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Fish Oil, Krill Oil, and Algal Oil Omega-3 (DHA & EPA) Supplements Review

See Our Omega-3 Top Picks and Avoid Rancid Fish Oils.

Latest Update

Fish Oil for Burning Mouth?



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Watch the video

Summary

• What are the benefits of fish oil? Taking a supplement with EPA and DHA from fish oil (or another marine source, such as krill oil or algae) offers a wide range of potential benefits for mental health, treating inflammatory disease, maintaining muscle, and even cancer prevention (see What It Does). In people with high triglyceride levels (which contributes to high cholesterol), high-dose, high-concentration fish oil, such as from prescription fish oils, may lower triglycerides.

However, eating fish at least twice each week may do you more good than taking a fish oil supplement for other types of cardiovascular benefit, for cognitive and memory benefits, or for reducing the risk of age-related macular degeneration (AMD) or of Alzheimer's disease (If you do eat fish, be aware that some types can be high in mercury – see <u>Getting EPA and DHA from Food</u> and our <u>Tuna, Salmon, Sardines & Herring Review</u>).

There is less evidence to support the use of other fatty acids in fish oil, such as DPA (docosapentaenoic acid) and omega-7 fatty acids (such as palmitoleic acid).

■ Which fish, krill, and algal oils are the best? Choose a supplement listed as Approved by ConsumerLab.com in the Results table, because some products may be rancid (including three products in this Review), contaminated, or fail to contain their listed amounts of omega-3 fatty acids (see How Products Were Evaluated and What CL Found). Compare prices to save money (see comparison graph and 5th column of the Results table). To save time, see our Top Picks — these are Approved products that offer exceptional value compared to other products in their categories, including fish oils in softgels, enteric-coated capsules, bottled liquids, as a prenatal supplement, for children, and for pets, as well as our Top Picks for krill oil and vegetarian algal oil (from algae). We also have Top Picks for getting DPA (the "other omega-3") and omega-7 fatty acids. You'll see that you can get high-quality supplements for just pennies a day. Be mindful of any added ingredients (see the last column of the Results

table), like vitamins, so you don't unintentionally exceed tolerable intake limits for these.

- How much fish oil should you take? Different amounts of EPA and DHA have been used for different purposes. A general daily dose is about 300 to 500 mg of EPA and DHA, while some treatments (such as for high triglycerides) involve doses as high as 4,000 mg per day (see What to Consider When Using Dosage). Focus on the amounts of EPA and DHA in a product rather than the amount of total oil, since the concentration of EPA and DHA in oils ranges from about 33% to 85% and, for some uses, you may want more EPA or more DHA (see the comparison graph and second column of the Results table below for amounts of EPA and DHA and concentration levels, as well as amounts of "the other omega-3" DPA, and omega-7 fatty acids). (Be aware that fish oils highly concentrated for omega-3s tend to have low levels of omega-7s).
- When is the best time to take fish oil? Taking fish oil with a meal containing other fats may improve absorption. If you need a high daily dose, dividing the dose over the course of the day may reduce any unpleasant aftertaste and "fishy burps." Enteric-coated capsules can also reduce these effects but may possibly reduce absorption if the coating doesn't release the oil in a timely fashion (CL tests enteric-coated fish oil supplements to ensure they properly release their ingredients).
- What is the best form of fish oil? Fish oil in supplements is generally first processed to purify it. This often involves modifying its chemical form. While all forms can help raise EPA and DHA levels and do so equally well if taken with a high-fat meal, if not taken with a high-fat meal the "re-esterified triglyceride" (or just "triglyceride") form may be the best absorbed, with up to 76% greater absorption than from the more common "ethyl ester" form (see ConsumerTips™ Forms of Fish Oil). You can check the form of each product in the 4th column of the Results table.

If you need a high dose, it may be more convenient to pick a product with a higher concentration (see the 4th column of the <u>Results</u> <u>table</u>) so that you can take fewer and/or smaller pills or other units.

- How should fish oil be stored? Store fish oil out of heat and light and, once opened, refrigerate. Freezing is also okay. When ordering products online, be sure to buy during a time of year when the weather is cold or mild (see Keep It Fresh).
- Which fish oil supplements are most like prescription omega-3 drugs? Some supplements have similarly high amounts and concentrations of EPA and DHA as found in prescription omega-3 drugs like Vascepa and Lovaza, but at lower cost than these brandname medications. See how fish oil supplements compare to prescription omega-3 drugs.
- Is fish oil safe? What are fish oil's side effects? Although generally safe, high amounts of EPA and DHA may suppress the immune system and increase the risk of abnormal heart rhythm (atrial fibrillation). It's best to limit daily intake of EPA and DHA from supplements to no more than 2 grams, unless medically indicated. Fish oil may also thin the blood and slightly lower blood pressure. See Concerns and Cautions for more information. As mentioned, take fish oil with food to reduce fishy burps, a common side effect.

Products tested in 2023

What It Is:

EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) are two principal fatty acids found in fish, krill, calamari, and green-lipped mussel. They belong to a family of nutrients known as omega-3 fatty acids. EPA and DHA can also be obtained from other marine sources, such as algae (algal oil). EPA and DHA are polyunsaturated fats ("good" fats, as opposed to saturated fats which are thought to increase the risk of heart disease). The body can only manufacture limited amounts of EPA and DHA from the essential fatty acid, alpha-linolenic acid (ALA) – found in flaxseed oil, canola oil, soy oil and walnut oil. For more information about ALA see the separate review covering ALA and GLA products.

What It Does:

Heart Disease and Stroke

Eating non-fried fish or taking high-dose *prescription* fish oil containing the omega-3 fatty acids EPA and DHA have a number of potentially heart-healthy effects, including reducing triglyceride levels, slightly raising levels of HDL ("good") cholesterol, possibly, "thinning" the blood, reducing levels of homocysteine, and reducing blood pressure. Fish oil *supplements*, on the other hand, have shown inconsistent and inconclusive evidence of cardiovascular benefit, particularly among people without risk factors for heart disease.

Increased consumption of fish oils from fish and high levels of omega-3s in the blood have been associated with reduced risk of cardiovascular disease and related mortality (Mozaffarian, Ann Int Med 2013). The researchers indicated that the high blood levels could be achieved with average daily intake of a moderate amount of fish providing 250 mg to 400 mg of EPA plus DHA (see Getting EPA and DHA from Food, below) and noted that greater intake would not yield much further benefit. In line with this, the American Heart Association recommends consuming at least 1 to 2 fish servings (3.5 oz per serving) of non-fried, preferably oily fish, per week to reduce the risk of cardiac death, coronary heart disease, and ischemic stroke (the most common type of stroke). It notes that mercury contamination is a concern with some types of fatty fish (i.e., swordfish, tuna, etc.), but the "benefits of 1 to 2 servings a week outweigh the risks, especially if a variety of seafood is consumed" (Rimm, Circulation 2018).

Clinical trials since 2010 cast *doubt* on some of the cardiovascular benefits of fish oil *supplements* (Kwak, Arch Intern Med 2012; Hu, Arch Intern Med 2012; Bosch, NEJM 2012; Rizos, JAMA 2012; Chowdhury, BMJ 2012; Roncaglioni, NEJM 2013; AREDS2 Study, JAMA 2014). This was demonstrated in the VITAL study, a 5-year study among a cross-section of older Americans, about half of whom had high blood pressure, 40% of whom had high cholesterol, and 14% of whom had diabetes. The VITAL study showed that supplementing with fish oil (460 mg of EPA and 380 mg of DHA daily) did not result in a lower incidence of major cardiovascular events than placebo. However, among people consuming less than 1.5 servings of fish per week, further analysis showed that the fish oil supplementation resulted in 19% and 40% reductions, respectively, in major cardiovascular events and heart attacks. In addition, African Americans had a 77% reduction in heart attacks with fish oil as compared to placebo (Manson, NEJM 2018). It should be noted, however, that a potential beneficial effect of the fish oil may have been masked in these trials by the fact that participants in most studies continued to take other heart medications and many participants already had significant intake of omega-3 fatty acids from fish in their diets.

Supplementation with fish oil may be helpful for people with **chronic heart failure**. In a study of 31 men and women with chronic heart failure given 2,000 mg of an extremely concentrated fish oil (providing 920 mg DHA and 760 EPA) or placebo daily for two months, those in the fish oil group experienced a 3% improvement in left ventricle ejection fraction (i.e., how well the heart pumps blood) and a 33% increase in flow-mediated dilation (which can be impaired by stiffness in the arteries) compared to the placebo group. Supplementation also decreased global longitudinal strain by 8.3%, inflammation and fibrosis of heart muscle (i.e., ST2) by 2.16% and the ratio of early and late filling of blood in the heart (i.e., E/e') by 7.37% compared to placebo. The researchers noted that individuals who had the greatest improvements in left ventricle ejection fraction were those who began the study with lower levels of NT-proBNP, a peptide secreted by the heart when it has to work harder to pump blood (Oikonomou, Clin Nutr 2019).

Fish oil supplementation has shown mixed evidence of benefit for **preventing heart failure hospitalization** among older people. It is possible that any benefit may depend on pre-existing risk factors for heart failure, such as type 2 diabetes. An analysis of data from the VITAL study among older American (described above) showed that supplementing with fish oil (460 mg of EPA and 380 mg of DHA) daily for about 5 years reduced the incidence of first heart failure hospitalization by 31% and the incidence of recurrent heart failure hospitalization by 47% compared to placebo *among those with type 2 diabetes* (a risk factor for heart failure), but there was no evidence of benefit among those *without* diabetes. There was also a 35% reduction in the risk of *recurrent* heart failure hospitalization compared to placebo *among people who were Black* (who may be at risk for heart failure due to higher prevalence of conditions such as obesity, hypertension and type 2 diabetes), but not among white people, and there was no reduction in the risk of *first* heart-failure related hospitalization among Black or white people (Djoussé, JAAC Heart Fail 2022). The potential benefit of fish oil in preventing heart failure among people with diabetes is supported by at least one earlier study in Italy among older people (about 60% of whom had type 2 diabetes), which showed that supplementing with 1 gram of fish oil daily for 5 years reduced the risk of hospitalization due to heart failure by 33% compared to placebo (Roncaglioni, N Engl J Med 2013). However, other studies have shown that supplementing with about 840 mg to 4,000 mg of EPA/DHA daily does *not* reduce the risk of nonfatal heart failure or heart failure hospitalization compared

to placebo, including among those with diabetes (<u>Bowman, J Engl J Med 2018</u>; <u>Bhatt, N Engl J Med 2019</u>; <u>Nicholls, JAMA 2020</u>). Reasons for these conflicting results are uncertain, although in some of the studies that did *not* find a benefit, as few as 21% of the participants had type 2 diabetes. [Interestingly, a post-hoc analysis of data from the Nicholls study found that high dose EPA/DHA *did* reduce the risk of major adverse cardiovascular events among certain trial participants (see <u>below</u>).]

A one-year study in Texas among 56 obese, middle-aged adults (average age 49) at **high risk of heart failure** (i.e., stage A) showed that taking 1.6 grams of fish oil daily did *not* reduce the accumulation of triglycerides within and around the heart (myocardial triglyceride content, which is a risk factor for cardiovascular disease) or excess "hidden" fat stored within the abdominal cavity (visceral adiposity), nor did it improve fitness parameters, heart structure, or vascular stiffness/function compared to placebo. Supplementing with fish oil in addition to participating in high-intensity interval training (HIIT) also did not improve any outcome more than HIIT alone (Hearon, JAAC: Heart Failure 2022).

There is some evidence that taking high dose fish oil may be beneficial **during recovery from heart attack**. In a study among 360 men and women who, in addition to standard lifestyle counseling and any required medications — statins, beta- blockers, etc., began taking high-dose, purified fish oil (four one-gram capsules of Lovaza daily — providing a total of 1,500 mg DHA and 1,860 mg of EPA) or a placebo within one month of hospitalization for a heart attack, the heart's ability to pump blood modestly improved after six months in those who took fish oil, while it worsened slightly in those who took the placebo (Heydari, Circulation 2016). There were no reports of bleeding (a potential concern with high-dose fish oil). However, follow-up of the participants for approximately 6.6 years showed that, overall, those who had received Lovaza did *not* have a lower risk of recurrent heart attack or unstable angina, heart failure-related hospitalizations, need for coronary artery bypass grafting (CABG), and/or death compared to those who received placebo, although the subgroup of individuals who achieved at least a 5% increase in omega-3 index (a measure of the amount of EPA and DHA in red blood cells) had a 41% lower rate of major adverse cardiovascular events compared to those who did not have a 5% increase in omega-3 index. It is possible that people with a genetic profile (e.g., the presence of FADS2 gene) that makes them more likely to experience an increase in omega-3 index upon fish oil supplementation may also be more likely to have favorable heart-related outcomes following a heart attack when supplementing with fish oil (Bernhard, Int J Cardiol 2024).

The American Heart Association has concluded that prescription n-3 FAs (EPA+DHA or EPA-only) at a dose of 4 grams/day (>3 grams/day total EPA+DHA) are an effective and safe option for reducing triglycerides as monotherapy or as an adjunct to other lipid-lowering agents (Skulas-Ray, Circulation 2019). However, be aware that not all prescription fish oils have shown the same benefits in reducing cardiovascular events, such as heart attack and stroke, in people with high triglyceride levels. For example, among people with high triglyceride levels, a high dose of Vascepa (a prescription fish oil highly concentrated for EPA rather than DHA) demonstrated a 25% reduction in the risk of initial heart attack, stroke or other major cardiac event in a five-year study, and a 30% reduction when subsequent cardiac events were counted. Vascepa was also shown to reduce coronary atherosclerosis progression among people with confirmed atherosclerosis and high triglyceride levels (see details for Vascepa). In contrast, a similar study with prescription Epanova (highly concentrated EPA + DHA) was halted due to a "low likelihood of demonstrating a benefit" (see details in Prescription Fish Oil vs.

Supplements). Several theories have been generated to explain the difference in benefit seen with Vascepa versus Epanova, and a recent post-hoc analysis of data from the Epanova trial has found that some of these hypotheses may not be valid (see below for details).

Taking into consideration the findings of clinical trials, as well as the American Heart Association's latest recommendations, the bottom line on fish oil for cardiovascular and cerebrovascular disease is that eating non-fried fatty fish twice per week as part of a healthy diet continues to be recommended and may help to reduce the risk of cardiac death, coronary heart disease, and ischemic stroke. [See ConsumerLab's Canned Fish Review for comparisons of EPA and DHA in canned fish.] In addition, high-dose, high-concentration fish oil, such as from prescription fish oils, can be helpful to people with high triglyceride levels.

However, regarding fish oil supplements:

• There is no reliable evidence that fish oil *supplements* prevent heart disease in healthy people who are not at risk for heart disease.

- Research does not support fish oil supplementation for preventing heart attacks in people who have heart disease or who are at
 risk for heart disease unless they have recently had a heart attack. [High-dose fish oil, however, may provide added benefit to lowdose statin therapy in people with stable coronary artery disease (see <u>Alfaddagh study</u> below)].
- Research does *not* support fish oil supplementation for preventing stroke or atrial fibrillation. (Doses of 2 grams or more may actually <u>increase the risk of atrial fibrillation</u>.)
- Fish oil supplementation may help people with chronic heart failure who have reduced left ventricular function, but it does not appear to be beneficial for people at high risk of heart failure.
- Fish oil supplementation, along with a high intake (3 or more servings per week) of fish may reduce the risk of venous thromboembolism.
- High-dose fish oil can help lower triglyceride levels in people with severe hypertriglyceridemia [including those whose triglycerides remain high while taking a statin (Kim, Clin Ther 2018)].
- Any other potential cardiovascular benefit of *supplementation* may be limited to people who do not regularly consume fish in their diets and who are not taking other medications for heart disease.

Consistent with the recommendations above, an analysis of 10 studies published from 1999 to 2014 involving 78,000 people with or at high risk for cardiovascular disease, found no significant association between supplementation with EPA and/or DHA and the occurrence of any major vascular events such as stroke, coronary heart disease, or death from coronary heart disease. It should be noted, however, that the analysis did not take into account the amounts of omega-3s people were already getting from their diets (Aung, JAMA 2018). Similarly, a much larger review of 79 clinical trials published from 1946 to 2017 involving over 112,000 people with or without cardiovascular disease concluded that taking omega-3 supplements does *not* reduce heart disease, stroke or death (Abdelhamid, Cochrane Database Syst Rev 2018). In addition, a major, long-term (7.4 year) study of adults with type 1 or type 2 diabetes showed no statistically significant cardiovascular benefit from a daily dose of 1 gram of fish oil (containing 460 mg EPA and 380 mg DHA) compared to a placebo (1 gram of olive oil): 8.9% and 9.2% of each group, respectively, experienced a serious vascular event (e.g., heart attack, stroke, transient ischemic attack) (ASCEND Study, NEJM 2018). In a separate arm of the study, patients were given low-dose aspirin (100 mg) or a matching placebo tablet each day, with 8.5% and 9.6% of each group, respectively, experiencing a serious vascular event, indicating a relative benefit with aspirin if not for the fact that it also caused significantly more major bleeding events (ASCEND Study, NEJM 2018). Although the two arms of the study were not compared, it is interesting to consider that the fish oil might have shown modest benefit if compared to the placebo tablet rather than to olive oil which, itself, may have some cardiovascular benefit, (particularly when substituted for saturated fat in the diet).

Perhaps the largest and longest-term study of fish oil supplement use, involving 427,678 individuals in England, Scotland, and Wales followed for 8 to 9 years, showed that the 31.2% of the studied individuals who indicated taking fish oil supplements (dose not specified) had a 13% lower risk of dying, a 16% lower risk of death from cardiovascular disease, and a 7% lower risk of any cardiovascular event than the general population after adjusting for consumption of oily fish and other demographic differences. The researchers speculated that the reason why this study, as opposed to others, found positive associations, may have been its size and duration (Li, BMJ 2020).

On June 19, 2019, the FDA <u>announced</u> that it would not object to the use of a qualified health claim similar to the following for foods and dietary supplements containing at least 0.8 grams (800 mg) of EPA and DHA (combined total) per serving: "Consuming EPA and DHA combined may reduce the risk of CHD (coronary heart disease) by lowering blood pressure." An important caveat is that any such claim must be followed by "However, FDA has concluded that the evidence is inconsistent and inconclusive."

Taking with statins

Adding high-dose fish oil to statin therapy has been shown to help lower triglyceride levels, but the evidence is mixed on whether it lowers total cholesterol, and it generally does not seem to slow the progression of coronary plaque. Fish oil does not appear to reduce the risk of cardiovascular death, non-fatal heart attack, or non-fatal stroke. Be aware that statins appear to decrease levels of omega-3 fatty acids in the body, although this does not argue against using fish oil with these drugs.

A study in South Korea found that high-dose omega-3 supplementation significantly **decreased triglyceride levels** in those whose triglyceride levels remained elevated while taking a statin. In the study, men and women with high cholesterol and triglyceride levels received 20 mg of rosuvastatin daily. After one month, those whose triglyceride levels remained high (average 263 mg/dL) continued to take rosuvastatin plus either a high daily dose of omega-3s (1,520 mg DHA + 1,840 EPA) or placebo, for two months. Average triglyceride levels decreased by 26% among those who took the omega-3s and by only 2% among those who took the placebo (<u>Kim, Clin Ther 2018</u>), and similar results were found when the same dose of omega-3s was taken with atorvastatin (<u>Jun, Diabetes Metab J 2019</u>). (Note: Both studies were funded by Kuhnil Pharmaceutical Co., Ltd of South Korea.)

In addition, a study in coronary heart disease patients already taking the statin drug simvastatin, but who continued to have high triglyceride levels, found that adding 2 grams twice a day of a highly concentrated omega-3 supplement (Omacor, which is discussed below under its current name, Lovaza) for 48 weeks decreased serum triglycerides by 20% to 30% and "bad" cholesterol - very low density lipoprotein (VLDL) - by 30% to 40% (Durrington, Heart 2001). And, in a study in the U.K. among 41 adults with high levels of LDL, VLDL, and triglyceride-rich lipoproteins despite being on stable-dose atorvastatin (Lipitor) showed that taking 1,000 mg of omega-3 fatty acids (750 mg of EPA and 250 mg of DHA ethyl esters by Wiley's Finest) four times daily for 8 weeks reduced total cholesterol by 6.55% (from 189.87 to 175.95 mg/dL), triglycerides by 21.51% (from 143.5 to 114.26 mg/dL), VLDL by 36.88% (from 34.75 to 21.24 mg/dL), and small, dense LDL cholesterol subclass (which is more likely to leave fatty deposits in the blood than other subclasses of LDL cholesterol) by 67.5% (from 3.48 to 0.77 mg/dL) compared to baseline, and these improvements were all significant compared placebo (olive oil). However, there was no significant improvement in LDL cholesterol (including the large or intermediate subclasses) or increase in HDL cholesterol compared to placebo (Us, Lipids Health Dis 2022).

A three-month study in Norway among 34 adults on statin therapy for **familial hypercholesterolemia** (a genetic disorder that results in elevated LDL cholesterol at birth and that is linked with increased risk of coronary heart disease) showed that supplementing with 1,840 mg of EPA and 1,520 mg of DHA daily lowered total cholesterol, LDL cholesterol and triglycerides, respectively, by an average of 9.28 mg/dL, 7.73 mg/dL, and 12.4 mg/dL more than placebo (olive oil). There was also a 2.0 mg/dL *increase* in large HDL cholesterol (which is inversely associated with cardiovascular disease) and a 2 mg/dL *decrease* in small HDL cholesterol (which is positively associated with heart disease) compared to placebo, although there was no significant difference in overall HDL cholesterol levels. Supplementing with fish oil did not, however, lower apolipoprotein B (ApoB), which is associated with cardiovascular disease risk (<u>Hande, Biomedicines</u> 2022).

Be aware that high-dose fish oil supplementation has *increased* LDL cholesterol in some studies and is noted as a possible side effect of prescription Lovaza and Epanova (see <u>Concerns and Cautions</u>).

A study in Japan among 75 men and women (average age 66) with coronary artery disease whose LDL cholesterol (average 71 mg/dL) and triglycerides (141 mg/dL) were already well-controlled with high-dose statin therapy (40 mg of pitavastatin daily) showed that adding 2 grams of omega-3 fatty acids (930 mg EPA + 750 mg DHA as ethyl esters, sold as Lotriga in Japan and as Lovaza in the U.S.) once or twice daily did not further reduce the **number or severity of coronary plaques**, or decrease LDL cholesterol or triglycerides, compared to those prescribed statin therapy alone (Nakao, J Atheroscler Thromb 2023). A broader, 3-year post-marketing surveillance study of the same prescription fish oil among 14,364 people in Japan with at least two cardiovascular risk factors and elevated triglycerides (150 mg/dL or higher) despite statin therapy also showed no decrease in the risk of adverse cardiovascular events compared to statin therapy alone (Teramoto, Expert Opin Drug Saf 2022; Tatsuno, J Clin Lipidol 2013).

Similarly, a well-controlled 30-month study found that taking daily, high-dose fish oil in addition to statin therapy did *not* decrease the progression of **coronary artery calcification** compared to statins (high or low-dose) taken without fish oil (<u>Hariri, Atherosclerosis 2023</u>). The study did show that fish oil prevented the progression of **fibrous coronary plaque** in people among people on low-dose statins (less than 40 mg of atorvastatin, 20 mg of rosuvastatin, or 80 mg of simvastatin). Among low-dose statin users, fibrous plaque increased 5% in those not receiving fish oil, but it did not increase among those receiving fish oil (1,860 mg of EPA and 1,500 mg DHA, from 4 softgels of Lovaza). However, fibrous plaque did not increase among those receiving high-dose statins. Musculoskeletal events, infectious diseases, and joint replacement were significantly lower among those taking the fish oil (Alfaddagh, J Am Heart Ass 2017).

A large, open-label study in Japan among 2,460 adults (average age 68) with **stable coronary artery disease** and a low ratio (<0.4) of blood levels of EPA to arachidonic acid (which has been linked with an increased risk of atherosclerotic cardiovascular events) who were already taking statins (mainly atorvastatin, pitavastatin, or rosuvastatin) showed that also taking 1,800 mg of icosapent ethyl (the form of EPA found in prescription Vascepa) daily for five years did *not* significantly reduce the combined risk of heart-related death, nonfatal heart attack, nonfatal stroke, unstable chest pain (angina) requiring hospitalization, or need for treatment to restore blood flow to the heart (coronary revascularization) compared to those in the control group, who took statins but did not receive EPA. Furthermore, the **rate of new-onset atrial fibrillation**, a heart rhythm problem, was about *twice as high* in the EPA group than the control group (3.1% vs. 1.6%, respectively), and this difference was statistically significant (Miyauchi, Circulation 2024).

Insulin sensitivity and blood sugar control

Limited evidence suggests that fish oil can modestly improve insulin sensitivity (note, a <u>study of krill oil</u> suggested a negative effect). A placebo-controlled study in Australia among 68 overweight and obese men and women (average age 51), most of whom had hyperinsulinemia, impaired fasting glucose, or high cholesterol, but none had diabetes, found that 1 gram of fish oil (*EPAX1050* – 460 mg DHA + 60 mg EPA) taken twice daily with meals for three months modestly reduced fasting insulin by an average of 1.62 µIU/L and improved insulin resistance (as measured by HOMA-IR) by - 0.40 units compared to a placebo (corn oil). Fish oil did not decrease fasting glucose, total or LDL cholesterol, or increase HDL cholesterol compared to placebo (<u>Abbott, Prostaglandins Leukot Essent Fatty Acids 2020</u>). Further analysis of the same study showed that fish oil supplementation also significantly increased total testosterone levels in men, but not in women (see <u>details below</u>).

An 8-week pilot study in Brazil among 32 overweight and/or obese adults with type 2 diabetes given a larger dose of fish oil (4 grams daily) suggested a benefit. Participants showed improved insulin sensitivity, reduced triglycerides, and increased HDL. However, the results are preliminary as there was no control group. Participants consumed *Nature's Bounty 2,400 mg* providing 1,440 mg EPA and 960 mg DHA from two capsules taken with food and water in the morning and in evening — a total of four capsules daily) (de Souza, J Diab Complications 2020).

A small study of healthy overweight/obese adults in Norway showed that consuming five ounces of *fatty* fish (salmon: 13% fat) five times per week for dinner for 8 weeks significantly improved blood sugar regulation (i.e., smaller increases in blood sugar) measured two hours after a meal, whereas *lean* fish (cod: 1% fat) did not. Neither type affected *fasting* blood sugar levels, and a previous study of healthy, young normal-weight adults showed no effect of either on blood sugar control (<u>Helland, Br J Nutr 2017</u>).

Arthritis and other inflammatory diseases

Increased intake of the omega-3 fatty acids in fish oil alter the body's production of inflammatory substances known as prostaglandins, and, consequently, reduces some forms of inflammation. Fish oil has also been associated with increased blood levels of certain precursors of protectins and resolvins (also known as specialized pro-resolving mediators, or SPMs), both in people with and without rheumatoid arthritis, that act to inhibit the inflammatory response (Marchland, Prostaglandins Leukot Essent Fat Acids 2023).

Rheumatoid arthritis

On the basis of this, EPA and DHA have been tried in the *treatment of symptoms* of rheumatoid arthritis with considerable success (especially in early stages of the disease). Unlike "disease modifying" drugs, however, fish oil probably doesn't slow the *progression* of the disease, although it possibly may reduce the risk of developing rheumatoid arthritis and some other autoimmune diseases.

A study of several thousand women in Sweden found that consistent, long-term term intake averaging more than 210 mg per day of omega-3 fatty acids from eating fish was associated with a 52% lower risk of developing rheumatoid arthritis compared with lower intakes over the period of the study – about 7.5 years (<u>Di Giuseppe, Ann Rheum Dis 2013</u>). This level of intake is equal to at least one serving per week of a fatty fish, such as salmon, or four servings per week of lean fish, such as cod. The study could not adequately assess the impact of supplement use due to limited use of supplements in the study population.

Supplementing with fish oil may reduce the risk of developing rheumatoid arthritis, although findings are not definitive. A large, multi-year study (the VITAL trial) of older individuals (average age of 67) across the U.S. found that taking 1 gram of extremely concentrated fish oil (460 EPA and 360 mg DHA) daily reduced the risk of developing autoimmune disease by 15% compared to taking placebo, although the difference was not statistically significant and the absolute reduction was small — 18 fewer confirmed cases out of about 13,000 people. Adding vitamin D had no effect. People with lower body mass index (BMI) seemed to benefit much more than those with higher BMI, as did people with a family history of autoimmune disease. Although risk reductions in specific autoimmune diseases were not statistically significant, apparent reductions were most notable for thyroid disease (47% reduction) and rheumatoid arthritis (42% reduction), while the risk of psoriasis appeared to *increase* by 57% (Hahn, BMJ 2022).

An analysis of twenty-two clinical studies also concluded that marine oils can reduce *pain* associated with rheumatoid arthritis – but not joint *function*. The results indicated that it may be best to use a product with at least 50% more EPA than DHA, but an ideal dose could not be determined (<u>Senftleber, Nutrients 2017</u>).

Despite the suggestion, above, regarding the importance of EPA, a later study found DHA alone to be somewhat helpful. In the study, 38 men and women with rheumatoid arthritis consumed either DHA-enriched food (providing 2,100 mg of DHA per day from 8 grams of microalgae oil) or food enriched with a placebo (8 grams of sunflower oil providing 4,700 mg of linoleic acid -- an omega-6 fatty acid) for ten weeks. It found that consuming the DHA-enriched food caused a statistically significant decrease in the average number of tender and swollen joints (from about 14 to 10), while consuming sunflower oil-enriched food *increased* the number of tender and swollen joints (from about 10 to 12). However, neither the DHA nor sunflower oil changed biochemical measures of inflammation (ESR and CRP) or patients' self-assessments of their conditions (<u>Dawczynskia, Clin Nutr 2017</u>).

Osteoarthritis

Most studies have *not* found fish oil supplementation to reduce pain associated with osteoarthritis (Senftleber, Nutrients 2017; Boe, Am J Orthop (Belle Mead NJ) 2015). However, researchers who analyzed data from a placebo-controlled study of older, sedentary, obese women and men (ages 50 to 80) in Australia who were not large consumers of fish or fish oil and had mild, chronic osteoarthritis pain (in the knees, lower back and/or shoulders) found that supplementation with 1,000 mg of DHA and 200 mg EPA (triglyceride forms) taken with breakfast and, again, with dinner reduced average self-reported overall pain by 42% compared to no treatment with fish oil. Interestingly, taking curcumin (*Longvida*, providing 160 mg of curcumin) daily in addition to the fish oil provided *less* pain relief than the fish oil alone (Kuszewski, Rheumatol Adv Pract 2020).

High doses of omega-3 fatty acids (1,860 mg of EPA and 1,500 mg of DHA daily from 4 softgels of Lovaza) taken for one year by adults with coronary artery disease resulted in no worsening of arthritic pain, stiffness, or physical function while all of these worsened in a similar control group not supplemented with fish oil. In contrast to the control group, the group given Lovaza reported more exercise per week (197 minutes vs. 135 minutes) and less joint replacement surgery (0% vs. 3.1%) (Alfaddagh, J Clin Lipidol 2018 – additional results from this clinical trial are reported above as Alfaddagh, J Amer Hearth Assoc 2017).

At best, **krill oil** may provide a small benefit after being taken for several months, although not all research agrees. A clinical study in Australia involving 222 people (average age 62) with knee osteoarthritis found no benefit with taking krill oil daily versus placebo (a mix of olive, maize, and palm kernel oils and medium-chain triglycerides). After 6 months, those receiving krill oil showed no statistically significant improvement in knee pain (including weight bearing pain, non-weight bearing pain, or function), hand pain, back pain, or lower limb strength compared to placebo. In fact, those in the *placebo* group showed a statistically significant reduction in joint swelling compared to those receiving krill oil, and more people taking krill oil experienced gastrointestinal discomfort compared to placebo (10% vs. 4.5%). Reasons for the lack of benefit are uncertain but may relate to the relatively low dose of krill oil used (2 grams of krill oil

containing 380 mg of EPA, 200 mg of DHA, and 24 mg of omega-6 fatty acids — provided by Aker Biomarine, which did *not* fund the study) and the fact that the participants were not required to limit dietary omega-3 intake, so even those in the placebo group may have been getting omega-3s from their diet (<u>Laslett, JAMA 2024</u>).

A high dose (4 grams) of krill oil was shown to provide only a modest and clinically insignificant reduction in knee pain compared to placebo (vegetable oil) in a study of 235 adults in Australia with mild to moderate osteoarthritis (the study was funded and designed by the provider of the krill oil product). There was no benefit of krill over placebo within the first three months of treatment, but by six months, the krill oil and placebo groups, respectively, had reductions in pain scores of 17.8 and 12.6 points (on a scale of 0 to 50), yielding a 5.2-point greater reduction with krill. There were also modest relative reductions in knee stiffness and function with krill oil but no reduction in a blood marker of inflammation (hs-CRP) or in voluntary use of anti-inflammatory medications. The krill oil (*Superba BOOST*, Aker Biomarine) was taken as four 1,000-mg capsules daily (providing a total of 600 mg of EPA, 280 mg of DHA, and 0.45 mg of astaxanthin) with, or shortly after, a meal (<u>Stonehouse, Am J Clin Nutr 2022</u>). Interestingly, a study in South Korea using a lower dose of the same krill oil but in combination with astaxanthin and hyaluronic acid showed some benefit for joint pain in people with mild osteoarthritis of the knee or hip. In the study, 75 people (average age 58) were given 600-mg capsules of FlexPro MD (by Valensa International), a combination of 321 mg of Antarctic krill oil (Superba by Aker BioMarine Antarctic US), 2 mg of astaxanthin (Zanthin Natural Astaxanthin by Valensa International) and 30 mg of hyaluronic acid (Flexonic by Valensa International), or placebo (palm, olive, and soybean oil and beeswax) daily for 12 weeks. Those in the FlexPro MD group showed significantly greater reduction (i.e., improvement) in self-reported joint pain compared to the placebo group (-20.8 vs. -10.6 on a scale of 0 to 100). The study was sponsored by Novarex, a partner of Valensa International (Hill, Nutrients 2023).

Gout

Eating fish low in purines may be helpful for people with gout, but there is no evidence that taking fish oil supplements is helpful or harmful.

Due to its anti-inflammatory effects, fish oil is sometimes promoted for gout — painful joint inflammation caused by elevated blood levels of uric acid. Preliminary research suggests the omega-3 fatty acids EPA and DHA may inhibit the inflammatory response involved in this form of arthritis (Yan, Immunity 2013). In men, higher blood levels of omega-3 fatty acids (>0.46 mmol/L) have been associated with a lower recurrence of acute gout attacks (Abhishek, Ann Rheum Dis 2016). According to an observational study among men and women who experienced gout, consuming fish rich in omega-3 fatty acids was associated with a protective effect against recurrent attacks, but taking fish oil supplements (fish oil, cod liver oil or omega-3 fatty acid supplements) did *not* have this effect (Zhang, American College of Rheumatology Annual Meeting 2015).

Be aware that people with gout are advised to limit intake of sardines, mackerel and herring because these fish contain high levels of purines in their meat, which can increase uric acid levels in the blood, aggravating gout symptoms (<u>American College of Rheumatology</u> 2012; <u>Kaneko, Biol Pharm Bull 2014</u>). However, purines are largely eliminated in the manufacture of fish oil supplements (<u>Roy, Food Nutr Sci 2013</u>).

Ulcerative colitis and Crohn's disease

The anti-inflammatory effects of EPA and DHA have also caused researchers to investigate possible benefits of fish oil for the treatment of menstrual cramps, inflammatory bowel disease (ulcerative colitis and Crohn's disease), lupus, and IgA nephropathy. For each of these conditions, at least one double-blind study has found positive results. A large European study (Hart 2009) showed that people with the highest consumption of DHA (410 mg to 2,000 mg per day) had a 77% reduction in the risk of developing ulcerative colitis over an average period of four years than those consuming the lowest amount (up to 110 mg per day). Conversely, those consuming the most (15 to 35 grams per day) of linoleic acid (an omega-6 fatty acid) were 2.3 times as likely to develop the disease as those consuming the lowest amount (8 grams - 11 grams per day). In a study in which people with stable ulcerative colitis were given 1,000 mg twice daily of EPA for 6 months, 76.7% remained in remission versus 50% of those given placebo. Levels of fecal calprotectin, a marker of mucosal inflammation, were also significantly reduced in 63.3% of those given EPA versus only 13.3% of those given placebo. The EPA was taken

as enteric-coated capsules (in order maximize intact delivery into the small intestine), each containing 500 mg of EPA in the free fatty acid form (ALFA, from SLA Pharma AG — apparently not currently sold in the U.S.) (Scaioli, Clin Gastro Hep 2018). However, in Crohn's disease, a trial of four grams per day of omega-3 fatty acids (50-60% EPA and 15-25% DHA) was ineffective at preventing relapses.

Dry eye

The majority of evidence from clinical studies has *not* found that supplementing with omega-3 fatty acids (typically from fish oil) alone helps treat or prevent dry eye (which is common in older people), or at least not much more than the small improvements reported for plant-based oils used as placebo controls. Small studies suggested some benefit for dry eye resulting from computer use in young adults and from contact lens use. Fish oil supplementation *in combination with other fatty acids and/or vitamins* may have some benefit. (Learn about other supplements for dry eye.)

Treatment

The largest and longest study to date, conducted by the University of Pennsylvania and the National Eye Institute, failed to show a benefit relative to placebo. The study involved giving fish oil or olive oil (intended as a placebo) to several hundred men and women with moderate to severe dry eye for 12 months. Symptoms and signs of dry eye improved among patients receiving fish oil treatment (providing 2,000 mg of EPA and 1,000 mg of DHA in the triglyceride form daily) and among those who received a similar amount of olive oil, with the disease severity score improving by about 13 points out of 100, although there was slightly greater improvement in the fish oil group (Asbell, N Engl J Med 2018).

Similarly, a study in Canada among 50 men and women with moderate to severe dry eye found that a combination of fish oil (providing 1,200 mg EPA and 300 mg DHA), evening primrose oil, and borage oil for three months led to a modest improvement in dry eye symptoms but this was *not* statistically better than the results with a placebo (a combination of coconut and olive pomace oils), despite the fact that omega-3 blood levels increased only in the treatment group (Ng, Optom Vis Sci 2021).

Several other short-term studies suggested that fish oil supplementation in combination with other fatty acids and/or vitamins may help. One study of postmenopausal women in the U.S. with dry eye showed improvements in eye irritation among those who took a formula consisting of fish oil with black currant seed oil and vitamins for six months versus those who took a placebo consisting sunflower oil (which contains < 0.1 % gamma-linolenic acid (GLA) and alpha-linolenic acid (ALA) and undetectable levels of n-3 EPA and DHA) (Sheppard, Cornea 2013). The daily dose given (4 softgels) provided fish oil (126 mg EPA and 99 mg DHA) and 1,570 mg of black currant seed oil (consisting of 240 mg GLA, 196 mg ALA, 710 mg of LA) in a formula (HydroEye) that also provided vitamins A, B6, C, and E. (Note: The amounts of fatty acids in the product during the study are slightly higher than listed on the HydroEye label.)

A study among 105 men and women diagnosed with mild to moderate dry eye found those who took 4 softgels containing re-esterified (triglyceride form) fish oil (providing a total daily dose of 1,680 mg of EPA and 560 mg of DHA) (*PRN Dry Eye Omega Benefits*, Physician Recommended Nutriceuticals) daily for 3 months had modest improvements in symptoms of dry eye, such as soreness, grittiness and sensitivity to light, and decreased dryness (as measured by tear osmolarity), compared to those who took a daily dose of linoleic acid (3,136 mg) (*Epitropoulos, Cornea 2016*). [Note: The label for this product, which is sold in the U.S., indicates that it also contains 1,000 IU of vitamin D₃]. However, a later and slightly larger 3-month study in South Korea using the same daily dosing of the same product (having a slightly different name: *De3 Omega Benefits*, LYS PHARMA) found *no* benefit compared to placebo (3,000 mg of grape seed oil daily). There was a similar level of improvement in dry eye symptoms with the product as with placebo (*Eom, JAMA Opthal 2024*).

A study among 54 people (average age 43) with mild to moderate dry eye disease found that supplementing with **krill oil** (providing 945 mg of EPA and 510 mg of DHA) daily for 3 months reduced the amount of salt in tears (too much salt in tears indicates that tears are evaporating too quickly) and improved self-reported symptoms of dry eye at the end of 3 months compared to placebo. However, there was no significant reduction in tear osmolarity after only 30 or 60 days compared to the placebo group, and, in general, the improvements in the krill oil group were similar to, but not significantly better than, improvements observed for those given fish oil

(1,000 mg/day EPA and 500 mg/day DHA). Neither the krill oil nor the fish oil group showed a significant increase in the volume of tears produced. (The study excluded people taking medications that could cause dry eye and those already taking fatty acid supplements) (Deinema, Ophthalmology 2017).

A large study of young adults found that taking a fish oil capsule twice daily (each capsule providing 180 mg EPA and 120 mg DHA) for three months improved symptoms of **dry eye associated with computer use**. The fish oil significantly decreased the rate of tear evaporation. The study was conducted in northern India, which has a largely vegetarian diet and low consumption of fish (<u>Bhargava</u>, <u>Contact Lens & Ant Eye 2015</u>).

