

Systematic Review - Cardiovascular Prevention with Omega-3 Fatty Acids

By Efrain Olszewer, MD

Complete References

Abstract

This systematic review involves studies and meta-analyses that looked at the intake of omega-3 polyunsaturated fatty acids (PUFAs) and their role in cardiovascular prevention and CVD pathologies. We identified and analyzed the benefits of different doses. The studies use varied dosages, which is why, we believe, the studies and meta-analyses have varied, and sometimes controversial, results.

We concluded that there is an inverse relationship between consuming omega-3s and cardiovascular pathologies; the higher the dose of omega-3, the better the results seem to be.

The authors recommend more studies with adequate doses of omega-3 to establish an ideal dosage with a strong inverse relationship between omega-3 consumption and cardiovascular disease.



1. Miles EA, Calder PC. [Influence of marine n-3 polyunsaturated fatty acids on immune function and a systematic review of their effects on clinical outcomes in rheumatoid arthritis.](#) *Br J Nutr.* 2012 Jun;107 Suppl 2:S171-84.
2. Calder PC. [Omega-3 polyunsaturated fatty acids and inflammatory processes: nutrition or pharmacology?](#) *Br J Clin Pharmacol.* 2013 Mar;75(3):645-62.
3. Calder PC. [Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance.](#) *Biochim Biophys Acta.* 2015 Apr;1851(4):469-84.
4. Calder PC. [Omega-3 fatty acids and inflammatory processes: from molecules to man.](#) *Biochem Soc Trans.* 2017 Oct 15;45(5):1105-1115.
5. Nowak JZ [Anti-inflammatory pro-resolving derivatives of omega-3 and omega-6 polyunsaturated fatty acids]. *Postepy Hig Med Dosw (Online).* 2010 Mar 17;64:115-32. Polish.
6. Calder PC. [Omega-3 fatty acids and inflammatory processes.](#) *Nutrients.* 2010 Mar;2(3):355-74.
7. Innes JK, Calder PC. Marine Omega-3 (N-3) Fatty Acids for Cardiovascular Health: An Update for 2020. *Int J Mol Sci.* Feb 18, 2020; 21(4).
8. Zhang et al. Association of Fish and Long-Chain omega-3 Fatty Acids Intakes With Total and Cause-Specific Mortality: Prospective Analysis of 421 309 Individuals. *J Intern Med.* 2018 Oct;284(4):399-417. doi: 10.1111/joim.12786. Epub 2018 Jul 17.
9. Kromhout D, et al. n-3 Fatty Acids and Cardiovascular Events after Myocardial Infarction. *N Engl J Med.* November 18, 2010; 363:2015-2026.

