

Your questions about complementary medicines answered: fish oil

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This is the third article in a series providing evidence-based answers to common questions about complementary medicines from consumers and healthcare professionals.

What is fish oil?

Fish oil, derived from fatty fish, is an important source of omega-3 polyunsaturated fatty acids (n-3 PUFA) including docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA). In Australia, it is widely used and 25.2% of respondents in the 2010 health survey reported that they had taken fish oil in the previous 24 hours.¹ Fish oil, in the form of cod liver oil, became popular in the 19th century as a source of vitamin D for sun-deprived children in Europe. Today it is used mostly by consumers hoping to prevent cardiovascular disease and stroke. The National Heart Foundation of Australia recommends an intake of 500 mg DHA and EPA daily for the general population, and double that for patients with confirmed heart disease² whereas others question this advice.³

Fish oil has also been used for inflammatory conditions such as joint pains, ulcerative colitis and Crohn's disease.⁴⁻⁶ There are few systematic reviews relating to indications for fish oils and controlled clinical trials continue to produce conflicting results, not only for effectiveness but also for the dose required for efficacy. Investigations across a variety of inflammatory diseases suggest efficacy is dose-dependent. Collectively, these studies indicate that the anti-inflammatory dose of fish oil requires 2.7 g or more of n-3 PUFA daily. However, this requires a daily dose of nine or more standard fish oil capsules, which typically

contain 30% long chain n-3 PUFAs w/w, whereas people who self-medicate with fish oil generally take one or two capsules daily.^{3,7}

Who asks about fish oil?

The medicine call centres received 1067 queries from consumers about fish oil (10.4% of all complementary medicine questions) and 323 from healthcare professionals (6.0%).⁸

The average age of consumers calling about fish oil was 59 years; 80% were women and most questions focused on interactions (33%), efficacy (20%) and adverse drug reactions (ADRs, 16%). Similarly, health professionals were predominantly concerned about interactions (43%) and ADRs (27%), but less about efficacy (9%).⁸

Common consumer and health professional question

Is it safe to combine fish oil with anticoagulants or antiplatelets?

If the dose of fish oil is <3 g daily, combinations of fish oil and warfarin or antiplatelet medication (eg aspirin or clopidogrel) are considered safe.^{4,9-11} However, no studies of fish oil used in combination with the new oral anticoagulants (dabigatran, rivaroxaban) or antiplatelets (abciximab, eptifibatide, prasugrel, ticagrelor) were retrieved.

The mechanism for the anticoagulant activity of fish oil relates to changes in the ratio of phospholipids in platelet membranes,

as fish oil decreases the synthesis of thromboxane A₂ from arachidonic acid in platelets.⁹ Consumption of fish-rich diets or fish oil supplements may reduce platelet aggregation.⁹ Therefore, combined use of fish oil with anticoagulant or antiplatelet agents may, theoretically, increase the risk of bleeding.

In commonly used doses (<3 g daily), fish oil does not seem to increase the risk of bleeding, as previously suggested.^{4,9-11} However, the safety of higher doses (>3 g/day) is less clear.⁹ Although not confirmed in trials, bruising and minor bleeding are frequently reported by people taking fish oils, so it is wise to monitor for these potential adverse effects and reduce the dose if they occur.

Common consumer question

How does fish oil compare with aspirin for prevention of cardiovascular disease?

Currently, neither aspirin nor fish oil is well supported by high-level evidence for primary prevention of cardiovascular disease. For aspirin, this is because the harms seem to outweigh the benefits.¹² In secondary prevention fish oil does not seem to provide any further benefit beyond modern medical therapy, particularly statins,^{13,14} whereas aspirin is effective in preventing further myocardial infarctions (MI) after a first cardiovascular event.¹⁵⁻¹⁸

In large, well-designed secondary prevention studies, fish oil did not prevent

cardiovascular death, Myocardial Infarction (MI) or stroke in patients with risk factors for heart disease or with previous MI.^{14,16,17} In contrast, there is ample evidence that aspirin is protective against these in patients at high risk of cardiovascular disease.^{14,18}

Common health professional question

Is it safe to take fish oil in pregnancy?

Although fish oil supplements are unlikely to be harmful in pregnancy, they are not routinely recommended for pregnant women. There is no strong evidence for benefits to the mother or child unless the mother has a deficiency of or inadequate intake of omega-3 fatty acids.^{19–22}

A joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Consultation on fats and oils in human nutrition recommended that pregnant women should consume at least 2.6 g of omega-3 fatty acids, incorporating 100–300 mg of DHA daily to cover fetal requirements.²³ Postnatal deficiencies caused by low maternal intake have been associated with reduced visual acuity, poor neurodevelopment and ill-effects on behaviour.^{23,24}

A number of studies have shown a positive effect on cognitive development and intelligence quotient of children whose mothers consumed greater amounts of essential fatty acids.^{21,25,26} However, the Evidence Report/Technology Assessment prepared for the Agency of Healthcare Research and Quality (AHRQ) of the US Department of Health and Human Services, and other reviews conclude that, based on the small number of current well-designed studies, there is no conclusive evidence of benefit.^{19–22,27}