Fish oil supplementation has been found to be helpful for **dry eye associated with wearing contact lenses**. A study in Australia among 65 adults who experienced dry eye and discomfort from daily use of soft disposable contact lenses found that fish oil capsules (providing 900 mg of EPA and 600 mg of DHA daily) taken for three months significantly reduced self-reported symptoms of dry eye compared to those who took a placebo (olive oil capsules providing 1,500 mg olive oil per day) or capsules containing a combination of fish oil and flaxseed oil (providing 900 mg of EPA, 600 mg of DHA and 900 mg of ALA per day). Fish oil supplementation also decreased certain markers of eye inflammation just as well as anti-inflammatory corticosteroid eye drops but took much longer to have this effect (three months vs. two weeks). The study also found that fish oil eye drops given four times daily (providing a total of 30 mg of EPA and 3 mg of DHA to each eye per day) for three months decreased certain markers of eye inflammation but did not reduce self-reported symptoms of dry eye compared to taking fish oil capsules (Downie, Invest Ophthalmol Vis Sci 2018).

Prevention

An ancillary study of the Vitamin D and Omega-3 Trial (VITAL) showed that, among the 23,523 adults (average age 67) who did not have dry eye at the start of the study, supplementing with 1 gram of omega-3 fatty acids from fish oil (providing 460 mg of EPA and 380 mg of DHA in the ethyl ester form) daily for about 5.3 years did *not* reduce the incidence of dry eye diagnosis at one-year follow-up compared to placebo, with 2.0% of participants in both groups developing this condition. Omega-3 index (a measure of EPA and DHA in the blood) increased by about 55% for those in the fish oil group compared to only 2% increase in the placebo group. Although many participants in the study consumed adequate amounts of fish at baseline (at least 1.5 servings per week), which may have limited any potential benefit of fish oil supplementation, there was still no reduced risk of dry eye among the subgroup of people who consumed less than 1.5 servings of fish weekly or among those with low blood levels of EPA and DHA (omega-3 index of <2.5%) at baseline. It is possible that the dose of fish oil was too low and/or the form (ethyl ester) was not well absorbed (the triglyceride form tends to have better absorption) (Christen, JAMA Ophthalmol 2022).

Liver disease

Although small clinical trials suggested that fish oil supplementation might reduce liver fat or improve liver function in people with **metabolic dysfunction-associated steatotic liver disease (MASLD)** (<u>Lu, Gastroenterol Res Pract 2016</u>), larger more recent studies have shown *no benefit*. Taking DHA alone also does not seem to be helpful. Nevertheless, omega-3 fatty acids are considered to be beneficial for managing high triglyceride levels among people with MASLD.

A study among 167 adults with early-stage MASLD found that taking fish oil capsules providing 1,140 mg of DHA and 1,380 mg of EPA (as *Hepaxa* from BASF) daily for 5 ½ months *did not* decrease liver fat compared to placebo (olive oil). In fact, both groups had similar decreases in the percentage of liver fat by the end of the study (a decrease of 26% and 28%, respectively), and those taking the *placebo* had greater improvements in certain liver enzymes than those taking *Hepaxa*. Although the researchers reported an association between increased levels of EPA + DHA (from the fish oil) in red blood cells and overall reduction in liver fat, they did not analyze this finding to determine if it was statistically significant (<u>Tobin, Nutrients 2018</u>). Despite the results, BASF, which funded the study, and *Hepaxa*'s U.S. distributor (DIEM Labs) promoted *Hepaxa* as "clinically proven" to reduce liver fat in people with MASLD. Both companies agreed in 2021 to pay a fine to settle <u>FTC charges</u> of deceptive advertising.

Another study among 51 adults (average age 52) with MASLD and metabolic syndrome, most of whom were men and five of whom were already experiencing liver cirrhosis, showed that taking 3.6 grams of fish oil (providing 1.72 grams of EPA and 1.24 grams of DHA) in four divided doses daily for one year did *not* improve liver fat content, fibrosis severity, most biomarkers of liver function, or lipid levels compared to placebo, although the study did find a greater reduction in liver fat among people who lost weight, which is a recommended strategy for managing MASLD (<u>Šmíd, Hepatol Commun 2022</u>).

A study in the U.S. among 203 adults (average age 51) with MASLD showed that taking 1,890 mg of DHA (in ethyl ester form and derived from DHASCO® marine microalgae), alone or along with 1,000 mg of synthetic vitamin E (as dl-alpha-tocopheryl acetate), daily for 6 months did not significantly reduce liver fat or improve levels of liver enzymes compared to placebo. Taking vitamin E alone was also not beneficial (Alkhouri, Aliment Pharmacol Ther 2024).

However, a meta-analysis of 22 clinical trials among 1,366 people with MASLD (which included data from the Tobin study described above) showed that supplementation with omega-3 fatty acids could help lower triglyceride levels among people with MASLD and high triglycerides compared to control (Lee, Nutrients 2020). The American Association for the Study of Liver Disease (AASLD) recommends omega-3 fatty acids along with statin therapy to help lower triglycerides among people with MASLD and hypertriglyceridemia not well controlled with statin therapy alone (Rinella, Hepatology 2023).

Asthma

Although giving <u>fish oil to pregnant women</u> has been shown to decrease the incidence of asthma in their offspring, it does not appear to help people who already have asthma. A study in the U.S. among 98 overweight/obese children and young adults ages 12 to 25 with poorly-controlled asthma found a high daily dose of highly-concentrated fish oil (providing 3,180 mg EPA, 822 mg DHA and 101 mg other omega-3 fatty acids — from Nordic Naturals) for 24 weeks did not improve measures of lung function or decrease exacerbations requiring urgent medical care and/or systemic corticosteroid medication compared to placebo (<u>Lang, Ann Am Thorac Soc 2019</u>). As noted <u>elsewhere</u>, a green-lipped mussel oil product has shown mixed results for asthma.

Cancer

Prevention

Some research suggests that consuming fish or taking fish or marine oil supplements may reduce the risk of precancerous colorectal growths in people with low blood levels of omega-3s and reduce the risk of dying from colorectal cancer. Fish oil may also reduce breast cancer risks. However, not all studies with supplementation have found a benefit. The evidence for fish oil reducing prostate cancer is weak.

A three-year, placebo-controlled study among 2,157 generally healthy men and women age 70 and older (average age 75) in five European countries without a history of cancer, about 40% of whom had blood levels of vitamin D below 20 ng/mL, found that daily supplementation with omega-3s (1 gram of algal oil providing about 167 mg of EPA and 333 mg of DHA per day) reduced the risk of *invasive cancer* by 30%, and by 48% if combined with regular strength training (30 minutes three times per week). Similarly, 50 mcg of vitamin D3 (2,000 IU) reduced the risk of invasive cancer by 24% and, if combined with strength training by 44%. Supplementing with both vitamin D and omega-3s decreased risk by 47%, while combining these with strength training had the greatest impact, decreasing the risk of an invasive cancer by 61%. It should be noted that the incidence of invasive cancer, overall, was only 3.8% (81 total cases) (Bischoff-Ferrari, Front Nutr 2022).

For example, daily supplementation with fish oil (460 mg of EPA and 380 mg of DHA) plus vitamin D3 (2,000 IU) was not shown to reduce the risk of cancer of any type in a major, 5-year, placebo-controlled study among over 25,000 of older Americans (average age 67) in the VITAL study (Manson, NEJM 2018). However, further analysis of data from the same study found that supplementation significantly reduced risk of **precancerous colorectal growths** (adenomas and polyps) by 41% in African Americans and by 24% in individuals who began the study with low blood levels of EPA and DHA (i.e. an omega-3 index of < 2.5%) (Song, JAMA Oncol 2019). Other research has shown that people diagnosed with **colorectal cancer** who then consume at least 300 mg per day of omega-3 fatty acids from fish and/or fish oil products have a 41% lower risk of dying from the disease than people consuming less than 100 mg per day (Song, Gut 2016).

It has been suggested that the anti-inflammatory effects of omega-3 fatty acids might reduce the risk of colorectal cancer by slowing the rate at which cells that line the colon reproduce or by offsetting the inflammatory effects of arachidonic acid, a fatty acid that may promote tumor growth. However, a study among 126 men and women (average age 58) with a history of **colorectal adenomas** (benign tumors that can become cancerous) who took 3 capsules per day of the highly concentrated prescription fish oil (*Lovaza*, providing a total daily dose of 1,395 mg EPA plus 1,125mg DHA) for six months found that the fish oil did not affect the rate of colorectal cell replication or cell death compared to placebo (olive oil). This was true regardless of whether or not participants had a genetic variant associated with increased tissue levels of arachidonic acid (Murff, Nutr Cancer 2021).

Eating fish is associated with a lower risk of recurrence, and risk of death, from **breast cancer**. In women with early stage breast cancer, higher intakes of DHA and EPA from fish (>73 mg/ day DHA+EPA) have been associated with a 25% lower risk of breast cancer recurrence (Patterson, J Nutr 2011). Another study found that over a 15 year period, women with primary in situ or invasive breast cancer who consumed the most tuna and/or other baked/broiled fish had a 25% to 34% reduction in risk of death from all causes, compared to those who reported eating no fish (Khankari, Cancer 2015). A study among postmenopausal women found that current use (but not past use) of fish oil supplements was associated with a 32% reduction in the risk of breast cancer. Risk was greatly reduced for ductal carcinoma of the breast (the most common form of breast cancer), but not lobular carcinoma (Brasky, Canc Epidemiol Biomarkers Prev 2010). It is speculated that the anti-inflammatory property of fish oil may be responsible for an anti-cancer effect because chronic inflammation is associated with cancer initiation and progression.

There is mixed evidence as to whether fish oil and omega-3 fatty acids help prevent **prostate cancer** development or progression. One study found no association between fish consumption and the development of prostate cancer although it found a large reduction in deaths from prostate cancer (Szymanski, Am J Clin Nutr 2010). A 6-year study of men who self-reported taking fish oil supplements also found no association between fish oil use and the development of prostate cancer (Brasky, Nutr Cancer 2011). A study at UCLA among 100 men on active surveillance for less aggressive (grade 1 or 2) prostate cancer found that taking 2.2 grams of fish oil (from Pharmavite LLC) daily while following a low-fat diet that limited intake of foods high in omega-6 fatty acids (i.e., fried foods, highly processed foods, chips, etc.) for one year had no significant impact on grade of prostate cancer, PSA levels, or tumor length compared to a group that did not take fish oil or receive dietary counseling. The fish oil group did have a 31% greater decline in the Ki-67 index — a measure of how fast cells in a tumor are dividing — but it's not clear if this was attributable to the use of fish oil or the reduced intake of omega-6 fatty acids (consumption of which has linked with increased risk of prostate cancer (Lu, J Am Coll Nutr 2007)). However, four men in the fish oil group were withdrawn from the study due to side effects including flatulence, constipation, bloating, diarrhea, gastrointestinal discomfort, belching and nausea (Aronson, J Clin Oncol 2024).

However, some studies that did not look directly at the consumption of fish or fish oil but at the ratios of fatty acids in blood serum, have found some unexpected associations with prostate cancer: One study of this kind found that men with the highest levels of DHA plus EPA and DPA (another omega-3 fatty acid) were 44% and 71%, respectively, more likely to develop low-grade and high-grade prostate cancers compared to men with the lowest levels (<u>Brasky, JNCI 2013</u>). This report included an additional analysis of several other blood-based studies, most of which, but not all, also showed associations between fatty acids in fish oil (particularly DHA) and development of prostate cancer (particularly high-grade cancer). However, whether or not there is a cause-and-effect relationship between intake of fish oils and prostate cancer is still not known. In fact, it has been suggested that the relationship with prostate cancer could stem from toxins in fish meat or introduced from frying or overcooking fish (<u>Aucoin, Integr Canc Ther 2017</u>).

Chemotherapy

Fish oil may prevent weight loss during cancer chemotherapy. Although some trials have not shown a benefit, one study (Murphy, Cancer 2011) showed significant benefit. In this study, patients with non-small cell lung cancer took fish oil throughout initial chemotherapy (approximately 10 weeks). During the course of chemotherapy, patients who did not take fish oil experienced an average weight loss of 5 lbs (of which approximately 2.2 lbs. was muscle). Those taking fish oil had, on average, no change in weight despite having lost, on average, 6.3% of their weight over the previous 6 months. In fact, many of those taking fish oil increased their muscle

mass — with the greatest increases corresponding to the greatest increases in plasma EPA concentrations. Cancer response rates to chemotherapy were similar in the two groups. Patients taking the fish oil were given an option consuming either four 1-gram gelatin capsules per day or 7.5 mL of liquid fish oil per day. Both formulations provided 2.2 grams of EPA per day.

However, some recent research suggests that fish oil (from supplements as well as fish) may *interfere with chemotherapy*. A fatty acid naturally found in fish oil known as 16:4(n-3) and into which other fatty acids, such as EPA, are converted in the body, has been shown in mice to activate white blood cells leading to resistance to chemotherapy. It is, therefore, advised to temporarily avoid fish oil from the day before chemotherapy until the day thereafter, as well as herring and mackerel (which raise 16:4(n-3) levels more than other fish such as salmon and tuna) in the 48 hours surrounding chemotherapy (<u>Daenen, JAMA Oncology 2015</u>).

Retinal disease

As explained below, consuming EPA and DHA from the diet (fish) is associated with lower risk of eye disease. However, taking EPA and DHA as supplements has not shown benefit.

Analyses of dietary intakes taken as part of the Age-Related Eye Disease Study (AREDS) show that participants who reported the highest intake of EPA and DHA were 30% less likely to develop diseases of the retina – neovascular age-related macular degeneration (AMD) and central geographic atrophy (CGA) – compared to those with the lowest intake (SanGiovanni, Am J Clin Nutr 2009). Decreased risk of developing AMD was also shown in a study of over 30,000 female health professionals: Those consuming at least one serving per week of fish had a 42% reduction in risk of developing AMD compared to those eating less than one serving per month – and the benefit was greatest with canned tuna or dark-meat fish (e.g., mackerel, salmon, sardines, bluefish, and swordfish) (Christen, Arch Opthamol 2011). Analyzed another way, the risk of developing AMD in this study was reduced by 38% and 36%, respectively, among those with the highest intakes from their diets of DHA (230 mg median intake) and EPA (100 mg median intake) compared to those consuming the least amount (median intakes of 60 mg of DHA and 10 mg of EPA). Based on these observations, EPA and DHA were included in the large AREDS2 (Age-Related Eye Disease Study 2) which evaluated a combination of supplements for preventing the progression of AMD. However, the addition of 350 mg DHA and 650 mg EPA to a combination vitamin A (from beta-carotene), vitamin C, vitamin E, zinc, and copper did not offer any additional benefits for slowing progression of AMD (AREDS2 Res Grp, JAMA 2013). See the Review of Eye Health Supplements for more information about AREDS and AREDS2.

Similarly, a five-year, placebo-controlled study of over 15,000 men and women (average age 67) (who were participants in the larger <u>VITAL</u> study) showed that daily supplementation with fish oil (providing 460 mg of EPA and 380 mg of DHA) plus vitamin D3 (2,000 IU) did not reduce the risk or slow the progression of AMD (<u>Christen, JAMA Ophthalmol 2020</u>).

A long-term observational study among 3,482 older men and women (average age 67) with type 2 diabetes found that those who reported consuming approximately 500 mg of EPA+ DHA from foods on a weekly basis were 46% less likely to develop sight-threatening diabetic retinopathy during the six-year study than those who consumed less this amount from their diet (Sala-Vila, JAMA Ophthalmol 2016). Even greater reductions in risk were observed among those who had advanced diabetes or who also had high blood pressure. The researchers noted that this amount of EPA + DHA can be met by consuming the American Heart Association's recommendation of two serving of fish (preferably oily fish) per week. However, a 6.5-year study in which 7,360 men and women aged 40 and older with type 1 or type 2 diabetes took 1 gram of fish oil daily (containing 460 mg EPA and 380 mg DHA) or placebo showed that fish oil did *not* decrease the risk of developing diabetic retinopathy (Sammons, Ophthalmology 2023 – a sub-study of the larger ASCEND trial).

Depression

Many studies have evaluated fish oil for depression. Fish oil seems to *help treat existing depression* at a dose of about 1,500 mg to 3,500 mg per day of omega-3 fatty acids that provides more EPA than DHA typically in populations not already getting much fish oil from their diets. In fact, treatment of depression using high-dose omega-3s containing more than 50% EPA was shown to have the strongest evidence of benefit of any type of supplement used for treating mental disorders according to an analysis of 33 meta-

analyses. The evidence was particularly strong for use in conjunction with SSRI medication (<u>Firth, World Psych 2019</u>). Fish oil supplementation has shown mixed evidence of benefit for *preventing depression*, with any benefit limited to people with a history of depression and when used at a dose greater than 1 gram/day.

In adults

Treatment

A study of depressed older women in a nursing home setting showed that after taking high-dose omega-3 fatty acids for eight weeks (2,500 mg once daily consisting of 1,670 mg EPA and 830 mg DHA), 40.9% had a remission of depression compared to 16.7% of those taking placebo (Rondanelli, J Am Col Nutr 2010). This study also found a statistically significant improvement in the self-assessed quality of life and that the fish oil treatment was well tolerated. In another study, the combination of EPA plus the prescription antidepressant fluoxetine (Prozac) was better than either EPA or fluoxetine alone for treating major depression in a short-term (8-week) study of 60 people. However, a study of people with congestive heart failure and depression failed to show any additional benefit from EPA (930 mg) and DHA (750 mg) daily when added to treatment with the prescription antidepressant sertraline (Zoloft) (Carney, JAMA 2009).

The best evidence for omega-3's has been in cases of major and moderate depression, but not mild depression, and one group of researchers has concluded that the antidepressant benefit is strongly dependent upon the EPA content of the supplement. After pooling and reviewing studies using a total of 1,000 mg to 6,000 mg of EPA and DHA, those in which EPA was 60% or more of the total showed a highly significant improvement, whereas those that were less than 60% EPA did not (Martins, Molec Psy 2012). An analysis of eight clinical studies which investigated the effects of taking EPA and/or DHA from fish oil with various anti-depressants (including SSRI drugs such as fluoxetine and sertraline and tricyclic drugs such as amitriptyline) found that, overall, there appeared to be additive benefit, especially from EPA in doses of about 1,000 mg to 2,000 mg per day, concluding, "EPA-rich omega-3 fish oil may be recommended for the adjunctive treatment of major depressive disorder." (Sarris, Am J Psychiatry 2016). Other researchers, however, believe that any benefit is, at best, small to negligible (Bloch, Molec Psy 2012). Nevertheless, further analysis of blood samples from the study by Rondanelli (above) found that elderly depression is characterized by very low levels of omega-3s, in particular EPA, in red blood cell membranes compared to those in healthy individuals and that EPA-rich supplementation restored EPA concentrations to normal values (Rizzo, Nutr J 2012). Interestingly, an earlier study using 1,000 mg, 2,000 mg, or 4,000 mg of EPA found that only the group receiving 1,000 mg had a significantly better outcome than a group receiving placebo (Peet, Arch Gen Psychiatry 2002).

A small study among young adults (average age 20) with mild to moderate depression but not taking antidepressant medication, found that those who took two fish oil capsules (providing a total of 1,000 mg EPA and 400 mg of DHA) daily for 21 days had significantly improved self-reported depression scores compared to those who took a placebo. At the end of the study, 67% of those who took EPA and DHA were no longer clinically depressed, compared to 20% in the placebo group (Ginty, Psychiatry Res 2015). It's worth noting that the amount of EPA given and ratio to DHA are consistent with those suggested by earlier research for treating depression.

A possible explanation for moderate improvements in depression among those who respond to fish oil, is that fish oil increases white matter (myelinated fibers that connect brain cells) in areas of the brain which can be compromised in depression. A small study of 16 acutely depressed adults with major depression found that among the 5 whose depression improved over the 6-week period of taking 4 grams of fish oil daily (OmegaLife-3, Unicity International, Inc., providing 1,600 mg of EPA and 800 mg DHA), 80% had increases in white matter in key brain regions, compared to only 45% of those whose depression did not improve (Chhetry, J Psychiatr Res 2016).

In 2019, the International Society for Nutritional Psychiatry Research issued clinician guidelines stating that in individuals with major depressive disorder, supplementing with omega-3s (1 to 2 grams per day for at least 8 weeks of either pure EPA or a combination of EPA + DHA in a ratio of > 2:1) can accelerate the effects of an antidepressant when started at the same time as the antidepressant, as well as enhance the effects of an antidepressant when results have been inadequate. The guidelines state that clinicians should consider relevant physical conditions, including fish hypersensitivities, before treatment with omega-3s is started, and monitor for common side effects as well as for potential adverse effects with high doses of fish oil, such as higher fasting blood sugar and increased LDL cholesterol (Guu, Psychother Psychosom 2019).

Interestingly, in a study among overweight adults with major depressive disorder who were *not* being treated with antidepressants, very high dose omega-3s were more effective than the suggested moderate dose: After supplementing with about 4 grams of EPA and about 1 gram of DHA daily for 12 weeks, 64% responded to treatment compared to only 36% of those who received half this dose, 38% of those who received one-quarter the dose, and 40% of those who received placebo. The fish oil was provided by Nordic Naturals as capsules containing 590 mg of EPA and 152 mg of DHA per capsule (high-dose was four capsules twice daily) (Mischoulon, J Clin Psychiatry 2022).

Fish oil providing a higher concentration of DHA than EPA (and a fairly low dose of EPA) was *not* helpful to people already being treated with medication in a small, 4-week study in Australia. Neither a low dose (1,000 mg of fish oil containing 260 mg of DHA + 70 mg EPA) or *twice* that dose reduced residual symptoms of depression or anxiety compared to placebo adults taking standard medications for major depressive disorder (SSRIs, desvenlafaxine, agomelatine, mirtazapine, vortioxetine) or bipolar disorder (lithium, lamotrigine, clonazepam) (Piperoglou, J Clin Psychopharmacol 2023).

A study in Turkey among 50 men and women (average age 36) with mild to moderate major depressive disorder, most of whom were taking a stable dose of antidepressant medication, found that taking 2,000 mg of either **krill oil** (providing a total of 340 mg EPA + 180 mg DHA per day) or fish oil (340 mg EPA + 240 mg DHA per day — a relatively low dose for depression) once daily after breakfast for 8 weeks resulted in similar, *slight* decreases in the severity of depression (average - 3.7 and - 4.7 points, respectively, on a 0 to 21-point scale) and anxiety (average - 2.8 and - 3.6 points, respectively, on a 0 to 21-point scale) symptoms, and these decreases were statistically significant compared no decrease in depression or anxiety severity among those who took a placebo (soybean oil). However, only decreases of 5 points or more are considered *clinically* meaningful for patients, suggesting a very limited benefit. Krill oil (but not fish oil) also slightly decreased HbA1c (a measure of blood sugar over time), but did not affect fasting blood sugar levels, which is notable as other research has raised concerns that high doses of krill oil might reduce insulin sensitivity (Acik, J Affect Disord 2025).

Prevention

There is mixed evidence regarding the effects of fish oil for preventing depression among older adults. Any benefit may be limited to people with a higher risk (i.e., those with a history of depression) and when used at a higher daily dose (>1 gram/day).

A 52-week study in China among 39 older adults (average age 69) with a history of major depressive disorder showed that taking fish oil concentrate providing 1.2 grams of EPA and 1 gram of DHA daily for 52 weeks significantly reduced the number of depression relapses compared to placebo (soybean oil). Ten out of 19 (53%) people in the fish oil group relapsed compared to 17 out of 20 (85%) in the placebo group. It is unclear whether the participants were or were not getting enough omega-3s from their diets, as dietary intake was not strictly controlled or monitored (Cheng, J Affect Disord 2024).

On the other hand, a study among 18,353 older adults (average age 68) *without* depression showed that taking 1 gram of prescription fish oil (*Omacor*) providing 465 mg of EPA and 375 mg of DHA daily for approximately 5.3 years increased blood omega-3 index levels by 55% but did *not* improve mood scores based on the 8-item Patient Health Questionnaire and slightly *increased* the incidence and recurrence of depression or depressive symptoms by about 13% compared to placebo. The researchers noted that it was unlikely that participants in the study were severely deficient in omega-3, and it is unclear whether higher doses of fish oil or supplementation with fish oil containing a higher ratio of EPA would be beneficial for depression prevention (<u>Okereke, JAMA 2021</u>).

In children, adolescents and young adults

Treatment

A benefit with fish oil was found in a small study in Slovakia among children and adolescents (average age 15) with depression. The children took fish oil (providing 1,000 mg EPA and 750 mg DHA) or a placebo (linoleic acid from sunflower oil) daily for three months. Most of the children in both groups were continued on SSRI antidepressants (sertraline, fluvoxamine or fluoxetine) throughout the study. Severity of depression symptoms was reduced by an average of 25% in those who took fish oil, compared to only 9% among those who took the placebo. However, the fish oil was not effective in those with mixed depression and anxiety (Trebaticka, Child Adolesc Psych Ment Hlth 2017). It's interesting to note that the fish oil used in this study is roughly in-line with what has been most likely to work in other studies: It provided 1,000 mg of EPA, which was nearly 60% the omega-3 content.

Fish oil provided no benefit in two studies in adolescents and/or young adults with depression. A 10-week study in New York of adolescents (aged 12 to 19 years) with moderate to severe major depressive disorder and not taking antidepressants found that both fish oil and a placebo (soybean and corn oil providing mainly omega-6 fatty acids) were equally effective at decreasing depression severity (about 40% to 50% of the participants in each group improved), but fish oil was *not superior to placebo*. However, participants reported consuming eight servings per week of foods high in omega-3 fatty acids, such as fish, i.e., they were generally not lacking intake of omega-3 fatty acids. The daily dose of omega-3s from fish oil (which was 67% EPA and 33% DHA) began at 1,200 mg but, if not effective, was increased during the study, such that ending doses averaged 3,200 to 3,400 mg of omega-3's or placebo (Gabbay, J Clin Psychiatry 2018). Similarly, daily fish oil supplementation (proving a total of 840 mg of EPA + 560 DHA per day) for three months did not improve symptoms of depression compared to placebo in a study in Australia among 181 adolescents and young adults (age 15 to 25, average age 18) with major depressive disorder who were not on antidepressant medications but received cognitive behavior management. Even among those with lower blood levels of EPA and DHA at the start of the study, fish oil was not helpful. It should be noted, however, the daily dosage of EPA and DHA given in this study is somewhat lower than in studies that have found a benefit (Amminger, Biol Psychiatry 2023).

Suicide

An analysis of blood samples from 1,600 military personnel showed those who committed suicide had, prior to suicide, significantly lower blood levels of DHA than personnel who did not commit suicide (<u>Lewis, J Clin Psychiatry 2011</u>). The population studied was predominantly male and the risk of suicide was found to be 62% greater among men with levels of serum DHA below 1.75% (% of total serum fatty acids) compared to those with higher levels. There was no such relationship with EPA levels. The researchers note that omega-3 fatty acid levels were generally low across the military personnel in the study, much lower than in the general population, and suggested that even greater risk reductions could be possible with higher serum levels of DHA.

Anxiety

Fish oil supplementation was associated with a modest improvement in anxiety symptoms among people with a clinically diagnosed neuropsychiatric or major physical illness, according to an analysis of 19 controlled clinical trials. The association was weaker in people without a diagnosed disease and it was greater when the dose was 2,000 mg or more of EPA and DHA per day and the ratio of EPA/DHA was less than 60% (Su, JAMA Network Open 2018). Among the studies analyzed was one of U.S. medical students that showed, over 12 weeks, that those who received high-dose omega-3 fatty acids (2,496 mg once daily providing 2,085 mg EPA and 348 mg DHA) had a 20% reduction in anxiety symptoms compared to those receiving placebo treatment. Treated students also had a 14% decrease in a marker of inflammation (stimulated IL-6 production) (Kiecolt-Glaser, Brain Behav Immun 2011). The study intentionally used an extremely concentrated fish oil (supplied by OmegaBrite) high in EPA due to earlier evidence that EPA has relatively stronger anti-inflammatory and antidepressant effects than DHA.

As <u>discussed above</u>, a study found that taking 2,000 mg of either krill oil (providing a total of 340 mg EPA + 180 mg DHA per day) or fish oil (340 mg EPA + 240 mg DHA per day) once daily after breakfast for 8 weeks *slightly* decreased anxiety among adults with mild to moderate major depression, but the small decrease is not considered *clinically* meaningful (having benefit that would be noticeable to patients or resulting in a change in treatment management) (<u>Acik, J Affect Disord 2025</u>).

Stress

Fish oil may slightly blunt some responses to mental stress, according to a study of young men and women given a large amount of fish oil (9 grams daily providing 1,600 mg EPA and 1,100 mg DHA) for eight weeks. When the participants were asked perform math calculations as quickly as possible for 5 minutes (a mental stress test), the mean heart rate increased by three beats less per minute after fish oil therapy than when the test had been taken at the beginning of the study, before therapy. The increase in total nervous activity (measured by nerve activity in the leg) was also significantly less after fish oil therapy. A control group, given olive oil instead of fish oil, did not have these reductions in heart rate and nervous activity (Carter, Am J Physiol 2013). However, in another study, fish oil was not found to be helpful. In the study, 90 men and women in Australia with self-reported chronic moderate to high levels of work stress took four capsules daily of predominately EPA fish oil (4 grams daily providing 2,200 mg of EPA and 440 mg of DHA) for three

months. Those taking the fish oil *did not* experience reductions in psychological stress compared to those taking placebo (olive oil) (<u>Bradbury, Front Pharmacol 2017</u>). There was also no improvement in other measures of stress, such as the ratio of cortisol to DHEA and levels of inflammatory cytokines.

Sleep

As discussed above, fish oil supplementation seems to have improved sleep in women experiencing menopausal symptoms. However, a small, company-funded study in Japan among 66 middle-aged men and women (average age 52) with poor sleep quality found that, compared to placebo (corn oil), taking 2,880 mg of fish oil (providing a total of 560 mg of DHA plus 284 mg of EPA) once daily for 12 weeks had little effect on most measures of sleep, despite significantly increasing blood levels of DHA and EPA compared to placebo. There were no improvements in the time it took to fall asleep or total sleep time compared to placebo, nor in most self-reported measures of sleep quality (such as feeling refreshed upon waking) or mood. Those who took fish oil had a slight reduction in the amount of time in bed spent asleep versus awake, although this was in comparison to a slight worsening in people given the placebo (Yokoi-Shimizu, Nutrients 2022).

Migraine headache

Getting more fish oil *from the diet* may reduce headache frequency in adults with migraine, with greatest benefit observed when intake of omega-6 fatty acids is also reduced. A study among 141 adults with chronic or episodic migraine showed that following a diet aimed at providing 1,500 mg of the omega-3 fatty acids EPA+DHA from fish daily, with or without reducing intake of linoleic acid (an essential fatty acid found in foods containing oils from corn, sunflower, safflower, soy, peanut and other plants, including **flaxseed**), decreased total headache hours per day by 1.7 and 1.3 hours, respectively, compared to following a diet providing little (less than <150 mg) of EPA+DHA daily. Increasing intake of omega-3 fatty acids and decreasing intake of linoleic (to about 3.2% of energy intake) decreased headache days per month by two days more than only increasing intake of omega-3 fatty acids. Both fish oil diets increased blood levels of 17-hydroxydocosahexaenoic acid (17-HDHA), a derivative of DHA with pain-relieving effects. However, neither of the fish oil diets significantly affected levels of other pain and inflammatory mediators with more established links to headaches (such as prostaglandin E2, leukotriene B4, cysteinyl leukotrienes, or calcitonin gene related peptide) (Ramsden, BMJ 2021).

Fish oil *supplements* may also help reduce the frequency of migraine headaches, although the evidence is somewhat mixed. Based on positive findings of some small, early studies, a placebo-controlled study involving 183 migraine patients was conducted in France in which roughly half the patients received 6 grams of fish oil (standardized to 18% EPA and 12% DHA) daily for 16 weeks and the other half received a placebo. During this period, 55% and 45% reductions in migraine attacks occurred, respectively, in the fish oil and placebo groups, indicating a strong placebo effect and a modest fish oil effect. However, the primary end-point of the study was the effect during only the last 4 weeks of treatment and, during that time, there was no statistically significant difference in the number of attacks between the two groups (Pradalier, Cephalalgia 2001). A placebo-controlled study of 60 migraine patients in Brazil found a significant benefit from giving fish oil containing 400 mg EPA plus 350 mg DHA twice-a-day before meals. For ethical reasons, the fish oil and placebo groups also received a low daily dose (10 mg) of amitriptyline (an antidepressant helpful for migraine). During 8 weeks of treatment, 66.7% of those given fish oil achieved an 80% reduction in the number of days of headache while only 33.3% of those given placebo achieved this level of reduction — a statistically significant difference (Soares, Nutr Neurosci, 2017).

EPA alone may also help migraine, particularly among women. A study in Taiwan among 70 men and women (average age 40) with episodic migraines, showed that those given 1 gram of fish oil containing 900 mg of EPA (in its ethyl ester form) with little (<1%) DHA daily for 12 weeks experienced a greater reduction in migraine frequency (-4.4 vs -0.6 days/month), days in which headache medication was needed (-1.3 vs. +0,1 days/month), and self-reported headache severity (-1.3 vs 0.0 points on a scale of 0 to 10) compared to placebo (100% soybean oil). Interestingly, when grouped by sex, men showed no significant between-group differences in any outcome measure, while women in the EPA group showed significantly greater reduction in migraine frequency (-4.9 vs -0.4 days/month), use of headache medication (-1.8 vs. +0.1 days/month), and headache severity (-1.3 vs 0.0 points) compared to placebo (Wang, Brain Behav Immun 2024).

Psychosis and schizophrenia

Prevention:

Despite promising evidence from initial research, studies have shown not shown fish oil to reduce the risk of psychosis among at-risk adolescents and adults.

An international, placebo-controlled study found no benefit when adding it to cognitive behavioral case management (CBCM) for adolescents and young adults at high risk for psychotic disorders. During the first six months of the study, subjects were given up to 20 sessions of CBCM and, each day, took four capsules of highly concentrated fish oil providing a total of 840 mg of EPA and 560 mg of DHA. Antipsychotic medication was not given, but antidepressant and anti-anxiety medication was permitted. Although a lower than expected percentage of subjects developed psychosis during the study, the percentage was not significantly different between those given the fish oil and those given placebo (paraffin oil). Over a full year (including six months after fish oil and regular CBCM treatment ended), about 11% of both the fish oil and placebo groups had progressed to psychosis (McGorry, JAMA Psychiatry 2016).

Similarly, a study conducted in eight European countries and Israel among 135 adolescents and adults (average age 16) at ultra-high risk for psychosis showed that, at 2-year follow-up, those who had supplemented with fish oil for the first 6 months of the study had a higher rate of transition to psychosis compared to placebo (8% vs. 4%), but the difference was not statistically significant. There were also no significant differences in the severity of symptoms such as depression, mania, positive symptoms (e.g., delusion, hallucinations, etc.), or negative symptoms (e.g., emotional and social withdrawal, difficulty in abstract thinking, etc.). Fish oil supplementation consisted of 2.4 grams of concentrated marine fish oil containing 720 mg of EPA plus 480 mg of DHA, which was taken daily for the first 6 months of the study (Winter-van Rossum, Schizophr Bull 2024).

These results conflict with those of earlier research. A year-long study in adolescents and young adults (ages 13 to 25) identified as at risk for developing psychosis or schizophrenia found those who took 700 mg EPA plus 480 DHA from fish oil daily for 3 months were much less likely to develop a psychotic disorder in the nine months following treatment compared to those who had taken a placebo: Among those who took the EPA and DHA, 4.9% developed psychosis compared to 27.5% of those in the placebo group (Amminger, Arch Gen Psychiatry 2010). In a follow-up study approximately 7 years after the original treatment with EPA and DHA, only 10% had developed psychosis, compared to 40% among the placebo group. Those who took the fish oil had significantly higher measures of psychosocial functioning and required less medication than those who took the placebo. The researchers speculated that omega-3 supplementation may be especially effective during adolescence, when the brain is still undergoing significant development (Amminger, Nature Communications 2015).

Treatment:

A study in Poland among first-episode schizophrenia patients (ages 16 to 35) found a small to moderate benefit from taking fish oil in addition to regular medication. During 26 weeks of taking four capsules daily of concentrated fish oil (providing a daily total of 1,320 mg of EPA and 880 mg of DHA) rather than a placebo containing olive oil, 69.4% experienced at least a 50% improvement in symptom severity while only 40% of those given the placebo experienced this level of improvement. The greatest improvements were in depressive symptoms. The researchers noted that studies of fish oil in people with chronic (long-term) schizophrenia have shown mixed results, suggesting that fish oil may be more effective at early stages of the disease (Pawelczyk, J Psych Res 2016).

Epilepsy

Omega-3 fatty acids inhibit neuronal excitability and reduce seizures in animal models, but, at high doses (1,700 mg to 2,200 mg of EPA + DHA daily), have failed to reduce seizures in people with drug-resistant epilepsy. However, a small, but well-controlled study using a lower dose (1,080 mg of EPA plus DHA per day) for 10 weeks found a 33.6% reduction in seizure frequency compared to placebo. A higher dose (twice the dose) was also tested but was not effective. The fish oil used in the study, which was funded by the National Institutes of Health, was Nature Made Fish Oil 360 mg OMEGA-3. The lower dose consisted of three gel capsules per day (each capsule containing 216 mg of EPA and 144 mg of DHA), while the higher dose was six capsules per day. During treatment with low-dose, patients had an average of 12.18 seizures per month, compared to 17.67 and 18.34 seizures per month, respectively, with the high-dose and placebo (DeGiorgio, J Neurol Neurosurg Psychiatry, 2014). The study authors note that a potential reason why the lower dose was

more beneficial than higher dose is that high-doses of fish oil may cause excessive reductions in non-esterified fatty acids (e.g., arachidonic acid), and that a study of fish oil in depression found a similar benefit using low-dose, but not higher-dose fish oil (Peet, Arch Gen Psychiatry 2002).

Attention deficit/hyperactivity disorder (ADHD) and executive functioning in children/adolescents

Studies using fish oil supplements in treating ADHD have yielded conflicting results. Evidence seems to suggest supplements may improve symptoms of inattention specifically, and not symptoms of ADHD more generally. A double-blind, placebo-controlled 16-week study giving boys aged 8 to 14 years fish oil (in a margarine spread containing 650 mg of EPA and 650 mg of DHA daily) found it to modestly improve parent-rated attention in boys with ADHD and in typically developing boys. Most of the boys with ADHD were also taking prescription medication. No effect, however, was seen in brain activity or on performance of cognitive control tasks (Bos, Neuropsychopharm 2015).

In contrast, an improvement in executive functioning was found in a study among 95 girls and boys (average age 11) with mood disorders (depression, bipolar disorder or unspecified) who took two capsules of fish oil providing a daily total of 700 mg EPA, 100 mg DHA and 134 mg other omega-3 fatty acids (*OmegaBrite* – which provided the capsules) in addition to twice-weekly therapy sessions for three months. Significant improvements in parent-reported executive functioning (working memory and cognitive skills such as attention, planning, organizing, switching between tasks) were found in comparison to those who had the same therapy but took a placebo. The same dose of fish oil also significantly improved parent-reported executive functioning compared to placebo in children who did not receive therapy sessions (<u>Vesco, J Child Psychol Psychiatry 2017</u>). It is difficult to say, however, to what extent the improvements may have been due to improvements in depressive symptoms, which also occurred (<u>Fristad, J Child Adolesc Psychol 2016</u>).

A 12-week, placebo-controlled study among 92 children (6 to 18 years old) with ADHD found that high-dose EPA (1,200 mg daily) improved "focused attention," particularly among those who started with low EPA levels. *However*, on measures of "impulsivity," the EPA-treated group improved *less* than those given placebo, and those who started with high EPA levels also showed less improvement on other ADHD and emotional symptoms than the placebo group. *The researchers supported the recommendation of a panel of ADHD experts* (*Banaschewski, Nutr Health 2018*) that patients who prefer omega-3 supplements over stimulants should take at least 750 mg daily of a combination of DHA and EPA for at least 12 weeks, but not if a patient is already getting these omega-3s from their diet (Chang, Translational Psych 2019).

A study in China among 95 children (ages 7 to 12) found that 800 mg of algal oil (providing a total of 300 mg of DHA and only about 2 mg of EPA) taken after breakfast daily for six months did not improve executive function (i.e., attention, abstract thinking, working memory) compared to placebo, although both the algal oil placebo groups had improvements at six months compared to the beginning of the study. However, it was not noted whether any of the children had been diagnosed with ADHD or other learning disorders (<u>Yang</u>, <u>Eur J Nutr 2020</u>).

Reading skills and other cognitive abilities in children

A double-blind, placebo-controlled study in boys and girls (ages 9 and 10) in Sweden found that a dose of 558 mg EPA, 174 mg DHA and 60 mg gamma-linolenic acid (GLA – an omega-6 fatty acid) taken daily for three months modestly improved reading ability, including the **ability to read** and pronounce unfamiliar words and the ability to read a series of letters quickly, as well as reading comprehension, compared to placebo. Although none of the children had a reading disability or ADHD, the researchers noted that the greatest improvements were found in children who had attention problems (as reported by parents) (Johnson, J Child Psychol Psychiatry 2016).