10. Manson JF, et al. The VITamin D and Omega-3 Trial (VITAL): Rationale and Design of a Large Randomized Controlled Trial of Vitamin D and Marine Omega-3 Fatty Acid Supplements for the Primary Prevention of Cancer and Cardiovascular Disease. *Contemp Clin Trials*. 2012 Jan; 33(1): 159–171.
11. Make KC, et al. Use of Supplemental Long-Chain omega-3 Fatty Acids and Risk for Cardiac Death: An Updated Meta-Analysis and Review of Research Gaps. *J Clin Lipidology*. Sep-Oct 2017;11(5): 1152-1160.e2. –
12. Maki KC, et al. Use of Supplemental Long-Chain Omega-3 Fatty Acids and Risk for Cardiac Death: An Updated Meta-Analysis and Review of Research Gaps. *J Clin Lipidol*. Sept-Oct 2017;11(5):1152-1160.
13. [Yun-Tao Zhao](#), [Qiang Chen](#), et al. Prevention of Sudden Cardiac Death With omega-3 Fatty Acids in Patients With Coronary Heart Disease: A Meta-Analysis of Randomized Controlled Trials. *Ann Med*. 2009;41(4): 301-10.
14. Singh S, et al. Eicosapentaenoic Acid Versus Docosahexaenoic Acid as Options for Vascular Risk Prevention: A Fish Story. *Am J Ther*. May-June 2016;23(3): e905-10.
15. Carracedo M, et al. The resolution of inflammation through omega-3 fatty acids in atherosclerosis, intimal hyperplasia, and vascular calcification. *Seminars in Immunopathology*. 2019;41:757–766.
16. Sekikawa A, et al. Association of blood levels of marine omega-3 fatty acids with coronary calcification and calcium density in Japanese men. *Eur J Clin Nutr*. 2019; 73(5):783–792.
17. Kanai S, et al. Eicosapentaenoic acid reduces warfarin-induced arterial calcification in rats. *Atherosclerosis*. 2011;215(1):43–51.
18. Nakamura K, et al. Eicosapentaenoic acid prevents arterial calcification in klotho mutant mice. *PLoS One*. 2017;12(8):e0181009.
19. Aung T, et al. Associations of omega-3 fatty acid supplement use with cardiovascular disease risks: meta-analysis of 10 trials involving 77917 individuals. *JAMA Cardiol*. 2018;3(3):225–34.
20. Nomura S, et al. Effects of eicosapentaenoic acid on endothelial cell-derived microparticles, angiopoietins and adiponectin in patients with type 2 diabetes. *Atheroscler Thromb*. 2009;16(2):83–90. 30.
21. Meisinger C, et al. Plasma oxidized low-density lipoprotein, a strong predictor for acute coronary heart disease events in apparently healthy, middle-aged men from the general population. *Circulation*. 2005;112(5):651–7.
22. Burr ML, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial infarction and reinfarction trial (DART). *Lancet*. 1989;2:757-761.
23. Ness AR, et al. The long-term effect of advice to eat more fish on blood pressure in men with coronary disease: results from the diet and reinfarction trial. *J Hum Hypertens*. 1999;13:729-733.
24. GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *Lancet*. 1999; 354: 447-455.
25. Macchia A, et al. Left ventricular systolic dysfunction, total mortality, and sudden death in patients with myocardial infarction treated with n-3 polyunsaturated fatty acids. *Eur J Heart Fail*. 2005;7:904-909.

26. Yokoyama M, et al. Effects of eicosapentaenoic acid on major coronary events in hypercholesterolemic patients (JELIS): a randomized open-label, blinded, end-point analysis. *Lancet*. 2007;369:1090-1098.
27. Tavazzi L, et al. Effect of n-3 polyunsaturated fatty acids in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2008;372:1223-1230.
28. Ness AR, et al.. The long-term effect of dietary advice in men with coronary disease: follow-up of the Diet and Reinfarction trial (DART). *Eu J Clin Nutr*. 2002;56:512-518. 87.
29. Kromhout D, Giltay EJ, Geleijnse JM. N-3 fatty acids and cardiovascular events after myocardial infarction. *N Engl J Med*. 2010;363:2015-2026.
30. Sala-Vila A, et al. Dietary α -linolenic acid, marine ω -3 fatty acids, and mortality in a population with high fish consumption: findings from the prevención con Dieta MEDiterránea (PREDIMED) Study. *J Am Heart Assoc*. 2016;5. pii: e002543.
31. Kris-Etherton PM, et al. Recent Clinical Trials Shed New Light on the Cardiovascular Benefits of Omega-3 Fatty Acids. *Methodist Debaquey Cardiovasc J*. Jul-Sept 2019;15(3).
32. Musa-Veloso K, et al. Systematic Review with Meta-analysis. Impact of low v.moderate intakes of long-chain n-3 fatty acids on risk of coronary heart disease. *British Journal of Nutrition*. 2011;106: 1129–1141.
33. Yang Hu, et al. Marine Omega-3 Supplementation and Cardiovascular Disease: An Updated Meta-Analysis of 13 Randomized Controlled Trials Involving 127 477 Participants. *J Am Heart Assoc*. 2019.
34. Amano T, et al. Impact of omega-3 polyunsaturated fatty acids on coronary plaque instability. [Atherosclerosis](#). September 2011;218(1):110-116.
35. He K, et al. Intakes of long-chain n-3 polyunsaturated fatty acids and fish in relation to measurements of subclinical atherosclerosis. *Am J Clin Nutr*. 2008;88:1111–8.
36. Erkkila AT, et al. Fish intake is associated with a reduced progression of coronary artery atherosclerosis in postmenopausal women with coronary artery disease. *Am J Clin Nutr*. 2004;80:626–32.
37. Sacks FM, et al. Controlled trial of fish oil for regression of human coronary atherosclerosis. HARP Research Group. *J Am Coll Cardiol*. 1995;25: 1492–8.
38. Manger MS, et al. Dietary intake of n-3 long-chain polyunsaturated fatty acids and coronary effects in Norwegian patients with coronary artery disease. *Am J Clin Nutr*. 2010;92:244–51.
39. Yokoyama M, et al. Effects of Eicosapentaenoic Acid on Major Coronary Events in Hypercholesterolaemic Patients (JELIS): A Randomised Open-Label, Blinded Endpoint Analysis. *Lancet*. 2007 Mar 31;369(9567):1090-8.
40. Hayati M, et al. Limited Impact of 2 g/day Omega-3 Fatty Acid Ethyl Esters (Omacor[®]) on Plasma Lipids and Inflammatory Markers in Patients Awaiting Carotid Endarterectomy. [Mar Drugs](#). 2013 Sep; 11(9): 3569–3581. Published online 2013 Sep 20.
41. Calder PC. Review The role of marine omega-4 (n-3) fatty acids in inflammatory processes, atherosclerosis and plaque stability. *Mol. Nutr. Food Res*. 2012; 56: 1073-1080.
42. Thies F et al, Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomized controlled trial, *Lancet*. 2003; 361:477-85.
43. Appel LJ, et al. Does Supplementation of Diet With 'Fish Oil' Reduce Blood Pressure? A Meta-analysis of Controlled Clinical Trials. *Arch Intern Med*. 1993;153(12):1429-1438.

