

OMEGA-3 FATTY ACIDS

It is well-established that dietary fats are an important part of a healthy and balanced diet. They add flavor and texture to foods and at the same time can be a source of health-promoting, vital nutrients. Of particular interest is a subgroup of dietary fats known as omega-3 fatty acids. These fats gained the attention of researchers in the late 1970s during observational studies of Greenland Inuits. The low occurrence of coronary heart disease (CHD) in Inuits was attributed to their traditional diet, which is

rich in marine animals and fish.¹ Other population studies have also shown that cultures with high fish consumption, such as Japan, have similarly low rates of CHD mortality.² Discoveries like these jumpstarted a massive body of research on omega-3 fatty acids and their effects on human health. This fact sheet covers the current state of the science on these important compounds, as well as dietary recommendations and food sources of omega-3 fatty acids.

WHAT ARE OMEGA-3 FATTY ACIDS?

Understanding the role of omega-3 fatty acids in human health begins with knowledge of the chemical makeup of fatty acids, which are distinguished based on the number of unsaturated bonds between carbon atoms in the fatty acid chain. Polyunsaturated fatty acids (PUFA) have more than one cis double bond in their carbon chain. Omega-3 fatty acids, including alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), are a type of PUFA. These omega-3

fatty acids contain their first double bond on the third carbon molecule from the methyl (or omega) end of the fatty acid's carbon chain³ (see figure below).

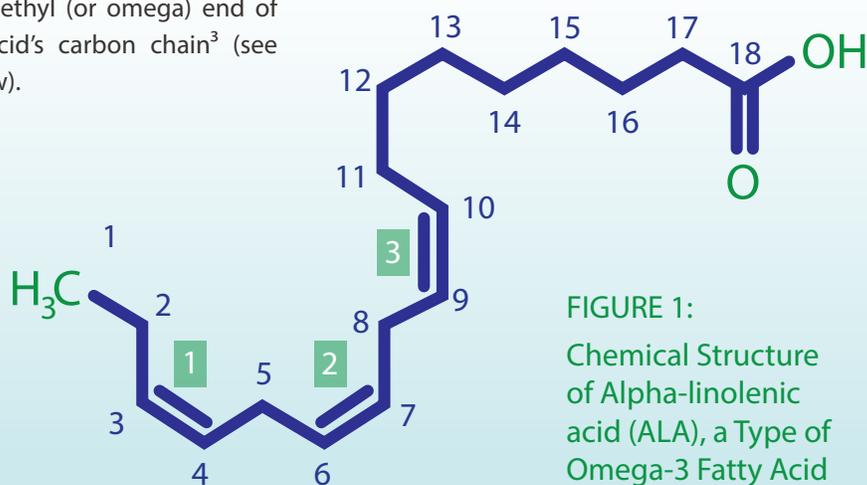


FIGURE 1:
 Chemical Structure
 of Alpha-linolenic
 acid (ALA), a Type of
 Omega-3 Fatty Acid

The naming of each fatty acid provides information regarding its chemical structure. As an example, DHA has a structure of 22:6n-3. The first part of the name (22:6) indicates that DHA is a 22-carbon fatty acid with six double bonds, whereas the second part (n-3) means that the first double bond is in the n-3 position, which qualifies it as an

omega-3 fatty acid.^{4,5} ALA contains 18 carbon atoms, while EPA and DHA contain 20 and 22 carbon atoms, respectively. EPA and DHA are considered to be “long-chain” omega-3s.⁶

ALA cannot be formed in the body, so it is considered an essential fatty acid and must be obtained through the diet.

ALA can be converted into EPA and further into DHA in the liver, although this process is inefficient. As a result, consuming EPA and DHA through foods or supplements may be a more realistic way to ensure that the body obtains an adequate amount of these omega-3s.