Consumption of oily fish itself has shown benefit in improving certain measures of cognitive function in children according to a study among 197 healthy boys and girls (8 to 9 years of age) in Denmark. The study found that those who consumed approximately 11 oz. of fish per week (salmon, mackerel or trout) for three months (which increased average intake of EPA + DHA from about 135 mg to 913 mg

per day) had modest improvements in tests of **attention and cognitive flexibility** (i.e., faster reaction times with fewer errors) than those who consumed an equivalent amount of poultry. Children who consumed fish also tended to have higher overall cognitive performance, although this did not reach statistical significance (<u>Teisen, Am J Clin Nutr 2020</u>).

Before pregnancy: Effects on infertility

A small, placebo-controlled study in Israel among 34 women (average age 33) with **polycystic ovary syndrome (PCOS)-related infertility** showed that supplementing with fish oil daily while undergoing ovulation stimulation with clomiphene citrate (50 mg) did *not* result in a statistically significant increase the rate of pregnancy among all participants. However, among those who were overweight or obese, supplementation with fish oil significantly increased the rate of pregnancies compared to placebo (29.6% vs. 5.3%). The daily dose of fish oil (*Omega Max-3* by Supherb, which supplied both the fish oil and placebo capsules used in the study) consisted of 3,000 mg of fish oil providing 1,080 mg of EPA and 720 mg of DHA. The fish oil supplementation was given for up to two clomiphene cycles (<u>Trop-Steinberg, Isr Med Assoc J 2023</u>).

During pregnancy: Effects on children

DHA is important for normal development and functioning of the brain and retina in the fetus and in infants. The benefits of fish oil supplementation during pregnancy with regard to brain function have not been established, although consuming a moderate amount of fish may be beneficial. Supplementation may also help prevent preterm labor among certain pregnant women, reduce the risk of colds in infants, and reduce the risk of allergy and asthma in children.

Experts in Europe recommend that all women who are pregnant should obtain, from foods and/or supplements, at least 250 mg/day of DHA plus EPA and an additional 100 to 200 mg/day of DHA, and women at risk of preterm birth due to inadequate DHA intake (<150 mg/day as determined using a dietary intake questionnaire such as the <u>7-question DHA-FFQ</u> or based on DHA measurement from a blood lipid component) should get 600 to 1,000 mg per day of DHA plus EPA or DHA alone. These intakes should start no later than 20 weeks of gestation and continue until 37 weeks gestation (<u>Cetin, Am J Obstet Gynecol MFM 2024</u>; <u>Savona-Ventura, Eur J Obstet Gynecol Reprod Biol 2024</u>).

In the U.S., there is no Dietary Recommended Intake (DRI) for DHA during pregnancy, but the <u>FAO/WHO recommends</u> a minimum intake of 200 to 300 mg of DHA per day and up to 1,000 mg during pregnancy and breastfeeding, which is similar to the European recommendation. (Be aware, however, that some experts advise avoiding omega-3 supplementation in late pregnancy due to a potential increased risk of post-partum hemorrhage — see <u>Concerns and Cautions</u>).

Cognitive effects:

An analysis that weighed the potential cognitive benefits with the risks (from exposure to mercury) of *consuming fish* during pregnancy suggested that consuming two seafood meals (8 to 12 oz) per week during pregnancy could **increase a child's IQ** an additional 3.3 IQ points by age 9. Consuming this recommended amount as tuna provided increases between 2.8 and 3.1 IQ points, while salmon (which generally has a <u>higher concentration of EPA and DHA</u>) provides 3.2 IQ points; however, as noted by the researchers, the benefit may be due, in part, to nutrients from fish other than EPA and DHA, such as vitamin D, selenium, and amino acids. No adverse cognitive effects from mercury were expected from consuming this amount of fish per week, and depending on the type of fish, you would have to consume many times this amount before getting the minimum amount of mercury known to cause adverse cognitive effects (for example, 120 light tuna sandwiches per week) (McGuire, Nutr J 2016).

However, fish oil *supplementation* during pregnancy does *not* seem to have significant cognitive benefit. In an Australian study, pregnant women less than 21 weeks' gestation were given 800 mg of DHA and 100 mg of EPA daily (from 1,500 mg of fish oil in capsules) until birth. Compared to women given placebo (vegetable oil capsules), there was **no statistically significant increase in cognitive or language development** in offspring during early childhood (<u>Makrides, JAMA 2010</u>), nor when the children were evaluated again at 4 years of age (<u>Makrides, JAMA 2014</u>), nor when the children were tested for IQ at age 7 – at which age they were reported to have slightly *more* behavioral and executive functioning problems than children in the placebo group (<u>Gould, JAMA 2017</u>). Similarly, a study in Spain evaluating the long-term effects of supplementing pregnant women with fish oil containing 500 mg of DHA and 150 mg of EPA

from 20 weeks of gestation until delivery found **no significant improvement in memory, attention, motor skills, language, or other measures of cognitive function** in the children when evaluated at 9 years of age compared to children of mothers not given no fish oil (Azaryah, Nutrients 2020).

Preventing premature birth:

Several studies suggest that DHA supplementation during pregnancy may reduce the risk of premature birth when given early, especially among women with low omega-3 levels or intake, but benefits may be limited among women with higher blood levels of DHA and supplementation may not reduce preterm births when given later in pregnancy.

The Australian study described above found that maternal supplementation with fish oil significantly decreased very premature births (1.09% in the treated group vs. 2.25% in the placebo group) as well as the risk of low-birth-weight infants and need for admission to neonatal intensive care units. There were also fewer fetal/infant deaths among those taking fish oil, although not by a statistically significant margin. At the same time, more of the treated women were induced or had cesarean sections because they were post-term (Makrides, JAMA 2010). Similarly, a placebo-controlled study in Kansas in which expectant mothers were given 600 mg of DHA daily from 14.5 weeks of gestation until delivery found that high-dose DHA reduced the risk of preterm birth (Colombo, Am J Clin Nutr 2019). Also, a study among 1,032 pregnant women in the U.S. who took either a low (200 mg) or high (1,000 mg) daily dose of DHA (from algal oil - Life's DHA-S oil, DSM Nutritional Products LLC) starting at 12 to 20 weeks gestation found that, among the women who began the study with low blood levels of DHA (< 6% RBC phospholipid DHA), those who took the high dose of DHA had half the rate of early preterm birth compared to those who received the lower dose (2% vs. 4.1%, respectively). Interestingly, women who began the study with high DHA levels had the lowest rate of early preterm birth (just 1.2%), regardless of whether they took low or high-dose DHA, suggesting DHA supplementation may not have added benefit for preventing early preterm birth among women already with adequate levels (Carlson, EClinicalMedicine 2021). This is supported by an earlier study that found no reduction in preterm births among mothers with higher levels of DHA (about 20% higher than studies showing benefit) who were given fish oil (providing a total of 800 mg of DHA and 100 EPA daily) within the first 20 weeks of pregnancy (Makrides, NEJM 2019). Nevertheless, all of the women in the Carlson study who took the higher dose had longer gestation, fewer spontaneous labors, and their infants had greater birth weight and length, and fewer neonatal admissions to an intensive care unit, compared to those that took the lower dose — suggesting some benefits even in women without low levels of DHA (Carlson, EClinical Medicine 2021).

On the other hand, DHA supplementation *later in pregnancy* does *not* appear to benefit women with threatened preterm labor (i.e., preterm contractions but no cervical dilation or thinning), as shown in a study of women in Thailand between 24 and 34 weeks gestation who were given 1,000 mg/day of DHA or no intervention until delivery or 37 weeks gestation. There were no significant between-group differences in preterm births, early preterm births, low birth weight, need for Cesarean delivery, or NICU admission (Phattharachindanuwong, Int J Women Health 2025).

Allergy and asthma:

A major study in Denmark found that fish oil supplementation during pregnancy **decreased the occurrence of persistent wheeze and asthma** in offspring. Starting at 24 weeks of pregnancy, women took 4 capsules daily, each containing 1 gram of concentrated fish oil providing 330 mg of EPA and 220 mg of DHA in the triglyceride form. By age 5, wheeze/asthma had developed in 23.7% of children whose mothers received a placebo (olive oil), compared to only 16.9% of those whose mothers received the fish oil supplement. Fish oil was particularly important for children of women who started with lower blood levels of fish oil (one-third of the women) — 35.1% in the placebo group developed asthma/wheeze compared to 17.5% in the supplemented group. Women in the U.S. tend to consume only half the amount of omega-3 fatty acids from their diets as those in Denmark, suggesting even greater potential benefit in the U.S. population (Bisgaard, NEJM 2016).

Follow up on the above study found that, at the age of 10, children whose mothers had taken the fish oil supplement had a 30% lower risk of developing **atopic dermatitis** (**eczema**) than those given a placebo if their mothers possessed the COX1 TT gene (which is most common and represented 61% of the mothers included in the study); however, if their mothers had the COX1 CC gene (which is least

common — present in only 6% of the mothers in the study, but more prevalent among African and Asian populations), the children were 500% *more likely* to develop atopic dermatitis. The risk of atopic dermatitis was not influenced by fish oil supplementation in children whose mothers had the COX1 CT gene (which represented 33% of the mothers in the study) (Chen, JAMA Dermatol 2024).

The Australian study described above found that babies born to women that had received maternal supplementation with fish oil were nearly 40% less likely to have egg allergies in their first year of life in comparison to babies of untreated women. They were also less likely to have eczema, although this association did not hold after the results were adjusted for factors such as maternal history of allergies (Palmer, BMJ 2012).

Respiratory infection:

Infants born to women in Mexico given 400 mg DHA daily (from algal oil from Martek Biosciences) during pregnancy (starting at about 20 weeks) had a **lower occurrence of colds** during the first three month of life than those whose mothers received placebo treatment (37.6% vs. 44.6%, respectively) (Imhoff-Kunsch, Pediatrics 2011). However, median daily intake of DHA among pregnant women in Mexico is much lower than in the U.S. (80 mg vs. 100 to 200 mg, respectively), so the findings may not apply to groups already consuming higher amounts of DHA.

During early childhood

A large study in which 1-year-olds in Ohio who were born preterm and had been weaned off breast milk and formula were given DHA (200 mg) and arachidonic acid (200 mg) daily for 6 months showed **no improvement in cognitive development and early measures of executive function** versus placebo, and possible negative effects on language development (Keim, JAMA Ped 2018). (Arachidonic acid (AA) is an omega-6 fatty acid believed to be important for infant growth and brain development. It is present in human milk and is commonly added to infant formula along with DHA (Hadley, Nutrients 2016).) The lack of effect on cognitive development is generally consistent with previous studies on infants and pre-term neonates, calling into question the benefit of DHA and AA supplementation in these groups.

Alzheimer's disease

Prevention:

Although population studies have suggested a link between consumption of DHA (generally from foods) and reduced incidence of Alzheimer's disease (Sala-Vila, Nutrients 2022), taking fish oil has not been shown to prevent Alzheimer's. A clinical study in Oregon among 102 older adults (average age 81) without dementia but with blood levels of omega-3 fatty acids below what is thought to be neuroprotective showed that taking 1.65 grams of fish oil (*ProOmega 3* by Nordic Naturals) containing 975 mg of EPA and 650 mg of DHA daily for three years did *not* significantly reduce the accumulation of **cerebral white matter lesions** ("bright spots" on MRI of the brain that are thought to play a role in cognitive decline and the development of dementia and Alzheimer's disease) compared to placebo (soybean oil). Fish oil supplementation also did *not* prevent brain atrophy or reduce nerve cell breakdown compared to placebo, although supplementation did significantly reduce the breakdown of nerve cells integrity compared to placebo among those who were carriers of a gene (APOE e4) that has been linked with Alzheimer's disease. However, the study did not determine whether fish oil reduced diagnoses of dementia among participants (Shinto, JAMA Netw Open 2024).

Treatment:

Fish oil alone has not shown a benefit in treating or slowing Alzheimer's disease, although there is some evidence that intake of omega-3s (EPA and DHA) along with adequate intake of B vitamins, or along with alpha-lipoic acid, may be beneficial in slowing Alzheimer's disease progression.

One of the studies that showed some benefit was in Sweden among people with mild to moderate Alzheimer's disease. It found that daily supplementation with 1,700 mg of DHA and 600 mg of EPA for six months benefitted only those with adequate B vitamin status (determined by blood levels of homocysteine). In comparison to those with higher homocysteine levels, people with levels below 11.7 mmol/L experienced a 7.1% improvement in cognitive performance and a 22.3% reduction on a rating scale of dementia. This was consistent with an <u>earlier study</u> by the same researchers that showed B vitamins were most helpful in reducing brain shrinkage in

Alzheimer's patients who had higher blood levels of EPA and DHA. The researchers explained that the two types of nutrients work together: B vitamins are necessary to form phosphatidylcholine which is necessary to carry DHA and EPA over the blood-brain barrier (<u>Jerneren, J Alz Dis 2019</u>). Somewhat similarly, an earlier placebo-controlled, one-year pilot study of 34 adults with mild to moderate impairment from Alzheimer's disease found that alpha-lipoic acid and fish oil slowed the decline in subjects' cognitive functioning. The combination also slowed the decline in subjects' abilities to perform daily activities, as did fish oil alone, but not alpha-lipoic acid alone. The participants normally ate fish no more than once per week and most continued to take Alzheimer's medications. A capsule of alpha-lipoic acid (600 mg) was taken each morning along with two fish oil capsules (each containing 1 gram of fish oil, providing 325 mg EPA and 225 mg DHA in the triglyceride form). Another fish oil capsule was taken with lunch (<u>Shinto, J Alzheimers Dis 2014</u>).

Among studies that have not shown any benefit in reducing declines in cognition or function was one in which individuals with mild to moderate Alzheimer's disease were given DHA from algae. There was also no apparent reduction in the decline in brain volume. In the study, patients received 2 grams of DHA from algal oil daily or placebo for 18 months. All of the patients had previously consumed less than 200 mg of DHA per day and had not taken supplements with DHA or EPA. Among those given DHA in the study, plasma levels of DHA tripled and the amount of DHA in cerebrospinal fluid increased by 38%, with no significant change in those taking placebo (Quinn, JAMA 2010). Similarly, a small study involving daily intake of a drink (Smartfish, Norway) providing 1,000 mg of EPA and 1,000 mg of DHA along with a modest amount of vitamin D (400 IU) and an undisclosed amount of antioxidants (pomegranate, chokeberry and resveratrol) found that the drink — consumed daily for 4 to 17 months — had no effect on cognition in people with Alzheimer's disease, nor in people with mild cognitive impairment. The study also evaluated the drink's effect on the ability of immune system cells in the subjects to remove amyloid beta — a neurotoxic molecule associated with Alzheimer's disease. No improvement in this immune function was found in Alzheimer's patients, although this did improve in people with mild cognitive impairment and normal cognitive function (Fiala, FASEB J 2015).

Age-related cognitive decline (ARCD)

Many studies have explored the use of DHA-rich fish oil for people with age-related cognitive decline (ARCD). Unlike Alzheimer's disease, ARCD is not considered a disease but a more gradual and, perhaps, normal consequence of aging. The effect of DHA on cognitive function in older adults has been mixed. Any benefit has generally been modest at best and may depend on the level of cognitive function prior to treatment, age, diabetes status, and whether or not fish is already being consuming fish in the diet, as discussed below.

Observational research among older individuals has found an association between use of fish oil *supplements* and less reduction in cognitive function and brain volume (size). However, this association has only been seen in those who started with normal cognitive function and did *not* have a gene known as APOE e4, which is associated with increased risk of Alzheimer's disease. Other studies have shown a positive association between *consumption of fatty fish* and better cognitive health and indicate that middle age may be a particularly significant period for the potential role of omega-3 fatty acids in better cognitive aging (<u>Daiello, Alzheimer's & Dementia 2015</u>; <u>Keenan, Alz Dem 2020</u>). Analyses of two studies that showed reduced cognitive decline and reduced brain shrinkage with a B vitamin combination concluded that the benefits were only found among people who began the studies with blood plasma levels of omega-3 fatty acids in the upper range of normal (see <u>B Vitamin Review</u>).

A placebo-controlled study among several hundred people with ARCD showed significant improvements in verbal recognition memory but no improvement in working memory or on executive function tests among those given DHA (900 mg per day from algal triglycerides) for 24 weeks. Plasma DHA levels doubled in the group receiving the supplementation (<u>Yurko-Mauro, Alzheimer's & Dementia 2010</u>).

An open-label study in Boston among 250 cognitively healthy people (average age 64) with coronary artery disease showed that those given high-dose, high-concentration fish oil (1,860 mg of EPA and 1,500 mg DHA in the ethyl ester form, from four softgels of Lovaza) for 30 months experienced higher verbal fluency, language, memory and visual-motor coordination scores compared to a control group that did not supplement with fish oil. The improvements in cognitive function for the fish oil group were observed beginning at 12 months and persisted through 30 months (Malik, Am J Clin Nutr 2021). The study did not discuss the amount of fish oil participants were consuming from their normal diet. (This study also showed cardiovascular benefits, as reported by Alfaddagh.)

However, not all studies have shown a benefit of DHA on cognitive function in older adults. A six-month study among 33 individuals aged 55 years and older (average age 69) who were cognitively unimpaired but with a first-degree family history of dementia showed that supplementing with 2,152 mg of DHA (in triglyceride form) and virtually no EPA daily did *not* affect changes in brain volume or cognitive scores compared to placebo (corn/soy oil), despite increasing DHA and EPA in the cerebral spinal fluid by 28% and 43%, respectively, with greater increases tending to occur more among participants who did *not* carry the APOE4 gene than those who did. All participants in the study were simultaneously supplemented with B vitamins (<u>Arellanes, EBioMedicine 2020</u>).

Fish oil supplementation doesn't seem to help people who already regularly consume fish. Neither daily fish oil (650 mg of EPA and 350 mg of DHA) nor lutein and zeaxanthin (10 mg and 2 mg, respectively) were found to reduce cognitive decline in a large, well-controlled, five-year study of older individuals in the U.S. (average age of 73) who were part of a larger study of supplements to slow age-related macular degeneration, an eye disease (see the <u>AREDS2 study</u>). Yearly decline in cognitive function was essentially the same for those taking these supplements as for those taking placebo (<u>Chew, JAMA 2015</u>). However, the study population was described as "well-nourished" and may have already been regularly consuming fish.

A large study in France among older adults (average age 75) with self-reported cognitive difficulties found that supplementing with 800 mg of DHA and 225 mg of EPA from fish oil daily did not reduce cognitive decline compared to placebo. There was also no benefit from a lifestyle intervention (physical activity, cognitive training, and nutritional advice) by itself or in combination with omega-3 supplementation (Andrieu, Lancet Neurol 2017). Similarly, an 18-month study in Australia among older adults (average age 73) found that daily supplementation with 1,720 mg of DHA and 600 mg of EPA did not help maintain or improve cognitive performance relative to results with placebo (an olive oil low in polyphenols). However, those in the study were consuming fish twice per week on average (Danthiir, Am J Clin Nutr 2018).

Mild cognitive impairment (MCI)

Mild cognitive impairment describes a decline in cognitive function among older individuals that is more severe than age-related cognitive decline but that does not interfere with daily living. Fish oil supplements high in DHA may help reduce further cognitive decline among people with MCI, although, at best, any benefit may be limited to those with lower IQs and lower blood levels among omega-3 fatty acids.

A placebo-controlled study of healthy older individuals in China with mild cognitive impairment found that taking 2 grams of DHA from algal oil daily for a year improved aspects of short- and long-term memory, but not other measures of cognition (e.g., arithmetic, vocabulary). MRI scans of those given algal oil (from Martek Biosciences, whose parent company, DSM, funded the study) showed a 4% increase in the volume of the hippocampus (a key area for memory formation), while those given a similar amount of corn oil did not have this improvement, nor improvements in cognitive function (Zhang, J Alz Disease 2016). Another study among older men and women (average age 71) in China with mild cognitive impairment found that 480 mg DHA and 720 mg EPA per day from fish oil slightly improved overall measures of cognitive function, perceptual speed and working memory, but not mental arithmetic efficiency or recognition memory, compared to placebo (olive oil) (Bo, Nutrients 2017). Blood levels of DHA and EPA in participants were somewhat low at the beginning of the study, which may help explain why supplementation was helpful.

A six-month study of people over age 65 with mild cognitive impairment showed that those receiving daily fish oil containing a large amount of DHA (1,550 mg) with EPA (400 mg) improved scores on verbal fluency, but not other measures of or cognition, compared to those in a control group receiving safflower oil (containing the omega-6 fatty acid, linoleic acid). A higher concentration of EPA to DHA (1,670 mg EPA with 160 mg DHA) did not affect any aspect of cognition or memory. However, both the EPA/DHA combination and, to a slightly greater extent, the DHA/EPA combination reduced depressive symptoms in these mildly cognitively impaired individuals (Sinn, Br J Nutr 2011). The researchers note that depression is a potential risk factor for progression to dementia, so the reduction of depressive symptoms may reduce the risk of dementia.

However, not all research has shown benefit in MCI. A study in New Zealand among 60 people with MCI who consumed less than two servings of fish per week showed that supplementing with 1,491 mg of DHA in the triglyceride form and 351 mg of EPA daily for a year did not improve cognitive measures overall compared to placebo (linoleic acid), despite increasing red blood cell concentrations of DHA by 51.8% and EPA by 10%, although depression and anxiety scores decreased among those who had the APOE e4 gene (associated

with increased risk of Alzheimer's disease). The researchers noted that participants in this trial had high average IQ score (119) despite having MCI and pointed out that people with high IQs tend to have greater cognitive reserve (i.e., ability of the brain to "improvise" to cope with cognitive declines), which might have accounted for the lack of benefit. Also, the researchers noted that the increase in red blood cell concentration of DHA was less than measured in other studies that used a similar dose of DHA/EPA and found cognitive benefit (for instance, in the Sinn study above, DHA levels increased by 90.1%) (Mengelberg, Int J Geriatr Psychiatry 2022). Similarly, no cognitive benefits or maintenance of brain volume were found with taking fish oil along with chocolate in a study in the UK and Australia among 197 men and women age 55 or older (average age 65) with mild cognitive impairment (MCI) or subjective cognitive impairment (SCI) who had averaged less than one serving of oily fish per week. Every day for a year, participants consumed 3 grams of fish oil (providing a daily total of 1,100 grams of DHA and 400 mg of EPA in the triglyceride form) plus 33 grams (about 1.5 oz. or 1/4 a cup) of chocolate chips (providing 508 mg of cocoa flavanols) (Vauzour, Am J Clin Nutr 2023).

Memory enhancement in healthy individuals

Most studies suggest only limited, if any, improvements in cognition and/or memory with omega-3 supplementation. Benefits tend to be limited to people starting with low blood levels of DHA, little fish intake, or lower baseline scores on cognitive measures.

A placebo-controlled study in 65 healthy **adults ages 50 to 75 years**, found that taking fish oil for 6 months resulted, on average, in a 26% improvement in executive functioning (e.g., verbal fluency, visual tasks, reading ability). There was no overall improvement in memory, although there was an improvement in memory consolidation – the recall of words after a 30-minute delay. Those who took the fish oil also had significant gains in the structure and volume of tissue in several areas of the brain, improvements in the lining of the carotid artery, and a 3.4% reduction in diastolic blood pressure. The participants took four fish oil capsules daily, each containing 1,000 mg of fish oil (300 mg EPA and 220 mg DHA) which included 15 mg of vitamin E as preservative, and continued eating their normal diet, with most consuming fish once per week (Witte, Cereb Cortex 2013).

A placebo-controlled study that looked at **blood flow to the brain** in older women and men (ages 50 to 80) in Australia who were sedentary and obese and were not large consumers of fish or fish oil found that supplementation with 1,000 mg of DHA and 200 mg EPA (triglyceride forms) taken with breakfast and, again, with dinner reduced stiffness of the cerebral arteries, although blood flow to the brain was found to increase only among men. The fish oil reduced heart rate and triglycerides and increased HDL cholesterol. The addition of <u>curcumin</u> provided no additional benefit (<u>Kuszewski, Nutr, Met Cardio Dis 2020</u>).

A small study among 20 older adults (average age 69) with **late-life depression** (which has been linked with increased risk of dementia) showed that taking 1.2 grams of EPA and 1 gram of DHA daily for 52 weeks did *not* significantly improve processing speed, executive function, memory, or language compared to placebo (soybean oil). The lack of significant clinical benefit, however, may be due, in part, to the fact that the participants already had adequate intake of omega-3s as, on average, they ate fish about 2.3 times per week (<u>Lin, J Affect Disord 2024</u>).

A study among 271 healthy **adults ages 30 to 54 years** with generally low intakes of omega-3 fatty acids from their diet (< 300 mg per day) found that taking two 1,000-mg fish oil capsules (each providing 500 mg EPA + 200 mg DHA) daily for four months did *not* lead to an improvement in executive functioning, psychomotor speed, learning/episodic memory, or fluid intelligence (i.e. reasoning) relative to placebo. Only among those who began the study with the *lowest* blood levels of DHA (< 2.45% of total fatty acids) was there a significant improvement with regard to executive functioning (<u>Leckie, Psychol Med 2019</u>).

Taking fish oil daily for six months was *not* found to improve cognitive measures (including visuospatial ability, working memory, episodic memory, and executive function) compared to placebo (soybean/corn oil) in a study in Canada among 193 healthy **adults ages 20 to 80 years** despite significantly increasing concentrations of EPA and DHA. The fish oil (2,000 mg providing 850 mg of EPA and 400 mg of DHA in ethyl ester form) was taken twice daily with breakfast and dinner. Only participants with low episodic memory scores at baseline showed improved scores following supplementation with omega-3 fatty acids compared to placebo. During the study, participants consumed less than two servings of fish weekly and did *not* consume other supplements (<u>Maltais, Prostaglandins Leukot Essent Fatty Acids 2022</u>).

In a small study of healthy **young adults**, better working memory performance has been found to correlate with higher levels of DHA (as measured in red blood cell membranes), but not EPA (Narendran, PLoS One 2012). Working memory performance was tested by showing a series of letters and numbers and asking what appeared one, two, and three times prior. Those who had higher DHA levels performed better on the "3-back" question than those with lower levels. The subjects were then asked to take 2 grams of highly-concentrated fish oil (Lovaza, 930 mg EPA and 750 mg DHA) daily for six months and tested again: Scores improved on the "3-back" question and those who previously had the lowest DHA levels improved the most. Similarly, another 6-month study in healthy young adults with diets low in omega-3 fatty acids found those given a DHA-rich fish oil supplement daily (2,250 mg of fish oil providing 1,160 mg of DHA and 170 mg EPA) had improved memory performance compared to those who received placebo (Stonehouse, Am J Clin Nutr 2013). Specifically, women had greater improvements in episodic memory — correctly remembering one more word or picture, while men experienced greater improvements in reaction times of working memory — completing tasks 20% faster than men in the placebo group. The report notes that six-months was chosen as the study period as this is required for DHA levels in tissue to plateau.

A study in Holland among **adolescents** with lower educational performance and generally low starting blood levels of omega-3 fatty acids who were given krill oil capsules (providing 520 mg of EPA + 280 mg DHA daily) for one year did not find improvements in measures of cognition compared to placebo, or any association between blood levels of omega-3 fatty acids and cognitive performance. However, it is difficult to draw conclusions from this study because average blood levels of omega-3 fatty acids actually decreased in those taking krill oil, possibly due to very low compliance (<u>van der Wurff Nutrients 2019</u>). Baseline testing (before starting krill) of the students had shown a positive association between levels of EPA + DHA in their blood and performance on two cognitive measures: processing speed and impulsivity control, but no association with short-term memory or six other cognitive measures (<u>van der Wurff, Nutrients 2016</u>).

Calanus oil, a source of omega-3 fatty acids from zooplankton, does *not* seem to improve memory among older adults. A study in the Czech Republic among 52 older women (average age 71) showed that taking 5 capsules of calanus oil (by Calanus A.S. Norway, which provided the capsules but did not fund the study) containing 105 mg of DHA and 125 mg of EPA daily for 16 weeks did *not* improve short-term memory compared to placebo, although both groups showed improvement compared to baseline. Both groups participated in exercise training for one hour, three times weekly, which may have contributed to the memory improvements observed in both groups (Dadova, Clin Interv Aging 2022). Dietary intake of omega-3 fatty acids from fish or other sources was not reported in the study, although fish consumption in the Czech Republic is relatively low. Calanus oil contains DHA and EPA in fatty alcohol and wax ester forms, which are thought to have high bioavailability.

Muscle, strength and falls

Many studies have evaluated the impact of taking fish oil (or krill oil) on aspects of muscle function, showing benefits in only some situations.

Among *older people*, several studies suggest that fish oil can modestly improve muscle *strength* (particularly for women) and might also *slightly reduce the risk of falls*, but there is conflicting evidence about whether fish oil helps maintain muscle *mass*. Fish oil does not appear to improve *endurance* among older individuals.

On the other hand, among *younger people* who are physically active, fish oil supplementation does not appear to significantly increase muscle *strength* but may improve *endurance*. It may also prevent decline in muscle volume during immobilization.

Older adults

A study in Scotland among 94 older adults (average age 71) who normally exercised less than 1 hour per week and ate two portions of oily fish or less per week showed that supplementing with 2 grams of krill oil (*SuperbaBoost* by Aker Biomarine Antarctic AS) twice daily (with lunch and dinner) for 6 months increased knee extensor muscle strength by 7.1% compared to a decrease of 2.2% for those in given placebo (a mixed vegetable oil). Grip strength also increased by 10.9% and muscle thickness by 3.5% for those in the krill oil group

compared to placebo, but there were no significant improvements in 4-meter walk speed or chair rise tests. Each 1-gram capsule of krill oil provided 193 mg of EPA and 96 mg of DHA, as well as 79 mg of choline (from the phosphatidylcholine in krill oil) (Alkhedhairi, Clin Nutr 2022).

A study among healthy older adults (average age 70) found that taking 3 grams of fish oil daily, providing a daily total of 2,100 mg of EPA and 600 mg of DHA (*Barlean's*), while performing resistance exercise (twice per week), increased muscle strength by 34% in women. This was significantly greater than the 16% increase among women given placebo. In men, however, fish oil did *not* result in significant improvement compared to placebo. The researchers speculated that older women may have a greater capacity for improvement from resistance exercise than older men (<u>Da Boit, Am J Clin Nutr 2016</u>).

A study in the U.S. among 63 healthy, older adults (average age 71) who normally exercised for less than 30 minutes three times weekly found that taking 2 grams of fish oil (*Ocean Blue Professional Omega-3 2100*) providing about 1,350 mg of EPA plus 600 mg of DHA twice daily (in the morning and evening) for 6 months, without changing normal daily physical activity, modestly improved muscle strength on a leg extension test by about 7.5% compared to a non-significant improvement of only 3.1% for those given placebo (corn oil). However, fish oil supplementation did *not* improve exercise endurance or increase muscle mass or muscle power, nor did it have any clear effects on muscle protein synthesis or breakdown (Kunz, Nutrients 2022).

There is mixed evidence about the effect of fish oil supplementation on muscle mass in older adults. A six-month, placebo-controlled study in healthy older men and women (60 to 85 years of age) found that high-dose, extremely concentrated fish oil increased muscle mass and function, while these declined in the placebo group receiving corn oil. The fish oil was Lovaza, taken as 2 pills with both breakfast and dinner, providing 1,860 mg of EPA and 1,500 mg of DHA daily (similar to amounts in about 3 servings of fatty fish). Compared to the control group, those getting the fish oil had about a 3.5% increase in muscle mass and a 6% increase in strength. The researchers noted that the therapy made up for 2 to 3 years of losses associated with normal aging and these changes were the same or greater than those which have been reported with testosterone, growth hormone, or DHEA, but less than what has been reported with exercise (Smith, AJCN 2015). However, in other studies discussed above, supplementing with fish oil did not improve muscle mass in older people compared to placebo (Kunz, Nutrients 2022; Da Boit, Am J Clin Nutr 2016).

A study of about two thousand generally healthy and active older adults (average age 75) with sufficient blood levels of vitamin D showed that those who supplemented daily with algal oil for three years were 10% less likely to experience falls than those not supplemented, although it did *not* reduce the rate of *injurious* falls. The dose given was 1 gram providing about 167 mg of EPA and 333 mg of DHA (Bischoff-Ferrari, Am J Clin Nutr 2022).

Young adults

A small study among male and female European competitive soccer players (average age 22) found that a high daily dose of fish oil (100 mg/kg of bodyweight; average dose 7 grams of fish oil providing 4,900 mg of EPA and 1,400 mg DHA daily) taken for one month modestly improved exercise endurance compared to placebo. After one month, those who took the fish oil were able to run an average of 203 meters further than before supplementation began, while those who took the placebo ran an average of 63 meters further (Gravina, Int J Sport Nutr Exerc Metab 2017).

A study among 20 recreationally active young women who had one leg experimentally immobilized with a knee brace for two weeks found that those who started taking daily high-dose fish oil four weeks before immobilization had less decline in muscle volume than those given sunflower oil (8% vs. 14% decline, respectively). In fact, two weeks after the brace was removed, muscle volume was back to normal for those who had taken fish oil but it remained reduced in the control group. Biopsies revealed that muscle synthesis was higher with the fish oil group throughout the study. Following immobilization, leg strength decreased more in the control group than in the fish oil group, but the difference was not statistically significant. The fish oil was taken as a liquid providing 2,970 mg of EPA and 2,030 mg of DHA daily (McGlory, FASEB J 2019).

Some studies suggest that high-dose fish oil supplementation (3 to 7 grams daily) does *not* significantly improve muscle strength among younger, physically active adults compared to placebo (Georges, J Nutr Metab 2018; Gravina, Int J Sport Nutr Exerc Metab 2017). A more recent study found mixed results: Fish oil increased the amount that could be bench pressed by an extra 5 kg (about 11 lbs) compared to placebo, but there were no statistically significant gains in back squats or changes in lean body mass or percent body fat among 21 recreationally active young adults who supplemented with 4.5 grams of fish oil daily (*ProOmega* by Nordic Naturals, standardized to 2.275 grams of EPA and 1.575 grams of DHA) while also participating in resistance exercise three days weekly for 10 weeks (Heileson, J Int Soc Sports Nutr 2023).

Muscle pain and inflammation after exercise (Omega XL)

A small study found that daily supplementation with a combination of green-lipped mussel oil, olive oil and vitamin E (*Omega XL/PCS0-524*, Pharmalink International) significantly reduced muscle damage, pain and inflammation after exercise in young men (average age 22) (Mickleborough, J Int Soc Sports Nutr 2015). In the study, the men took eight *Omega XL* capsules per day (providing a total daily dose of 800 mg olive oil, 400 mg green lipped mussel oil extract (58 mg EPA + 44 mg DHA) and 1.8 mg vitamin E) or 8 placebo capsules (containing 1,200 mg olive oil) daily for one month. On the 26th day of supplementation, the men performed a downhill running exercise designed to induce muscle damage. Those who took the green-lipped mussel oil combination had significantly less delayed-onset muscle soreness (DOMS) on the third and fourth day after exercise, as well as lower levels of certain blood markers for muscle damage and inflammation, compared to those who took a placebo. The study was funded by Pharmalink International. [Note: this product was tested by ConsumerLab.com in 2014 and 2016 and was neither "Approved" or "Not Approved" because the label did not claim to contain a specific amount of omega-3 fatty acids — it was found each time to contain only about 6 mg of EPA and 5 mg of DHA per softgel, very low amounts compared to other omega-3 fatty acid supplements, although consistent with the amounts per pill in the above study.]

There is mixed evidence that Omega XL/PCSO-524 may also be helpful for other conditions, and many of the clinical studies on this product were not properly designed (i.e., not double-blinded, placebo-controlled, etc.). For example, one study found it significantly reduced pain and improved physical function in men and women with **osteoarthritis** of the knee and/or hip when compared to fish oil (<u>Zawadzki, Mar Drugs 2013</u>), but another study found no such benefit when compared to a placebo (<u>Lau, Progress in Nutrition 2004</u>). In addition, a study found Omega XL/PCSO-524 to reduce the occurrence of wheezing in adults with **asthma** (<u>Emelyanov, Eur Respir J 2002</u>), while a study in children with asthma found no benefit compared to placebo (<u>Lello, Inter J of Asthma, Allergy and Immunol 2012</u>). Any promotion of the product for heart health appears to be based on the fact that it contains omega-3 fatty acids, not published clinical studies, although, as noted, it contains a scant amount of omega-3s. (See <u>Cautions and Concerns</u> for safety concerns about green-lipped mussel extract).

Acne

A small study found that daily supplementation with either omega-3 fatty acids (EPA and DHA) or the omega-6 fatty acid GLA significantly reduced the number and severity of acne lesions in men and women ages 18 to 33 years old with mild to moderate acne (Jung Acta Derm Venereol 2014). Participants received two capsules daily containing either omega-3 fatty acids (providing a total of 1,000 mg EPA and 1,000 mg DHA) or GLA (providing a total of 400 mg GLA from 2,000 mg borage oil) for 10 weeks. A third group, serving as the control, did not receive supplementation or any other treatment. At the end of the study, both treatment groups experienced a significant reduction in the number of inflammatory acne lesions (42.6% and 32.7%, respectively) and non-inflammatory acne lesions (19.6% and 15.8%, respectively). There was also a significant reduction in the severity of acne lesions in both groups (29% and 22%, respectively). No significant changes were seen in the control group.

Periodontitis (inflammation around teeth)

A small, controlled, 3-month study found that giving 2,000 mg per day of DHA (from four capsules of algal oil which was 53.6% DHA) along with low-dose aspirin (81 mg per day) improved outcomes in people with periodontitis (inflammation around teeth causing pocketing) in comparison to aspirin plus placebo (soy/corn oil). Those receiving the DHA had greater reductions in local inflammation and pocketing around teeth (Naqvi, J Dent Res 2014). The researchers speculate that, in the presence of aspirin, DHA is converted to a compound used by certain white blood cells to produce other compounds (e.g., resolvins and protectins) that help resolve

inflammation. Aspirin alone does not have this effect, and it is not known whether DHA *alone* has this effect, although a small study found that DHA *along with* EPA does not significantly help. The study, which included 40 people (average age 48) with severe or advanced periodontitis, showed that taking about 9 grams of fish oil (that contained 900 mg of DHA and 1,300 mg of EPA) twice daily starting at 3 weeks after an initial dental "deep cleaning" session (i.e., scaling and root planning) and continuing for 6 months did *not* significantly reduce the depth of pockets between the gumline and teeth compared to deep cleaning alone (Stando-Retecka, BMC Oral Health 2023). An earlier pilot study of EPA alone did not affect periodontitis, although positive results were seen with 2,000 mg per day of GLA (an omega-6 fatty acid) (Rosenstein, Prosta Leukot Essent Fatty Acids 2003).

Protection from effects of air pollution

A small study by scientists at the U.S. Environmental Protection Agency (EPA) in middle-aged people found that fish oil supplementation protected against adverse cardiac and lipid effects associated with air pollution exposure (<u>Tong, Env Health Perp 2012</u>). Participants in the study were given daily capsules of fish oil (3 grams, providing 1230 mg EPA and 822 mg DHA) or olive oil for four weeks and then exposed to air containing particles for two hours. This caused the group taking olive oil to experience undesirable changes in blood lipids (increased LDL and triglyceride levels), but this did not occur in the fish oil group. The fish oil group also experienced fewer negative effects on heart functioning than the olive oil group.

However, a second small study found that supplementation with olive oil provided protection against other vascular effects of air pollution that fish oil supplementation did not. In the study, middle-aged men and women who took 3 grams of olive oil daily for four weeks experienced significantly better endothelial function after being exposed to air conditioning particles for two hours compared to those who took 3 grams of fish oil or placebo (Tong AJRCCM 2014). This suggests that olive oil and fish oil may each offer different cardio-protective benefits when it comes to air pollution exposure.

Testosterone, fertility and semen quality

Despite animals studies suggesting that consumption of omega-3 fatty acids increases testosterone levels in males (Zaima, Biochem Biophys Rep 2016; Sebokova, J Nutr 1990), studies in men have shown mixed results, although an association between fish oil use and improved semen and sperm levels was found in one analysis. A study in 26 men (average age 37) found that a high daily dose fish oil (5 grams of EPA + DHA) taken for one month did not increase free (biologically active) or total testosterone levels compared to placebo (Hughes, Atherosclerosis 1990). Similarly, a large, placebo-controlled study of older men (ages 60 to 80) with a history of heart attack (which increases the risk of testosterone deficiency), a modest daily dose of 400 mg of EPA + DHA did not increase total testosterone levels, nor the risk of testosterone deficiency, compared to placebo (Giltay, Int J Androl 2012). On the other hand, a placebo-controlled study in Australia among overweight and obese men and women (average age 51) found that 1 gram of fish oil (EPAX1050 - 430 mg DHA + 60 mg EPA) taken twice daily with meals for three months significantly increased total testosterone levels in men (by 1.95 nmol/L compared to placebo, which is more than a 10% increase) but not in women. However, levels of free ("active") testosterone were not measured (Kylie, Prostaglandins Leukot Essent Fatty Acids 2020).

A study of 1,679 healthy young men in Denmark found that use of fish oil supplements (dosage not recorded) over the prior three months was associated with significantly better testicular function with regard to semen volume, sperm count, and testicular size, particularly if fish oil had been taken for 60 or more days in that period. There was no such association with the use of other supplements, such as multivitamins or vitamins C or D. The authors noted that these results are consistent with previous studies of men at fertility clinics and of healthy men given a significant amount (75 grams) of nuts to consume daily, possibly due to the fact both fish oil and nuts provide polyunsaturated fatty acids which are important constituents of sperm cell membranes. Conversely, saturated fat has been associated with lower sperm counts (Jensen, JAMA Net Open 2020).

