo-Mediterranean Diet Heart Study,11 suggest n-3 fatty acids have a protective mechanism of reducing the risk of irregular heartbeats. Furthermore, the GISSI-Prevenzione trial—the longest of the three trials, which enrolled 11,323 subjects who survived their first heart attack—demonstrated that even a small amount (1 g/d) of n-3 fatty acids is effective in reducing overall mortality and risk of cardiac death by 20 percent and 45 percent, respectively.

Omega-3 fatty acids are also shown to be beneficial at various life stages and with several health conditions. DHA is naturally found in breast milk and has been shown to support the visual and cognitive development in infants. Various infant formulas now contain DHA along with ARA to
more closely mimic breast milk. Evidence has also emerged showing benefits from n-3 fatty acid consumption in health conditions such as, depression, cancer, lupus, and asthma. A cross-sectional study in Australia showed an inverse association between age-related maculopathy (ARM)—a leading cause of blindness in older adults—and fish consumption. Subjects who ate fish more than once per week reduced their risk of having ARM by half compared to those who ate fish less than once per month. Patients with rheumatoid arthritis, who received fish oil supplements in addition to background medication, had a significant decrease in the number of tender joints and morning stiffness. The continued study of n-3 fatty acids will lead to further understanding of their effects on development, health, and disease risk reduction.

**Recommendations**

In general, the scientific community has not yet arrived at a consensus in terms of the ideal LA to ALA dietary ratio, the optimal intake of n-3 fatty acids, or the comparative efficacy of plant and marine n-3 fatty acids. The current ratio of LA to ALA consumption in Western Europe and the US ranges from 15:1 to 20:1.20 This is due to the increased consumption of LA-rich vegetable oils and meats and declining fish consumption. These ratios are much higher than the ratio found in the Paleolithic diet from which humans evolved. That diet had roughly equal amounts of LA and ALA (1:2:1).3 Concerned about the imbalance of LA and ALA in the diet and its potential negative impact on health, some experts believe the evidence indicates a 4:1 ratio—similar to that of the Lyon Heart Study and the traditional Japanese diet—would be optimal. Based on limited studies in animals, children, and adults, the Institute of Medicine has determined that a LA to ALA ratio range from 5:1 to 10:1 is a reasonable recommendation for adults. However, an expert workshop concluded that it is the absolute amount of LA in the diet, not its ratio to ALA, that is important for reducing CHD risk.

The Dietary Reference Intakes (DRIs)—released by the Institute of Medicine in collaboration with Health Canada—recommend an ALA intake of 0.6-1.2 percent of energy, or 1.3 to 2.7 g/d, on the basis of a 2000-calorie diet.5 The World Health Organization and North Atlantic Treaty Organization (WHO-NATO) recommend consuming 0.3 to 0.5 g/d of EPA + DHA.5 These recommendations can be met by eating two servings of fish per week, with emphasis on fatty fish—salmon, herring, and mackerel—and by using liquid vegetable oils containing ALA. The 2005 Dietary Guidelines Advisory Committee also recommended the consumption of two, 4-ounce servings of fish high in EPA and DHA per week to reduce the risk of CHD. The American Heart Association recommends 0.5 to 1.8 g/d of EPA + DHA to reduce cardiac disease and 1.5 to 3 g/d of ALA for beneficial health effects. The current average intake of n-3 fatty acids in the US is about 1.6 g/d (~0.7% of total calories); of this, only 0.1-0.2 g/d is EPA+DHA.

While much of the current scientific research supports the health effects of fish and fish oils, it is not yet clear whether there are functional differences between marine and plant n-3 PUFAs. A large clinical trial, the Indo-Mediterranean Diet Heart Study, found that mustard seed oil and fish oil were both effective in reducing cardiovascular disease outcomes when compared to a placebo, but detected no differences between the two supplements. In addition, only a few studies on ALA are available, and variations in study design and methodology make comparisons difficult. Factors such as population characteristics can confound results. For instance, if the population under study already had high overall intakes of fish, eating more fish is not associated with increased benefits. Also, reduced CHD mortality has been found only among high-risk groups. Furthermore, background dietary components make it difficult to identify the benefits specific to n-3 fatty acids. Studies on n-3 fatty acids from Mediterranean-type diets identified fiber, phytochemicals, and antioxidants in fruits, vegetables, whole grains, and nuts as other potential contributors to observed health benefits.

In October of 2000, after a review of the scientific literature on dietary supplements containing EPA
and DHA, the US Food and Drug Administration (FDA) concluded that a direct CHD risk reduction benefit from consuming n-3 fatty acids could not be established because their effects in the general healthy population are unknown compared to that of diseased populations.\cite{24} Although n-3 fatty acids were associated with decreased triglycerides,\cite{6,12} omega-3 fatty acids generally have no effect on LDL-cholesterol, a validated surrogate marker of CHD.\cite{24} Given the inconclusive evidence, the FDA has permitted a qualified health claim for dietary supplements—provided the labeling does not recommend exceeding a daily intake of two grams combined EPA and DHA.\cite{25} In September of 2004, the FDA announced they would allow a qualified health claim for reduced risk of coronary heart disease (CHD) for conventional foods that contain EPA and DHA omega-3 fatty acids. The claim states: “Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. One serving of [name of food] provides [x] grams of EPA and DHA omega-3 fatty acids. [See nutrition information for total fat, saturated fat and cholesterol content.]”\cite{26} Further research is necessary for significant scientific consensus/agreement regarding the relationship between n-3 fatty acids and coronary heart disease as well as other health benefits.

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**The Bottom Line**

Omega-3 fatty acids from fish and fish oils have a beneficial effect in people with pre-existing cardiovascular heart disease (CHD). One serving of fish weekly may decrease the risk of fatal CHD by approximately 40 percent. For the general, healthy population, two, 4-ounce servings of fish high in DHA and EPA per week are recommended as part of a healthful diet. Currently, the FDA allows a qualified health claim for these omega-3 fatty acids (EPA and DHA) and coronary heart disease for dietary supplements and conventional foods.

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**Omega-3 Fatty Acids:**

Found in plant and marine sources

**Plant Sources:**

- Flax
- Walnuts
- Canola Oil

**Marine Sources:**

- Salmon
- Sardines
- Tuna

**Properties:**

- May reduce risk of coronary heart disease.
- May contribute to maintenance of mental and visual function.
References:


25 Letter responding to a request to reconsider the qualified claim for a dietary supplement health claim for omega-3 fatty acids and coronary heart disease (Docket No. 91N-0103).


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