TABLE 1: Types of Omega-3 Fatty Acids

NAME OF OMEGA-3	ABBREVIATION	STRUCTURE	FOOD SOURCES
Alpha-linolenic acid	ALA	18:3n-3	Chia seed, flaxseed and flaxseed oil, walnuts, canola oil
Eicosapentaenoic acid	EPA	20:5n-3	Fatty fish and seafood, fish oils, krill oil, cod liver oil, algal oils
Docosahexaenoic acid	DHA	22:6n:3	Fatty fish and seafood, fish oils, krill oil, cod liver oil, algal oils

OMEGA-3 FATTY ACIDS AND HUMAN HEALTH

Omega-3 fatty acids are perhaps best known for their potential heart health benefits,⁷⁻⁹ although not all evidence supports these outcomes.^{10,11} A growing body of research continues to examine the effects of omega-3s in other areas, such as certain types of cancers, neurological disorders, arthritis and infant neurocognitive development.^{6,12}

Observational research often notes a relationship between a higher intake of fish and other seafood with improved health-related outcomes. Unfortunately, it is often difficult to determine whether or not those benefits are a result of greater intake of omega-3 fatty acids; if fish or seafood choices replace other, unhealthier diet choices; or if the benefits are due to a combination of factors.⁶ In all areas, additional research in the form of long-term, placebo-controlled, clinical trials will be useful in understanding the health outcomes associated with omega-3 intake.

CARDIOVASCULAR HEALTH

Observational studies have reported that greater intakes of fish and seafood as well as higher

dietary levels or plasma levels of omega-3s are associated with lower risks of heart failure, CHD and fatal coronary heart disease.⁶ Several systematic reviews and meta-analyses based on observational data completed before 2014 reported that omega-3s reduce the risk of cardiac death.¹³⁻¹⁵ However, the results of randomized clinical trials have not always consistently aligned with the observational findings. A 2016 review reported that higher intakes of omega-3s (EPA and DHA from fish, seafood, and dietary supplements) reduced triglyceride levels and increased high-density lipoprotein (HDL, or “good” cholesterol) levels but also increased low-density lipoprotein (LDL, or “bad” cholesterol) levels. In addition, the review stated that these higher intakes did not affect major adverse cardiovascular events, sudden cardiac death, or all-cause mortality.¹⁶

In 2017, a review by the American Heart Association (AHA) found that the available evidence did not support the use of omega-3 supplements for those in the general population who were not at a high risk of cardiovascular disease (including people with diabetes mellitus and prediabetes). However, the AHA continues to suggest that physician-





monitored omega-3 supplementation may be a reasonable addition for secondary prevention of CHD in people with a recent CHD-related event, such as a heart attack.¹¹ After removing studies deemed to be at high risk of bias, a 2018 Cochrane systematic review found that “moderate- and high-quality evidence suggests that increasing EPA and DHA has little or no effect on mortality or cardiovascular health (evidence mainly from supplement trials).”¹⁰ Additional clinical trials investigating omega-3 fatty acids and cardiovascular events are needed. However, in general, research still supports the idea that consuming a balanced diet, including omega-3 containing fatty fish and other seafood, or omega-3 supplementation (following a physician’s guidance), helps promote heart health.¹⁷

CANCER

It has been hypothesized that greater consumption of omega-3s from foods or supplements might decrease the risk of cancer as a result of anti-inflammatory properties of omega-3s and their potential to inhibit cell growth factors.¹⁸ However, results from observational studies have been inconsistent and differ by the location of the cancer in the body as well as factors such as gender and genetic risk.⁶ Some studies have noted associations between higher intake of omega-3s (or blood levels of omega-3s) and a reduction in risk for

cancers such as breast or colorectal cancer, while others report no effect of omega-3 intake on cancer risk. Further, some researchers have suggested that intake of omega-3s might contribute to the risk of developing prostate cancer.⁶ A 2020 review of 15 meta-analyses of observational studies focusing on brain, breast, endometrial, liver, prostate and skin cancers found no convincing, highly suggestive or suggestive evidence of an association between fish or omega-3 fatty acid consumption and cancer risk.¹⁹