Menopausal symptoms

A randomized, placebo-controlled study in Iran among 180 postmenopausal women (average age 53) suggested that, based on self-reported outcomes, fish oil supplementation once daily for three months reduced menopausal symptoms — including sweating, hot flashes, sleep problems, depressed mood and anxiety but not joint discomfort, bladder problems or vaginal dryness — better than

placebo and similar to taking soybean extract. Fish oil was given as *Omega-rex* 1,000 mg softgels (providing a total of 180 mg of EPA and 120 mg of DHA daily), and soybean extract was given as *Soygan* 500 mg capsules (containing 500 mg of soybean powder and extract) daily (<u>Purzand, Complement Ther Clin Pract 2020</u>).

COVID-19

Fish oil does not appear to reduce the risk of hospitalization or death with COVID. It also does not improve symptoms of long COVID.

A placebo-controlled trial among 2,052 patients with mild to moderate COVID in which high-dose, high-concentration prescription fish oil (Vascepa) or placebo was given daily (8 grams for 3 days followed by 4 grams for 25 days) found no statistically significant difference in the percentage of COVID-19-related **hospitalizations** with fish oil versus placebo (11.2% vs. 13.7%) or **deaths** (16% vs. 22%) at day 28, and those who received placebo had slightly shorter hospital stays (<u>Dharam, J Am Coll Cardiol 2021</u>).

A preliminary study among 91 COVID patients given the same type and dose of fish oil in the study above reported reductions in **inflammation** and **flu-like symptoms** compared to standard treatment alone; however, there was no placebo control, as needed to prove a benefit. Over the 14 days of treatment, symptoms were reduced by 52% in the Vascepa-treated group compared 24% in patients who did not receive Vascepa. Those who received Vascepa also had a greater decrease in the inflammatory biomarker, C-reactive protein (CRP), compared to those who received standard treatment alone (25% vs. 5.6% decreases, respectively), after adjusting for age, sex, and cardiovascular risk (Kosmopoulos, iScience 2021).

A small study in New Jersey among 18 healthcare workers (average age 50) experiencing **long COVID** (i.e., symptoms lasting more than 12 weeks) showed that taking about 2,100 mg of fish oil (*OceanBlue Omega-3 EPA+DHA* by KD Pharma) in two divided doses daily for 12 weeks did *not* improve symptoms such as shortness of breath, cough, fatigue, lack of taste, or loss of smell compared to placebo (soybean oil). The daily dose of fish oil contained 1,512 mg of EPA and 612 mg of DHA (<u>Sarkar, Cureus 2024</u>). These results differ from earlier preliminary research suggesting that fish oil supplementation (2,000 mg of omega-3 fatty acids/day) *may* be beneficial for loss of smell with COVID when used in addition to standard treatment (olfactory training, oral steroids and steroid rinses), as noted in The British Rhinological Society guidelines. (Those guidelines did *not* find sufficient evidence to recommend <u>vitamin A</u> drops or <u>alpha lipoic</u> acid for COVID-19 related loss of smell (<u>Hopkins, Clin Otolaryngol 2021</u>).)

Other uses

A study in India among 110 people (average age 58) with **burning mouth syndrome (BMS)**, a condition characterized by unexplained scalding sensations in the mouth, showed that taking 2 grams of omega-3 fatty acids (1,200 mg of EPA and 800 mg of DHA) daily for 12 weeks reduced the severity of self-reported burning pain by 4.4 points (on a 10-point scale) compared to only 1.2 points for the placebo group, and this difference was statistically significant (<u>Srivastava, J Pharm Bioallied Sci 2025</u>). More research is needed to confirm this effect. (Also see: Alpha-Lipoic Acid for burning mouth syndrome).

Other proposed uses of fish oil with some support include chronic fatigue syndrome, cystic fibrosis, and osteoporosis.

More research is needed to determine if fish oil supplementation is helpful for **Raynaud's phenomenon** (abnormal sensitivity of hands and feet to cold). In a small clinical trial, supplementation with 12 fish oil capsules daily (providing a total of 3, 960 mg EPA and 2,640 DHA daily) for six weeks modestly increased the time of onset of symptoms when exposed to cold (which correlated with increased systolic blood pressure in the fingers), compared to before supplementation, in people with primary Raynaud's phenomenon, but did not appear to be helpful in people with Raynaud's phenomenon due to other health conditions (<u>DiGiamcomo</u>, <u>Am J Med 1989</u>). On the other hand, another study found no association between total dietary fish oil consumption and the length or frequency of attacks in people with Reynaud's (<u>Foley</u>, <u>FASB J 2016</u>).

The balance of current evidence suggests that fish oil is not effective for **psoriasis** and enhancing immunity in **people with HIV**. Although some research has indicated that omega-3 fatty acid supplements might have anti-inflammatory effects that could benefit patients with **multiple sclerosis (MS)**, a placebo-controlled study of 92 MS patients found no beneficial effect with daily fish oil (1,350).

mg EPA and 850 mg DHA) for 2 years whether taken alone (for 6 months) or in combination with interferon (for 18 months) (<u>Torkildsen</u>, <u>Arch Neurol 2012</u>).

Pet use

Fish oil supplements are commonly given to pets to help maintain their coats and skin. [Reviews of other pet supplements by ConsumerLab.com include ALA and GLA, Joint Supplements and Multivitamins/Multiminerals.]

For information on dosages see What to Consider When Using.

Quality Concerns and Tests Performed:

Because omega-3 fatty acids are obtained from natural sources, **levels of fatty acids** in supplements can vary, depending on the source and method of processing.

Contamination has also been a concern because fish can accumulate toxins such as mercury, dioxins, and polychlorinated biphenyls (PCBs). Mercury can damage the nervous system – particularly in a fetus. Dioxins and PCBs may be carcinogenic at low levels of exposure over time and may have other deleterious effects. However, while these contaminants remain of concern in fish meat, they have generally not been found to occur at dangerous levels in fish oil likely due to the purification processes used in preparing fish oil as well as the fact that contaminants like mercury bind to protein (meat) and not to oil.

The **freshness** of the oil is also an important consideration because rancid fish oils can have an extremely unpleasant odor and taste, and oxidized fish oil may be less safe and effective. A 7-week study in Norway, for example, found that high-quality (non-oxidized) fish oil taken daily by healthy adults resulted in a 6% decrease in LDL ("bad") cholesterol, while oxidized fish oil resulted in a 19% increase in LDL. Total cholesterol also decreased with high-quality fish oil compared to oxidized fish oil. Each fish oil contained the same amount of omega-3 fatty acids (700 mg EPA and 900 mg DHA). The researchers speculated that oxidized fish oil might enhance the solubility of cholesterol in the gut and increase its absorption, thus *raising* cholesterol levels (Rundblad, Br J Nutr 2017). Similarly, an earlier study found that highly oxidized (spoiled) omega-3 fatty acids from capsules had a negative effect on cholesterol levels in contrast to less oxidized omega-3 fatty acids which reduced triglyceride and cholesterol levels (Garcia-Hernandez, Int J Food Sci Nutr 2013).

While you can sometimes tell that a fish oil is rancid when you take it directly as a liquid, this can be masked by added flavors and not readily detected if you use a softgel and other encapsulated product. There may be safety considerations with oxidized fish oils due to a variety of compounds produced, some of which are odorless, such as peroxides. A study commissioned by the government of Norway (where fish oil supplement use is extremely high) concluded there would be some health concern related to the regular consumption of oxidized fish/marine oils, particularly in regards to the gastrointestinal tract, but there is not enough data to determine the risk (The Norwegian Scientific Committee for Food Safety, 2011). The study explained that the amount of spoilage and contamination in a supplement depends on the raw materials and processes of extraction, refining, concentration, encapsulation, storage and transportation. However, it saw no significant risk of contamination by microorganisms, proteins, lysophospholipids, cholesterol, and trans-fats. (ConsumerLab.com's tests of fish oil also indicate only insignificant amounts (less than 1%) of trans-fats, meaning that a capsule with 1,000 mg of fish oil contains less than 10 mg, or 0.01 grams, of trans-fat.)

Studies of the freshness of supplements have suggested that a large percentage may be oxidized. An analysis of data from ConsumerLab.com's tests of omega-3 supplements sampled between 2014 and 2020 showed that 13% of unflavored products exceeded the GOED limit for total oxidation (TOTOX) (GOED is the Global Organization for EPA and DHA — a fish oil trade group). An even greater percentage of flavored products exceeded this limit, but, as noted, the limit does not apply to such products because flavorings as well as colored compounds can inflate oxidation measures (Hands, J Diet Suppl 2023). Similarly, a study in Canada of mostly fish oil supplements (Jackowski, J Nutr Sci 2015) found that 50% exceeded voluntary oxidation limits. However, this study did not necessarily exclude products containing flavors that can interfere with testing, and this may have led to misleading findings and the

conclusion that children's products (80% of which included flavorings) were more likely to be oxidized. The study also concluded that encapsulated, unflavored fish oil appears to be the safest and most readily testable type of product. It should be noted, however, that several of the researchers were employees of Pivotal Therapeutics, Inc., which exclusively sells encapsulated, unflavored fish oil.

A private research group in Boston reported that three "top-selling" fish oil dietary supplements "exceeded maximum international industry standards" with regard to oxidization, but an extremely concentrated prescription fish oil did not (product identities were not disclosed). It also reported that each supplement contained "significant levels of saturated fat in addition to desirable omega-3 fatty acids." The report, however, is somewhat misleading in that 1) the oxidation values for the supplements were inflated by the researchers to "normalize" them to one gram of omega-3 fatty acids, rather than to one gram of fish oil — which is the true industry standard, and 2) fish oil naturally contains saturated fats as well as unsaturated fats, so finding some saturated fats is expected and is not surprising.

Amarin Pharma, the maker of a prescription fish oil (VASCEPA) funded the writing of the report (Mason, Biochem and Biophy Res Comm 2016).

A study of 33 fish and marine oil supplements purchased on the internet and in retail stores in Norway found peroxide levels (one measure of oxidation) to vary almost 10-fold, from 1.04 to 10.83 meq/kg, but the average level among products was 3.61 meq/kg, which is well below the GOED limit of 5 meq/kg which ConsumerLab.com applies in its reviews (Halvorsen, Food Nutr Res 2011). GOED (the Global Organization for EPA and DHA — a fish oil trade group) funded its own study of popular U.S. fish oil supplements purchased in 2016 and found that "nearly half of 17 tested products for which all quality parameters could be tested did not meet at least one of the oxidative quality criteria or their label claim for EPA + DHA." The GOED report includes product-specific findings (Bannenberg, J Food Comp Analys 2020 — Table 1, pg. 35). Interestingly, two of the products that passed testing were also Approved in Reviews by ConsumerLab (Spring Valley Fish Oil 1200 mg [2018] and Natural Factors Rx Omega-3 400 EPA/200 DHA [2016]), while none that failed GOED's tests had been Approved by CL.

Another study funded by GOED found that the susceptibility of fish oil to oxidation depends on the specific fish oil evaluated and the oxidation conditions to which the fish oil is exposed. Incorporating antioxidants such as mixed tocopherols into fish oil tends to delay oxidation. For instance, refined anchovy oil stabilized with added mixed tocopherols resisted oxidation following exposure to light and oxygen (i.e., photo-oxidation), while hoki liver oil containing only some natural alpha-tocopherol (but no added mixed tocopherols) became rancid rapidly. Refined anchovy oil also resisted degradation at higher temperatures (i.e., thermal degradation) better than hoki liver oil, although both fish oils lost antioxidant protection at longer exposure times. The researchers noted that the oxidation conditions used in the study were severe and that commercially available fish oil products are unlikely to be exposed to such conditions, although they did note that some of the oxidation byproducts were present in both fish oils even at baseline, indicating the byproducts may be formed at low levels during processing or storage (Phung, Foods 2020).

ConsumerLab.com's tests for spoilage were conducted on newly opened products, maintained out of heat and moisture. However, be aware that spoilage may occur after products are opened and exposed to air and/or excessive heat (see Keep It Fresh for storage tips). Lemon and other citrus flavorings, which are common in marine oil supplements, as well as vanillin, can interfere with spoilage testing, giving a falsely high reading. In addition, deeply colored oils, such as krill, cannot be evaluated in this test. Consequently, ConsumerLab.com was not able to determine spoilage in such products, as indicated with "N/A" (not applicable) in the "Freshness" column of the results table below). To be sure a product was not spoiled and passed oxidation tests, look for a "pass" in for "Freshness" in the 3rd column of the Results table.

Capsules that are **enteric-coated** and are expected to release the oil *after* the stomach to theoretically reduce fishy aftertaste or burp. If they release too soon they lose that potential benefit. If they release too late, the oil may not get absorbed. ConsumerLab.com tested enteric-coated fish oil products according to the specifications set forth by the United States Pharmacopeia (USP).

Neither the FDA nor any other federal or state agency routinely tests fish or marine oil supplements for quality prior to sale.

ConsumerLab.com, as part of its mission to independently evaluate products that affect health, wellness, and nutrition, purchased many dietary supplements sold in the U.S. claiming to contain EPA and/or DHA and tested them for their levels of omega-3 fatty acids (EPA, DHA, DPA, and if listed, ALA), omega-7 fatty acids, lead, cadmium, arsenic, mercury, and signs of spoilage (unless the product had

issues preventing accurate testing for spoilage, as noted above). Enteric-coated capsules were tested to see if they properly released their ingredients. Krill oils were additionally tested for amounts of phospholipids and astaxanthin. Among the products purchased and tested, the majority were for use by people and some were for pets. Most of the supplements were softgel capsules or liquids.

For more information about the testing, see How Products Were Evaluated.

What CL Found:

Among the 14 products that ConsumerLab.com selected for review (including two products for pets), 11 were "Approved" for quality — meaning that they passed tests for freshness (i.e., not rancid) and purity (i.e., lack of contamination by heavy metals), contained their claimed amounts omega-3 fatty acids, and, if enteric coated, disintegrated properly. An additional 12 products that were tested through CL's Quality Certification Program passed testing and were also Approved.

Problems Discovered

Three products were found to be rancid. As <u>noted earlier</u> "freshness" in Quality Concerns, rancid (oxidized) fish oils can have an unpleasant odor and taste and may be less safe and effective. This problem was confirmed in a second, independent laboratory. All samples were newly opened and within their listed expiration or "best by" dates.

- Jamieson Omega-3 Complete 600 mg (a Canadian product) failed for being heavily oxidized. Fish oil that is fresh should have a level of peroxide (which is formed when oils are exposed to oxygen) that is no more than 5 mEq/kg, but the level was 48 mEq/kg in Jamieson. This gave Jamieson a Total Oxidation (TOTOX) score of 109.9, while the limit is 26. (TOTOX is calculated as twice the peroxide level plus the level of anisidine a compound formed later in the oxidation process).
- Wiley's Finest Wild Alaskan Fish Oil also failed for being overly oxidized, although not as heavily as Jamieson. Peroxide in Wiley's was 11.6 mEq/kg and the TOTOX score was 32.6.
- Iceland Pure Pharmaceutical Human Grade Fish Oils Salmon Oil (for dogs and cats) also failed for being oxidized, having 9.1 mEq/kg of peroxide and a TOTOX score of 32.3.

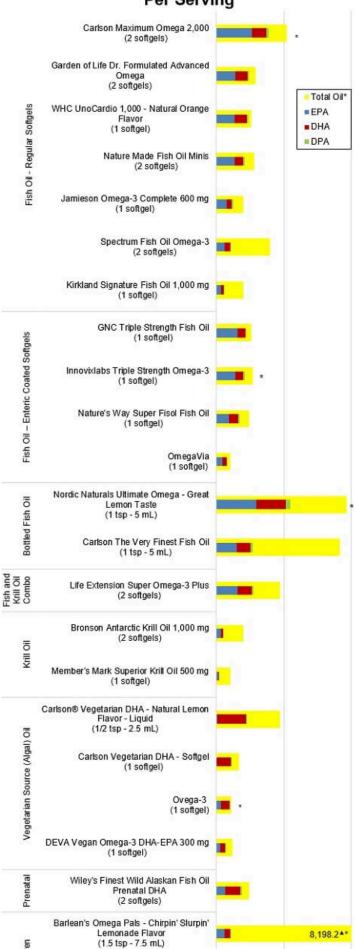
Although no other products failed for being rancid, be aware that, due to chemical interference with colored compounds (such as astaxanthin in krill) and certain flavorings (such as lemon), some products with these features could not be reliably analyzed for oxidation. They are marked "NA" for "Freshness" in the 3rd column in the results table below or with a "Partial Pass" if peroxide level was below 10 mEq/kg.

Range of EPA + DHA Concentrations and Pill Sizes

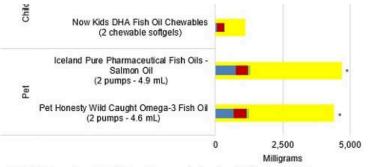
As depicted in the bar graph below (and in more detail in the Results table), amounts of omega-3 fatty acids (EPA, DHA, as well as DPA) found per serving ranged from as much as 2,946.8 mg in a teaspoon of Nordic Naturals Ultimate Omega (due to highly concentrated fish oil and a relatively large dose) down just 116.6 mg in a softgel of Member's Mark [Sam's Club] Extra Strength Krill Oil (due to the naturally low concentration of omega-3s in krill oil and a small dose — about 0.5 g per softgel).

The bar graph also shows that some supplements are more highly concentrated in EPA and DHA than others, i.e., they contain a higher ratio of EPA (blue bar) and DHA (red bar) to total oil (the encompassing yellow bar). Concentration depends on the source of the omega-3s, how the oil is processed, and the amounts of other oils included in the supplement. A more concentrated product allows you to consume a smaller amount of oil (e.g., fewer or smaller pills) to get the same amount omega-3s as you would get from a larger amount of less concentrated oil. This is also why *it's important to look at the amount of omega-3s, and not just the total amount of fish oil*, in a supplement. An example of an extremely concentrated product is *WHC UnoCardio 1,000*, while *Ovega-3* has a low concentration.

Omega-3s Found In Supplements Per Serving







^{*} Total oil for most products is based on amount of marine oil listed on label. If marked with an asterisk, amount is based on listed voume of oil in liquid product multiplied by density of the liquid or, for softgels, the weight of softgel contents.

▲ Exceeds scale of graph.

As a guide to how concentrated a product is, we applied the following scale based on amounts of EPA and DHA found in the listed amount of fish oil or other marine oil. The concentration of each is noted in the 4th column of the Results table. If a product did not list the total amount of marine or algal oil, we used the claimed amount of fat or, if that was not listed, the measured weight of its contents.

Relative Concentrations of EPA + DHA in Tested Products:

- Extremely high: 80% to 90% (Note: This is the concentration of the prescription medications Lovaza and Epanova.)

- Very high: 65% to 79%

- High: 45% to 64%

- Moderate: 24% to 44%

- Low: 17% to 23% - Very low: 8% to 16%

When Size Matters

If you have trouble swallowing large softgels, the 4th column of the <u>Results table</u> also includes descriptions of the pill size. As some softgels are more narrow than others, and this can make swallowing a bit easier, we've also indicated which are "narrow" (i.e., a width/length ratio <0.37). Most of the supplements were softgels and ranged from just under one-half inch to over one inch in length. These are fairly large sizes compared to capsules of other types of supplements. The tested softgels are grouped by length as follows:

Softgel Sizes by Length: (Oblong shape unless noted otherwise)

- Very large: over 25.4 mm (> 1 inch)

- Large: up to 25.4 mm (1 inch)

- Medium/Large: up to 19 mm (3/4 inch)

- Medium: up to 12.7 mm (1/2 inch)

Cost

To help you compare the cost of products and determine those that offer the best value, the graph below (and 5th column of the Results table) shows the cost to obtain 500 mg of EPA and DHA from each product based on the price we paid. After all, it's not how much "oil" that matters, but how much actual EPA and DHA you get.

Interestingly, the two products with the lowest cost to obtain 500 mg of EPA and DHA are very different. The lowest cost (8 cents) was from *Kirkland Signature Fish Oil 1,000 mg* due to its low price (\$16.99 for 400 softgels) despite its low concentration, while this cost was only one cent higher from *Innovix Triple Strength Omega-3* due to its very high concentration despite its higher price (\$30.99 for 200 enteric-coated softgels).

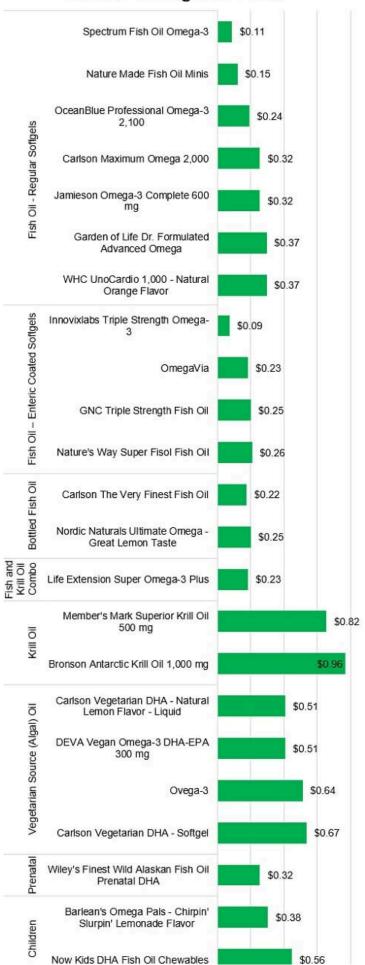
The highest cost to get 500 mg of EPA and DHA among fish oil softgels and bottled oils was 37 cents from both WHC UnoCardio 1,000 (\$49.95 for 60 softgels) and Garden of Life Dr. Formulated Advanced Omega, and both products are extremely highly concentrated.

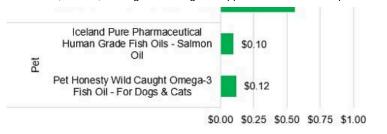
Krill oils tend to be more expensive sources of EPA and DHA than fish oils as they naturally have lower concentrations of these, explaining why the cost to obtain 500 mg of EPA and DHA from them ranged from 82 cents from *Member's Mark Superior Krill Oil* to 96 cents from *Bronson Antarctic Krill Oil*.

Products with additional ingredients and/or special formulations, such as the chewables in *NOW Kids DHA Fish Oil Chewables*, tend to cost more.

Keep in mind that prices can vary across merchants and your cost per serving will depend on how large a dose of EPA and DHA you choose to take -- which can range from as little as about 25 mg to more than 5,000 mg per day (see <u>Dosage</u> information).

Cost Per 500 mg EPA + DHA*





Top Picks:

Below are our *Top Picks* for omega-3 marine oils that were Approved for their quality in our tests and provide superior value within their respective categories.

In addition to focusing on products shown to deliver what they promise, be aware that our selections include a preference for products that were:

- 1. In the triglyceride form (as it may allow better absorption than the ethyl ester form)
- 2. Not enteric-coated, due to the theoretical possibility that enteric coatings may delay normal release and absorption of the oils although the coating may also reduce fishy burps
- 3. Narrower in shape, for ease of swallowing
- 4. Able to be accurately tested for freshness without interference from flavors or colors (although the presence of flavors or colors is not necessarily a problem)
- 5. Lowest in cost for obtaining omega-3s within its category

Softgels

Fish oil in softgels is generally the least expensive way to get good-quality EPA and DHA. If you just want to be sure you're getting a decent amount of EPA and DHA (perhaps because you don't eat fish) such as 250 mg to 499 mg, you can choose a product with a moderate or high concentration. If you need larger amounts, such as 500 mg to 1,000 mg, or even as much as 3,000 mg to 4,000 mg (perhaps to lower triglyceride levels — although beware of an <u>increased risk of atrial fibrillation</u>), consider products with very or extremely high concentrations to avoid getting too much fish oil (which can have a blood-thinning effect).

If you want to reduce the chance of fishy burps after taking fish oil, choose a capsule or softgel that is **enteric-coated**, which is designed to release the oil in the small intestine rather than in the stomach. However, it's theoretically possible that this could somewhat decrease absorption of omega-3s if it reduces the time during which omega-3s mix in the small intestine with bile acids which cause the oil to be emulsified (broken into smaller droplets), making absorption easier. So, if fish burps are not a problem for you, you may be better off choosing a product that is not enteric-coated.

- Low concentration: If cost is more of an issue than the size and number of pills you take, our *Top Pick* is *Kirkland*Signature [Costco] Fish Oil 1000 mg, which promises 250 mg of EPA plus DHA per softgel (we found a bit more 270.9 mg) per 1,000 mg of fish oil, i.e., a "low concentration" or actually not concentrated. The cost is only 4 cents per softgel (\$16.99 for 400 softgels), making it, by far, the lowest cost product. In addition, although not stated on the label, its omega-3s appear to be in the triglyceride form and it is not enteric-coated, so you're likely to get the best absorption. Be aware that the softgels are very large, but are narrow to make swallowing a bit easier.
- Moderate concentration: For even easier swallowing and only slightly higher cost, consider *Spectrum Fish Oil Omega-3* which provides about the same amount of EPA and DHA per softgel as *Kirkland* but the softgels are somewhat smaller because the oil is somewhat more concentrated. It also seems to be in the triglyceride form. The cost per softgel is 11 cents (\$27.99 for 250 softgels).

(Spectrum, as well as Kirkland, also provides about 100 mg of omega-7 fatty acids, which you typically won't get from higher concentration products, although the clinical value of this is not clear.)

- Very/Extremely high concentration: If you want a very or extremely concentrated fish oil, allowing you to get the most omega-3s with the least amount of total oil and pills, our *Top Pick* is *Carlson Maximum Omega 2,000*, which promises 875 mg of EPA and DHA in the triglyceride form (and we found somewhat more) in each softgel — although the softgels are very large. Each softgel costs 59 cents (\$52.87 for 90 softgels). If you want the highest concentration of omega-3s and the highest dose of these in a single softgel, *WHC Unocardio 1000* provided 1,226.5 mg of EPA and DHA per softgel for 83 cents - its concentration of omega-3s is similar to that of prescription fish oils. If you prefer a somewhat smaller, enteric-coated softgel, you can get 1,040 mg of EPA and DHA in the triglyceride form *OmegaVia* for 50 cents per softgel (\$29.85 for 60 softgels).

Fish Oil Supplements Comparable to Prescription Omega-3s

Very and extremely highly concentrated omega-3s are not only sold as supplements, but some versions are <u>approved as drugs</u> for lowering elevated triglycerides. As shown in the table below, supplements can provide approximately the same omega-3s as prescription drugs at a lower cost than the branded drugs — although the cost of generic versions of these drugs is roughly similar to the cost of supplements — and, sometimes better. Note, however, that prescription drugs are held to higher standards than fish oil dietary supplements, including the clinical demonstration of safety and efficacy and more rigorous manufacturing standards and oversight. This should be considered when comparing products.

Attention has focused on the EPA-only drug **Vascepa** (icosapent ethyl), as it was shown to <u>reduce the risk of cardiovascular disease</u> in people with elevated levels of triglycerides. Vascepa claims to be 96% EPA, providing 960 mg of EPA per capsule; two of these are taken twice daily with meals. The cash price for each capsule is about \$2.27, or \$9.10 per day, although a generic version can be purchased for just 71 cents per capsule, or \$2.84 per day.

You can get similar amounts of EPA in a single large softgel of *Carlson Elite EPA GEMS* (tested in CL in 2020) as in Vascepa. *Carlson's* softgels provide 1,000 mg of EPA and 16.5 mg of DHA, which appear to be in the ethyl ester form, like Vascepa. The cost per capsule of *Carlson* is 75 cents, which is just slightly *more* than the cost per capsule (71 cents) of the generic equivalent of Vascepa. Like Vascepa, Carlson's capsule is not enteric-coated.

If you are looking for a fish oil supplement similar to prescription **Lovaza** (465 mg EPA and 375 mg DHA in the ethyl ester form), **Solgar Triple Strength Omega 3 950 mg** (tested by CL in 2018) provides a bit more – 504 mg of EPA and 378 mg DHA per large softgel – for \$1.16 per day, making it less expensive than even the generic form of Lovaza costing \$2.08 per day (and, like Lovaza, is in the ethyl ester form). Spring Valley [Walmart] *Maximum Care Omega-3 2000 mg* provides even more EPA and almost as much DHA but at the very low cost of just 14 cents per softgel, which, as shown in the table below, is a fraction of the cost of the generic version of Lovaza.

Comparison of Omega-3 Prescription Drugs to Very or Extremely Concentrated Supplements Approved by ConsumerLab.com

| Product | EPA and DHA Per 1 Capsule or Softgel | Cost Per Capsule or Softgel ¹ | Rx Dose and Comparable Dose ² | EPA and DHA Per Day | Cost Per Day | Chemical Form/Other |
|-----------------------------|---|--|---|-------------------------------|--------------------------------|---------------------------|
| Vascepa (Rx) | EPA: 960 mg DHA: <40 mg (High EPA) | \$2.27 (Generic: \$0.71 ³) | 4 capsules | EPA: 3,840 mg DHA: <160 mg | \$9.10 (Generic: \$2.84) | Ethyl ester |
| Carlson Elite EPA Gems** | EPA: 1,000 mg DHA: 16.5 mg (High EPA) | \$0.75 | 4 softgels | EPA: 4,000 mg DHA: 66 mg | \$3.00 | Appears to be ethyl ester |

| Lovaza (Rx) | EPA: 465 mg DHA: 375 mg (EPA/DHA) | \$7.14 (Generic: \$0.52 ³) | 4 capsules | EPA: 1,860 mg DHA: 1,500 mg | \$28.56 (Generic: \$2.08) | Ethyl ester |
|---|---|--|------------|--------------------------------|---------------------------------|--------------|
| Solgar Triple Strength Omega 3 950 mg* | EPA: 504 mg DHA: 378 mg (EPA/DHA) | \$0.29 | 4 softgels | EPA: 2,016 mg DPA: 1,512 mg | \$1.16 | Ethyl ester |
| Spring Valley Maximum Care Omega-3 2000 mg* | EPA: 645 mg DHA: 310 mg (Mostly EPA) | \$0.14 | 4 softgels | EPA: 2,580 mg DHA: 1,240 mg | \$0.56 | Ethyl ester |
| Carlson Maximum Omega 2000*** | EPA: 625 mg DHA: 250 mg (EPA/DHA) | \$0.59 | 4 capsules | EPA: 2,500 mg DHA: 1,000 mg | \$2.36 | Triglyceride |
| Garden of Life Dr. Formulated Advanced Omega*** | EPA: 347.5 mg DHA: 232.5 mg (EPA/DHA) | \$0.43 | 6 capsules | EPA: 2,085 mg DHA: 1,395 mg | \$2.58 | Triglyceride |
| WHC UnoCardio 1,000*** | EPA: 665 mg DHA: 445 mg (EPA/DHA) | \$0.83 | 3 capsules | EPA: 1,995 mg DHA: 1,335 mg | \$2.50 | Triglyceride |

Excludes enteric-coated supplements. Amounts of omega-3s in supplements based on those listed on label.

- * Tested by ConsumerLab in 2018 or 2019.
- ** Tested by ConsumerLab in 2020.
- ***Tested by ConsumerLab in 2023.
- 1 Prices are from 2023 and may vary over time.
- 2 Comparable doses from supplements were calculated by ConsumerLab to provide amounts of EPA and DHA comparable to those from prescription drugs; they are typically greater than the suggested serving sizes indicated on the supplements. 3 Price on GoodRx.com with discount coupon.

Bottled Fish Oil (Liquid)

Bottled fish oil is a good option if you don't like to swallow softgels or need a large dose and don't want to have to take multiple softgels. A teaspoon of oil is about 5 grams, or roughly the amount in about 5 softgels. You can also more easily adjust dosage oil from a bottle.

Our overall *Top Pick* for liquids is *Carlson The Very Finest Fish Oil*. This is a moderately concentrated fish oil. The clear, pale-yellow oil has a light lemony flavor and is not "fishy" tasting. One teaspoon promises 1,300 mg of EPA and DHA (we found slightly less, but well within acceptable margin of error) and costs 56 cents (\$22.53 for 6.7 fl oz or 200 mL). If this is more omega-3 than you want per serving, you can easily reduce the serving size. We found one teaspoon to also provide 466.8 mg of omega-7 fatty acids.

The other bottled fish oil that we tested was *Nordic Naturals Ultimate Omega*. It is also lemony, but has a slight anchovy flavor. It is a higher-concentration fish oil, promising a whopping 2,560 mg of EPA and DHA per teaspoon (we found slightly more) but was also more expensive at \$1.29 per teaspoon. As it is more concentrated in omega-3s than *Carlson*, it has a lower amount of omega-7s (142 mg per teaspoon).

The oil in both bottled products appears to be in the triglyceride form, although this is not claimed. *Carlson* has a spout, which makes pouring a bit easier, while *Nordic* does not.

Be sure to keep liquid fish oils refrigerated as they begin to spoil once opened, and shake the bottle before each use.

Krill Oil

Krill oil is generally the most expensive source of omega-3 fatty acids. Our *Top Pick* for krill oil is *Member's Mark* [Sam's Club] *Extra Strength Krill Oil*. One of these medium/large softgels promises 94 mg of EPA and DHA (we found somewhat less) for 15 cents (\$23.48 for 160 softgels). In terms of getting omega-3s from krill oil, *Member's Mark* was somewhat less expensive than *Bronson Antarctic Krill Oil 1000 mg*. *Member's Mark* is less than half the cost of the krill oils tested in 2020 -- *Kori Pure Antarctic Krill Oil* and *Viva Naturals Antarctic Krill Oil*. *Member's Mark* is essentially identical in its ingredients and quality to *Schiff MegaRed* and *CVS Health Extra Strength 100% Pure Omega-3 Krill Oil*, both of which were tested and Approved by CL in 2018 but were slightly more expensive than *Member's Mark*.

There is concern about krill being overharvested from oceans. While some may choose to avoid krill oil for this reason, if you choose to use krill oil it may be best to choose a product, like *Member's Mark* krill oil, that has the <u>Marine Stewardship Council (MSC) Certified</u>

<u>Sustainable Seafood seal</u>. *Bronson* krill oil does not have the MSC seal.

ConsumerLab.com also tested the amounts of phospholipids in these products, as phospholipids naturally occur with krill oil and appear to enhance absorption of EPA and DHA. Both products had somewhat more than their expected amounts of phospholipids. These krill oil products provide small amounts of choline because 65% to 69% of the phospholipids were phosphatidylcholine, of which 13.7% is **choline**. So, per serving, *Member's Mark* provided about 19 mg of choline and *Bronson* provided about 21.5 mg.

All krill products also claim amounts of <u>astaxanthin</u>, an antioxidant pigment that occurs in krill. *Member's Mark* and *Bronson* were found to contain, respectively, 226.7 mcg and 255 mcg of astaxanthin per softgel — both somewhat above their listed amounts. *Life Extension Super Omega-3 Plus*, which is a combination of fish and krill oils, actually had much more astaxanthin (we found over 1,000 mg per softgel), although this astaxanthin is added and not only from its krill oil.

Algal Oil

Algal oil is a good source of omega-3s — particularly DHA — and is assumed to be in the triglyceride form, which is likely good for absorption. CL's *Top Pick* is *Deva Vegan Omega-3 DHA-EPA*, in which we found 122.7 mg of EPA and 195.6 mg of DHA per softgel — both within the listed ranges claimed on its label. A softgel of *Deva* costs 32 cents and provided omega-3s at a slightly lower cost than the other algal oil that we tested, *Ovega-3*. If you want even more DHA and less EPA, you can get it from *Carlson Vegetarian DHA — Softgel*, which promises 500 mg of DHA and just 3.4 mg of EPA per softgel, although the these are expensive (71 cents per softgel).

Be aware that in 2020 we tested *Freshfield Vegan Omega-3 EPA + DPA* but it was not Approved because it was inaccurately labeled, claiming 500 mg of total omega-3s but providing only 46.8% of that amount.

Prenatal

Prenatal supplements tend to have much higher DHA content than EPA due to DHA's role in brain development. However, supplements with DHA have not been shown to provide cognitive benefits to offspring, although they may reduce the risk of preterm birth (see What It Does: During Pregnancy above). Also be aware that some research suggests that getting omega-3s from supplements during late pregnancy may increase the risk of post-partum hemorrhage — see Concerns and Cautions).

Unfortunately, the prenatal DHA supplement that we tested, Wiley's Finest Wild Alaskan Fish Oil Prenatal DHA, failed for being rancid, as noted earlier. Our previous Top Pick in this category from 2020 was Whole Foods Market Prenatal DHA but it no longer seems to be available.

If you want DHA and with less EPA, consider the children's supplement (see below), Now Kids DHA Fish Oil Chewables. Also, consider one of the algal oils above.

(You can find ConsumerLab.com's tests of prenatal multivitamins in the Multivitamin Review).

Children's

Children's supplements with fish oil, such as liquids, chewables, and gummies, tend to sell at premium prices because of their special, child-oriented formulations. This holds true for our *Top Pick* for children's supplements is *Barlean's Omega Pals — Chirpin' Slurpin'*Lemonade Flavor, which costs 38 cents per 1 ½ teaspoon serving. It is a slightly thick liquid that has a pleasant, somewhat sweet, lemony flavor that does a good job hiding the taste of fish oil. The suggested serving promises 330 mg of EPA and 210 mg of DHA — we found somewhat less but within an acceptable margin. *Barlean's Omega Pals* can be given to children 1 year and older.

We also liked *Now Kids DHA Fish Oil Chewables*. It promises mostly DHA (200 mg) and a small amount of EPA (48 mg) — we found a bit more of each. It's about the same cost per serving as *Barlean's* at 35 cents for 2 chewables, although it provides a lower dose of omega-3s. Its soft, fish-shaped softgels release a mildly sweet, non-fishy tasting liquid when chewed. It's a good option for women looking primarily for DHA as a prenatal supplement, although one might want to take a larger dose.

For Dogs and Cats

Pet supplements with omega-3s need to be chosen with particular care, as CL's tests have found many problems over the years. In 2016, *Amazing Nutritionals Omega 3 Chews* contained only tiny amounts of omega-3s -- even less than listed on the label. In 2020, *Doctor's Foster + Smith Premium Plus Omega-3 For Dogs* was found to contain only 51% of its listed EPA and 44.2% of its listed DHA. And this year, *Iceland Pure Pharmaceutical Human Grade Fish Oils — Salmon Oil* was found to be rancid, as noted earlier.

Our *Top Pick* for dogs as well as cats is *Pet Honesty Wild Caught Omega-3 Fish Oil — For Dogs & Cats*, which comes in a squeezable, pour-top bottle that, like all fish oil liquids, should be refrigerated after opening. It also comes with an alternative, pump top, with each pump providing 582 mg of EPA and DHA — this is a bit less than the 663 mg expected from the label, but within an acceptable margin for a natural product. The oil can be applied directly to pet food and costs just 14 cents per pump (\$28.99 for 16 fl oz or 473 mL).

DPA the "other" omega-3 in fish oil

The omega-3 <u>DPA</u> (as discussed elsewhere) may have some cardiovascular benefit. Amounts of DPA that we found per serving of each product are shown in the 2nd column of the Results table below. The highest amount of DPA per serving (177.7 mg per teaspoon) was in highly concentrated *Nordic Naturals Ultimate Omega* and it is our *Top Pick* for DPA, although the cost per serving (which includes large amounts of EPA and DHA) is \$1.29.

Omega-7

Omega-7 fatty acids are best obtained from fish oil that is not highly concentrated for omega-3s (because omega-7s are removed to increase the concentration of omega-3s) or from the plant sea buckthorn. One of the most commonly occurring omega-7s is palmitoleic acid. Although sometimes promoted for improving insulin sensitivity and lipid levels and having other benefits, there is no good clinical research to back this up. The product that provided by far the greatest amount of omega-7s (466.8 mg per teaspoon for 56 cents, and including large amounts of EPA and DHA) was *Carlson The Very Finest Fish Oil*, making our *Top Pick* for Omega-7s. It is also our *Top Pick* for bottled fish oil, as noted earlier.

Although not tested in this Review, in 2018 we tested one sea buckthorn product — *New Chapter Sea Buckthorn Force*, which passed our testing. It contained its listed 100 mg of omega-7s per vegetarian capsule and 77.9% of this was palmitoleic acid. However, the cost to obtain omega-7 from this product was significantly higher than from two omega-7 products CL tested two years earlier, which were *SeabuckWonders Sea Buckthorn Oil Blend Omega-7 Complete* (155 mg of omega-7s along with a range of other omega-3, -6, and -9 oils from seed oils in a softgel and *Doctor's Best Omega-7* (roughly 200 mg of omega-7s per softgel).

Other Marine Oils

Green-lipped mussel oil has been promoted for containing "omega" fatty acids. Although not included in this year's testing, be aware that *Omega XL*, a proprietary blend that includes "green lipped mussel oil extract," was neither "Approved" nor "Not Approved" by ConsumerLab.com when tested in 2016 because it did not claim to contain a specific amount of omega-3 fatty acids: its label simply indicated that it contained "30 free fatty acids including EPA, DHA, ETA and OTA." Each softgel, listed as containing 300 mg of a proprietary blend, was found to contain just 5.8 mg of EPA and 5.0 mg of DHA. The only substantial amount of omega fatty acids found were omega-9s (76 mg per capsule) nearly all of which was oleic acid, which may, at least in part, come from the "Extra Virgin Olive Oil" listed as an ingredient after "Green Lipped Mussel Oil Extract (PCSO-524®) containing Omega Fatty Acids" and before the only other listed ingredient "d-alpha Tocopherol (Vitamin E)." Many of the fish oil supplements provide a comparable amount of omega-9s per capsule (results not shown). It is somewhat surprising that a product named *Omega XL* provides relatively small amounts of omega fatty acids and a chemical profile similar to olive oil. The formulation in this product appears to be that of Lyprinol®, which is listed as containing 50 mg of PCSO-524, 100 mg of mono-unsaturated olive oil, and 0.225 mg of vitamin E. (Also see the information about *Omega XL* in the What It Does section.) The product was also fairly expensive — \$2 per 2 softgel serving.