44. Miller PE, et al. Experimental Biology and medicine. Long-Chain Omega-3 Fatty Acids Eicosapentaenoic Acid and Docosahexaenoic Acid and Blood Pressure: A Meta-Analysis of Randomized Controlled Trials. *Am J Hypertens*. July 2014;27(7).
45. Geleijnse JM, et al.. Blood Pressure Response to Fish Oil Supplementation: Metaregression Analysis of Randomized Trials. *J Hypertens*, Aug 2002;20(8):1493-9.
46. Hoshi T, et al. Omega-3 fatty acids lower blood pressure by directly activating large-conductance Ca²⁺-dependent K⁺ channels. [Proc Natl Acad Sci U S A](#). 2013 Mar 19; 110(12): 4816–4821.
47. Pase MP, Grima NA, Sarris J. Do Long-Chain n-3 Fatty Acids Reduce Arterial Stiffness? A Meta-Analysis of Randomised Controlled Trials. *Br J. Nutr*, Oct 2011;106 (7): 974-80.
48. Siasos G, et al. Effects of Ω-3 Fatty Acids on Endothelial Function, Arterial Wall Properties, Inflammatory and Fibrinolytic Status in Smokers: A Cross Over Study.*Int J Cardiol*. 2013 Jun 20;166(2):340-6.
49. Casanova MA, et al. Omega-3 Fatty Acids Supplementation Improves Endothelial Function and Arterial Stiffness in Hypertensive Patients With Hypertriglyceridemia and High Cardiovascular Risk.*J Am Soc Hypertens*. 2017 Jan;11(1):10-19.
50. Delgado-Lista J, et al. Long chain omega-3 fatty acids and cardiovascular disease: a systemic review. *BJN*. May 17, 2012.

Efrain Olszewer, MD, who specializes in internal medicine and cardiology, is clinical director of the International Center of Prevention Medicine (CMP) in Brazil. He is the president of the Brazilian Orthomolecular Society and editorial director of the Journal of Orthomolecular Practice. He has written 93 books on health and medicine.

MycoPul™ Exceptionally pure, vigorous mycotoxin binder

Researched Nutritionals
MycoPul™
Advanced Binder Complex™

- Breaks Mycotoxins in the GI tract*
- Combines with EnzoiPul™ for optimal detox support*
- GMO Free

Researched Nutritionals
solutions for life