ALZHEIMER'S DISEASE AND COGNITIVE FUNCTION

Many, but not all, observational studies report that high dietary intake of omega-3s is associated with a reduced risk of cognitive decline, Alzheimer’s disease, and dementia.⁶ Conversely, the results of multiple systematic reviews and meta-analyses have noted that supplementation with omega-3s does not affect cognitive function in healthy people or those with Alzheimer’s disease.⁶ However, for people who suffer from milder forms of cognitive dysfunction, consuming omega-3s may improve key areas of cognitive function, like processing speed and memory.²⁰

ARTHRITIS

Omega-3 fatty acids have anti-inflammatory properties and as a result have been theorized to help mitigate symptoms of rheumatoid arthritis (RA). A 2017 meta-analysis noted that the use of supplemental omega-3 in subjects with RA was associated with a reduction in tender joints, early morning stiffness, and pain levels compared with a placebo.²¹ However, a 2017 systematic review of the effects of omega-3 supplements on subjects with RA noted that only four of 18 placebo-controlled trials saw a benefit of omega-3s for pain level.²²

INFANT NEUROCOGNITIVE DEVELOPMENT (MATERNAL CONSUMPTION)

Results from observational studies have shown that maternal intake of at least eight ounces of DHA-containing seafood per week during pregnancy and breastfeeding is associated with better infant health-related outcomes.¹² However, results from a 2013 systematic review of maternal omega-3 intake and potential effects on early childhood cognitive development found no difference between the DHA and control groups in measures of cognition or neurodevelopment (including language, behavior, or motor function).²³ Most recently, the Scientific Report of the 2020 Dietary Guidelines Advisory Committee (DGAC)’s review of the literature aligns with current recommendations for pregnant women to consume eight to 12 ounces of seafood lower in methylmercury and higher in omega-3 fatty acids.²⁴

OMEGA-3 FATTY ACID DIETARY RECOMMENDATIONS AND CURRENT INTAKE

When the Institute of Medicine (or IOM, now called the National Academy of Medicine) last reviewed omega-3 fatty acids, there were insufficient data to establish an estimated average requirement (EAR), so adequate intakes (AIs) were developed for all ages based on omega-3 intakes in healthy populations. Human breast milk contains ALA, EPA, and DHA, so the AI for infants from birth to 12 months is equal to the average intake of omega-3s in healthy, breastfed infants. The AIs for infants refer to total omega-3s. For ages one and older, the AI refers only to ALA because it is the only essential omega-3. Specific intake recommendations for EPA, DHA, or other long-chain omega-3s have not been established.⁶ Additionally, the National Academy of Medicine has not established a tolerable upper intake level (UL) for omega-3 fatty acids,⁴ and the U.S. Food and Drug Administration (FDA) has ruled that intakes of EPA and DHA of up to three grams per day are Generally Recognized as Safe (GRAS) for inclusion in the diet.²⁶ Doses of greater than five grams of EPA and DHA per day are generally not recommended by the FDA due to evidence that intake at those levels may lengthen bleeding time in susceptible people.²⁶

Table 2 lists the AIs for omega-3s in grams per day.

The 2015–2020 Dietary Guidelines for Americans (DGA) provide intake goals for ALA that are based on the AIs and include a goal of consuming

intake of key nutrients and as part of an overall healthy dietary pattern.” Also, consuming fish and seafood species with higher amounts of omega-3s and low levels of methylmercury is advised, using guidance from federal and local fish and seafood advisories. The

TABLE 2: Adequate Intakes (AIs) for Omega-3 Fatty Acids (grams per day)⁴

AGE	MALE	FEMALE	PREGNANCY	LACTATION
Birth to 6 months*	0.5 g	0.5 g	--	--
7 to 12 months*	0.5 g	0.5 g	--	--
1 to 3 years **	0.7 g	0.7 g	--	--
4 to 8 years**	0.9 g	0.9 g	--	--
9 to 13 years **	1.2 g	1.0 g	--	--
14 to 18 years**	1.6 g	1.1 g	1.4 g	1.3 g
19 to 50 years**	1.6 g	1.1 g	1.4 g	1.3 g
51+ years**	1.6 g	1.1 g	--	--