Calamari oil — Although not included in this year's testing, in 2018 we tested one calamari (squid) oil product: *Dr. Sinatra Omega Q Plus*, which passed testing. A two softgel serving provided 200 mg of EPA and 350 mg of DHA and cost \$1.43 — making it a relatively expensive way to get omega-3 fatty acids, although it included vitamins B6 & B12, L-carnitine, and relatively modest amounts of CoQ10

and trans resveratrol. Be aware that the amounts of <u>B6 and B12</u> in this product were much higher than one needs unless significantly deficient in those vitamins.

Test Results by Product:

Listed alphabetically below are the test results for 26 supplements containing omega-3 fatty acids (including two for pets). Fourteen of these were selected by ConsumerLab.com for review. Twelve others (each indicated with a CL flask icon) were tested at the request of their manufacturers/distributors through CL's Quality Certification Program and are included for having passed testing.

The full list of ingredients is shown for each product in the last column on the right. All "Approved" products met their label claims for omega-3s, quality standards regarding lead, cadmium, arsenic, and mercury, were not rancid (if they could be reliably tested), and, if labeled as "enteric coated," passed disintegration testing.

| | Results of (| | • | of Omega-3 Ma | arine Oil Supplen | nents |
|------------------------------|--|---|---|--|---|--------------------------------------|
| Approval Status Product Name | Omega-3 Fatty Acids Per Serving Astaxanthin & Phospholipids (Krill only) | Freshness Heavy Metals Suggested Serving on Label | Unit Size Concentration of EPA + DHA Chemical Form Storage | Cost Per Suggested Serving [Cost Per 500 mg EPA + DHA Found] Price | Notable Features and Precautions on Label | Full List of Ingredients Per Serving |
| Fish Oil - Regular Softge | ıls: | | 1 | 1 | 1 | |

| 1/25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algai Oil Omega | a-3 Supplements Rev | iew & Top Picks - Cons | umerLab.com |
|--|------------------------|-------------------------|-------------------|---------------------|------------------------|---------------------------|
| 2 | 2 softgels | Freshness: Pass | Very large | \$1.17/2 softgels | IFOS seal. Igen® | 2 softgels |
| APPROVED | | Peroxide: 1 | softgel | | Non-GMO Tested | |
| K | EPA: 1,250 mg | meq/kg | | [\$0.32] | seal. Gluten-free. | Calories 30, Total Fat |
| 3 | [found: 1,314.5 | Anisidine: 24.4 | Very high | | No Artificial | 2.5 g, Protein <1 g, |
| Top Pick | mg √] | TOTOX: 26.4 | concentration | \$52.87/90 | Preservatives. It | Norwegian Fish Oil |
| K | DHA: 500 mg | (Natural lemon | | softgels | has been | Concentrate [Total |
| for | [found: 547.2 | flavor) | Triglyceride | | determined to be | Omega-3 Fatty Acids |
| very/extremely | mg √] | | | | fresh and potent | [EPA (Eicosapentaenoic |
| high | DPA: 76.6 mg | Heavy Metals: | | | (per AOCS | Acid) 1,250 mg, DHA |
| concentration | Total Omega- | <u>Pass</u> | | | international | (Docosahexaenoic Acid) |
| Carlson® | 3 : 2,000 mg | Lead: 0.002 | | | protocols) and is | 500 mg] 2,000 mg] |
| Maximum | [found: 2,150.2 | mcg/day (0.005 | | | free of detrimental | 2,600 mg. |
| Omega 2,000 🗥 * | mg √] | mcg/g) | | | levels of mercury, | |
| | Total Omega- | Cadmium: <0.01 | | | cadmium, lead, | Other Ingredients: Soft |
| Carlson. | 7: 9.4 mg | mcg/g | | | PCBs and 28 other | gel shell (beef gelatin, |
| Maximum Omega 2000 | (42.9% | Arsenic: <0.01 | | | contaminants. | glycerin, water), natural |
| Abbasis of transfer of the state of the stat | palmitoleic | mcg/g | | | | mixed tocopherols, d- |
| Dist. by Carlson | acid) | Mercury: <0.001 | | | Precaution: | alpha tocopherol, |
| Division of J.R. | | mcg/g | | | Contains fish | natural flavors. |
| Carlson | Total Oil: 2,600 | | | | (anchovy, sardine, | |
| Laboratories, | mg | Adults: Take two | | | and mackerel). | |
| Inc. | | soft gels daily at | | | | |
| | Complies with | mealtime. | | | | |
| | aspects of | | | | | |
| | GOED | | | | | |
| | monograph | | | | | |

| 21 | /25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algai Oil Omega | -3 Supplements Rev | iew & Top Picks - Consi | umerLab.com |
|----|------------------|----------------------|-------------------------|-------------------|--------------------|-------------------------|--------------------------|
| | 3 | 2 softgels | Freshness: Partial | Medium/large | \$0.85/2 softgels | MSC seal. Non | 2 softgels |
| | APPROVED | | <u>Pass</u> | softgel | | GMO Project | |
| | K | EPA: 695 mg | Peroxide: 2.4 | | [\$0.37] | Verified seal. NSF® | Calories 15, Total Fat |
| | Garden of Life® | [found: 700.4 | meq/kg | Extremely | | Contents Certified | 1.5 g, Unsaturated Fat |
| | Dr. Formulated | mg √] | Anisidine: | high | \$25.59/60 | seal. Made without | 1.5 mg, |
| | Advanced | DHA: 465 mg | тотох: | concentration | softgels | dairy or soy | PureSeaOmega3™ MSC |
| | Omega 🕰 " | [found: 463.9 | (Citrus flavor) | | | ingredients, peanut | CoC-Grade Fish Oil with |
| | | mg √] | | Triglyceride | | or shellfish. | naturally occurring |
| | | DPA: 30 mg | Heavy Metals: | | | | SPMs, including |
| | Advanced Omega | [found: 49.1 | <u>Pass</u> | | | Precaution: | Resolvins & Protectins |
| | 1-33 or EPA COLO | mg √] | Lead: 0.002 | | | Contains: Fish. | [Total Omega-3s |
| | Dist. by Garden | Total Omega- | mcg/day (0.005 | | | Manufactured in a | (Triglyceride Form) [EPA |
| | of Life LLC | 3 : 1,290 mg | mcg/g) | | | facility that also | (Eicosapentaenoic Acid) |
| | | [found: 1,236.7 | Cadmium: <0.01 | | | processes milk, | 695 mg, DHA |
| | | mg √] | mcg/g | | | egg, fish, | (Docosahexaenoic Acid) |
| | | Total Omega- | Arsenic: <0.01 | | | crustacean | 465 mg, DPA (Total |
| | | 7: 4.5 mg | mcg/g | | | shellfish, tree nuts, | Docosapentaenoic |
| | | (53.7% | Mercury: <0.001 | | | wheat and | Acid) 30 mg] 1,290 mg] |
| | | palmitoleic | mcg/g | | | soybeans. | 1,450 mg |
| | | acid) | | | | | Additional |
| | | | Adults take 2 | | | | Information |
| | | Total Oil: 1,450 | softgels daily with | | | | |
| | | mg | food. No intended | | | | 2 softgels |
| | | | for children. | | | | |
| | | | | | | | Calories 15, Total Fat |
| | | | | | | | 1.5 g, Unsaturated Fat |
| | | | | | | | 1.5 mg, |
| | | | | | | | PureSea0mega3™ |
| | | | | | | | MSC CoC-Grade Fish |
| | | | | | | | Oil with naturally |
| | | | | | | | occurring SPMs, |
| | | | | | | | including Resolvins & |
| | | | | | | | Protectins [Total |
| | | | | | | | Omega-3s |
| | | | | | | | (Triglyceride Form) |
| | | | | | | | [EPA |
| | | | | | | | (Eicosapentaenoic |
| | | | | | | | Acid) 695 mg, DHA |
| | | | | | | | (Docosahexaenoic |
| | | | | | | | Acid) 465 mg, DPA |
| | | | | | | | (Total |
| | | | | | | | Docosapentaenoic |
| | | | | | | | Acid) 30 mg] 1,290 |
| | | | | | | | mg] 1,450 mg. |
| | | | | | | | Ingredients: |
| | | | | | | | |

| 8/2 | 8/21/25, 9:54 AM Fish Oil, Krill Oil, and Algal Oil Omega-3 Supplements Review & Top Picks - ConsumerL | | | | | | ımerLab.com | |
|-----|--|--|--|--|--|--|-----------------------|---|
| | | | | | | | PureSea0mega3™ | ı |
| | | | | | | | Mercury-Free Tuna Oil | |
| | | | | | | | (Thunnus spp.), Non- | |
| | | | | | | | GMO PlantGel™ | |
| | | | | | | | Softgel, Non-GMO | |
| | | | | | | | Flavor, Non-GMO | |
| | | | | | | | Rosemary Extract. | |

| 2′ | 1/25, 9:54 AM | 25, 9:54 AM Fish Oil, Krill Oil, and Algal Oil Omega-3 Supplements Review & Top Picks - ConsumerLab.com | | | | | | | | |
|----|---|---|-------------------|---------------|----------------|----------------------|--------------------------|--|--|--|
| | 3 | 1 softgel | Freshness: Fail | Very large | \$0.36/softgel | No starch, gluten, | 1 softgel | | | |
| | <i>NOT</i> APPROVED | | Peroxide: 48 | (narrow) | | lactose, artificial | | | | |
| | ĸ | EPA: 400 mg | meq/kg | softgel | [\$0.32] | colours, flavours or | Molecularly distilled | | | |
| | Jamieson™ | [found: 375.5 | Anisidine: 13.9 | | | preservatives. | Fish Oil (Anchovy, Tuna) | | | |
| | Omega-3 | mg √] | TOTOX: 109.9 | High | \$28.95/80 | | [Providing 600 mg of | | | |
| | Complete 600 | DHA: 200 mg | | concentration | softgels | | omega-3 fatty acids: | | | |
| | mg | [found: 196 mg | Heavy Metals: | | | | Eicosapentaenoic Acid | | | |
| | | ✓] | <u>Pass</u> | Ethyl ester | | | EE (EPA) 400 mg, | | | |
| | Jamieson: | DPA : 50.4 mg | Lead: 0.001 mcg | | | | Docosahexaenoic Acid | | | |
| | Omega-3 | Total Omega- | to 0.003 mcg/day | Store between | | | EE (DHA) 200 mg] 1,000 | | | |
| | 80 Noige reduce doubt-devial among promote heart health | 3: 600 mg | (0.001 mcg/g) | 15°C and | | | mg. | | | |
| | Dist. by | [found: 665.9 | Cadmium: <0.01 | 25°C. | | | | | | |
| | Jamieson | mg √] | mcg/g | | | | Also contain: Gelatin | | | |
| | Laboratories | Total Omega- | Arsenic: <0.01 | | | | (bovine), glycerin. | | | |
| | | 7: 32.2 mg | mcg/g | | | | | | | |
| | | (16.7% | Mercury: <0.001 | | | | | | | |
| | | palmitoleic | mcg/g | | | | | | | |
| | | acid) | | | | | | | | |
| | | | Take 1 softgel to | | | | | | | |
| | | Total Oil: 1,000 | support | | | | | | | |
| | | mg | cardiovascular | | | | | | | |
| | | | and cognitive | | | | | | | |
| | | | health | | | | | | | |
| | | | Additional | | | | | | | |
| | | | Information | | | | | | | |
| | | | Freshness: Fail | | | | | | | |
| | | | Peroxide: 48 | | | | | | | |
| | | | meq/kg | | | | | | | |
| | | | Anisidine: 13.9 | | | | | | | |
| | | | TOTOX: 109.9 | | | | | | | |
| | | | Heavy Metals: | | | | | | | |
| | | | <u>Pass</u> | | | | | | | |
| | | | Lead: 0.001 | | | | | | | |
| | | | mcg to 0.003 | | | | | | | |
| | | | mcg/day (0.001 | | | | | | | |
| | | | mcg/g) | | | | | | | |
| | | | Cadmium: <0.01 | | | | | | | |
| | | | mcg/g | | | | | | | |
| | | | Arsenic: <0.01 | | | | | | | |
| | | | mcg/g | | | | | | | |
| | | | Mercury: <0.001 | | | | | | | |
| | | | mcg/g | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

| 21/25, 9:54 AM | | Fish Oii, Kriii Oii, an | d Algai Oli Omega | -3 Supplements Rev | riew & Top Picks - Cons | umerLab.com |
|--|---------------------|-------------------------|-------------------|--------------------|-------------------------|--------------------------|
| | | Take 1 softgel | | | | |
| | | to support | | | | |
| | | cardiovascular | | | | |
| | | and cognitive | | | | |
| | | health. Take 3 | | | | |
| | | softgels daily to | | | | |
| | | help reduce | | | | |
| | | serum | | | | |
| | | triglycerols/ | | | | |
| | | triglycerides | | | | |
| | | and support | | | | |
| | | healthy mood | | | | |
| | | balance. | | | | |
| 2 | 1 softgel | Freshness: Pass | Very large | \$0.04/softgel | USP Dietary | 1 softgel |
| APPROVED | | Peroxide: 4 | (narrow) | | Supplement | |
| E | EPA + DHA: | meq/kg | softgel | [\$0.08] | Verified® seal. No | Calories 10, Total Fat 1 |
| 2 | 250 mg [found: | Anisidine: 6.4 | | | Artificial Colors. No | g, Cholesterol 10 mg, |
| Top Pick | 151.8 mg EPA | TOTOX: 14.4 | Low | \$16.99/400 | Artificial Flavors. | Fish [Omega-3 Fatty |
| K | and 119.1 mg | | concentration | softgels | No Yeast or Gluten. | Acids (EPA+DHA) 250 |
| for low | DHA √] | Heavy Metals: | | | | mg, Other Omega-3 |
| concentration | DPA: 16.7 mg | <u>Pass</u> | Form not | | Fish Oil Country of | Fatty Acids 50 mg] |
| Kirkland | Total Omega- | Lead: <0.001 | listed, but | | Origin: Peru. | 1,000 mg. |
| Signature | 3: 300 mg | mcg/g | appears to be | | | |
| [Costco] Fish Oil | [found: 336.1 | Cadmium: <0.01 | triglyceride | | Precaution: | Ingredients: Fish Oil, |
| 1,000 mg | mg √] | mcg/g | | | Contains: Fish | Gelatin (Porcine), |
| | Total Omega- | Arsenic: <0.01 | Store at room | | (Mackerel, | Glycerin, Water, |
| KIRKLAND | 7: 100.6 mg | mcg/g | temperature, | | Anchovy, | Tocopherols. |
| FISH OIL 1000 mg Prints 500 mg d Canage Farm penda | (73.9% | Mercury: <0.001 | tightly closed. | | Menhaden, | |
| 400 | palmitoleic | mcg/g | | | Herring, Sardine). | |
| Dist. by Costco | acid) | | | | | |
| Wholesale | | Take one (1) | | | | |
| Corporation | Total Oil: 1,000 | softgel two times | | | | |
| | mg | daily with a full | | | | |
| | | glass of water | | | | |
| | Complies with | preferably with a | | | | |
| | aspects of | meal. | | | | |
| | GOED | | | | | |
| | monograph | | | | | |

| 2 softgels | | | | | |
|----------------------|--|---|---|--|---|
| 2 dortgeto | Freshness: Pass | Large (narrow) | \$0.29/2 softgels | No Color Added. | 2 softgels |
| | Peroxide: 3.8 | softgel | | Gluten Free. No | |
| EPA: 680 mg | meq/kg | | [\$0.15] | Milk. No Shellfish. | Calories 15, Total Fat 1 |
| [found: 668.8 | Anisidine: 3.4 | Very high | | Purified to remove | g, Polyunsaturated Fat 1 |
| mg √] | TOTOX: 11 | concentration | \$8.61/60 | PCBs, dioxins and | g, Cholesterol 15 mg, |
| DHA: 250 mg | (Lemon scent) | | softgels | furans, and mercury | Omega Concentrate |
| [found: 319.9 | | Ethyl ester | | to ensure levels | from Fish Oil [Total |
| mg √] | Heavy Metals: | | | below 0.09 ppm, 2 | Omega-3 Fatty Acids |
| DPA: 56.9 mg | <u>Pass</u> | | | ppt WHO TEQs, and | [EPA (Eicosapentaenoic |
| Total Omega- | Lead: <0.001 | | | 0.1 ppm | Acid) Omega-3 600 mg, |
| 3 : 1,000 mg | mcg/g | | | respectively. | DHA (Docosahexaenoic |
| [found: 1,100 | Cadmium: <0.01 | | | | Acid) Omega-3 250 mg, |
| mg √] | mcg/g | | | Fish Oil Country of | Other Omega-3 70 mg] |
| Total Omega- | Arsenic: <0.01 | | | Origin: Norway or | 1,000 mg] 1,400 mg |
| 7: 13.7 mg | mcg/g | | | Canada or Chile. | Additional |
| (14.1% | Mercury: <0.001 | | | | Information |
| palmitoleic | mcg/g | | | | illioilliation |
| acid) | | | | | 2 softgels |
| | Adults, take 2 | | | | |
| Total Oil: 1,400 | softgels daily with | | | | Calories 15, Total Fat |
| mg | water and a meal | | | | 1 g, Polyunsaturated |
| | for optimal | | | | Fat 1 g, Cholesterol 15 |
| Complies with | absorption. | | | | mg, Omega |
| aspects of | | | | | Concentrate from Fish |
| GOED | | | | | Oil [Total Omega-3 |
| monograph | | | | | Fatty Acids [EPA |
| | | | | | (Eicosapentaenoic |
| | | | | | Acid) Omega-3 600 |
| | | | | | mg, DHA |
| | | | | | (Docosahexaenoic |
| | | | | | Acid) Omega-3 250 |
| | | | | | mg, Other Omega-3 |
| | | | | | 70 mg] 1,000 mg] |
| | | | | | 1,400 mg. |
| | | | | | Other Ingredients: |
| | | | | | Gelatin, Glycerin, |
| | | | | | Tocopherols. |
| | [found: 668.8 mg √] DHA: 250 mg [found: 319.9 mg √] DPA: 56.9 mg Total Omega- 3: 1,000 mg [found: 1,100 mg √] Total Omega- 7: 13.7 mg (14.1% palmitoleic acid) Total Oil: 1,400 mg Complies with aspects of GOED | [found: 668.8 meq/kg [found: 668.8 Anisidine: 3.4 mg √] TOTOX: 11 DHA: 250 mg [found: 319.9 mg √] Heavy Metals: DPA: 56.9 mg Total Omega- 3: 1,000 mg [found: 1,100 Cadmium: <0.01 mg √] mcg/g Total Omega- 7: 13.7 mg (14.1% Mercury: <0.001 palmitoleic acid) Adults, take 2 Total Oil: 1,400 mg Complies with aspects of GOED Merouv: 3.4 TOTOX: 11 (Lemon scent) Heavy Metals: Pass Lead: <0.001 mcg/g Admium: <0.01 mcg/g Arsenic: <0.01 mcg/g Adults, take 2 softgels daily with water and a meal for optimal absorption. | [found: 668.8 Anisidine: 3.4 Very high mg √] TOTOX: 11 concentration DHA: 250 mg (Lemon scent) [found: 319.9 Heavy Metals: DPA: 56.9 mg Total Omega- 3: 1,000 mg [found: 1,100 Cadmium: <0.01 mcg/g Total Omega- 7: 13.7 mg (14.1% Mercury: <0.001 mcg/g (14.1% Mercury: <0.001 mcg/g Codulits, take 2 Total Oil: 1,400 softgels daily with water and a meal for optimal absorption. Complies with aspects of GOED | EPA: 680 mgmeq/kgVery high[found: 668.8]Anisidine: 3.4Very highmg √]TOTOX: 11concentration\$8.61/60DHA: 250 mg(Lemon scent)Ethyl ester[found: 319.9]Heavy Metals:Ethyl esterDPA: 56.9 mgPassLead: <0.001 | EPA: 680 mg [found: 668.8 Anisidine: 3.4 TOTOX: 11 Concentration phases and purified to remove softgels furans, and mercury to ensure levels below 0.09 ppm, 2 ppt WHO TEQs, and 0.1 ppm respectively. Pass Lead: <0.001 mcg/g [found: 1,100 mcg/g [found: 1,100 mcg/g Total Omega- Arsenic: <0.01 mcg/g (14.1% Mercury: <0.001 mcg/g acid) Adults, take 2 softgels daily with mg water and a meal for optimal absorption. |

| 1/25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algai Oil Omega | -3 Supplements Rev | iew & Top Picks - Cons | umerLab.com |
|---------------|------------------------|-------------------------|-------------------|--------------------|------------------------|--------------------------|
| 3 | 2 softgels | Freshness: | Very large | \$0.90/2 softgels | Friend Of The Sea® | 2 softgels |
| APPROVED | | Peroxide: | softgel | | seal. No Detectable | |
| r. | EPA : 1,350 mg | Anisidine: | | [\$0.24] | Mercury. | Calories 30, Total Fat |
| but unable to | [found: 1,302.5 | тотох: | Very high | | | 2.5 g, Polyunsaturated |
| evaluate for | mg √] | (Natural orange | concentration | \$27.00/60 | Precaution: | Fat 2 g, Cholesterol 15 |
| freshness | DHA: 600 mg | oil) | | softgels | Allergen Warning: | mg, Protein <1 g, Total |
| OceanBlue® | [found: 600.3 | | Ethyl ester | | Contains fish and | Omega-3 [EPA |
| Professional | mg √] | Heavy Metals: | | | soy derivatives. | (Eicosapentaenoic Acid) |
| Omega-3 | DPA : 150 mg | <u>Pass</u> | Store in a cool, | | | 1,350 mg, DHA |
| 2,100® 🗥* | [found: 136.7 | Lead: <0.001 | dry place. | | | (Docosahexaenoic Acid) |
| | mg √] | mcg/g | | | | 600 mg, DPA |
| Ω oceanblus | Total Omega- | Cadmium: <0.01 | | | | (Docosapentaenoic |
| OMEGA-3 2100° | 3: 2,100 mg | mcg/g | | | | Acid) 150 mg] 2,100 mg |
| 600 | [found: 2,107.2 | Arsenic: <0.01 | | | | Additional |
| Dist. by | mg √] | mcg/g | | | | Information |
| OceanBlue LLC | Total Omega- | Mercury: <0.001 | | | | |
| Occumbiae EEO | 7: 12.3 mg | mcg/g | | | | 2 softgels |
| | (39.8% | | | | | |
| | palmitoleic | Take 1 or 2 | | | | Calories 30, Total Fat |
| | acid) | softgels daily with | | | | 2.5 g, Polyunsaturated |
| | | meal. | | | | Fat 2 g, Cholesterol 15 |
| | Total Oil: 2,680 | | | | | mg, Protein <1 g, Total |
| | mg | | | | | Omega-3 [EPA |
| | | | | | | (Eicosapentaenoic |
| | | | | | | Acid) 1,350 mg, DHA |
| | | | | | | (Docosahexaenoic |
| | | | | | | Acid) 600 mg, DPA |
| | | | | | | (Docosapentaenoic |
| | | | | | | Acid) 150 mg] 2,100 |
| | | | | | | mg. |
| | | | | | | |
| | | | | | | Ingredients: Omega-3 |
| | | | | | | marine oil (one or |
| | | | | | | more of anchovy, |
| | | | | | | squid, sardine, herring, |
| | | | | | | and mackerel), |
| | | | | | | capsule shell (gelatin, |
| | | | | | | glycerin, purified |
| | | | | | | water), natural orange |
| | | | | | | oil and natural mixed |
| | | | | | | tocopherols (soy). |
| | | | | | | |

| /25, 9:54 AM | | Fish Oil, Krill Oil, an | id Algai Oli Omega | -3 Supplements Rev | iew & Top Picks - Cor | nsumerLab.com |
|---|----------------------|-------------------------|--------------------|--------------------|-----------------------|--------------------------|
| 3 | 2 softgels | Freshness: Pass | Large (narrow) | \$0.22/2 softgels | Precaution: | 2 softgels |
| APPROVED | | Peroxide: 1.2 | softgel | | Contains: Fish | |
| K | EPA: 320 mg | meq/kg | | [\$0.11] | (Anchovies, | Calories 20, Total Fat 2 |
| Spectrum® Fish | [found: 305.1 | Anisidine: 2.2 | Moderate | | Sardines, | g, Saturated Fat 0.5 g, |
| Oil Omega-3 | mg √] | TOTOX: 4.6 | concentration | \$27.99/250 | Mackerel). | Cholesterol 10 mg, Fish |
| Man and | DHA: 200 mg | | | softgels | | Oil [Total Omega-3 Fatty |
| Spectrum. Fish OIL | [found: 203.4 | Heavy Metals: | Form not | | | Acids [EPA |
| OMEGAN DEPLACED AND AND AND AND AND AND AND AND AND AN | mg √] | <u>Pass</u> | listed, but | | | (eicosapentaenoic acid) |
| To the humanish p Lacourd Fish Control Fish | DPA: 36.3 mg | Lead: <0.001 | appears to be | | | 320 mg, DHA |
| Dist. by The | Total Omega- | mcg/g | triglyceride | | | (docosahexaenoic acid) |
| Hain Celestial | 3: 600 mg | Cadmium: <0.01 | | | | 200 mg, Other Omega-3 |
| Group, Inc. | [found: 608.4 | mcg/g | Refrigerate | | | Fatty Acids 80 mg] 600 |
| | mg √] | Arsenic: <0.01 | after opening | | | mg] 2,000 mg |
| | Total Omega- | mcg/g | | | | Additional |
| | 7: 232.8 mg | Mercury: <0.001 | | | | Information |
| | (70.8% | mcg/g | | | | IIIIOIIIIatioii |
| | palmitoleic | | | | | 2 softgels |
| | acid) | 2 softgels daily | | | | |
| | | with food. | | | | Calories 20, Total Fat |
| | Total Oil: 2,000 | | | | | 2 g, Saturated Fat 0.5 |
| | mg | | | | | g, Cholesterol 10 mg, |
| | | | | | | Fish Oil [Total Omega- |
| | Complies with | | | | | 3 Fatty Acids [EPA |
| | aspects of | | | | | (eicosapentaenoic |
| | GOED | | | | | acid) 320 mg, DHA |
| | monograph | | | | | (docosahexaenoic |
| | | | | | | acid) 200 mg, Other |
| | | | | | | Omega-3 Fatty Acids |
| | | | | | | 80 mg] 600 mg] 2,000 |
| | | | | | | mg. |
| | | | | | | Other Ingredients: |
| | | | | | | Gelatin, glycerin, |
| | | | | | | purified water, mixed |
| | | | | | | natural tocopherols. |

| | 1 softgel | Freshness: Pass | Large softgel | \$0.83/softgel | Vitamin D3 25 mcg | 1 softgel |
|--|-----------------------|--------------------|---------------|----------------|-----------------------|----------------------------|
| APPROVED | | Peroxide: 2.2 | | | (1,000 IU) per | |
| 5 | EPA: 665 mg | meq/kg | Extremely | [\$0.37] | softgel | Calories 15, Total Fat |
| WHC | [found: 662.7 | Anisidine: 19.6 | high | | | 1.5 g, Vitamin D3 (as |
| UnoCardio® | mg √] | TOTOX: 24 | concentration | \$49.95/60 | Friend Of The Sea | Cholecaliferol) 25 mcg |
| 1,000 - Natural | DHA: 445 mg | (Natural orange | | softgels | seal. IFOS™ Purity | (1,000 IU), Fish Oil [Tota |
| Orange Flavor | [found: 464.6 | oil) | Triglyceride | | Certified seal. | Omega-3 [EPA |
| <u>√</u> 20,≈ | mg √] | | | | Labdoor seal. No | (Eicosapentaenoic Acid |
| | DPA: 57.1 mg | Heavy Metals: | | | beef gelatin, | 665 mg, DHA |
| WHIC W UnoCardio 1000 | Total Omega- | <u>Pass</u> | | | suitable for pesco- | (Docosahexaenoic Acid |
| 17500 NO. REAL CO. HE 1 SCHILLY SEE OF SEE OF SEE STREET, SEE OF SEE STREET, SEE | 3: 1,180 mg | Lead: 0.001 | | | vegetarians. Gluten- | 445 mg, Other Omega- |
| | [found: 1,226.5 | mcg/day (0.001 | | | free - lactose free / | 3's 70 mg] 1,800 mg] |
| Dist. by | mg √] | mcg/g) | | | Non GMO. | 1,300 mg. |
| QuattroMega | Total Omega- | Cadmium: <0.01 | | | | |
| Inc. | 7: 1.4 mg (40% | mcg/g | | | Precaution: | Other Ingredients: Fish |
| | palmitoleic | Arsenic: <0.01 | | | Contains: Fish oil | gelatin, water, glycerol, |
| | acid) | mcg/g | | | (anchovy, | natural orange flavor, |
| | | Mercury: <0.001 | | | mackerel, sardine) | rosemary extract |
| | Total Oil: 1,300 | mcg/g | | | and fish gelatin | (preservative), mixed |
| | mg | | | | (tilapia). | tocopherols |
| | | 1 softgel per day. | | | | (preservative). |
| | Complies with | | | | | |
| | aspects of | | | | | |
| | GOED | | | | | |
| | monograph | | | | | |
| Fish Oil - Enteric Coated | Softgels: | I | I . | I | I | |

| | I | 1 | T | | Towa Top Floks - Colls | I |
|--|----------------------|--------------------|---------------|-----------------|------------------------|--------------------------|
| 2 | 1 enteric- | Freshness: Pass | Large softgel | \$0.50/enteric- | No Sugar, No | 1 enteric-coated softgel |
| APPROVED | coated softgel | Peroxide: 5.6 | | coated softgel | Starch, No Artificial | |
| K | | meq/kg | Very high | | Colors, No Artificial | Calories 15, Total Fat |
| GNC Triple | EPA: 734 mg | Anisidine: 5 | concentration | [\$0.25] | Flavors, No | 1.5 g, Cholesterol 0 mg, |
| Strength Fish Oil | [found: 711.8 | TOTOX: 16.2 | | | Preservatives, | Total Omega-3s [Total |
| <u>₩</u> * | mg √] | | Form not | \$29.99/60 | Sodium Free, No | EPA + DHA [EPA |
| | DHA: 266 mg | Heavy Metals: | listed, but | enteric-coated | Wheat, Gluten Free, | (Eicosapentaenoic Acid) |
| GINC HINGSHASON FISH OIL | [found: 288.9 | <u>Pass</u> | appears to be | softgels | No Corn, No Dairy, | Omega-3 734 mg, DHA |
| FISH OIL | mg √] | Lead: <0.001 | ethyl ester | | Cholesterol Free. | (Docosahexaenoic Acid) |
| Greate a summered (a) and the service of the servic | DPA: 53.7 mg | mcg/g | | | | Omega-3 266 mg] 1,000 |
| Dist. by General | Total Omega- | Cadmium: <0.01 | | | Precaution: | mg, Other Omega-3 65 |
| Nutrition | 3: 1,065 mg | mcg/g | | | Contains: | mg] 1,065 mg. |
| Corporation | [found: 1,115.9 | Arsenic: 0.027 | | | Soybeans and Fish | |
| | mg √] | mcg/day (0.02 | | | (Anchovy, | Ingredients: Fish Oil, |
| | Total Omega- | mcg/g) | | | Mackerel, Sardine, | Softgel & Enteric |
| | 7: 8.9 mg | Mercury: <0.001 | | | Smelt, Salmon, | Coating (Gelatin |
| | (18.2% | mcg/g | | | Tuna, Cod or a | Additional |
| | palmitoleic | | | | Combination | Information |
| | acid) | Disintegration: | | | Thereof). | IIIIOIIIIatioii |
| | | Pass | | | | 1 enteric-coated |
| | Total Oil: | | | | | softgel |
| | 1,355.2 mg | Take one softgel | | | | |
| | | capsule daily with | | | | Calories 15, Total Fat |
| | Complies with | food. | | | | 1.5 g, Cholesterol 0 |
| | aspects of | | | | | mg, Total Omega-3s |
| | GOED | | | | | [Total EPA + DHA [EPA |
| | monograph | | | | | (Eicosapentaenoic |
| | | | | | | Acid) Omega-3 734 |
| | | | | | | mg, DHA |
| | | | | | | (Docosahexaenoic |
| | | | | | | Acid) Omega-3 266 |
| | | | | | | mg] 1,000 mg, Other |
| | | | | | | Omega-3 65 mg] |
| | | | | | | 1,065 mg. |
| | | | | | | |
| | | | | | | Ingredients: Fish Oil, |
| | | | | | | Softgel & Enteric |
| | | | | | | Coating (Gelatin, |
| | | | | | | Glycerin, Stearic Acid, |
| | | | | | | Sodium Alginate, |
| | | | | | | Ethylcellulose, |
| | | | | | | Medium Chain |
| | | | | | | Triglycerides, Oleic), |
| | | | | | | Mixed Tocopherols. |
| | | | | | | |

| _ | 1/25, 9:54 AIVI | | risii Oii, Kiiii Oii, aii | u Algai Oil Oillega | -5 Supplements Nev | riew & Top Picks - Consi | |
|---|--|----------------------|---------------------------|---------------------|--------------------|--------------------------|--------------------------|
| | 3 | 1 enteric- | Freshness: Pass | Large softgel | \$0.15/enteric- | IFOS seal. Does Not | 1 enteric-coated softgel |
| | APPROVED | coated softgel | Peroxide: 3 | | coated softgel | Contain: Dairy, | |
| | K | | meq/kg | Very high | | eggs, corn, | Calories 15, Calories |
| | Innovixlabs | EPA: 480 mg | Anisidine: 3.2 | concentration | [\$0.09] | shellfish, tree nuts, | from Fat 15, Total Fat |
| | Triple Strength | [found: 451.2 | TOTOX: 9.2 | | | peanuts, | 1.5 g, Cholesterol 0 g, |
| | Omega-3 🕰* | mg √] | | Form not | \$30.99/200 | wheat/gluten, soy | Fish Oil Concentrate |
| | The second secon | DHA: 360 mg | Heavy Metals: | listed, but | enteric-coated | protein, sugar, | (75% Omega-3) 1,200 |
| | (Company) | [found: 367.7 | <u>Pass</u> | appears to be | softgels | yeast, artificial | mg, Total Omega-3 [EPA |
| | Miple Strength OMEGA-3 | mg √] | Lead: <0.001 | ethyl ester | | colors or flavors. | Omega-3 |
| | OSCICIONACION PROFICIO STRAINGE DEL COCCUMENTO STRAINGE COCCUMENTO ST | DPA : 24 mg | mcg/g | | | Sustainably | (Eicosapentaenoic Acid) |
| | Dist. by | [found: 51.6 | Cadmium:<0.01 | | | sourced fish oil | 480 mg, DHA Omega-3 |
| | InnovixLabs - A | mg √] | mcg/g | | | from Anchovy, | (Docosahexaenoic Acid) |
| | Division of | Total Omega- | Arsenic: <0.01 | | | Sardine, Mackerel | 360 mg, DPA |
| | Innovix Pharma | 3: 900 mg | mcg/g | | | (Peru/Chile). | (Docosapentaenoic |
| | Inc. | [found: 905.6 | Mercury: <0.001 | | | | Acid) 24 mg, Other |
| | IIIC. | | mcg/g | | | Precaution: Allergy | Omega-3 36 mg] 900 |
| | | Total Omega- | 3. 3 | | | Information: If you | mg |
| | | 7: 9.7 mg | Disintegration: | | | are allergic to fish, | |
| | | (23.1% | Pass | | | you should not | Additional |
| | | palmitoleic | . 433 | | | take this product | Information |
| | | acid) | Take 1 - 2 softgels | | | or other fish oil | 1 enteric-coated |
| | | (3.2) | daily | | | supplements. | softgel |
| | | Total Oil: 1,200 | dany | | | ouppioments. | |
| | | mg | Additional | | | | Calories 15, Calories |
| | | 9 | Information | | | | from Fat 15, Total Fat |
| | | Complies with | Freshness: | | | | 1.5 g, Cholesterol 0 g, |
| | | aspects of | Pass | | | | Fish Oil Concentrate |
| | | GOED | Peroxide: 3 | | | | (75% Omega-3) 1,200 |
| | | monograph | meq/kg | | | | mg, Total Omega-3 |
| | | | Anisidine: 3.2 | | | | [EPA Omega-3 |
| | | | TOTOX: 9.2 | | | | (Eicosapentaenoic |
| | | | | | | | Acid) 480 mg, DHA |
| | | | Heavy Metals: | | | | Omega-3 |
| | | | Pass Pass | | | | (Docosahexaenoic |
| | | | Lead: <0.001 | | | | Acid) 360 mg, DPA |
| | | | mcg/g | | | | (Docosapentaenoic |
| | | | Cadmium:<0.01 | | | | Acid) 24 mg, Other |
| | | | mcg/g | | | | Omega-3 36 mg] 900 |
| | | | Arsenic: <0.01 | | | | mg. |
| | | | mcg/g | | | | J. |
| | | | Mercury: <0.001 | | | | Other Ingredients: |
| | | | mcg/g | | | | Gelatin Softgel, |
| | | | , | | | | Glycerin, Purified |
| | | | Disintegration: | | | | Water, Plant-based |
| | | | Pass | | | | Enteric Coating |
| | | | . 400 | | | | (Alginate, Stearic |
| | | | | | | | y againste, otedino |
| | ı | I | I | I | I | I | I |

| 8/21/25, 9:54 AM | Fish Oil, Krill Oil, and Algal Oil Omega-3 Supplement | Fish Oil, Krill Oil, and Algal Oil Omega-3 Supplements Review & Top Picks - ConsumerLab.com | | | | | |
|------------------|---|---|--|--|--|--|--|
| | Take 1 - 2 | Acid), Mixed | | | | | |
| | softgels daily. | Tocopherols. | | | | | |
| | Do not take | | | | | | |
| | more than 4 | | | | | | |
| | softgels per day | | | | | | |
| | unless | | | | | | |
| | recommended | | | | | | |

by a doctor.