Resources

www.nps.org.au/health-professionals/health-news-evidence/2012/fish-oil

www.heartfoundation.org.au/SiteCollectionDocuments/Dietary-fats-summary-evidence.pdf

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References

- Morgan TK, Williamson M, Pirotta M, Stewart K, Myers SP, Barnes J. A national census of medicines use: A 24-hour snapshot of Australians aged 50 years and older. *Med J Aust* 2012;196:50–53.
- Heart Foundation. Position statement. Fish, fish oils, n-3 polyunsaturated fatty acids and cardiovascular health. Updated November 2008. Available at www.heartfoundation.org.au/SiteCollectionDocuments/Fish-FishOils-position-statement.pdf [Accessed 11 June 2014].
- Greene J, Ashburn SM, Razzouk L, Smith DA. Fish oils, coronary heart disease, and the environment. *Am J Public Health* 2013;103:1568–76.
- Villani AM, Crotty M, Cleland LG, et al. Fish oil administration in older adults: Is there potential for adverse events? A systematic review of the literature. *BMC Geriatr* 2013;13:41.
- Goldberg RJ, Katz J. A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. *Pain* 2007;129:210–23.
- Turner D, Shah PS, Steinhart AH, Zlotkin S, Griffiths AM. Maintenance of remission in inflammatory bowel disease using omega-3 fatty acids (fish oil): A systematic review and meta-analyses. *Inflamm Bowel Dis* 2011;17:336–45.
- Cleland LG, James MJ, Proudman SM. Fish oil: What the prescriber needs to know. *Arthritis Res Ther* 2006;8:202.
- Kreijkamp-Kaspers S, McGuire T, Bedford S, et al. Your questions about complementary medicines answered. *Aust Fam Physician* 2015;44:373–74.
- Harris WS. Expert opinion: Omega-3 fatty acids and bleeding-cause for concern? *Am J Cardiol* 2007;99:44C–46C.
- Buckley MS, Goff AD, Knapp WE. Fish oil interaction with warfarin. *Ann Pharmacother* 2004;38:50–52.
- Wang C, Chung M, Lichtenstein A, et al. Effects of omega-3 fatty acids on cardiovascular disease. *Evid Rep Technol Assess (Summ)* 2004;1–8.
- Sutcliffe P, Connock M, Gurung T, et al. Aspirin in primary prevention of cardiovascular disease and cancer: A systematic review of the balance of

evidence from reviews of randomized trials. *PLoS One* 2013;8:e81970.

- Marik PE, Varon J. Omega-3 dietary supplements and the risk of cardiovascular events: A systematic review. *Clin Cardiol* 2009;32:365–72.
- Rizos EC, Ntzani EE, Bika E, Kostapanos MS, Elisaf MS. Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: A systematic review and meta-analysis. *JAMA* 2012;308:1024–33.
- Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71–86.
- Kwak SM, Myung SK, Lee YJ, Seo HG, Korean Meta-analysis Study G. Efficacy of omega-3 fatty acid supplements (eicosapentaenoic acid and docosahexaenoic acid) in the secondary prevention of cardiovascular disease: A meta-analysis of randomized, double-blind, placebo-controlled trials. *Arch Intern Med* 2012;172:686–94.
- Roncaglioni MC, Tombesi M, Silletta MG. N-3 fatty acids in patients with cardiac risk factors. *N Engl J Med* 2013;369:781–82.
- Antithrombotic Trialists C. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71–86.
- Mozurkewich EL, Klemens C. Omega-3 fatty acids and pregnancy: Current implications for practice. *Curr Opin Obstet Gynecol* 2012;24:72–77.
- Makrides M, Duley L, Olsen SF. Marine oil, and other prostaglandin precursor, supplementation for pregnancy uncomplicated by preclampsia or intrauterine growth restriction. *Cochrane Database Syst Rev* 2006;CD003402.
- Moher D. Effects of omega-3 fatty acids on child and maternal health. US Department of Health and Human Services, 2005.
- Dennehy C. Omega-3 fatty acids and ginger in maternal health: Pharmacology, efficacy, and safety. *J Midwifery Womens Health* 2011;56:584–90.
- FDA. Section b: Overview of scientific information on the effect of fish consumption and omega-3 fatty acids on neurodevelopmental health benefits, January 2009. Available at www.fda.gov/Food/FoodbornIllnessContaminants/ChemicalContaminants/ucm153054.htm [Accessed 4 June 2014].
- Bambrick HJ, Kjellstrom TE. Good for your heart but bad for your baby? Revised guidelines for fish consumption in pregnancy. *Med J Aust* 2004;181:61–62.
- Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA. Maternal supplementation with very-long-chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. *Pediatrics* 2003;111:e39–44.
- Helland IB, Saugstad OD, Saarem K, Van Houwelingen AC, Nylander G, Drevon CA. Supplementation of n-3 fatty acids during pregnancy and lactation reduces maternal plasma lipid levels and provides dha to the infants. *J Matern Fetal Neonatal Med* 2006;19:397–406.
- Makrides M, Gould JF, Gawlik NR, et al. Four-year follow-up of children born to women in a randomized trial of prenatal dha supplementation. *JAMA* 2014;311:1802–04.

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