*As total omega-3s **As ALA

eight ounce-equivalents of seafood per week.¹² The Scientific Report of the 2020 DGAC is consistent with the seafood-related recommendations of the 2010 and 2015 DGAC reports, with minor revisions.²⁴ The 2020 DGAC report states that “[t]wo or more servings of cooked seafood per week are recommended for ages 2 years and older to ensure

upcoming 2020–2025 DGA may provide information on the types of seafood and amounts to consume (or avoid) based on methylmercury content.²⁴ For people wishing to avoid seafood intake, regular intake of other foods high in omega-3s, such as flaxseed, walnuts, algae, and soybean oil may be adequate.

The National Health and Nutrition Examination Survey (NHANES) from 2011–2012 reported that most children and adults consume the recommended amounts of omega-3s as ALA: the average intake of ALA from foods is 1.32 grams in females and 1.55 in males ages 2 to 19 years. In adults ages 20 and older the average intake of ALA from food is 1.59 grams per day for females and 2.06 grams per day for males.²⁷ Food sources of EPA and DHA provide about 40 milligrams (mg) in children and teens and about 90 milligrams in adults.²⁷

The Safety of Omega-3s

A common safety concern regarding omega-3 intake from fish and seafood relates to the risk of unsafe intake levels of methylmercury, a toxic and heavy metal. However, this risk can be mitigated somewhat through avoidance of certain fish and seafood species that tend to contain higher amounts of methylmercury, including king mackerel, marlin, orange roughy, shark, swordfish, tilefish (from the Gulf of Mexico), and bigeye tuna.²⁵ Omega-3 supplements have not been found to contain methylmercury, an outcome of rigorous processing and purification steps.

SOURCES OF OMEGA-3 FATTY ACIDS

Table 3 captures a list of common foods that provide ALA, EPA, and DHA.^{28,29}

Certain foods, such as specific brands of juice, milk, yogurt and soy beverages are fortified with DHA and other omega-3s. Omega-3 enriched eggs are also available; their omega-3 content is enhanced by feeding hens a diet that is supplemented with omega-3 fatty acids. Additionally, since 2002, infant formula manufacturers in the United States have added DHA and arachidonic acid (two of the most prevalent long-chain PUFAs in the brain) to their products.³¹

Omega-3s are also available as dietary supplements in the form of fish oil, cod liver oil, krill oil, and algal (vegetarian) oils. In general, fish oil supplements that are roughly 1,000 mg fish oil may contain about 180 mg EPA and 120 mg DHA, although doses can vary considerably.³²

TABLE 3: Food Sources of ALA, EPA, and DHA^{28,30} (grams per serving)

FOOD	SERVING	ALA	DHA	EPA
Flaxseed oil	1 tbsp	7.26		
Chia seeds	1 ounce	5.06		
Walnuts, English	1 ounce	2.57		
Flaxseeds, whole	1 tbsp	2.35		
Salmon, Atlantic, farmed, cooked	3 ounces		1.24	0.59
Salmon, Atlantic, wild, cooked	3 ounces		1.22	0.35
Canola oil	1 tbps	1.28		
Sardines, canned in tomato sauce, drained	3 ounces		0.74	0.45
Salmon, pink, canned, drained	3 ounces	0.04	0.63	0.28
Soybean oil	1 tbsp	0.92		
Edamame, frozen, prepared	1/2 cup	0.28		
Tuna, light, canned in water, drained	3 ounces		0.17	0.02
Shrimp, cooked	3 ounces		0.12	0.12
Reduced fat milk, fortified with DHA	8 ounces		0.03	
Soy milk, fortified with DHA	8 ounces		0.03	
Orange juice, omega-3 enriched	8 ounces		0.03	0.02
Egg, omega-3 enriched*	1 egg	0.048	0.002	0.1-0.15

*The amount of ALA, DHA, and EPA in omega-3 enriched eggs can vary considerably among brands.