| 2 | 1/25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algai Oil Omega | i-3 Supplements Rev | iew & Top Picks - Consi | umerLab.com |
|---|---|----------------------|-------------------------|-------------------|---------------------|-------------------------|----------------------------|
| | 3 | 1 enteric- | Freshness: Pass | Medium/large | \$0.20/enteric- | Gluten Free: No | 1 enteric-coated softgel |
| | APPROVED | coated softgel | Peroxide: 5.8 | softgel | coated softgel | yeast-derived | |
| | K | | meq/kg | | | ingredients, wheat, | Calories 5, Total Fat 0.5 |
| | Nature's Way® | EPA: 200 mg | Anisidine: 10 | Very high | [\$0.26] | dairy products, or | g, Saturated Fat 0 g, |
| | Super Fisol™ | [found: 216.2 | TOTOX: 21.6 | concentration | | artificial colors. | Trans Fat 0 g, |
| | Fish Oil | mg √] | | | \$35.69/180 | Sustainably | Polyunsaturated Fat 0 g, |
| | SUPER | DHA: 150 mg | Heavy Metals: | Form not | softgels | Sourced. Tested For | Monounsaturated 0 g, |
| | SUPER FISOL* FISH OIL \$ ARROWAGULAR \$ JOHN TREATH | [found: 167.9 | <u>Pass</u> | listed, but | | PCBs, Heavy | Cholesterol <5 mg, Fish |
| | (5) | mg √] | Lead: 0.001 mcg | appears to be | | Metals (Including | Oil [Omega-3 Fatty |
| | 70% EPA AND DHA | DPA: 26.8 mg | to 0.002 mcg/day | triglyceride | | Mercury), And | Acids |
| | Dist. by Nature's | Total Omega- | (0.001 mcg/g) | | | Other Impurities. | [Eicosapentaenoic Acid |
| | Way Brands, | 3 : 350 mg | Cadmium: <0.01 | Store at room | | | (EPA) 200 mg, |
| | LLC | [found: 427.9 | mcg/g | temperature | | Precaution: | Docosahexaenoic Acid |
| | | mg √] | Arsenic: <0.01 | | | Contains fish | (DHA) 150 mg] 350 mg] |
| | | Total Omega- | mcg/g | | | (Anchovy, Sardine, | 500 mg. |
| | | 7: 3.4 mg | Mercury: <0.001 | | | Mackerel). | |
| | | (32.3% | mcg/g | | | | Other Ingredients: |
| | | palmitoleic | | | | | Gelatin (softgel), |
| | | acid) | Disintegration: | | | | glycerin, purified water, |
| | | | Pass | | | | ethylcellulose, sodium |
| | | Total Oil: 500 | | | | | alginate, medium chain |
| | | mg | Take 1 softgel up | | | | triglycerides, oleic acid, |
| | | | to three times | | | | sunflower oil, mixed |
| | | Complies with | daily with water. If | | | | tocopherols |
| | | aspects of | you are pregnant, | | | | Additional |
| | | GOED | nursing, or taking | | | | Information |
| | | monograph | any medications, | | | | momation |
| | | | consult a | | | | 1 enteric-coated |
| | | | healthcare | | | | softgel |
| | | | professional | | | | |
| | | | before use. | | | | Calories 5, Total Fat |
| | | | | | | | 0.5 g, Saturated Fat 0 |
| | | | | | | | g, Trans Fat 0 g, |
| | | | | | | | Polyunsaturated Fat 0 |
| | | | | | | | g, Monounsaturated 0 |
| | | | | | | | g, Cholesterol <5 mg, |
| | | | | | | | Fish Oil [Omega-3 |
| | | | | | | | Fatty Acids |
| | | | | | | | [Eicosapentaenoic |
| | | | | | | | Acid (EPA) 200 mg, |
| | | | | | | | Docosahexaenoic |
| | | | | | | | Acid (DHA) 150 mg] |
| | | | | | | | 350 mg] 500 mg. |
| | | | | | | | |
| | | | | | | | Other Ingredients: |
| | | | | | | | Gelatin (softgel), |
| | | | | | | | 1 |

| 8/21 | /25, 9:54 AM | Fish Oil, Krill Oil, an | d Algal Oil Omega | -3 Supplements Revi | iew & Top Picks - Consu | ımerLab.com |
|------|--------------|-------------------------|-------------------|---------------------|-------------------------|-------------------------|
| | | | | | | glycerin, purified |
| | | | | | | water, ethylcellulose, |
| | | | | | | sodium alginate, |
| | | | | | | medium chain |
| | | | | | | triglycerides, oleic |
| | | | | | | acid, sunflower oil, |
| | | | | | | mixed tocopherols |
| | | | | | | (preservative to |
| | | | | | | maintain freshness), |
| | | | | | | rosemary extract |
| | | | | | | (leaf) (preservative to |
| | | | | | | maintain freshness), |
| | | | | | | stearic acid, ascorbyl |
| | | | | | | palmitate |
| | | | | | | (preservative to |
| | | | | | | maintain freshness). |

| 2 | 1/25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algal Oil Omega | i-3 Supplements Rev | iew & Top Picks - Cons | umerLab.com |
|---|---|----------------------|-------------------------|-------------------|---------------------|------------------------|--------------------------|
| | 3 | 1 enteric- | Freshness: Pass | Large softgel | \$0.50/enteric- | IFOS seal. Does Not | 1 enteric-coated softgel |
| | APPROVED | coated softgel | Peroxide: 3 | | coated softgel | Contain: Dairy, | |
| | r | | meq/kg | Very high | | eggs, corn, | Calories 15, Total Fat |
| | OmegaVia® 🔼® | EPA: 780 mg | Anisidine: 3.2 | concentration | [\$0.23] | shellfish, tree nuts, | 1.5 g, Ultra |
| | | [found: 790.9 | TOTOX: 9.2 | | | peanuts, | Concentrated Oil (>85% |
| | omega <mark>via</mark> | mg √] | | Triglyceride | \$29.85/60 | wheat/gluten, soy | Omega-3) 1,300 mg, |
| | Ultra Concentrated Omogo4 Proved Sevella sea Avenda Sea Marin Omogo 2 as Separa del Explorated Maringary | DHA: 260 mg | Heavy Metals: | | enteric-coated | protein, sugar, | Total Omega-3 [EPA |
| | | [found: 274.2 | <u>Pass</u> | Store at room | softgels | yeast, artificial | Omega-3 |
| | Dist. by Innovix | mg √] | Lead: <0.001 | temperature | | colors or flavors. All | (Eicosapentaenoic Acid) |
| | Pharma Inc. | DPA: 40 mg | mcg/g | | | Ingredients are | 780 mg, DHA Omega-3 |
| | | [found: 47.3 | Cadmium: <0.01 | | | Non-Bioengineered. | (Docosahexaenoic Acid) |
| | | mg √] | mcg/g | | | Sustainably | 260 mg, DPA Omega-3 |
| | | Total Omega- | Arsenic: <0.01 | | | sourced fish oil | (Docosapentaenoic |
| | | 3 : 1,135 mg | mcg/g | | | from Anchovy, | Acid) 40 mg, Other |
| | | [found: 1,164.9 | Mercury: <0.001 | | | Sardine, Mackerel | Omega-3 (SDA, ETA, |
| | | mg √] | mcg/g | | | (Peru/Chile). | ETE, ALA) 55 mg] 1,135 |
| | | Total Omega- | | | | | mg |
| | | 7: 1.6 mg | Disintegration: | | | Precaution: | Additional |
| | | (58.3% | Pass | | | Allergen: contains | Information |
| | | palmitoleic | | | | fish. Do not take if | illioilliation |
| | | acid) | Take 1 to 4 | | | you are allergic to | 1 enteric-coated |
| | | | softgels per day. | | | fish. | softgel |
| | | Total Oil: 1,300 | Best if consumer | | | | |
| | | mg | with a meal. | | | | Calories 15, Total Fat |
| | | | | | | | 1.5 g, Ultra |
| | | Complies with | | | | | Concentrated Oil |
| | | aspects of | | | | | (>85% Omega-3) |
| | | GOED | | | | | 1,300 mg, Total |
| | | monograph | | | | | Omega-3 [EPA |
| | | | | | | | Omega-3 |
| | | | | | | | (Eicosapentaenoic |
| | | | | | | | Acid) 780 mg, DHA |
| | | | | | | | Omega-3 |
| | | | | | | | (Docosahexaenoic |
| | | | | | | | Acid) 260 mg, DPA |
| | | | | | | | Omega-3 |
| | | | | | | | (Docosapentaenoic |
| | | | | | | | Acid) 40 mg, Other |
| | | | | | | | Omega-3 (SDA, ETA, |
| | | | | | | | ETE, ALA) 55 mg] |
| | | | | | | | 1,135 mg. |
| | | | | | | | Other Ingredients: |
| | | | | | | | Fish Gelatin, |
| | | | | | | | Vegetable Glycerin, |
| | | | | | | | Purified Water, |
| | | | | | | | |

| 8/21/25, 9:54 AM | | | Fish Oil, Krill Oil, and Algal Oil Omega-3 Supplements Review & Top Picks - ConsumerLab.com | | | | |
|------------------|----------------------------|--|---|--|--|--|----------------------|
| | | | | | | | Vegetable Enteric |
| | | | | | | | Coating (Alginate, |
| | | | | | | | Stearic Acid), Mixed |
| | | | | | | | Tocopherols, |
| | | | | | | | Rosemary Extract. |
| | Bottled Fish Oil (Liquid): | | | | | | |

| ۷, | 1/25, 9.54 AIVI | | FISH OII, KIIII OII, aH | u Algai Oli Olliega | -3 Supplements Revi | ew & Top Picks - Const | intercap.com |
|----|--------------------------|----------------------|-------------------------|---------------------|---------------------|------------------------|---------------------------|
| | 3 | 1 tsp [5 mL] | Freshness: Partial | Taste: Clear, | \$0.56/tsp | Friend Of The Sea® | 1 tsp |
| | APPROVED | | <u>Pass</u> | pale yellow oil | | seal. IFOS® seal. | |
| | K | EPA: 800 mg | Peroxide: 3.8 | with light | [\$0.22] | Gluten-free. No | Calories 40, Total Fat |
| | 3 | [found: 751.1 | meq/kg | lemony flavor. | | Artificial | 4.5 g, Saturated Fat 1 g, |
| | Top Pick | mg √] | Anisidine: | Not fishy. | \$22.53/6.7 fl oz | Preservatives. It | Cholesterol 20 mg, |
| | K | DHA: 500 mg | тотох: | | [200 mL] bottle | has been | Vitamin E (as d-alpha |
| | for bottled fish | [found: 515.4 | (Lemon flavor) | Moderate | (approx. 40 | determined to be | tocopherol) 6.7 mg, |
| | oil (liquid) and | mg √] | | concentration | servings) | fresh and potent | Norwegian Fish Oil |
| | for omega-7s | DPA : 90 mg | Heavy Metals: | | | (per AOCS | [Total Omega-3 Fatty |
| | Carlson® The | [found: 82 mg | <u>Pass</u> | Form not | | international | Acids [EPA |
| | Very Finest Fish | √] | Lead: <0.001 | listed, but | | protocols) and is | (Eicosapentaenoic Acid) |
| | Oil <u>Æ</u> ® | Total Omega- | mcg/g | appears to be | | free of detrimental | 800 mg, DHA |
| | | 3 : 1,600 mg | Cadmium: <0.01 | triglyceride | | levels of mercury, | (Docosahexaenoic Acid) |
| | Caba | [found: 1,530 | mcg/g | | | cadmium, lead, | 500 mg, DPA |
| | The Very Finest Fish Oil | mg √] | Arsenic: <0.01 | Refrigerate | | PCBs and 28 other | (Docosapentaenoic |
| | 1, Sulting Groups Is | Total Omega- | mcg/g | after opening, | | contaminants. | Acid) 90 mg] 1,600 mg] |
| | Diet by ID | 7: 466.8 mg | Mercury: <0.001 | and use with | | o o mammama. | 4,600 mg. |
| | Dist. by J.R. | (75.6% | mcg/g | 100 days. | | Precaution: | 1,000 mg. |
| | Carlson | palmitoleic | ,og, g | l co dayo. | | Contains fish | Other Ingredients: |
| | Laboratories, | acid) | Adults: take one | | | (anchovy, sardine, | Natural flavors |
| | Inc. | acia) | teaspoonful once | | | sardine, mackerel). | Natural navors |
| | | Total Oil: 4,600 | or twice daily at | | | Saraine, mackerer). | Additional |
| | | | mealtime. | | | | Information |
| | | mg | meaitime. | | | | 1 tsp |
| | | | | | | | 1 top |
| | | | | | | | Calories 40, Total Fat |
| | | | | | | | 4.5 g, Saturated Fat 1 |
| | | | | | | | g, Cholesterol 20 mg, |
| | | | | | | | Vitamin E (as d-alpha |
| | | | | | | | ` . |
| | | | | | | | tocopherol) 6.7 mg, |
| | | | | | | | Norwegian Fish Oil |
| | | | | | | | [Total Omega-3 Fatty |
| | | | | | | | Acids [EPA |
| | | | | | | | (Eicosapentaenoic |
| | | | | | | | Acid) 800 mg, DHA |
| | | | | | | | (Docosahexaenoic |
| | | | | | | | Acid) 500 mg, DPA |
| | | | | | | | (Docosapentaenoic |
| | | | | | | | Acid) 90 mg] 1,600 |
| | | | | | | | mg] 4,600 mg. |
| | | | | | | | |
| | | | | | | | Other Ingredients: |
| | | | | | | | Natural flavors. |
| | | | | | | | Contains <0.5% of the |
| | | | | | | | following: antioxidant |
| | | | | | | | blend (natural mixed |
| | | | | | | | |

| | | | | | | *************************************** |
|-------------------------------|----------------------|--------------------|-----------------|-----------------|----------------------|---|
| | | | | | | tocopherols, rosemary extract). |
| 3 | 1 tsp [5 mL] | Freshness: Partial | Taste: Clear, | \$1.29/tsp | No gluten, milk | 1 tsp |
| APPROVED | | <u>Pass</u> | pale yellow oil | | derivatives, or | Calories 45, Total Fat 5 |
| EF EF | PA: 1,460 mg | Peroxide: 5.2 | with slight | [\$0.25] | artificial colors or | g, Saturated Fat 0 g, |
| i [fc | ound: 1,472.7 | meq/kg | lemony, | | flavors. | Trans Fat 0 g, |
| Top Pick me | ng √] | Anisidine: | anchovy flavor. | \$61.16/8 fl oz | | Cholesterol 10 mg, Total |
| r DI | HA: 1,010 mg | тотох: | | [237 mL] bottle | Fish oil processed | Omega-3s [EPA |
| for DPA [fo | ound: 1,094 | (Natural lemon | High | (approx. 47.4 | in Norway. | (Eicosapentaenoic Acid) |
| Nordic m | ng √] | flavor) | concentration | servings) | | 1,460 mg, DHA |
| Naturals® DF | PA: 177.7 mg | | | | | (Docosahexaenoic Acid) |
| Ultimate To | otal Omega- | Heavy Metals: | Form not | | | 1,010 mg] 2,840 mg. |
| Omega® - Great 3: | : 2,840 mg | <u>Pass</u> | listed, but | | | |
| Lemon Taste [fo | ound: 2,946.8 | Lead: 0.002 mcg | appears to be | | | Ingredients: Purified |
| m | ng √] | to 0.005 mcg/day | triglyceride | | | deep sea fish oil (from |
| To | otal Omega- | (0.001 mcg/g) | | | | anchovies and |
| NORDIC MAYUMATE ORDEGA OTTES | : 142 mg | Cadmium: <0.01 | Refrigerate | | | sardines), natural lemon |
| 2840 70 | 16.3% | mcg/g | after opening | | | flavor, d-alpha |
| Mfd. by Nordic pa | almitoleic | Arsenic: 0.46 mcg | | | | tocopherol (antioxidant), |
| | cid) | to 0.92 mcg/day | | | | rosemary extract (a |
| | | (0.19 mcg/g) | | | | natural preservative). |
| To | otal Oil: 4,830 | Mercury: <0.001 | | | | |
| m | ng | mcg/g | | | | |
| | | One-half to one | | | | |
| | | teaspoon daily, | | | | |
| | | with food, or as | | | | |
| | | directed by your | | | | |
| | | health care | | | | |
| | | professional. | | | | |
| Fish and Krill Oil Combinatio | on: | | <u> </u> | 1 | 1 | <u> </u> |

| 2 | I/25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algal Oil Omega | -3 Supplements Rev | iew & Top Picks - Cons | umerLab.com |
|---|---|----------------------|-------------------------|-------------------|--------------------|------------------------|--------------------------|
| | 3 | 2 softgels | Freshness: Pass | Very large | \$0.61/2 softgels | Polyphen-Oil™ olive | 2 softgels |
| | APPROVED | | Peroxide: 0.6 | softgel | | extract 200 mg & | |
| | ĸ | EPA: 750 mg | meq/kg | | [\$0.23] | sesame seed | Calories 25, Total Fat |
| | Life Extension® | [found: 779.4 | Anisidine: 5.5 | High | | lignan extract 5 mg | 2.5 g, Cholesterol <5 |
| | Super Omega-3 | mg √] | тотох: 6.7 | concentration | \$36.75/120 | per 2 softgels | mg, Pure+™ Wild Fish Oil |
| | Plus 🕰* | DHA: 510 mg | (Krill) | | softgels | | and Antarctic Krill |
| | | [found: 529.8 | | Triglyceride, | | Gluten Free. | (Euphausia superba) Oil |
| | LIFE EXTENSION | mg √] | Heavy Metals: | ethyl ester & | | | Concentrates [Yielding: |
| | Super Omega-3 Plus EA/DHA Fish Od. Science Lighters Over Entrock Kirls | DPA: 66.2 mg | <u>Pass</u> | phospholipid | | Precaution: | EPA (eicosapentaenoic |
| | Tollywoods, bittel Color shootholgad Compay 3 Forms 120 sorress, a second | Total Omega- | Lead: 0.029 | | | Contains | acid) 750 mg, DHA |
| | Dist. by Quality | 3: 1,511.2 mg | mcg/day (0.005 | | | crustacean | (docosahexaenoic acid) |
| | Supplements | Total Omega- | mcg/g) | | | shellfish (krill), | 510 mg, Phospholipids |
| | and Vitamins, | 7: 76.1 mg | Cadmium: <0.01 | | | sesame. | 60 mg] 2,350 mg, |
| | Inc. | (27% | mcg/g | | | | Polyphen-Oil™ Olive |
| | | palmitoleic | Arsenic: 1.4 | | | | extract (fruit and leaf) |
| | | acid) | mcg/day (0.24 | | | | [providing 45 mg |
| | | Phospholipids: | mcg/g) | | | | polyphenols, 11.25 mg |
| | | 60 mg [found: | Mercury: <0.001 | | | | verbacoside/ |
| | | 60.8 mg √] | mcg/g | | | | oleuropein, 9 mg |
| | | Astaxanthin: | | | | | hydroxytyrosol/ tyrosol] |
| | | 2,000 mcg | Take two (2) | | | | 200 mg |
| | | [found: 2,155 | softgels twice | | | | Additional |
| | | mcg √] | daily with meals, | | | | Information |
| | | | or as | | | | Information |
| | | Total Oil: 2,350 | recommended by | | | | 2 softgels |
| | | mg | a healthcare | | | | |
| | | | practitioner. | | | | Calories 25, Total Fat |
| | | | | | | | 2.5 g, Cholesterol <5 |
| | | | | | | | mg, Pure+™ Wild Fish |
| | | | | | | | Oil and Antarctic Krill |
| | | | | | | | (Euphausia superba) |
| | | | | | | | Oil Concentrates |
| | | | | | | | [Yielding: EPA |
| | | | | | | | (eicosapentaenoic |
| | | | | | | | acid) 750 mg, DHA |
| | | | | | | | (docosahexaenoic |
| | | | | | | | acid) 510 mg, |
| | | | | | | | Phospholipids 60 mg] |
| | | | | | | | 2,350 mg, Polyphen- |
| | | | | | | | Oil™ Olive extract |
| | | | | | | | (fruit and leaf) |
| | | | | | | | [providing 45 mg |
| | | | | | | | polyphenols, 11.25 |
| | | | | | | | mg verbacoside/ |
| | | | | | | | oleuropein, 9 mg |
| | | | | | | | hydroxytyrosol/ |
| | | | | | | | |

| 21/25, 9:54 AIVI | | FISH OII, KIIII OII, an | d Algai Oil Offlega | i-s supplements kev | iew & Top Picks - Cons | umercab.com |
|--|----------------------|-------------------------|---------------------|---------------------|------------------------|-----------------------------|
| 2 | 2 softgels | Freshness: Partial | Medium/large | \$0.47/2 softgels | Precaution: | 2 softgels |
| APPROVED | | <u>Pass</u> | softgel | | Contains: Shellfish | |
| K | EPA: 120 mg | Peroxide: 0.1 | | [\$0.96] | (Krill). | Calories 10, Total Fat 1 |
| Bronson® | [found: 154.7 | meq/kg | Low | | | g, Antarctic Krill Oil |
| Antarctic Krill | mg √] | Anisidine: | concentration | \$27.99/120 | | [Total Omega 3 Fatty |
| Oil 1,000 mg | DHA: 80 mg | тотох: | | softgels | | Acids [20:5 - EPA |
| ANTARCTIC KRILL OIL | [found: 89 mg | (Ethyl vanillin, krill) | Form not | | | (Eicosapentaenoic Acid) |
| OMEGA-3 EPA/OHA EDITENDE STUDIEST SOMETH DOOK PURE PREMIUM KEILL MEANY METAL TESTED | ✓] | | listed, but | | | 120 mg, 22:6 - DHA |
| NOS | DPA: 12.6 mg | Heavy Metals: | assumed to | | | (Docosahexaenoic Acid) |
| BRONSON SON | Total Omega- | <u>Pass</u> | be | | | 80 mg] 200 mg, |
| Dist. by Bronson | 3: 200 mg | Lead: 0.002 | phospholipid | | | Phospholipids 200 mg, |
| Laboratories | [found: 283.7 | mcg/day (0.002 | | | | Astaxanthin 200 mcg] |
| | mg √] | mcg/g) | Store at room | | | 1,000 mg. |
| | Total Omega- | Cadmium: <0.01 | temperature. | | | |
| | 7 : 97 mg | mcg/g | | | | Other Ingredients: |
| | (55.4% | Arsenic: 3.2 | | | | Gelatin, glycerin, purified |
| | palmitoleic | mcg/day (3 | | | | water, ethyl vanillin. |
| | acid) | mcg/g) | | | | |
| | Phospholipids: | Mercury: <0.001 | | | | |
| | 200 mg [found: | mcg/g | | | | |
| | 234 mg 🗸] | | | | | |
| | Astaxanthin: | As a dietary | | | | |
| | 200 mcg | supplement for | | | | |
| | [found: 255 | adults, take 2 | | | | |
| | mcg √] | softgels daily with | | | | |
| | | the first meal or | | | | |
| | Total Oil: 1,000 | as directed by a | | | | |
| | mg | healthcare | | | | |
| | | professional. | | | | |
| | | | | | | |

| 1/25, 9:54 AIVI | | Fish Oil, Krill Oil, an | d Algai Oli Omega | i-3 Supplements Rev | iew & Top Picks - Cons | umerLab.com |
|--|---------------------|-------------------------|-------------------|---------------------|------------------------|---------------------------|
| 3 | 1 softgel | Freshness: Partial | Medium/large | \$0.15/softgel | Certified | 1 softgel |
| APPROVED | | <u>Pass</u> | softgel | | Sustainable | |
| r | EPA: 64 mg | Peroxide: 0.1 | | [\$0.82] | Seafood MSC™ | Calories 5, Total Fat 0.5 |
| Member's Mark | [found: 58.2 | meq/kg | Low | | seal. No Milk. No | g, Cholesterol 10 mg, |
| [Sam's Club] | mg √] | Anisidine: | concentration | \$23.48/160 | Gluten. No Egg. No | Krill Oil [Omega-3 Fatty |
| Superior Krill Oil | DHA: 30 mg | тотох: | | softgels | Soy. No Tree Nuts. | Acids [EPA |
| 500 mg | [found: 30.8 | (Ethyl vanillin, krill) | Form not | | No Wheat. No | (eicosapentaenoic acid) |
| | mg √] | | listed, but | | Peanuts. | 64 mg, DPA |
| MICARCOM SYLEGES | DPA: 1.3 mg | Heavy Metals: | assumed to | | | (docosahexaenoic acid) |
| Extra Strength | Total Omega- | <u>Pass</u> | be | | Precaution: | 30 mg] 120 mg, |
| The Section of the Se | 3: 120 mg | Lead: 0.001 | phospholipid | | Contains: | Phospholipids 200 mg, |
| Dist. by Sam's | [found: 116.6 | mcg/day (0.002 | | | Crustacean | Esterified Astaxanthin |
| West, Inc. | mg √] | mcg/g) | | | Shellfish (krill). | 150 mcg] 500 mg. |
| | Total Omega- | Cadmium: <0.01 | | | | |
| | 7: 48.5 mg | mcg/g | | | | Other Ingredients: |
| | (51.8% | Arsenic: 2.6 | | | | Gelatin Capsule |
| | palmitoleic | mcg/day (4.7 | | | | (Gelatin, Glycerin, |
| | acid) | mcg/g) | | | | Purified Water, Ethyl |
| | Phospholipids: | Mercury: <0.001 | | | | Vanillin, Sorbitol). |
| | 200 mg [found: | mcg/g | | | | |
| | 203.5 mg √] | | | | | |
| | Astaxanthin: | Take one (1) | | | | |
| | 150 mcg | softgel daily with | | | | |
| | [found: 226.7 | a meal. For adults | | | | |
| | mcg √] | only. | | | | |
| | Total Oil: 500 | | | | | |
| | mg | | | | | |
| Vegetarian Source (Alga | l) Oil: | | | | | |
| | | | | | | |

| 1/25, 9:54 AM | | risii Oii, Kiiii Oii, aii | u Algai Oil Oillega | i-5 Supplements Nevi | iew & Top Picks - Cons | Sumer Lab. Com |
|---|------------------------|---------------------------|---------------------|----------------------|------------------------|--------------------------|
| 2 | 1/2 tsp [2.5 | Freshness: Partial | Taste: Clear, | \$1.11 per 1/2 tsp | igen™ Non-GMO | 1/2 tsp |
| APPROVED | mL] | <u>Pass</u> | pale yellow oil | | Tested seal. | |
| K | | Peroxide: 2.8 | with light | [\$0.51] | Vegetarian. No | Calories 20, Total Fat |
| Carlson® | EPA: 122.7 mg | meq/kg | lemony flavor. | | Artificial | 2.5 g, Marine Algae Oil |
| Vegetarian DHA | DHA: 910 mg | Anisidine: | Not fishy. | \$26.52/2 fl oz | Preservatives. | (Schizochytrium sp.) |
| - Natural Lemon | [found: 1,055.8 | тотох: | | [60 mL] bottle | Gluten-free. | [Total Omega-3 Fatty |
| Flavor - Liquid | mg √] | (Natural lemon | High | (approx. 24 | | Acids (as Triglycerides) |
| <u>~</u> | DPA: 8.1 mg | flavor) | concentration | servings) | | [DHA (Docosahexaenoic |
| - Carlson | Total Omega- | | | | | Acid) 910 mg] 1,100 mg] |
| Vegetarian DHA | 3 : 1,100 mg | Heavy Metals: | Triglyceride | | | 2.35 g. |
| 910 mg DHA | [found: 1,113.4 | <u>Pass</u> | | | | |
| Conjunctor Constitution Vision Support The Number automates | mg √] | Lead: <0.001 | Refrigerate | | | Other Ingredients: |
| Dist. by Carlson | Total Omega- | mcg/g | after opening, | | | Natural flavors. |
| Div. of J.R. | 7: 192.3 mg | Cadmium: <0.01 | and use within | | | Contains <0.5% of the |
| Carlson | (45.3% | mcg/g | 100 days. | | | following: antioxidant |
| Laboratories, | palmitoleic | Arsenic: <0.01 | | | | blend (natural mixed |
| Inc. | acid) | mcg/g | | | | tocopherols, rosemary |
| | | Mercury: <0.001 | | | | extract). |
| | Total Oil: 2,350 | mcg/g | | | | |
| | mg | | | | | |
| | | Adults: take 1/2 | | | | |
| | Complies with | teaspoonful once | | | | |
| | aspects of | daily at mealtime. | | | | |
| | GOED | | | | | |
| | monograph | | | | | |

| 1/25, 9.54 AIVI | | r isir Oii, itilii Oii, aii | | o oupplements rev | iew & Top Ficks - Colls | |
|--|----------------------|-----------------------------|---------------|-------------------|-------------------------|----------------------------|
| 2 | 1 vegetarian | Freshness:Pass | Large | \$0.71/vegetarian | No Artificial | 1 vegetarian softgel |
| APPROVED | softgel | Peroxide: 2 | vegetarian | softgel | Ingredients. Gluten- | |
| K | | meq/kg | softgel | | Free. Vegetarian. | Calories 10, Total Fat 1 |
| Carlson® | EPA: 3.4 mg | Anisidine: 3.9 | | [\$0.67] | This product is | g, Algal Oil (derived |
| Vegetarian DHA | DHA: 500 mg | TOTOX: 7.9 | High | | regularly tested by | from Schizochytrium |
| - Softgel <u>™</u> * | [found: 527.4 | | concentration | \$42.42/60 | independent FDA | sp.) [DHA |
| | mg √] | Heavy Metals: | | vegetarian | registered | (Docosahexaenoic Acid) |
| Carlson | DPA: 1.3 mg | <u>Pass</u> | Triglyceride | softgels | laboratories. It has | 500 mg] 830 mg. |
| Vegetarian DHA | Total Omega- | Lead: 0.002 | | | been determined to | |
| ************************************** | 3: 540.8 mg | mcg/day (0.002 | | | be fresh and fully | Other Ingredients: |
| Dist. by Carlson | Total Omega- | mcg/g) | | | potent (per AOCS | Vegetarian capsule |
| Division of J.R. | 7: 2.4 mg | Cadmium: <0.01 | | | international | (modified food starch, |
| Carlson | (39.3% | mcg/g | | | protocols) and is | carrageenan, glycerin, |
| Laboratories, | palmitoleic | Arsenic: <0.01 | | | free of detrimental | sorbitol, purified water), |
| Inc. | acid) | mcg/g | | | levels of mercury, | antioxidant blend |
| | | Mercury: <0.001 | | | cadmium, lead, | (mixed tocopherol, |
| | Total Oil: 830 | mcg/g | | | PCBs and 28 other | rosemary extract, and |
| | mg | | | | contaminants. | ascorbyl palmitate). |
| | | Adults: take one | | | | |
| | Complies with | soft gel daily at | | | | |
| | aspects of | mealtime. | | | | |
| | GOED | | | | | |
| | monograph | | | | | |

| _ | 1/25, 9.54 AIVI | | FISH OII, KIIII OII, all | u Algai Oli Offiega | -3 Supplements Kev | iew & Top Picks - Const | unierLab.com |
|---|--|----------------------|----------------------------------|---------------------|--------------------|-------------------------|---------------------------|
| | 3 | 1 softgel | Freshness: Pass | Large (narrow) | \$0.32/softgel | Vegan Society seal. | 1 softgel |
| | APPROVED | | Peroxide: 2.6 | softgel | | This product does | |
| | K | EPA: 90 mg to | meq/kg | | [\$0.51] | NOT contain animal | Calories 10, Total Fat 1 |
| | 2 | 126 mg [found: | Anisidine: 3.8 | High | | products, | g, Microalgae (50% |
| | Top Pick | 122.7 mg √] | ТОТОХ: 9 | concentration | \$28.99/90 | derivatives or | DHA/EPA) [which |
| | K | DHA: 180 mg | (Orange oil) | | softgels | products. Food | typically provides: Total |
| | for vegetarian | to 252 mg | | Form not | | Sensitivity: Free of | DHA + EPA (Omega-3) |
| | source (algal) | [found: 195.6 | Heavy Metals: | listed, but | | yeast, soy | [DHA (docosahexaenoic |
| | oil | mg √] | <u>Pass</u> | appears to be | | allergens, | acid) 180 to 252 mg, |
| | DEVA® Vegan | DPA: 24.9 mg | Lead: <0.001 | triglyceride | | carrageenan, | EPA (eicosapentaenoic |
| | Omega-3 DHA- | Total Omega- | mcg/g | | | wheat, gluten, | acid) 180 to 252 mg] |
| | EPA 300 mg 🗥 | 3: 348.7 mg | Cadmium: <0.01 | | | hexane, egg, dairy, | 300 mg] 600 mg. |
| | | Total Omega- | mcg/g | | | fish, shellfish and | |
| | DEVA" | 7: 0.3 mg | Arsenic: <0.01 | | | salt. | Other Ingredients: Non- |
| | OMEGA-3 DHA-EPA EDIM | (100% | mcg/g | | | | gmo tapioca starch, |
| | Carageons free | palmitoleic | Mercury: <0.001 | | | | vegetable glycerin, |
| | W 18 18 18 18 18 18 18 18 18 18 18 18 18 | acid) | mcg/g | | | | purified water |
| | Dist. by DEVA | aciu) | meg/g | | | | pullied water |
| | Nutrition LLC | Total Oil: 600 | For adults, take | | | | Additional |
| | | | | | | | Information |
| | | mg | one (1) vegan softgel daily with | | | | 1 softgel |
| | | 0 1: | | | | | i sortger |
| | | Complies with | food, or as | | | | Colorino 10 Total Fat |
| | | aspects of | directed by a | | | | Calories 10, Total Fat |
| | | GOED | doctor. | | | | 1 g, Microalgae (50% |
| | | monograph | | | | | DHA/EPA) [which |
| | | | | | | | typically provides: |
| | | | | | | | Total DHA + EPA |
| | | | | | | | (Omega-3) [DHA |
| | | | | | | | (docosahexaenoic |
| | | | | | | | acid) 180 to 252 mg, |
| | | | | | | | EPA |
| | | | | | | | (eicosapentaenoic |
| | | | | | | | acid) 180 to 252 mg] |
| | | | | | | | 300 mg] 600 mg. |
| | | | | | | | |
| | | | | | | | Other Ingredients: |
| | | | | | | | Non-gmo tapioca |
| | | | | | | | starch, vegetable |
| | | | | | | | glycerin, purified |
| | | | | | | | water, high oleic |
| | | | | | | | sunflower oil, mixed |
| | | | | | | | tocopherols, orange |
| | | | | | | | oil (organic), |
| | | | | | | | rosemary extract, |
| | | | | | | | annatto color, |
| | | | | | | | ascorbyl palmitate. |
| | | | | | | | |
| | | | | | | | |

| 3/21/25, 9:54 AM | | Fish Oil, Krill Oil, and Algal Oil Omega-3 Supplements Review & Top Picks - ConsumerLab.com | | | | | |
|------------------|--|---|--|--|--|----------------------|--|
| | | | | | | (All from non-animal | |
| | | | | | | sources) | |

| 2 | 1/25, 9:54 AM | | Fish Oil, Krill Oil, an | d Algai Oil Omega | -3 Supplements Rev | iew & Top Picks - Cons | JmerLab.com |
|---|--|-----------------------|-------------------------|-------------------|--------------------|------------------------|----------------------------|
| | 3 | 1 vegetarian | Freshness: Pass | Large | \$0.62/vegetarian | Vegetarian/vegan. | 1 vegetarian softgel |
| | APPROVED | softgel | Peroxide: 5.6 | vegetarian | softgel | Ovega-3® is GMO- | |
| | K | | meq/kg | softgel | | Free, Gluten-Free, | Calories 10, Total Fat 1 |
| | Ovega-3 | EPA: 135 mg | Anisidine: 7.2 | | [\$0.64] | Soy-Free, Lactose- | g, Total Carbohydrate 0 |
| | PROCEEDINGS OF THE PROPERTY OF | [found: 166.1 | TOTOX: 18.4 | High | | Free And Sugar- | g, Total Sugars [Incl. 0 g |
| | Ovega3 | mg √] | | concentration | \$37.33/60 | Free. | Added Sugars] 0 g, |
| | SOUND CHARGON AND THE PARTY OF | DHA: 270 mg | Heavy Metals: | | vegetarian | | Sugar Alcohol <1 g, |
| | NO FERRI CONTROL CONTR | [found: 317.8 | <u>Pass</u> | Form not | softgels | | Omega-3 fatty acids |
| | Dist. by i-Health, | mg √] | Lead: 0.001 | listed, but | | | (from Algal Oil) [DHA |
| | Inc. | DPA: 39.7 mg | mcg/day (0.001 | appears to be | | | (docosahexaenoic acid) |
| | | Total Omega- | mcg/g) | triglyceride | | | 270 mg, EPA |
| | | 3 : 500 mg | Cadmium: <0.01 | | | | (eicosapentaenoic acid) |
| | | [found: 524.4 | mcg/g | Store at room | | | 135 mg] 500 mg. |
| | | mg √] | Arsenic: <0.01 | temperature. | | | |
| | | Total Omega- | mcg/g | | | | Ingredients: Algal Oil |
| | | 7: 1.1 mg (36% | Mercury: <0.001 | | | | (which contains high |
| | | palmitoleic | mcg/g | | | | oleic sunflower oil |
| | | acid) | | | | | Additional |
| | | | Take one softgel | | | | Information |
| | | Total Oil: 827.5 | per day. | | | | imorridation |
| | | mg | | | | | 1 vegetarian softgel |
| | | | | | | | |
| | | Complies with | | | | | Calories 10, Total Fat |
| | | aspects of | | | | | 1 g, Total |
| | | GOED | | | | | Carbohydrate 0 g, |
| | | monograph | | | | | Total Sugars [Incl. 0 g |
| | | | | | | | Added Sugars] 0 g, |
| | | | | | | | Sugar Alcohol <1 g, |
| | | | | | | | Omega-3 fatty acids |
| | | | | | | | (from Algal Oil) [DHA |
| | | | | | | | (docosahexaenoic |
| | | | | | | | acid) 270 mg, EPA |
| | | | | | | | (eicosapentaenoic |
| | | | | | | | acid) 135 mg] 500 |
| | | | | | | | mg. |
| | | | | | | | |
| | | | | | | | Ingredients: Algal Oil |
| | | | | | | | (which contains high |
| | | | | | | | oleic sunflower oil, |
| | | | | | | | rosemary extract, |
| | | | | | | | antioxidants |
| | | | | | | | [tocopherols and |
| | | | | | | | ascorbyl palmitate]), |
| | | | | | | | Corn Starch, Glycerin |
| | | | | | | | (from palm oil), |
| | | | | | | | Sorbitol, Carrageenan, |
| | | | | | | | |

| | | | | | | Purified Water, Colors |
|-------------------------------|----------------------|------------------|------------------|-------------------|----------------------|---------------------------|
| | | | | | | (Beta Carotene and |
| | | | | | | Caramel). |
| Prenatal: | | | | | | |
| 3 | 2 softgels | Freshness: Fail | Large (narrow) | \$0.59/2 softgels | Certified By Eagle | 2 softgels |
| <i>NOT</i> APPROVED | | Peroxide: 11.6 | softgel | | Certification Group | |
| E | EPA: 300 mg | meq/kg | | [\$0.32] | seal. Certified | Calories 15, Total Fat |
| Wiley's Finest® | [found: 311.1 | Anisidine: 9.4 | Very high | | Sustainable | 1.5 g, Cholesterol 15 |
| Wild Alaskan | mg √] | TOTOX: 32.6 | concentration | \$35.61/120 | Seafood MSC™ | mg, Concentrated Fish |
| Fish Oil Prenatal | DHA : 600 mg | | | softgels | seal. Does Not | Oil [EPA |
| DHA | [found: 586.7 | Heavy Metals: | Ethyl ester | | Contain: Sugar, | (Eicosapentaenoic Acid) |
| | mg √] | <u>Pass</u> | | | Gluten, Starch, | 300 mg, DHA |
| 2 MONTH SUPPLY: WILEYS FINES! | DPA: 54.7 mg | Lead: 0.001 | Store in a cool, | | Yeast, Wheat, Dairy, | (Docosahexaenoic Acid) |
| FISH OIL | Total Omega- | mcg/day (0.001 | dry place. | | Artificial Flavors, | 600 mg] 1,200 mg. |
| 0300 | 3: 994.8 mg | mcg/g) | | | Artificial Colors, | |
| Mfd. by Wiley's | Total Omega- | Cadmium: <0.01 | | | Nuts, Shellfish, | Ingredients: |
| Finest® A Wiley | 7 : 0 mg | mcg/g | | | Eggs, Peanuts, Soy | Concentrated Omega-3 |
| Companies | | Arsenic: <0.01 | | | or Corn. | Ethyl Esters from Wild |
| Brand™ | Total Oil: 1,200 | mcg/g | | | | Alaska Pollock (Fish) |
| | mg | Mercury: <0.001 | | | Precaution: | Oil, Fish Gelatin, |
| | | mcg/g | | | Contains Fish: | Glycerin, Purified Water, |
| | | | | | Alaska Pollock | Non-GMO Mixed |
| | | Take 2 softgels | | | (Gadus | Tocopherols. |
| | | daily with food. | | | chalcogrammus). | |
| Children: | I | I | 1 | I | I | I |

| _ | 1/25, 9.54 AIVI | | FISH OII, KIIII OII, an | d Algai Oil Offiega | -s Supplements Rev | iew & Top Picks - Cons | umercab.com |
|---|-------------------|----------------------|-------------------------|---------------------|--------------------|------------------------|--------------------------|
| | 3 | 1.5 tsp [7.5 | Freshness: Pass | _ | \$0.38/1.5 tsp | Non-GMO. Gluten | 1.5 tsp |
| | APPROVED | mL] | Peroxide: 0.1 | yellow | | Free. Sugar Free. | |
| | K | | meq/kg | emulsion with | [\$0.38] | Dairy Free. | Calories 30, Total Fat 2 |
| | 3 | EPA: 330 mg | Anisidine: 19.9 | strong | | | g, Saturated Fat 0.5 g, |
| | Top Pick | [found: 301.7 | TOTOX: 20.1 | sour/sweet | \$13.49/8 fl oz | | Polyunsaturated Fat 1 g, |
| | K. | mg √] | (Lemon flavor) | lemony flavor. | [266.2 mL] bottle | | Monounsaturated Fat 0 |
| | for children's | DHA: 210 mg | | Not fishy. | (approx. 35.5 | | g, Cholesterol 15 mg, |
| | product | [found: 196.8 | Heavy Metals: | | servings) | | Total Carbohydrate 3 g, |
| | Barlean's | mg √] | <u>Pass</u> | Very low | | | Total Sugars [Includes 0 |
| | Omega Pals - | DPA: 33.6 mg | Lead: 0.016 | concentration | | | g Added Sugars] 0 g, |
| | Chirpin' Slurpin' | Total Omega- | mcg/day (0.002 | | | | Sugar Alcohol 2 g, |
| | Lemonade | 3: 675 mg | mcg/g) | Form not | | | Omega-3 |
| | Flavor | [found: 609.9 | Cadmium: <0.01 | listed, but | | | Polyunsaturated Fat |
| | | mg √] | mcg/g | appears to be | | | [Eicosapentaenoic Acid |
| | BISLEANS . | Total Omega- | Arsenic: <0.01 | triglyceride | | | (EPA) 330 mg, |
| | | 7: 205.8 mg | mcg/g | | | | Docosahexaenoic Acid |
| | Emonada 220 E | (74.9% | Mercury: <0.001 | Refrigerate | | | (DHA) 210 mg, Other |
| | Dist. by | palmitoleic | mcg/g | after opening | | | Omega-3 Fatty Acids |
| | Barlean's | acid) | | | | | 135 mg] |
| | | | 1 1/2 tsp daily. | | | | Additional |
| | | Total Oil: | Slurp from a | | | | Information |
| | | 8,198.2 mg | spoon or mix into | | | | |
| | | | smoothies, yogurt, | | | | 1.5 tsp |
| | | | oatmeal and | | | | |
| | | | more. | | | | Calories 30, Total Fat |
| | | | | | | | 2 g, Saturated Fat 0.5 |
| | | | | | | | g, Polyunsaturated Fat |
| | | | | | | | 1 g, Monounsaturated |
| | | | | | | | Fat 0 g, Cholesterol 15 |
| | | | | | | | mg, Total |
| | | | | | | | Carbohydrate 3 g, |
| | | | | | | | Total Sugars [Includes |
| | | | | | | | 0 g Added Sugars] 0 |
| | | | | | | | g, Sugar Alcohol 2 g, |
| | | | | | | | Omega-3 |
| | | | | | | | Polyunsaturated Fat |
| | | | | | | | [Eicosapentaenoic |
| | | | | | | | Acid (EPA) 330 mg, |
| | | | | | | | Docosahexaenoic |
| | | | | | | | Acid (DHA) 210 mg, |
| | | | | | | | Other Omega-3 Fatty |
| | | | | | | | Acids 135 mg]. |
| | | | | | | | |
| | | | | | | | Ingredients: Water, |
| | | | | | | | fish oil (anchovy, |
| | | | | | | | sardine and/or |
| | | | | | | | |

| 1/25, 9:54 AM | ı | ı ısıı olı, ıxılıı olı, alı | u Aigai Oil Oillega | | iew & Top Picks - Consi | I |
|--|----------------------|-----------------------------|---------------------|------------------|-------------------------|------------------------------|
| | | | | | | mackerel), xylitol, |
| | | | | | | glycerine, gum arabic, |
| | | | | | | natural flavors, citric |
| | | | | | | acid, xanthan gum, |
| | | | | | | antioxidant blend |
| | | | | | | (Vitamin E (as d-alpha |
| | | | | | | tocopherol), rosemary |
| | | | | | | extract, green tea |
| | | | | | | extract, and ascorbyl |
| | | | | | | palmitate), guar gum, |
| | | | | | | turmeric, sorbic acid. |
| 3 | 2 chewable | Freshness: Partial | Taste: Soft, | \$0.35/2 | GOED Omega-3 | 2 chewable softgels |
| APPROVED | softgels | <u>Pass</u> | fish-shaped | chewable | Proud Member | |
| K | | Peroxide: 6.8 | softgel, that | softgels | seal. Non-GMO. | Calories 10, Total Fat 1 |
| Now® Kids DHA | EPA: 48 mg | meq/kg | releases a | | Kosher. Halal. This | g, Rich Oil Concentrate |
| Fish Oil | [found: 58.8 | Anisidine: | mildly sweet, | [\$0.56] | fish oil concentrate | (BioPureDHA®) |
| Chewables | mg √] | тотох: | non-fishy | | is manufactured | [Docosahexaenoic Acid |
| == | DHA: 200 mg | (Fruit punch | tasting liquid | \$10.61/60 | under strict quality | (DHA) 200 mg, |
| newkia | [found: 255.4 | flavor) | when chewed. | chewable softgel | control standards. | Eicosapentaenoic Acid |
| PISH OIL SHEWABLES | mg √] | | | | It is tested to be | (EPA) 48 mg] 1,100 mg. |
| The Control of Control | DPA: 14.8 mg | Heavy Metals: | Large (narrow) | | free of potentially | |
| Dist. by Now | Total Omega- | <u>Pass</u> | fish-shaped | | harmful levels of | Other Ingredients: |
| Foods | 3: 347.5 mg | Lead: 0.001 mcg | chewable | | contaminants such | Softgel Capsule [bovine |
| | Total Omega- | to 0.002 mcg/day | softgel | | as PCBs, dioxins, | gelatin (BSE-free), |
| | 7: 69.4 mg | (0.001 mcg/g) | | | mercury and other | glycerin, water, natural |
| | (69.1% | Cadmium: <0.01 | Very low | | heavy metals. | fruit punch flavor, xylitol, |
| | palmitoleic | mcg/g | concentration | | | cellulose] and Mixed |
| | acid) | Arsenic: <0.01 | | | Precaution: | Tocopherols. |
| | | mcg/g | Form not | | Contains fish | |
| | Total Oil: 1,100 | Mercury: <0.001 | listed, but | | (tuna). Mixed | |
| | mg | mcg/g | appears to be | | Tocopherols from | |
| | | | triglyceride | | non-GMO soy. | |
| | | For children and | | | Contains Xylitol, | |
| | | adults, take 2 | | | which is harmful to | |
| | | chewable softgels | | | pets. | |
| | | 1 to 2 times daily | | | | |
| | | with food, or as | | | | |
| | | directed by your | | | | |
| | | healthcare | | | | |
| | | practitioner. | | | | |
| Pet: | | | | | | |

| | ,, | a / ugai o ii o iii oga | o cappionionio i tot | iew & Top Picks - Cons | amereab.com |
|----------------------|--|-------------------------|---|------------------------|--------------------------|
| 2 pumps [4.9 | Freshness: Fail | Description: | \$0.25/2 pumps | GMO Free | 2 pumps |
| mL] | Peroxide: 9.1 | Clear, slightly | | Ingredients. No | |
| | meq/kg | salmon- | [\$0.10] | Rosemary Extract. | Crude Protein min. 0%, |
| EPA: 644 mg | Anisidine: 13.5 | colored oil with | | | Crude Fat min. 99.9%, |
| [found: 746.5 | TOTOX: 32.3 | faint stale | \$25.20/17 fl oz | Product of Norway. | Crude Fiber max. 0%, |
| mg √] | | fishy odor. | [502 mL] bottle | | Moisture max 0.5%, |
| DHA: 476 mg | Heavy Metals: | | (approx. 102.4 | | Crude max. Ash 0%, |
| [found: 467.9 | Pass | Moderate | servings) | | Eicosapentaenoic Acid |
| mg √] | Lead: 0.005 mcg | concentration | | | min (EPA) 644 mg/tsp, |
| DPA: 83.8 mg | to 0.019 mcg/day | | | | Docosahexaenoic Acid |
| Total Omega- | (0.001 mcg/g) | Form not | | | min (DHA) 476 mg/tsp, |
| 3: 1,118 mg | Cadmium: <0.01 | listed, but | | | Total Omega 3 fatty |
| [found: 1,477.1 | mcg/g | appears to be | | | Acids min 1,118 mg/tsp, |
| mg √] | Arsenic: <0.01 | triglyceride | | | Total Omega 6 fatty |
| Total Omega- | mcg/g | | | | Acids min 82 mg/tsp. |
| 6: 82 mg | Mercury: <0.001 | Fine to | | | |
| [found: 112 mg | mcg/g | refrigerate but | | | Ingredients: Salmon Oil, |
| √] | | not necessary. | | | Tocopherols |
| Total Omega- | Recommended | Use Within 90 | | | (preservative). |
| 7: 466 mg | Feeding Amount | days after | | | |
| (74.5% | (1 Pump is | opening. | | | |
| palmitoleic | approximately 1/2 | | | | |
| acid) | tsp): Dogs & Cats | | | | |
| | up to 35 lb 2 | | | | |
| Total Oil: | pumps x day = 1 | | | | |
| 4,707.1 mg | tsp 1,118 mg; | | | | |
| | Dogs 36 lb to 60 | | | | |
| | lb 3 pumps x day | | | | |
| | = 1.5 tsp 1,677 | | | | |
| | mg; Dogs 61 lb to | | | | |
| | 100 lb 6 pumps x | | | | |
| | day = 3 tsp 3,354 | | | | |
| | mg; Dogs + 101 lb | | | | |
| | 8 pumps x day = 4 | | | | |
| | tbsp 4,472 mg. | | | | |
| | mL] EPA: 644 mg [found: 746.5 mg √] DHA: 476 mg [found: 467.9 mg √] DPA: 83.8 mg Total Omega- 3: 1,118 mg [found: 1,477.1 mg √] Total Omega- 6: 82 mg [found: 112 mg √] Total Omega- 7: 466 mg (74.5% palmitoleic acid) Total Oil: | mL] | mL] meq/kg EPA: 644 mg [found: 746.5] mg ✓] DHA: 476 mg [found: 467.9] mg ✓] DPA: 83.8 mg Total Omega- 6: 82 mg [found: 112 mg ✓] Total Omega- 7: 466 mg (74.5% palmitoleic acid) palmitoleic approximately 1/2 tsp): Dogs & Cats up to 35 lb 2 pumps x day = 1 tsp 1,118 mg; Dogs 36 lb to 60 lb 3 pumps x day = 1.5 tsp 1,677 mg; Dogs 61 lb to 100 lb 6 pumps x day = 3 tsp 3,354 mg; Dogs + 101 lb 8 pumps x day = 4 | mL] | mL] |

| 131 Oil, Mill Oil, and Algar Oil Official Neview & 100 Fisher Official Control of Contro | | | | | | | |
|--|--|----------------------|--------------------|-----------------|------------------|-----------------|----------------------------|
| | 3 | 2 pumps [4.6 | Freshness: Pass | Description: | \$0.28/2 pumps | National Animal | 2 pumps |
| | APPROVED | mL] | Peroxide: 3.4 | Clear, pale | | Supplement | |
| | K | | meq/kg | yellow oil with | [\$0.12] | Council [NASC] | Crude Fat 99.5%, |
| | E | EPA: 800 mg | Anisidine: 11.9 | faint fishy | | seal. | Moisture 0.5% (max), |
| | Top Pick | [found: 663.3 | TOTOX: 18.7 | odor. | \$28.99/16 fl oz | | EPA 18.0%, DHA 12.0%, |
| | K | mg √] | | | [473 mL] bottle | | Total Omegas [Omega- |
| | for pet's product | DHA: 525 mg | Heavy Metals: | Moderate | (approx. 102.8 | | 3s 1,438 mg, EPA 800 |
| | Pet Honesty | [found: 500.4 | <u>Pass</u> | concentration | servings) | | mg, DHA 525 mg] 1,598 |
| | Wild Caught | mg √] | Lead: <0.001 | | | | mg. |
| | Omega-3 Fish | DPA: 72.9 mg | mcg/g | Form not | | | |
| | Oil - For Dogs & | Total Omega- | Cadmium: <0.01 | listed, but | | | Ingredients: Anchovy |
| | Cats | 3 : 1,438 mg | mcg/g | appears to be | | | Oil, Herring Oil, Mackerel |
| | | [found: 1,406.6 | Arsenic: <0.01 | triglyceride | | | Oil and Sardine Oil. |
| | OMEGA-3 PISH OIL | mg √] | mcg/g | | | | |
| | ************************************** | Total Omega- | Mercury: <0.001 | Store between | | | |
| | 16 To | 7: 452 mg | mcg/g | 55°-65°F | | | |
| | Dist. by Pet | (75.7% | | | | | |
| | Honesty | palmitoleic | Feeding | | | | |
| | | acid) | Directions: 0-15 | | | | |
| | | | lbs - 1/2 pump; | | | | |
| | | Total Oil: 4,393 | 15-25 lbs - 1 | | | | |
| | | mg | pump; 25-50 lbs - | | | | |
| | | | 2 pumps; 50-75 | | | | |
| | | Complies with | lbs - 3 pumps; 75+ | | | | |
| | | aspects of | lbs - 4 pumps. | | | | |
| | | GOED | | | | | |
| | | monograph | | | | | |
| | | | | | | | |

Unless otherwise noted, information about the products listed above is based on the samples purchased by ConsumerLab.com (CL) for this Product Review. The samples are from a single lot of the respective product. Be aware that there may lot-to-lot variation in products, particularly natural products. Manufacturers may change ingredients and label information at any time, so be sure to check labels carefully when evaluating the product you use or buy as it may be different from the product we tested. Manufacturers may also change ingredient suppliers, which can affect product quality. Pricing can change over time and vary based on retailer, promotions, and other factors.

The information contained in this report is based on the compilation and review of information from product labeling and analytic testing. CL applies what it believes to be the most appropriate testing methods and standards. The information in this report does not reflect the opinion or recommendation of CL, its officers or employees. CL cannot assure the accuracy of information.

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Products tested in 2023

ConsumerTips™:

What to Consider When Buying:

Getting EPA and DHA From Supplements:

When buying supplements containing EPA and/or DHA, keep in mind that products vary significantly in terms of the amounts and ratios of EPA and DHA. Be aware that only about a third of the total oil from fish is EPA and DHA, although this may be higher (up to about 85%)

as EPA and DHA) in a "concentrated" product". With a more concentrated product, one may be able to take fewer capsules of the same size. Your daily intake should be based on your reason for taking it (see below) and the amount that you are already getting from your diet.

The ratio of EPA to DHA in marine oils will also vary. Products made from menhaden and other small oily fish, for example, tend to have a ratio of EPA to DHA of 1.5:1 so that a capsule claiming 1 gram (1,000 mg) of fish oil, of which 30% is EPA and DHA, provides 180 mg of EPA and 120 mg of DHA. Salmon oil naturally contains more DHA than EPA (often several times more), and algal oil also typically contains more DHA than EPA. Does the ratio matter? It's not clear, but EPA may have slight benefits. A study of people with normal cholesterol levels found that both EPA-rich and DHA-rich fish oils at a very high daily dose of 12 grams (of which about 40% was EPA and/or DHA) for 8 weeks equally decreased triglyceride levels by about 14% but had little overall effect on LDL "bad" cholesterol or HDL "good" cholesterol. Both down-regulated several proteins, such as gelsolin, involved in inflammation, but fish oil rich in EPA did this to a greater extent than fish oil rich in DHA, suggesting a more anti-inflammatory effect of EPA. EPA also resulted in greater increases in ApoM (a subfraction of HDL), which has potential anti-atherosclerotic functions (Yang, Nutrients, 2020).

"Fishy" Labeling:

To distinguish themselves, some products sport terms that, in actuality, are meaningless and misleading:

- "Pharmaceutical grade" Although some products claim to be "pharmaceutical grade" this term means nothing, as the FDA has not defined what would constitute a pharmaceutical grade fish oil product.
- "Tested in FDA approved laboratories" -- The FDA does not approve analytical laboratories so these claims are not correct, although laboratories may be FDA registered and inspected. (None of the products in this Review make this statement.)
- "Krill Oil" -- Be aware that the term "krill oil" in the name of a product does not necessarily mean it's all krill oil. For example, in the past we found that if you looked carefully at the label of one krill oil product, the "Other Ingredients" section (which is in order of amount) showed "fish oil" first on the list. In fact, even the astaxanthin (naturally found in real krill oil, giving it its red color) has been added from an algal source, although this is not always disclosed on labels. (Fortunately, all of the products labeled as "krill oil" products in this review list only krill oil as the source of its omega-3 fatty acids).
- "Daily value for EPA and DHA" -- In the Supplement Facts panels of some products are claims that they provide a specific
 percentage of the DV (Daily Value) for EPA and DHA. DVs are developed by the USDA and FDA and relate to the recommended
 daily allowance of a required nutrient. However, no DV has been established for EPA and DHA. (None of the products in this
 review make this claim.)

Forms of Fish Oil — Natural Triglycerides, Ethyl Esters, Re-Esterified Triglycerides, or Monoglycerides: Is One Better? The Forms:

The omega-3 fatty acids (EPA and DHA) in fish oil naturally occur in the form of **triglycerides** (fatty acids attached to glycerol). However, in most supplements, fish oil is not in this natural triglyceride form, but has been converted other forms in order to purify, concentrate, and/or stabilize it. Natural fish oil may also be purified and concentrated without solvents using methods such as **supercritical CO2 extraction** (which uses a gas and some heat) or **winterization** (which uses cold temperatures).

One of the most common forms of fish oil in supplements and medications is the **ethyl ester** form, which is created by exposing the fish oil to ethanol, replacing the glycerol molecule. This allows the fish oil to undergo molecular distillation: the oil is heated under high vacuum, causing certain other compounds, such as contaminants, to be removed while concentrating the omega-3 fatty acid ethyl esters. This distillation may also reduce levels of some potentially beneficial compounds (such as small amounts of vitamins) found in fish oil, but this has to be weighed against the benefit of removing contaminants and concentrating the EPA and DHA.

A third common form of fish oil on the market is known as **re-esterified triglycerides**. It is made by chemically converting ethyl esters back to triglycerides, so that most of the omega-3 fatty acids are, once again, triglycerides. A very small amount of ethanol (pure

alcohol) is released from the ethyl ester form into the gut during this process (about 13% of EPA/DHA ethyl ester is ethanol), although the amount is likely to be insignificant (just a few drops of ethanol per softgel) for most people. (Note: It has been demonstrated, typically as part of a sales pitch, that the ethyl ester form of fish oil will dissolve Styrofoam — going through a cup, for example, in just a few minutes, while the triglyceride forms will not. While this effect is real — due to differences in the polarity of the forms — this is not a health concern).

Another marketed form of fish oil is the **monoglyceride** form, which is made by "predigesting" the triglyceride form of fish oil (<u>Castejon</u>, <u>N Biotechnol 2020</u>), although after you swallow any form of fish oil, your body's digestive enzymes free the omega-3 fatty acids so they can be absorbed.

Absorption: While a sufficient dose of any of these forms can significantly raise the levels of EPA and DHA in your blood, a study found that people absorb more of these omega-3 fatty acids (about 76% more) from the re-esterified triglyceride form of fish oil than from the ethyl ester form (Dyerberg, PLEFA 2010). This study, in which each form was taken daily for two weeks (with the recommendation that it be taken at "meal times"), found that re-esterified triglyceride fish oil is absorbed even better than natural fish oil (34% more fatty acids are absorbed). Fish oil in a free fatty acid form was not absorbed as well as natural fish oil (about 14% lower absorption of EPA and DHA), although this difference was not statistically significant.

Quite often, some of the omega-3s in re-esterified triglyceride fish oil is not all triglycerides, but can be diglycerides or monoglycerides. A study among 48 healthy, young adults (average age 24) who received 5,000 mg of fish oil (that was about 50% omega-3s) in either a greater than 95% re-esterified triglyceride form (*Ultimate Omega* by Nordic Naturals, which was involved in funding and conducting the study) or a less than 70% re-esterified triglyceride form (*MEG-3* bulk oil by DSM), once daily at breakfast with water, found that omega-3 fatty acids (including DHA, EPA, and docosapentaenoic acid) from *Ultimate Omega* were incorporated into red blood cell membranes slightly more than from *MEG-3* bulk oil after 4 months. However, the total daily intake of omega-3 fatty acids from *Ultimate Omega* was slightly greater than that of *MEG-3* bulk oil (daily amount of EPA+DHA: 2,750 mg vs. 2,500 mg), and both products were taken on an empty stomach rather than with a high-fat meal, which helps increase absorption. Therefore, it's unclear how meaningful the observed difference in absorption is to a consumer (Minton, PLoS One 2023).

A study in 20 healthy people found that giving a single oral dose of 6,000 mg of the monoglyceride form of fish oil (*MaxSimil 3020*), providing 1,800 mg of EPA and 1,200 mg of DHA and given with a low-fat meal, resulted in double the blood level of DHA plus EPA than the same amount of fish oil in ethyl ester form over the following 24 hours, and about four times the level during the first 5 hours after eating (the critical period for absorption) (*Chevalier, Eur J Clin Nutr 2020*). The study was funded by a seller of *MaxSimil*, Neptune Wellness.

A subsequent study led by the same researcher (and also funded by Neptune Wellness) among 22 adults (average age 28) compared absorption of equal amounts of fish oil (880 mg of EPA and 332 mg of DHA) in monoglyceride (*MaxSimil*), ethyl ester, and triglyceride forms, all given with a low-fat meal. The study, over 24 hours, showed no difference in blood levels of DHA, although levels of EPA were twice and three times as high with the monoglyceride form compared to the triglyceride and ethyl ester forms, respectively (*Chevalier*, *J Nutr* 2021). Another study found that the absorption of fish oil in the monoglyceride form is similar to that of the free fatty acid form and similar to or slightly better than that of the triglyceride form when given to people following a low-fat diet (*Cuenoud*, *Nutrients* 2020).

It should be noted that none of the studies with the monoglyceride form were given with a high-fat meal, and studies that have expressly required fish oil to be taken with a high-fat meal have shown little difference in absorption among the various other forms (Nordoy, Am J Clin Nutr 1991; Lawson, Biochem Biophys Res Commun 1988).

Because the ethyl ester form has been the most widely available form on the market, most of the clinical studies with fish oil

supplements have been conducted with this form, which have shown it to be generally safe, as well as effective for certain conditions such as improving cholesterol levels in people with high triglycerides (see What It Does).

An experiment in mice showed that DHA from natural fish oil relaxed smooth muscle in vascular tissue and temporarily lowered blood pressure, while DHA in the ethyl ester form did not. In fact, the ethyl ester form blocked natural DHA from having this blood pressure-lowering effect. Similar effects were found when comparing natural and ethyl ester forms of EPA (Hoshi, PNAS 2013). Although these findings might, at first, seem concerning, the doses were administered to the mice intravenously (IV), thereby allowing the ethyl esters into the blood; this could not happen if they had been taken by mouth, like a supplement. The findings, however, may raise issues for people who get fish oil as part of parenteral (IV) nutrition, as the ethyl ester and triglyceride forms may affect their blood pressure differently.

In summary, each of the four forms of fish oil, after being digested, will end up in the same form in your blood and, if taken with a fatty meal, will be equally well absorbed over 24 hours. However, if you are taking fish oil with just a small meal or no food, it may be fair to pay some premium for fish oil in the natural or re-esterified triglyceride forms. If you choose to use either of these two forms, look for products which list EPA and DHA as "triglycerides." Be aware that some products with "natural" in the name don't seem to provide truly natural fish oil, but may just start with natural fish oil which is then chemically treated or simply have "natural" as part of their brand name. Although the monoglyceride form of fish oil seems to have somewhat better absorption than the triglyceride form when fish oil is not taken with a high-fat meal, less is known about the safety and effectiveness of this form.

Note that to avoid contaminants in an *un*refined supplement, it's best to choose those made from small, oily fish that are low in food chain, such as anchovy, sardines or menhaden. Also be aware that fish "liver" oils can contain high levels of vitamins, such as vitamin A, which can be toxic at excessive doses (see <u>Concerns and Cautions</u> below, as well as our separate <u>Review of Vitamin A and Cod Liver</u> <u>Oil Supplements</u>).

You'll find that many products also contain vitamin E or other antioxidants to stabilize the oils and prevent them from becoming rancid.

Algal and DHA-Rich Oil

Algae (including microalgae) are aquatic organisms which are sources of DHA and, to a lesser extent, EPA.

A recent analysis of clinical studies using relatively high dose DHA from algal oil (averaging 1,680 mg of DHA per day) found it to be similar to high dose EPA and DHA in lowering triglycerides and increasing HDL cholesterol (Bernstein, J Nutr 2012). The high-dose algal oil lowered triglycerides by about 15% and increased HDL cholesterol by about 5%. The algal oil also caused an 8% increase in LDL cholesterol. LDL cholesterol is often thought of as "bad" cholesterol; however, the LDL particles themselves became larger in size, which may make them less likely to harden arteries. Similar results have been seen with purified DHA from fish oil. DHA has also been found to be more effective than EPA at increasing HDL2 cholesterol the subfraction of HDL cholesterol that may be most protective against coronary heart disease (Mori, Am J Clin Nutr 2000).

If you are primarily interested in DHA or are vegetarian, algal oil supplements — although more expensive than most fish oil supplements — are a good option and they are typically very low in contaminants since algae is low on the food chain. The EPA and DHA in algal oil supplements is normally in the triglyceride form.

Krill Oil (and Astaxanthin)

Like fish oil, oil from krill (a shrimp-like crustacean) contains significant amounts of both EPA and DHA. Preliminary studies indicate that krill oil, like fish oil, has a beneficial effect on cholesterol and triglyceride levels and anti-inflammatory applications. The phospholipids in krill oil may enhance absorption of its EPA and DHA, and a 4-week study funded by a krill oil manufacturer (AkerBioMarine) showed that EPA and DHA from krill oil are absorbed at least as well, if not somewhat better, as they are from fish oil. The daily quantity of EPA

provided in the krill and fish oil supplements were comparable; however, the amount of DHA present in the krill oil was approximately one half that provided in the fish. At the end of the treatment period, the mean plasma EPA concentration was 28% higher in the krill oil group compared with the fish oil group, whereas the DHA concentrations were comparable – suggesting twice the absorption of DHA from the krill oil, although this was not evaluated for statistical significance (Maki, Nutr Res 2009).

Astaxanthin:

Krill oil also contains astaxanthin, a carotenoid is naturally produced by microalgae (*Haematococcus pluvialis*) which, through the food chain, provides the pink coloration of shrimp and other crustaceans, as well as salmon and trout. (A typical 4-ounce serving of farmed Atlantic salmon provides approximately 1 mg of astaxanthin and a similar serving of wild Pacific salmon provides about 4.5 mg.)

Astaxanthin itself has a range of potential uses (see the <u>Astaxanthin Supplements Review</u> for more information), although all based on preliminary evidence. It may also be helpful in <u>preventing sunburn</u>.

ConsumerLab.com has found that some krill oil supplements contain additional astaxanthin — which may be naturally derived or synthetic, as this is often not disclosed on the label. Overall, there is currently not enough evidence to determine whether natural or synthetic astaxanthin provides any advantage over the other. Brands of natural astaxanthin derived from microalgae include *BioAstin* (Cyanotech), *AstaREAL* (Fuji Health Science) and *AstaPure* (Algatechnologies Ltd). In these products, astaxanthin exists in a single isomeric form (i.e., molecular configuration) known as 3S, 3S', which is the predominate form of astaxanthin naturally found in fish oil. Synthetic astaxanthin differs from natural astaxanthin in that it includes additional isomers, so that one quarter of synthetic astaxanthin is in the 3S, 3S' form. The other forms, however, are believed to be active anti-oxidants. Synthetic versions also provide astaxanthin in its "free form," while natural astaxanthin is in an "esterified" form; both forms can increase blood levels of astaxanthin in people. Although there is some very preliminary evidence that the free (synthetic) form of astaxanthin may be slightly more bioavailable (Coral-Hinostroza, Comp Biochem Physiol C Toxicol Pharmacol 2004), some *in-vitro* research that suggests the natural, esterified form may have more antioxidant activity (Capelli, Nutrafoods 2013). Synthetic astaxanthin appears to be safe in amounts typically used in foods and supplements — one brand of synthetic astaxanthin, *AstaSana* (DSM) has been approved for use as a food additive.

Krill Harvesting: Krill is a primary food source for certain whales, seals, penguins and other animals. Its harvesting has been a subject of environmental debate. Proponents of the use of krill oil in supplements argue that it is plentiful and only a small percentage of total krill biomass is being harvested, most of which is used in fish meal and not for direct human consumption. There are also catch limits for sustainable exploitation established by a conservation commission known as CCAMLR, and registration and monitoring is required of harvesting vessels. However, other groups, such as the Antarctic Krill Conservation Project counter that krill harvesting may have detrimental effects on sea life and on other animals that depend directly or indirectly on krill, and that current limits and monitoring are insufficient. If you decide to use krill oil, it may be best to look for products marked as Certified Sustainable Seafood with a blue-colored seal from MSC (Marine Stewardship Council). Our Top Pick for krill oil has the MSC seal. MSC is a nonprofit originally founded by Unilever and the World Wildlife Fund (NPR 2013), reflecting the interests of both industry and the environment. To carry the MSC seal, the seafood ingredients in a product must come from fisheries certified to only fish healthy stocks, be well-managed so stocks can be fished for the long-term, and minimize their impact on other species and the wider ecosystem. The MSC approach is not perfect, and some certified fisheries have been noted as not being in full-compliance and not making improvements necessary for compliance (WWF 2020).

Calamari Oil

Squid, also known as calamari (particularly when referring to it as a food) are a rich source of omega-3s. Unlike fish oil, calamari oil contains a higher amount of DHA than EPA (as you can see from the results table above). As squid have a short life cycle, they may be less likely to accumulate toxins than longer-lived fish, particularly those higher up on the food chain. A common source of calamari oil in supplements is trademarked Calamarine, which, according to the website of its manufacturer, Pharma Marine, is a socially responsible source of marine omega-3s as it is "produced solely from by-products of existing food production of calamari" and may be more ecofriendly than other animal sources based on how it is harvested.

Enteric-coated Pills:

Some fish oils come in enteric-coated pills, designed to release the oils in the intestine rather than the stomach — to help avoid fishy aftertaste or fishy smelling burps. As long as these pills release on time, this should not compromise your absorption of omega-3s because oils are not absorbed in the stomach, but in the intestine. With the help of bile acids, oils get emulsified (made into smaller droplets) in the upper intestine so they can be more effectively acted on by pancreatic lipase (an enzyme) and absorbed further down the small intestine. If this doesn't happen, less oil may be absorbed.

So while enteric-coated pills may be fine, if you notice more oily stools, this would be an indication that the oils are not being well absorbed. Also, be aware that some of these enteric coatings are made with acrylics (such as methacrylic acid copolymer) that don't break down – they are like thin latex balloons intended to pop open under specific conditions (they are also somewhat stiffer than regular softgels). You might find remains of these pills in your stool, but there is no reason to be concerned.

Getting EPA and DHA from Food:

You may want to consider getting omega-3 fatty acids directly from fish. For the general population, the American Heart Association (AHA) recommends at least two 3.5 oz servings of non-fried fish (preferably fatty fish) per week. For people with heart disease or cardiac risk factors, some experts recommend eating four 3-ounce servings of fatty fish per week. Fatty fish, such as the following, have higher levels of omega-3 fatty acids:

- Anchovies
- Bluefish
- Carp
- Catfish
- Halibut
- Herring
- Lake trout †
- Mackerel
- Pompano
- Salmon *
- Sardines
- Striped Sea Bass
- White Tuna (Albacore) **
- Whitefish

Source: U.S. Department of Agriculture, Agricultural Research Service. 2001; <u>Oregon State University, Omega-3 Fatty Acid Content in</u> Fish.

- * Farmed salmon may contain more PCBs than other salmon.
- ** May contain an excessive amount of mercury.
- [†] Lake trout may be a good source of EPA and DHA (about 500 mg of EPA and 1,100 mg of DHA per 3.5 ounces), but many canned trout products contain *rainbow* trout, which contains only about 1/3 the amount of these omega-3 fatty acids (100 mg of EPA and 400 mg of

DHA per 3.5 ounces).

Total amounts of omega-3s vary among fish. ConsumerLab.com's <u>tests of canned tuna and canned salmon</u> found some tuna to provide less than 100 mg of EPA and DHA per suggested serving (2 ounces), while others provided more. In general, canned salmon provided significantly more EPA and DHA than canned tuna (as salmon is an oilier fish) as well as lower concentrations of mercury and arsenic.

A three-ounce serving of canned salmon contains about 4.5 grams of fat of which 17% is EPA (166 mg) and DHA (587 mg). In salmon steaks and fillets, the fatty layer underneath the skin is richest in omega-3s. However, if you prefer not to eat this part, there is also a significant amount of DHA and EPA distributed throughout the flesh of the salmon, especially in the red muscle (located at the outside edges of a cut piece of salmon steak) and in the area surrounding the belly (this area is located in the outer portion of the "u" shape in a cut piece of salmon steak) (Aursand, J Sci Agr 2006).

(See our Canned Fish Review to learn about the differences between farmed and wild salmon).

Omega-3 Fortified Foods

Eggs fortified with DHA are also available in the U.S. and claim to contain about 150 mg of DHA in each egg. Chickens producing these eggs are typically fed algal DHA. Algal DHA is also an approved food ingredient, so that foods and beverages can be fortified with DHA and be considered vegetarian. Because some formula-fed infants may not be converting enough ALA to DHA, some formulas are also available with DHA -- which has been added to formulas for premature infants for many years.

Amounts of EPA and/or DHA in fortified foods and beverages tend to be about 50 to 100 mg per serving -- much lower than that found in a serving of fish or in a traditional fish oil supplement. While omega-3 fortified products can contribute to your intake of these fatty acids, they are typically not sufficient in themselves to provide the full generally recommended amounts of EPA or DHA.

Be aware that ConsumerLab.com found, in the past, that some fortified foods or beverages claimed to supply certain percentages of a "Daily Value" of EPA and DHA, stating the Daily Value for these to be 160 mg of EPA and DHA. Such statements are not correct. A "Daily Value" for omega-3 fatty acids has not been established. In April 2014, the FDA <u>ruled</u> that statements on the labels that claim a product is "high in" DHA or EPA (or statements using similar language, such as "rich in" or "excellent source of") are prohibited, as these types of statements are only permitted for nutrients for which reference levels have been established (<u>FDA, Nutrient Content Claims: Final Rule 2014</u>).

DPA: The "other" omega-3

After EPA and DHA, DPA (docosapentaenoic acid) is often the third most prevalent omega-3 fatty acid in fish oil – although it often occurs in much smaller amounts and is typically not included in labels, yet some products contain over 100 mg per serving.

ConsumerLab and other researchers have found DPA to represent about 2% to 5% of the total omega-3 fatty acids in fish oil (Byelashov, Lipid Technol 2015). However, much larger amounts of DPA can be obtained from eating a 3.5 oz. portion of the following fish: raw salmon (393 mg) Atlantic mackerel, (200 mg), and Pacific herring, bluefin tuna, and rainbow trout (between 100 mg and 200 mg) (Byelashov, Lipid Technol 2015). Similarly high amounts can be obtained from canned salmon, particularly sockeye (red) salmon, while canned tuna tends to contain smaller amounts (as well as lower overall amounts of omega-3 fatty acids) (see ConsumerLab's Canned Tuna and Salmon Review).

In the body, DPA can be produced from EPA, and structurally, the two fatty acids are very similar (<u>Dyall, Front Aging Neurosci 2015</u>). Higher blood levels of DPA have been associated with lower blood triglycerides, cholesterol and inflammation, and a lower risk of heart attack and overall risk of coronary heart diseases (<u>Byelashov, Lipid Technol 2015</u>). Having higher blood levels of EPA and DPA, but not DHA, has been associated with healthier aging (longer life free from major cardiovascular, lung and kidney disease, cancer, physical or mental dysfunction). A 13-year-study of over 2,500 older men and women (with an average age of 74 at the start of the study) found

that having the highest blood levels of EPA and DPA, as opposed to the lowest levels, was associated, respectively, with a 24% and 18% lower risk of unhealthy aging. No such association was found with blood levels of DHA (<u>Lai, BMJ 2018</u>).

However, there are very few clinical studies on the effects of DPA supplementation. A preliminary study in Australia among ten healthy young women found that DPA supplementation (2 grams of 99.8% pure DPA taken for one day, followed by 1 gram per day for six days) significantly increased blood levels of DPA, as well as EPA plus DHA, and the researchers proposed that DPA may act as a "reservoir" for EPA and DHA for the body to use as-needed (Miller, Eur J Nutr 2013). A small, company-funded study among men and women with moderate to high triglyceride levels found that 4 grams of a prescription DPA/EPA formula (MAT9001, Matinas BioPharma) taken for two weeks lowered triglyceride levels by about 13% more, and lowered very low density lipoprotein (VLDL) by 24% more than the same dose of a prescription ethyl ester EPA (Vascepa, Amerin). However, the exact amount of DPA in the product is not known, and the product does not appear to be on the market.

Contaminants in Fish vs. Supplements

Mercury is not a known contaminant in fish oil or other marine oil supplements. ConsumerLab.com has never found mercury in such supplements. Mercury is a potential problem, however, in fish meat. Levels of pollutants, such as mercury, tend to be higher in long-lived, larger fish, particularly shark, swordfish, king mackerel, and tilefish. These fish tend to average about 1,000 ppb (parts per billion) of mercury — the FDA limit for human consumption — while most other fish tend to have about one-tenth to one-third of this amount. Eating a fish with 1,000 ppb of mercury is not necessarily toxic, but it should not be consumed by young children and pregnant or nursing women, or by anyone on a regular basis. The Environmental Protection Agency (EPA) has also advised that fresh-water fish may contain more mercury than commercially caught fish and advises that "If you are pregnant or could become pregnant, are nursing a baby, or feeding a young child, limit consumption of fish caught by family and friends to one meal (about 6 ounces) of fish per week." The same limit is recommended for albacore ("white") tuna, as it may occasionally contain excessive levels of mercury.

Microplastics are small fibers and particles of plastic in the environment that can be ingested by fish. There is evidence of microplastic contamination in the flesh of fish and other seafood (see our Review of Canned and Packaged Fish). Due to the filtration process used to produce fish oil, it is much less likely to contain the amounts of microplastics found in fish flesh. The industry organization GOED (Global Organization for EPA and DHA) has stated that "it can be said with a high level of certainty that microplastic particles with a diameter larger than 0.5 to 1 micrometer are not present in refined fish oils." (GOED 2018). The organization notes that fish oil in supplements could potentially contain much smaller plastic particles known as nanoplastics (0.001 to 0.1 micrometers), but there are currently no methods to assess this. Microplastics also contain and can leach compounds such PCBs (polychlorinated biphenyls) and a chemically similar group of compounds known as PBDEs (polybrominated diphenylethers), but, as discussed below, amounts of these compounds in fish oil have been found to be extremely low in comparison to amounts that would be ingested when eating fish.

PCBs (polychlorinated biphenyls) occur in nearly all fish oil supplements but almost always at extremely low levels, as shown in our testing. You are likely to get a much higher amount of PCBs from eating fish. A study of fish sold in markets in Germany, for example, looked at a dioxin-like PCBs (dl-PCBs) which are a small subset of PCBs but which are known to be most toxic. It found that oily fish (such as salmon) to contain about 2 picograms of dioxin-like PCBs (dl-PCBs) per gram (Karl, J Verbr Lebensm 2008). A small serving (3 ounces or 85 grams) of salmon, therefore, would contain about 170 picograms of dl-PCBs. Even a serving of less oily fish (which tend to have fewer PCBs but also less omega-3s) is likely to contain several times more PCBs than a typical fish oil supplement.

The FDA permits a 3-ounce serving of fish to contain about 169,000,000 picograms of total PCBs, 1,000 times more than in any of the products in this review. The EPA, using a more conservative approach, estimates that the average adult can consume 1,400,000 picograms of total PCBs per day without harmful effects. If you are concerned about mercury and other potential contaminants, concentrated fish oil products may be a better choice, provided that they contain the claimed amount of oils and meet other quality parameters tested for in this review.

PBDEs (polybrominated diphenylethers) are chemically similar to PCBs. Although low concentrations of PBDEs have been detected in fish oil supplements, they occur in much lower concentrations than one would ingest if consuming fish. For example, the concentration of PBDEs in 10 fish oil supplements purchased online or in retail stores in the U.S. between 2007 and 2009 was found to be very low (average 3 ng/g) (Ashely, Food Addit Contam 2010), while concentrations of PBDEs in fish such as Norwegian wild herring and farmed salmon have been reported to be much higher (16.63 ng/g and 19.52 ng/g, respectively (Bethune, National Institute of Nutrition and Seafood Research 2004). Even including fish consumption, overall exposure to PBDEs from all dietary sources is estimated to be only 17%, while 85% of exposure is estimated to come from soil, dust, and dermal exposure (Wu, Environ Sci Technol 2007).

PFAS (per- and polyfluoroalkyl substances) are a class of chemicals used in products such as Teflon, dental floss and packaging. PFAS exposure has been linked with negative health effects, including altered immune and thyroid function, liver disease, lipid and insulin dysregulation, kidney disease, adverse reproductive and developmental outcomes such as low infant birth weights, and cancer (Fenton, Environ Toxicol Chem 2021; EPA 2018; CDC 2020). They break down slowly, or in some cases, not at all, and can accumulate in the environment. Once plants or animals are exposed to PFAS, these chemicals are taken up into protein-rich tissues. Concerning levels of PFAS have been found in canned clams sold in the U.S., but not in other seafood samples such as canned tuna, salmon, shrimp and other seafood products (see CL Answer about PFAS for more details). Furthermore, fish oil supplements do not appear to be a significant source of PFAS. A study comparing blood levels of 5 different PFAS compounds among more than 4,500 people in the U.S. found that taking fish oil supplements (at least one serving per day) was not associated with increased blood levels of any PFAS compound compared to not taking fish oil supplements (Onteeru, Environ Res 2022).

Omega-3 vs. Omega-6 Fatty Acids:

Some experts suggest that the American diet contains too little omega-3 fatty acids and too much of another essential fatty acid family called the omega-6 fatty acids. Omega-6s are found in oils from corn, sunflower, soy, peanut and other plants. The typical ratio of omega-6's to omega-3's in the American diet is believed to be as high as 14:1 (14 grams of omega 6's for every gram of omega-3's); these experts suggest that a ratio of no more than 3:1 (3 grams of omega-6's for every 1 gram of omega-3) may be preferable. However, the evidence for this recommendation is sketchy at best.

Omega-7 Fatty Acids:

Omega-7s are a class of unsaturated fatty acids including palmitoleic acid, vaccenic acid and margaroleic acid. Palmitoleic acid is one the most commonly occurring omega-7s, found in foods like eggs, salmon, anchovy, sardines, macadamia nuts, olive oil and cod liver oil. It is also synthesized in the body by the liver and found in fat tissue. Palmitoleic acid should not be confused with *palmitic acid*, a saturated fatty acid found in many of the same foods as palmitoleic acid.

As noted earlier, some fish and marine oil supplements may also contain palmitoleic acid, although amounts are typically not listed on the label and, in general, it appears that the more highly concentrated a fish oil is in EPA and/or DHA, the lower the concentration of omega-7 fatty acids will be. Products made from algae oil contain virtually no omega-7s, although it is abundant in the sea buckthorn. (See the 2nd column of the Results Table for amounts of total omega-7s and the percentage of palmitoleic acid found in each product.)