THE BOTTOM LINE

Omega-3 fatty acids may have beneficial effects on infant development and, in adults, on cardiovascular health and other disease conditions such as cancer, arthritis, Alzheimer’s disease and cognitive function. People at varying stages of the life cycle, including during pregnancy, may benefit from consuming appropriate amounts of omega-3 fatty acids. The current food supply offers a variety of sources of dietary omega-3 fatty acids. Additional research is needed to better understand the complexities of omega-3 fatty acids and the impacts they have on the body and on disease prevention and management.



REFERENCES

- Bang HO, Dyerberg J, Sinclair HM. The composition of the Eskimo food in north western Greenland. *Am J Clin Nutr.* 1980;33(12):2657-2661.
- Harris WS. Omega-3 Fatty Acids In: Coates PM, Betz JM, Blackman MR, al. e, eds. *Encyclopedia of Dietary Supplements.* 2nd Edition. London and New York: Informa Healthcare; 2010:577-586.
- Kostoglou-Athanassiou I, Athanassiou L, Athanassiou P. The Effect of Omega-3 Fatty Acids on Rheumatoid Arthritis. *Mediterr J Rheumatol.* 2020;31(2):190-194.
- Board FaN, Medicine Io. Dietary Fats: Total Fat and Fatty Acids. In: *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids.* Washington, DC: National Academies Press 2002:422-541.
- Cholewski M, Tomczykowa M, Tomczyk M. A Comprehensive Review of Chemistry, Sources and Bioavailability of Omega-3 Fatty Acids. *Nutrients.* 2018;10(11).
- U.S. Department of Health and Human Services, National Institutes of Health OoDS. Omega-3 Fatty Acids, Fact Sheet for Health Professionals <https://ods.od.nih.gov/factsheets/Omega3FattyAcids-HealthProfessional/#en5>. Published 2019. Accessed 2020.
- Bowen KJ, Harris WS, Kris-Etherton PM. Omega-3 Fatty Acids and Cardiovascular Disease: Are There Benefits? *Curr Treat Options Cardiovasc Med.* 2016;18(11):69.
- Wei J, Hou R, Xi Y, et al. The association and dose-response relationship between dietary intake of alpha-linolenic acid and risk of CHD: a systematic review and meta-analysis of cohort studies. *Br J Nutr.* 2018;119(1):83-89.
- Rimm EB, Appel LJ, Chiuve SE, et al. Seafood Long-Chain n-3 Polyunsaturated Fatty Acids and Cardiovascular Disease: A Science Advisory From the American Heart Association. *Circulation.* 2018;138(1):e35-e47.
- Abdelhamid AS, Brown TJ, Brainard JS, et al. Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease. *Cochrane Database Syst Rev.* 2018;11:CD003177.
- Siscovick DS, Barringer TA, Fretts AM, et al. Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease: A Science Advisory From the American Heart Association. *Circulation.* 2017;135(15):e867-e884.
- U.S. Department of Health and Human Services, Agriculture USDo. 2015-2020 Dietary Guidelines for Americans. 8th Edition. 2015.
- Casula M, Soranna D, Catapano AL, Corrao G. Long-term effect of high dose omega-3 fatty acid supplementation for secondary prevention of cardiovascular outcomes: A meta-analysis of randomized, placebo controlled trials [corrected]. *Atheroscler Suppl.* 2013;14(2):243-251.
- Delgado-Lista J, Perez-Martinez P, Lopez-Miranda J, Perez-Jimenez F. Long chain omega-3 fatty acids and cardiovascular disease: a systematic review. *Br J Nutr.* 2012;107 Suppl 2:S201-213.