Unfortunately, clinical studies have failed to show cardiovascular benefit with omega-7 fatty acids and palmitoleic acid. A study that reported benefits on lipid levels with daily supplementation with 220 mg of palmitoleic acid daily for 30 days was later retracted due to concerns over its statistical accuracy (Bernstein, J Clin Lipid 2014).

In a study among 50 men and women with **chronic musculoskeletal discomfort** and slightly elevated levels of c-reactive protein (CRP, a blood marker of inflammation in the body sometimes also used to assess cardiovascular risk), 688 mg of palmitoleate from an omega-7 fish oil blend (*Barlean's*) taken daily for three weeks did *not* reduce levels of CRP or other blood markers of inflammation, or decrease muscle discomfort or improve self-reported quality of life compared to placebo (medium-chain triglycerides, i.e., MCT oil) (Sasagawa, Nutrients 2021).

A study in South Korea among 98 middle-aged women (average age 46) found that those who took one capsule containing 500 mg of refined Alaskan pollock fish oil providing 250 mg of palmitoleic acid (7-MEGA, by VITECH — which funded the study) twice daily (with breakfast and dinner) for three months had a *slight*, but statistically significant decrease in the roughness and depth of wrinkles at the outer corner of the eyes (i.e., "crow's feet") and a slight increase in skin elasticity compared to placebo. Taking 7-MEGA did not, however, prevent loss of skin moisture (Sung, Nutrients 2024).

A branded, "purified" form of palmitoleic acid found in a number of omega-7 supplements, called <u>Provinal®</u> (Tersus Pharmaceuticals) is processed to reduce the amount of palmitic acid it contains to less than 1%. <u>Provinal®</u> is derived from anchovy and contains 50% palmitoleic acid (most of the omega-3 fatty acids have also been removed). Many of the supplements on the market containing this brand provide the omega-7 oil in a softgel or capsule containing 460 mg of <u>Provinal®</u> (210 mg of palmitoleic acid) each, and cost between \$14 and \$25 dollars for 30 pills (a one-month supply).

Clinical studies assessing cardiovascular and other potential effects of sea buckthorn berry juice or puree have failed to show a benefit.

A study in China among 99 people with high cholesterol who were not taking cholesterol-lowering medication found that taking 30 grams (about 1 ounce) of de-seeded sea buckthorn berry puree three times daily for 90 days did not improve total cholesterol, LDL cholesterol, HDL cholesterol or triglycerides, nor did it improve blood pressure, body mass index or biomarkers of atherosclerosis and inflammation, compared to placebo (Zhou, Anim Biotechnol 2020).

A puree made from frozen sea buckthorn berry, has been tried in healthy men and women to try to prevent colds. It did not have that effect, although it did decrease levels of the inflammatory marker CRP compared to placebo (<u>Larmo, Eur J Clin 2008</u>).

Be aware that sea buckthorn seed oil is very different than the juice and has only about 1/10th the concentration of omega-7 fatty acids.

Also, be aware that some supplements containing omega-3 and omega-7 fatty acids are marketed as omega-10 fatty acids — claiming provide a "more complete" fatty acid formula (i.e., omega-3 plus omega-7) for cardiovascular health. However, as noted above, there is no evidence to support this, there is no "omega-10" fatty acid, and many fish oil supplements already do contain omega-7 fatty acids.

What to Consider When Using:

Dosage:

- In the U.S., there is no official recommended intake for EPA and DHA in healthy people (See <u>Daily Value</u> for more information). However, some other countries recommend from 300 mg to 500 mg per day of a combination of EPA and DHA. This is roughly equivalent, if not greater than, the amount of omega-3s obtained from two servings of fish per week, as suggested by the American Heart Association (See <u>Getting EPA and DHA from Food</u>).
- The most recent evidence does not support fish oil supplementation for reducing heart attacks and strokes (Kwak, Arch Intern Med 2012). Any potential cardiovascular benefit of supplementation may be limited to people who do not regularly consume fish in their diets and who are not taking other medications for heart disease. A diet high in fatty fish (2 servings of marine fish per week) continues to be recommended as it provides omega-3 fatty acids and replaces less healthful protein sources, such as red meat (Hu, Arch Intern Med 2012). A study in Norway among CAD patients showed only those with intakes lower than 300 mg per day of omega-3 fatty acids had a slightly increased risk of coronary events. There was no significant difference in risk among groups with high (580 mg), very high (1,360 mg) or even extremely high (2,640 mg) daily intakes of omega-3's (Manger, Am J Clin Nutr 2010).

- A typical dose of fish oil for specific therapeutic uses is 6-12 grams daily. However, as noted above, EPA and DHA represent only part of the total oil in fish and their levels vary among products. For most therapeutic uses of omega-3s, the daily dosage of total EPA and DHA tested in studies has ranged from 1-6 grams daily. Higher dosages have been tried by some researchers, especially for the treatment of **schizophrenia**, **Raynaud's phenomenon**, and **lupus**.
- For maintaining remission in ulcerative colitis, 1,000 mg twice daily of EPA in enteric-coated capsules (<u>Scaioli, Clin Gastro Hep 2018</u>).
- For pregnant and nursing women, the recommended dose of DHA, from either supplements or fish, is 100 to 200 mg per day. 400 mg DHA daily has been shown to reduce colds during initial months of infancy among women with otherwise low DHA intake (Imhoff-Kunsch, Pediatrics 2011). A study using higher amounts of omega-3's (800 mg DHA and 100 mg EPA daily) showed reduced risk of very premature birth as well as lower risk of egg allergy in infants (Makrides, JAMA 2010, Palmer, BMJ 2012). Even higher amounts (1,320 mg EPA and 880 mg DHA) have been shown to reduce the risk of persistent wheezing and asthma in offspring when taken starting at 24 weeks of pregnancy (Bisgaard, NEJM 2016).
- For potentially reducing the risk of developing of **retinal disease**, eating fish providing approximately 200 mg or more of EPA and DHA per day may be helpful. This is based on the dietary intakes of participants in the AREDS study who had the lowest incidence of retinal disease. A separate study suggests benefit with consumption of at least one serving of fish per week, particularly canned tuna or dark-meat fish (salmon e.g., mackerel, salmon, sardines, bluefish, and swordfish), which works out to consumption from the diet of about 100 mg of EPA and 230 mg of DHA per day (<u>Christen, Arch Opthamol 2011</u>). However, as noted in the <u>Eye Disease</u> section above, fish oil *supplementation* has not been found to reduce the risk or progression of age-related macular degeneration.
- For treating symptoms of **dry eye**, a combination of fish oil (126 mg EPA and 99 mg DHA) in a formula with black currant seed oil, vitamins A, B6, C, and E, magnesium sold as <u>HydroEye</u> been successfully used (<u>Sheppard, Corna 2013</u>). A large study of young adults found that taking a fish oil capsule twice daily (each capsule providing 180 mg EPA and 120 mg DHA) improved symptoms of dry eye associated with computer use (<u>Bhargava, Contact Lens & Ant Eye 2015</u>).
- For maintaining weight during initial **chemotherapy**, fish oil providing 2.2 grams of EPA per day (<u>Murphy, Cancer 2011</u>). (Note: Despite this apparent benefit, fish oil maybe contraindicated during chemo, as explained in the <u>Concerns and Cautions</u> section).
- For depression, 2,500 mg (consisting of 1,670 mg EPA and 830 mg DHA) taken once daily for eight weeks (Rondanelli, J Am Col Nutr 2010). In mildly cognitively impaired individuals, combinations providing either 1,550 mg DHA with 400 mg EPA or 1,670 EPA with 160 mg DHA have also shown benefit over 6 months (Sinn, Br J Nutr 2011). Also, 1,000 mg per day of EPA together with the prescription drug fluoxetine (Prozac) appears to be more effective than either EPA or fluoxetine alone. A daily dose of 1,000 mg EPA in people with depression who were taking a standard antidepressant medication was also shown to result in a significantly better outcome compared to placebo (Peet, Arch Gen Psychiatry 2002). In the study, this dose was more effective than higher doses of EPA.
- For anxiety, 2,496 mg (providing 2,085 mg EPA and 348 mg DHA), taken once daily (Kiecolt-Glaser, Brain Behav Immun 2011).
- For stress, 9 grams (providing 1,600 mg EPA and 1,100 mg DHA), taken once daily (<u>Carter, Am J Physiol 2013</u>).
- For **migraine headache**, 400 mg EPA and 350 mg DHA taken twice daily along with medication (amitriptyline 10 mg) (<u>Soares</u>, <u>Nutr Neurosci 2017</u>).
- For **epilepsy**, 1,080 mg EPA plus DHA taken daily for 10 weeks has been shown to reduce the frequency of seizures (<u>DeGiorgio</u>, <u>J</u> Neurol Neurosurg Psychiatry 2014).
- For improving attention in boys with **ADHD**, 650 mg of EPA and 650 mg of DHA daily (<u>Bos, Neuropsychopharm 2015</u>)—but not in children already getting these omega-3's from diets (<u>Chang, Translational Psych 2019</u>).

- For improvement in working memory in healthy, young adults, 2,000 mg of fish oil (providing 930 mg EPA and 750 mg DHA) daily (Narendran, PLoS One 2012) or 2,250 mg of fish oil (providing 1,160 mg of DHA and 170 mg EPA) (Stonehouse, Am J Clin Nutr 2013). Best results may take 6-months the period required for DHA levels in tissue to plateau. In healthy older adults, executive functioning improved with 4 fish oil capsules daily, each containing 1,000 mg of fish oil (300 mg EPA and 220 mg DHA) (Witte, Cereb Cortex 2013).
- For **Alzheimer's disease**, taking 2 fish oil capsules each morning (each containing 1 gram of fish oil, providing 325 mg EPA and 225 mg DHA in the triglyceride form) and another capsule with lunch, slowed the decline in subjects' abilities to perform daily activities. Adding 600 mg of alpha-lipoic acid in the morning slowed the decline in the subjects' cognitive functioning. (Shinto, J Alzheimers Dis 2014).
- For **strength training**, 1,000 mg of fish oil (providing 180 mg EPA and 120 mg DHA) twice daily (<u>Rodacki, Am J Clin Nutr 2012</u>). For increasing **muscle and strength** in older people, 4,000 mg of extremely concentrated fish oil (providing 1,860 mg of EPA and 1,500 mg of DHA daily) (<u>Smith, AJCN 2015</u>).
- For acne, 1,000 mg EPA and 1,000 mg DHA taken daily reduces the number and severity of lesions (<u>Jung Acta Derm Venereol</u> 2014).
- For **periodontitis**, 2,000 mg per day of DHA (from four capsules of algal oil which was 53.6% DHA) along with low-dose aspirin (81 mg per day) has shown improved outcomes (Nagyi, J Dent Res 2014).

Prescription Fish Oil vs. Supplements

For people with **high triglycerides** who have not responded well to other treatments, the American Heart Association (AHA) has stated that prescription n-3 FAs (EPA + DHA or EPA-only) at a dose of 4 g/d (>3 g/d total EPA + DHA) are an effective and safe option for reducing triglycerides as monotherapy or as an adjunct to other lipid-lowering agents (<u>Skulas-Ray, Circulation 2019</u>). The AHA notes that omega-3 fatty acids with EPA + DHA or with EPA only appear roughly comparable for triglyceride lowering and do not increase low-density lipoprotein cholesterol when used as monotherapy or in combination with a statin. (Prior to the FDA approving specific fish oil products as drugs, earlier recommendations from the AHA had referred to "fish oil capsules" rather than prescription products.) Due to the large dose of omega-3s required, fish oil products highly concentrated in omega-3s are used, as these can reduce the total amount of oil needed by about two-thirds compared to unconcentrated fish oil.

A prescription fish oil, **Lovaza** (previously known as Omacor and still sold under that name in other countries), provides 840 mg of EPA and DHA per 1-gram capsule (an 84% concentration), of which approximately 465 mg is EPA and 375 mg is DHA. Generic versions of Lovaza sold as 1-gram capsules of "omega-3-acid ethyl esters" have been approved by the FDA as providing approximately the same amounts of EPA and DHA in the same chemical form as Lovaza. [Note: A generic version from Teva Pharmaceuticals, for example, was approved in 2014, but Teva withdrew it from the market in 2020, providing no specific reason for the withdrawal]. Another prescription fish oil, **Epanova** (*AstraZeneca*), which was approved by the FDA (but is not being sold), contains a similar concentration of fatty acids per 1 gram capsule (85%) but slightly more EPA (500 – 600 mg) and slightly less DHA (150 to 250 mg) – provided in a "free fatty acid form" rather than the ethyl ester form found in Lovaza. Both of these prescription fish oils have been approved by the FDA to reduce triglyceride levels in adults with severe hypertriglyceridaemia (triglyceride levels greater than or equal to 500 mg/dL), in conjunction with a low-fat diet. Lovaza and Epanova have also both been shown to help lower triglyceride levels in people taking statin drugs.

It may be possible to significantly lower triglyceride levels with a lower dose (and fewer pills) of Epanova than Lovaza. While Lovaza has been shown in clinical studies to lower triglyceride levels by 20 - 30% and has been approved for use at a dose of four 1-gram capsules per day (Koski, PT 2008), Epanova has been shown in clinical studies to significantly lower triglyceride levels and has been approved for use at the same dose -- as well as a lower dose of two 1-gram capsules per day (Kastelein, J Clin Lipidol 2014). Epanova lowered triglyceride levels by 30% at the 4-gram daily dose, and by 26% at the 2-gram daily dose.

Another difference between Epanova and Lovaza may be the way they are absorbed. While Lovaza contains fatty acids in the ethyl ester

form (the form found in most fish oil supplements), the fatty acids in Epanova are in a "free fatty acid" form. The maker of Epanova claims that this form is more bioavailable than the ethyl ester form because it does not have to be broken down by enzymes before it is absorbed, and therefore does not need to be taken with food or a high-fat meal. (See the discussion on the <u>different forms of fish oil</u> for more information).

A clinical study comparing Epanova and Lovaza (funded by the makers of Epanova) found Epanova significantly raised levels of DHA and EPA, and lowered triglyceride levels, compared to Lovaza (Offman, Vasc Health Risk Manag 2013). In the study, 52 healthy men and women were instructed to follow a low-fat diet, and were given either four 1-gram capsules of either Epanova or Lovaza once daily, 30 minutes prior to a low-fat breakfast, for two weeks. Blood levels of EPA and DHA were 3 and 4 times higher, respectively, and triglyceride levels were reduced by 13% more, in those taking Epanova.

The most commonly reported side-effects for Epanova are diarrhea, nausea and abdominal pain, while those for Lovaza include burping, upset stomach and a change in the sense of taste (<u>AstraZeneca, Epanova Prescribing Information</u>; <u>Koski, PT 2008</u>). Both have the potential to increase LDL cholesterol or levels of certain liver enzymes in some people (see <u>Concerns and Cautions</u>).

A third fish oil supplement available by prescription **Vascepa** (*Amarin*), contains a 96% concentration of the ethyl ester form of EPA - but no DHA — and has been shown in clinical studies to significantly reduce triglyceride levels *without increasing* LDL cholesterol levels. Like Lovaza and Epanova, Vascepa has been approved for use in conjunction with a low-fat diet to reduce triglyceride levels in adults with hypertriglyceridemia. The recommended daily dose of 4 grams (taken as 2 capsules twice daily with food) has been shown to decrease triglyceride levels by 21- 33% over three months with no significant change in LDL cholesterol levels (<u>Nelson, Ann Pharmacother 2013</u>). Interestingly, the most commonly reported side effects were not the gastrointestinal issues reported with use of Lovaza and Epanova, but joint and throat pain (Amarin, Vascepa Prescribing Information).

In a study that ran for nearly 5 years, Vascepa (4 grams per day) demonstrated a 25% reduction in the risk of first-time heart attack, stroke or other major cardiac event among statin-treated adults with persistently elevated triglycerides (150 to 499 mg/dL) and other cardiovascular risk factors. The proportion of adverse events was similar between those treated with Vascepa and placebo, although there was increase in cases of atrial fibrillation or flutter (3.1% vs. 2.1% for placebo) (Bhatt, NEJM 2018). A second analysis of the same study that also took into account second, third and any additional cardiovascular events during the same 5-year time period found an even greater decrease in risk (30%) of events compared to placebo (Bhatt, J Am Coll Cardiol 2019). However, as discussed below, questions have been raised as to whether the placebo used in this trial (mineral oil) may have affected the results.

In a separate study, 4 grams per day of Vascepa or placebo taken for 18 months by 80 people with elevated triglyceride levels (despite statin treatment) and atherosclerosis showed that Vascepa reduced coronary atherosclerosis progression, in terms of total plaque, by 9% versus an 11% increase among those given placebo. Even more notable was a 17% decrease in "low-attenuation" plaque (a strong predictor of heart attack) versus a 109% increase with placebo (Budoff, Eur Heart J 2020). Vascepa was initially approved for treating patients with *very high* (severe) triglyceride levels (over 500 mg/dL) and this was extended in December 2019 to include its use as an adjunctive therapy (i.e., in addition to statins) to reduce the risk of cardiovascular events among adults with *elevated* triglyceride levels of 150 mg/dL or higher who also have either established cardiovascular disease or diabetes and two or more additional risk factors for cardiovascular disease. Patients are advised to continue physical activity and maintain a healthy diet when using Vascepa.

[Note: A <u>clinical trial</u> of Epanova (highly concentrated, free-form, EPA/DHA) was undertaken to determine whether it could, similar to Vascepa, reduce the risk of cardiovascular events among more than 13,000 statin-treated adults with moderately high triglyceride levels (175 to 499 mg/dL) and low levels of "good" HDL cholesterol. However, in January 2020, the maker of Epanova <u>announced</u> it would halt the study due to its "low likelihood of demonstrating a benefit." Publication of the results in November 2020 showed that although Epanova (4 grams per day) reduced triglyceride levels by 19% (versus 0.9% with corn oil as a placebo) and modestly decreased a measure of inflammation (c-reactive protein), there was no reduction in cardiovascular events, and, concerningly, it increased the risk of atrial fibrillation (2.2% vs. 1.3% for placebo). Epanova also caused more gastrointestinal complaints (24.7% vs. 14.7%) (Nicholls, JAMA)

2020).] As a result, Epanova is not being marketed in the U.S. Interestingly, a later analysis showed that participants in the study who lived in Asian countries (including China, Japan, South Korea and Taiwan) *did* benefit from taking Epanova: After taking it daily for about 3½ years, Epanova reduced the risk of major adverse cardiovascular events (such as heart attacks, non-fatal stroke, and unstable angina hospitalization) by 28% compared to placebo. There was no reduction in the risk of cardiovascular events among other participants. No definitive reason for the difference in the effect of Epanova among Asians vs. non-Asians could be identified, although factors such as differences in diet, exercise, or genetics may have influenced the results (these factors were not recorded during the study) (Wang, Atherosclerosis 2025).]

One theory as to why Vascepa showed a benefit in major studies but Epanova did not is that Vascepa raised EPA levels more than Epanova. However, an analysis showed that those who achieved the highest levels of EPA with Epanova (which was higher than the average reported with Vascepa) had no benefit. Perhaps a more plausible explanation is that the placebo used in the Vascepa trial (mineral oil) may have had adverse cardiovascular effects, thus making Vascepa look better than it was. In fact, researchers who compared the results of the Epanova and Vascepa trials with data modeled on the general population proposed that approximately half of the estimated benefit found with Vascepa versus Epanova might be due to the negative effects of mineral oil on triglyceride levels, LDL cholesterol, and C-reactive protein (CRP) (Doi, Eur Heart J 2021). The placebo used in the Epanova study (corn oil) is not believed to cause negative cardiovascular effects. More research is needed to understand these differences (Nissen, JAMA Cardiol 2021).

The annual cost of Vascepa is approximately \$3,000. Fish oil supplements tend to be less expensive than prescription fish oil capsules. Similarly high concentrations of EPA and DHA can be found among dietary supplements at lower cost (see <u>Softgels Compared to Prescription Omega-3s</u>).

High-Dose Krill Oil: A krill-based omega-3 product (**CaPre**, Acasti Pharma) had been under development as a prescription product. It contained about half the concentration of EPA and DHA (about 1,240 mg per 4,000 mg daily dose) as the prescription fish oils in "a combination of phospholipid esters and free fatty acids." Two clinical trials showed over 30% reductions triglycerides among people with severely high triglyceride levels (500 mg/dL to 1,500 mg/dL) given the product, but these reductions were not considered statistically significant due to the fact that people given a placebo in each study also had large reductions (just under 30%) in triglycerides. By combining the results from the two studies and reanalyzing the data, the triglyceride reduction with the krill oil was considered statistically significant (due to the larger sample base), although still not much better than placebo (Mozaffarian, JAMA Netw Open 2022). It appears that development of this drug has been halted.

How to Take:

Taking fish oil with fatty meals helps increase its absorption (<u>Dyerberg, PLEFA 2010</u>). Fish oils are also best tolerated when taken with meals, and, if possible, should be taken in divided doses, i.e., divide the dose in half and take twice daily, or in thirds and take three times a day.

The reason why fish oil is better absorbed with a fatty (or oily) meal is that fats trigger the release of bile into the small intestine and this causes the oil to be emulsified (broken into smaller droplets), making absorption easier. Some fish oil is sold in an emulsified form, such as *Coromega*. If you only take fish oil without food, you may absorb somewhat more if you use an emulsified product, although they tend to cost more than regular fish oil. On the other hand, if you tend to take fish oil with meals that contain reasonable amounts of fats or oils, the fish oil will likely be absorbed just as well regardless of whether it's emulsified or regular fish oil.

Interestingly, a study that compared taking *Coromega* liquid to regular fish oil from a capsule found that the EPA from *Coromega* was absorbed almost twice as well as the EPA from the capsule. However, overall, the total amount of EPA and DHA was not absorbed significantly better from *Coromega* (Raatz, Lipids 2016). Furthermore, the fish oils were taken along with a low-fat breakfast and it's possible that any comparative benefit of *Coromega* would have disappeared if the fish oils had, instead, been taken with fatty meal.

A "self-emulsifying" fish oil is also sold as *Nature Made Omega-3 with Xtra Absorb Technology*. A study in which it was given *without any food* showed it to have 8.2-fold higher bioavailability for EPA + DHA than a non-emulsified fish oil (the prescription fish oil Lovaza), particularly for EPA (18.3-fold higher), while DHA was 4.5-fold higher. Both products contained EPA and DHA in the ethyl ester form, as

this permits greater concentration than the natural triglyceride form (<u>Maki, Clin Therapeutics 2018</u>). However, as with the *Coromega* study, had the fish oils been taken *with food*, there may have been little or no difference in bioavailability.

Keep It Fresh:

Omega-3 fatty acids can spoil, so it is best to keep products out of heat and light. Once opened, tightly reseal the container. If possible, refrigeration can help prolong freshness and is particularly important with bottled liquids. A slight cloudy appearance of the oil is normal after refrigeration -- just shake the bottle before use. If you use a bottled liquid, purchase a size that you will completely use within a few weeks because once air is introduced into the bottle, spoilage may begin. As noted earlier, all products in this review were tested for freshness unless deeply colored (such as krill oil) or containing flavorings, as these characteristics can prevent accurate testing.

If you won't be using a portion of the product soon, you can also freeze fish oil. This will extend its freshness and not have an adverse effect on the oil (and this generally will not affect capsules, either).

Some products contain added antioxidant ingredients, such vitamin E, rosemary or ascorbic acid, which can help keep fish and marine oil fresh.

Should You Test Your Omega-3 Level?

There are several tests to determine your omega-3 status. These can tell you how much omega-3 is in your blood, or components of your blood, and this may be helpful in estimating the risk of death from coronary heart disease (Harris, Prev Med 2004). However, even if your results come back "low," it has not been established that taking omega-3 supplements will reduce your risk of heart disease and the evidence is mixed for other conditions (see What It Does). Therefore, it is not clear if using these tests is worthwhile. Also, the only available over-the-counter omega-3 test, which costs about \$55 per test and may require retesting up to four times per year, is not covered by insurance.

Nevertheless, if you remain interested in using one of these tests, we compare them below:

The **Omega-3 Index** measures the amount of EPA and DHA in red blood cells and reports it as a percentage of total fatty acids in these cells. Research supported by one of the main providers of the test (OmegaQuant) has suggested that an Omega-3 Index of about 8% (i.e., more than 8% of the fatty acids in your red bloods cells are omega-3s) is associated with lower risk of atherosclerotic cardiovascular disease. An index of below 4% is associated with the highest (<u>Harris, Atherosclerosis 2017</u>). About 89% of people in the U.S. are estimated to have an Omega-3 Index in the "high risk" category (<u>Murphy, BMJ Open 2021</u>). OmegaQuant offers this test directly to consumers, while Boston Heart Diagnostics and Quest Diagnostics make it available through a healthcare provider (<u>Dicklin, J Nutr 2024</u>)

However, the Omega-3 Index test appears to have certain limitations. The analytical methods used to measure the Omega-3 Index can vary from laboratory to laboratory because there is no standardized method. Consequently, Omega-3 Index test results can vary significantly from lab to lab (von Schacky, Nutrients 2014). Be aware that this test does not distinguish between EPA and DHA and, since these may have different biological effects, a test that assesses the levels of these omega-3 fatty acids separately might be more informative (Dicklin, J Nutr 2024).

Two other tests look at omega-3 levels in *whole blood* — but this approach is thought to reflect only more recent intake of omega-3 fatty acids compared to the Omega-3 Index, which is thought to reflect intake over a longer time period (<u>Dicklin, J Nutr 2024</u>).

One whole blood test is **OmegaCheck** (by Quest Diagnostics and LabCorp), which measures EPA plus DHA *along with other* omega-3s. Based on population studies, low cardiovascular risk is associated with a finding of 5.5% or higher, while medium risk is 3.8% to 5.4%, and high risk is 3.7% or lower.

The other test based on omega-3s in whole blood is **OmegaScore** (by Lipid Analytical Laboratories), which measures levels of EPA+DHA+DPA. Its results are claimed to not only determine risk of sudden cardiac death, but all-cause mortality (i.e., death regardless of cause), and age-related cognitive deterioration.

Concerns and Cautions:

While fish oil supplements are generally considered safe, there are a few caveats and cautions you should take into consideration before you buy. While krill oil has not been as extensively studied as fish oil, it is reasonable to assume that the same concerns and cautions apply.

- The most common side effects are fishy smelling burps and diarrhea. Fish oil supplementation may also cause gastrointestinal upset, indigestion, heartburn or reflux (Freeman, Prostaglandins Leukot Essent Fatty Acids 2007; Mozaffarian, JAMA 2012). Fish oil and krill oil have been found to have similar GI side effects, such as nausea, gas, bloating and diarrhea, although one study reported that gas and bloating were more frequent with krill oil supplementation than with fish oil supplementation (Maki, Nutr Res 2009). Taking fish oil in smaller, divided doses, just before a meal may reduce reflux from fish oil supplements. If you lie down after eating, lie on your left side, allowing easier passage of the oil into the intestine (Cleland, Arthritis Res Ther 2006). An enteric-coated fish oil supplement may also help.
- Unless medically prescribed, it seems best not exceed more than a total of 3 grams per day of EPA and DHA omega-3 fatty acids, with no more than 2 grams per day from a dietary supplement. Such high doses may suppress the immune system. Unless medically necessary, such doses should be avoided, particularly by immunocompromised individuals. The potential for immune suppression was highlighted in a review of several studies in animals which found very high amounts of EPA and DHA to dampen immunity, resulting in reduced survival from bacterial, viral and fungal infections (Fenton, Prostag Leukotri EFAs 2013). These adverse effects occurred when EPA & DHA consumption contributed as much as 1% to 10% of an animal's total daily energy intake. In terms of human consumption, this would be about 2,200 mg to 22,000 mg of EPA and DHA daily, although the dosage taken to lower triglycerides would fall in the lower end of this range. Commenting on these findings, a researcher noted, "Our main concern here is the hyper-supplemented individual, who may be taking high dose omega-3 supplements and eating four to five omega-3 enriched foods per day." (OSU website, 2013).
- Fish oil may also have a **blood-thinning effect**, especially at doses above 3 grams of EPA + DHA per day (<u>Zucker</u>, <u>Atherosclerosis 1998</u>), and particularly among those on blood thinning medication. Lower doses (less than 1 gram of omega-3 fatty acids, including EPA + DHA, per day) do not appear to have this effect (<u>Bays</u>, <u>Am J Cardio 2007</u>). Use of high-dose, highly concentrated prescription fish oil (<u>Vascepa</u> typical daily dose 3,840 mg EPA) was associated with a tripling in the risk of a bleeding event among people also taking antithrombotic drugs, such as **aspirin**, **clopidogrel** (**Plavix**), **or warfarin** (**Coumadin**), **heparin**, **or apixaban** (**Eliquis**), according to a review of Vascepa adverse events. It did not increase bleeding events among those not on such medications (<u>Cai</u>, <u>Expert Opin Drug Saf 2023</u>). Among people on warfarin, clotting time (INR) has been shown to increase upon beginning or increasing fish oil supplementation, returning to normal after discontinuing fish oil. However, there are cases among older people on warfarin and fish oil who have suffered traumatic injuries and clotting time could not be adequately reduced. In one case, an 87-year old man with head trauma due to a motor vehicle collision died from uncontrollable bleeding into his brain despite the use of treatments (prothrombin and vitamin K) which normally reverse the effects of warfarin (<u>Gross</u>, <u>J Trauma Nursing 2017</u>).
- Use of supplements containing omega-3s during pregnancy was associated with a 25% increased risk of postpartum hemorrhage for both vaginal and cesarean delivery and a 470% increased the risk of massive postpartum hemorrhage after cesarean (but not vaginal) delivery, compared to no omega-3 supplementation, according to a large study in Sweden. The researchers advised that it may be best to discontinue omega-3 supplementation in late pregnancy (the third trimester) to reduce this risk (<u>Lichtenstein, Acta Obstet Gynecol Scand 2024</u>). However, more research is needed and the significance of this study is limited by the fact that women only reported on their use of supplements once, in early pregnancy (so duration of supplementation was not considered), and data was not collected on the amount of omega-3 intake.

- Although patients are often advised to stop taking fish oil several weeks before surgery, a large study of over 1,500 men and women who underwent cardiac surgery (such as coronary artery bypass or valve surgery) found that taking 8 to 10 grams of the prescription fish oil Lovaza two to five days before surgery, and 2 grams per day after surgery until discharge or up to ten days, did not increase bleeding during or after surgery compared to placebo. In fact, those who took the fish oil were less likely to need a blood transfusion, and those with higher blood levels of omega-3s had a lower risk of bleeding compared to those with lower blood levels (Akintoye, Circ Cardiovasc Qual Outcomes 2018).
- High-dose fish oil supplementation may also increase the risk of bleeding in the eye. A 32-year old Chinese man with extreme nearsightedness experienced a macular hemorrhage (bleeding in the retina) in his left eye without having other risk factors for hemorrhage. Ten weeks later the man experienced a second macular hemorrhage, at which time his doctor's learned that he began taking two 1,000-mg capsules of fish oil (providing 400 mg of DHA and 600 mg of EPA) daily beginning one month prior to the first bleeding event and continuing through the second event. After he discontinued the fish oil, the second hemorrhage healed within 8 weeks, and no further bleeding events were reported (Li, SAGE Open Med Case Rep 2020).
- If you take blood pressure lowering medication, be aware that fish oil may further lower blood pressure.
- Contrary to earlier reports, fish oil does not appear to adversely affect **blood sugar levels** in people with diabetes. However, a study in which a large amount of krill oil (including a modest amount of salmon oil) was given daily with water for 8 weeks to overweight, middle-aged men in New Zealand showed, to the researchers' surprise, that it reduced insulin sensitivity (by about 27%, factoring in potential benefits from EPA and DHA) and could, therefore, increase the risk of diabetes and cardiovascular disease. The men were given 5 grams (5,000 mg) of the oil daily (88% krill oil and 12% fish oil providing just 230 mg of EPA and 154 mg of DHA). Two men in the study (4%) withdrew after experiencing krill allergy; 47% reported experiencing "fishy burps." Due to the krill component, 42% of the oil used in the study was phospholipids. Phospholipids are not known to impair insulin sensitivity, but the researchers speculate that krill proteins attached to the phospholipids may have impaired insulin sensitivity (Albert, Am J Clin Nutr 2015).
- Despite some concern, taking fish oil long-term does **not seem to adversely affect the liver**. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) considers fish oil to be unlikely to cause clinically apparent liver injury (<u>LiverTox</u>: <u>Clinical and Research Information on Drug-Induced Liver Injury</u>, 2012-2017). One study in rats given fish oil, virgin olive oil, or sunflower oil throughout their life (i.e., for 24 months) found that the animals given fish oil showed increased oxidation and decreased mitochondrial function in the liver, which the researchers stated *might* make the liver susceptible to nonalcoholic steatosis (NASH), a form of fatty liver disease. However, there was no worsening of fat content in the liver (steatosis), inflammation, severity of NASH, or fibrosis (liver scarring) compared to the animals fed with the other oils, although all three groups showed worsening of these outcomes over their lifetime, which was attributed to aging. The animals given fish oil also showed changes in the expression of certain genes that that may help the liver adapt to aging (<u>Varela-Lopez</u>, <u>J Nutr Biochem 2018</u>). Be aware, however, that taking fish oil containing <u>large amounts of vitamin A</u> (as is commonly found in fish liver oils, such as **cod liver oil**) can cause liver toxicity, particularly if taken with other supplements containing vitamin A.
- A study of mice fed a diet *extremely* high in fish oil showed that it caused **hair loss**, but this is likely not a risk for people eating a normal diet and supplementing with standard amounts of fish oil or taking prescription fish oil. The researchers had increased fish oil in the diets of the mice to represent 45% of total calories, up from what is usually just 10% from all oils and fats (<u>Hao, Cell Report 2023</u>). The researchers noted that countries that rely heavily on fatty fish as a food source (such as Japan) exhibit the most hair loss when compared with other Asian nations, but this may relate to overconsumption of retinol (vitamin A) that naturally occurs in fish oil (from the fish liver) and is known to cause hair loss (<u>Hagino, Clin Cos Investig Derm 2021</u>).
- Some people are **allergic** to proteins in fish, krill, and calamari/squid (among other foods). Supplements are required to identify foods with allergic potential (including the species name) with a statement, e.g., "Contains: Fish (mackerel)." Not all of the fish oil products tested provided this complete labeling (those that did not have been indicated with a footnote in the sixth column in the results table above). It is possible that some manufacturers did not include this labeling because they considered the oil to

be highly refined (and contain minimal protein). A small study among six fish-allergic patients administered fish oil supplements had no reaction to the supplements (Mark, Allergy Asthma Proc 2008). However, there is at least one case report of a person having a reaction to an "omega-3-6-9 fish oil capsule" (the specific product and its ingredients were not disclosed) (Kmet, Can Fam Phys 2012). In short, if you are allergic to fish, krill, or calamari, you may not have a problem with refined oils made from them, but use caution.

- Be aware that statins and other cholesterol-lowering drugs, like fenofibrate (Tricor), may alter the metabolism of omega fatty acids in the body, lowering omega-3 levels, although this does not argue against using fish oil with these drugs, as the combination may be beneficial. A study in healthy young men showed that taking 4 grams of fish oil (*Omacor*, containing 1,520 mg of DHA and 1,840 mg of EPA) in addition to 40 mg of atorvastatin (Lipitor) decreased blood levels of DHA and EPA compared to atorvastatin alone, but the significance of this is not clear, and it did not increase adverse effects compared to atorvastatin alone (Kim, Pharmaceuticals (Basel) 2022), while a study in older men with elevated triglyceride levels showed the same combination taken daily for eight weeks decreased triglyceride levels compared to atorvastatin alone, and without an increase in adverse effects, suggesting this combination may be beneficial (Woo, Clin Ther 2021). A 3-month study of men with high cholesterol showed that taking 200 mg of fenofibrate caused a significant decrease in the omega-3 fatty acids alpha-linolenic acid (ALA) and DHA, while among those taking 20 mg of a statin drug (simvastatin) there was a trend toward a decrease in all fatty acids, but it was not significant (de Lorgeril, Nutr Metab and Cardiovasc Dis 2005).
- Although high-dose fish oil supplementation (4 grams daily) did not affect LDL cholesterol (a general form of "bad" cholesterol) in one study (<u>Us, Lipids Health Dis 2022</u>), **elevations in LDL cholesterol**, as well as **elevations in the results of blood tests used to check liver function**, are noted as possible serious side effects with prescription Lovaza and Epanova (i.e., concentrated fish oils taken at a high daily dose up to 4 grams) (prescribing information for <u>Lovaza</u> and <u>Epanova</u>).
- High doses of fish oil from supplements may increase the risk of atrial fibrillation, or atrial flutter, a heart rhythm problem, particularly in people with heart problems, possibly by affecting the timing of electrical impulses in the heart. An observational study in the U.K. found that, even among people without cardiovascular disease, fish oil supplementation was associated with a slightly higher rate of atrial fibrillation compared to non-users (5.3% vs. 4.1%, respectively). Oily fish consumption did not affect the association between fish oil supplementation and atrial fibrillation risk (Zhang, Eur J Prev Cardiol 2022). A subsequent observational study in the U.K. found similar results: Among healthy people, regular use of fish oil supplements was linked with a 13% higher risk of developing atrial fibrillation and 5% higher risk of having a stroke compared to non-use over a follow-up period of about 12 years, although regular use of fish oil supplements was associated with an 8% reduced risk of heart failure. The study included over 415,000 participants (average age 56), most of whom consumed fish less than twice weekly (Chen, BMJ Med 2024).

In people with pre-existing heart disease, supplementation for one year or longer with high-dose fish oil (1 to 4 grams of omega-3 fatty acids per day) may increase the overall relative risk of atrial fibrillation by 25% (Gencer, Circulation 2021; Bork, Curr Opin Clin Nutr Metab Care 2023). Atrial fibrillation occurred in 2.2% of people on 4 grams of Epanova daily compared to 1.3% of those given 4 grams of corn oil placebo (Nicholls, JAMA 2020). Icosapent ethyl (including Vascepa) has also caused an increase in the incidence of atrial fibrillation (3.1% vs 1.6% to 2.1% of patients in the control groups (Miyauchi, Circulation 2024; Bhatt, N Engl J Med 2018), and increased risk of heart rhythm problem is also noted in the prescribing information for Lovaza (Lovaza Prescribing Information 2015). Even a lower dose of concentrated fish oil (1.8 grams providing 930 mg of EPA and 660 mg of DHA) resulted in a trend toward increased incidence of atrial fibrillation (7.2% vs. 4% on placebo) in a two-year study among older people with recent heart attacks in Norway (Kalstad, Circulation 2020). A review of five large clinical trials (including two trials noted above) using fish oil doses ranging from 840 mg to 4 grams per day, concluded that omega-3 supplementation is associated with an increased risk of atrial fibrillation in people with elevated triglyceride levels and/or cardiovascular risk (Lombardi, Eur Heart J Cardiovasc Pharmacother 2021). If taking high-dose fish oil, your physician should monitor you for atrial fibrillation and other potential side effects, particularly if you have had heart problems in the past. Even in people without heart problems, one gram of highly concentrated prescription fish oil (Omacor, now known as Lovaza) taken daily for two years

resulted in statistically significant changes in electrical signals in the heart, including a slowing of the conduction between the atria of the heart (<u>Tikkanen, Sci Rep 2023</u>).

- Vascepa can cause joint and throat pain (<u>Vascepa Prescribing Information</u>).
- High-dose fish oil can increase blood levels of the immunosuppressant drug tacrolimus (sold as Astagraf, Envarsus, Protopic), as was demonstrated in a small study in Norway that showed blood concentrations of tacrolimus increased by 25% in organ transplant recipients who took 2,600 mg of omega-3 fatty acids daily (Lovaza/Omacor) for 4 weeks. This interaction may occur due to potential inhibition of intestinal CYP3A enzymes by omega-3 fatty acids. The researchers also warned that since the resulting increased systemic exposure of tacrolimus may not be reflected in "trough concentrations" (the lowest concentration reached by a drug before the next dose is administered) it may be difficult to monitor tacrolimus levels following the initiation and discontinuation of marine omega-3 fatty acid supplementation (Robertsen, Transpl Int 2021). High-doses of omega-3 fatty acids have been reported to raise levels of other immunosuppressant drugs metabolized by CYP3A enzymes, including cyclosporine (Neoral, Sandimmune) and sirolimus (Rapamune) (Cortinovis, Transplantation 2010; Busnach, J Nephrol 1998).
- Fish oil (from supplements as well as fish) may **interfere with chemotherapy**. A fatty acid naturally found in fish oil known as 16:4(n-3) and into which other fatty acids, such as EPA, are converted in the body, has been shown in mice to activate white blood cells leading to resistance to chemotherapy. It is, therefore, advised to temporarily avoid fish oil from the day before chemotherapy until the day thereafter, as well as herring and mackerel (which raise 16:4(n-3) levels more than other fish such as salmon and tuna) in the 48 hours surrounding chemotherapy (<u>Daenen, JAMA Oncology 2015</u>).
- Green-lipped mussel extract should not be taken by women who are **pregnant or nursing**, as an animal study suggests it may interfere with fetal development (Miller, N Z Med J 1984).
- Be aware that cod or other fish liver oils are not always a good substitute for fish oil supplements as these may be high in
 vitamins A and D. Because these vitamins can be toxic, make sure that you do not exceed safe levels (see <u>Tolerable Upper</u>
 Intake Levels (ULs) for vitamins and minerals).

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back to top

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