- Kotwal S, Jun M, Sullivan D, Perkovic V, Neal B. Omega 3 Fatty acids and cardiovascular outcomes: systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes.* 2012;5(6):808-818.
- Balk EM, Adam GP, Langberg V, al. e. Omega-3 Fatty Acids and Cardiovascular Disease: An Updated Systematic Review. Evidence Report/Technology Assessment No. 223. Rockville, MD Agency for Healthcare Research and Quality; 2016.
- Bernasconi AA, Wiest MM, Lavie CJ, Milani RV, Laukkanen JA. Effect of Omega-3 Dosage on Cardiovascular Outcomes: An Updated Meta-Analysis and Meta-Regression of Interventional Trials. *Mayo Clin Proc.* 2020.
- Weylandt KH, Serini S, Chen YQ, et al. Omega-3 Polyunsaturated Fatty Acids: The Way Forward in Times of Mixed Evidence. *Biomed Res Int.* 2015;2015:143109.
- Lee KH, Seong HJ, Kim G, et al. Consumption of Fish and omega-3 Fatty Acids and Cancer Risk: An Umbrella Review of Meta-Analyses of Observational Studies. *Adv Nutr.* 2020;11(5):1134-1149.
- Mazereeuw G, Lanctot KL, Chau SA, Swardfager W, Herrmann N. Effects of omega-3 fatty acids on cognitive performance: a meta-analysis. *Neurobiol Aging.* 2012;33(7):1482 e1417-1429.
- Gioxari A, Kaliora AC, Marantidou F, Panagiotakos DP. Intake of omega-3 polyunsaturated fatty acids in patients with rheumatoid arthritis: A systematic review and meta-analysis. *Nutrition.* 2018;45:114-124.
- Abdulrazaq M, Innes JK, Calder PC. Effect of omega-3 polyunsaturated fatty acids on arthritic pain: A systematic review. *Nutrition.* 2017;39-40:57-66.
- Gould JF, Smithers LG, Makrides M. The effect of maternal omega-3 (n-3) LCPUFA supplementation during pregnancy on early childhood cognitive and visual development: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr.* 2013;97(3):531-544.
- Committee DGA. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services Washington, DC: U.S. Department of Agriculture, Agricultural Research Service; 2020.
- Administration USFaD. Advice about Eating Fish. <https://www.fda.gov/food/consumers/advice-about-eating-fish>. Published 2020. Accessed 2020.
- Administration USFaD, Labeling OoNaF, Nutrition CFFSaA. FDA Response: Petition for a Health Claim for Eicosapentaenoic Acid and Docosahexaenoic Acid and Reduction of Blood Pressure in the General Population (Docket No. FDA-2014-Q-1146). In: 2019.
- Agriculture USDo, Service AR. What we eat in America, NHANES 2011-2012. https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/1112/Table_1_NIN_GEN_11.pdf. Published 2015. Accessed 2020.
- Agriculture USDo, Service AR. FoodData Central <https://fdc.nal.usda.gov/>. Published 2019. Accessed 2020.
- Bellows L, Clifford J, Niebaum K, Bunning M. Omega-3 Fatty Acids <https://extension.colostate.edu/topic-areas/nutrition-food-safety-health/omega-3-fatty-acids-9-382/>. Published 2015. Accessed 2020.
- Canada FCo. Omega-3 Enriched Eggs <https://flaxcouncil.ca/resources/nutrition/general-nutrition-information/flax-in-a-vegetarian-diet/omega-3-enriched-eggs/>. Accessed 2020.
- Administration USFaD. Questions and Answers for Consumers Concerning Infant Formula. <https://www.fda.gov/food/people-risk-foodborne-illness/questions-answers-consumers-concerning-infant-formula>. Published 2015. Accessed 2020.
- Health NIo. Dietary Supplement Label Database (DSLDB). <https://dsslod.od.nih.gov/dsslod/>. Published in 2015. Accessed 2020.