

# BONUS: THE OMEGA-3 SCIENCE REPORT

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*The American Heart Association: “Omega-3 fatty acids benefit the heart of healthy people, and those at high risk of, or who have cardiovascular disease.”*

*Compiled by Garey Simmons, CHC, AADP*

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MEDITERRANEAN DIET AND N-3 FATTY ACIDS IN THE PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASE. DE LORGERIL M, SALEN P.

Source

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Abstract

Consumption of a traditional Mediterranean diet and n-3 polyunsaturated fatty acids (PUFAs) was shown

to be effective in reducing the complications of coronary heart disease in randomized controlled trials. Epidemiological studies and controlled trials indicate that plant- and sea-derived n-3 PUFAs are likely to be important mediators of the protection provided by traditional Mediterranean diets. Of note, consumption of marine n-3 PUFAs from fish and other seafood is high in certain Mediterranean countries (Spain, Portugal), but quite low in others (Italy, Greece).

A relative insufficiency of dietary marine n-3 PUFAs among Italians might in part explain the results of the GISSIPrevenzione trial, in which a modest supplementation of eicosapentaenoic acid + docosahexaenoic acid (approximately 850 mg/day) produced striking reductions in coronary heart disease death (-30%) and sudden cardiac death (-45%) among patients with known heart disease. The protection provided by n-3 PUFAs from both plant and marine sources may be partly dependent on other dietary factors. Plant and marine n-3 PUFAs are likely to be major mediators of the protective effect provided by traditional Mediterranean diets.

PMID: 17876197

[PUBMED - INDEXED FOR MEDLINE]

PATHOPHYSIOLOGY. 2007 OCT;14(2):127-32. EPUB 2007 JUN 28.

N-3 PUFAS-FROM DIETARY SUPPLEMENTS TO MEDICINES.

FEDACKO J, PELLA D, MECHÍROVÁ V, HORVATH P, RYBÁR R, VARJASSYOVÁ P, VARGOVÁ V.

Source

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Kosice, Slovakia.

## Abstract

Although there has been a great progress in the prevention of cardiovascular diseases, the mortality of patients with acute myocardial infarction (AMI) still remains high. One of the most important underlying causes explaining this phenomenon is the sudden cardiac death. Nearly half of all cardiovascular deaths in the USA each year is attributed to this unpredictable and unexpected complication of AMI. Hence, there is an urgent medical need for a targeted therapy to reduce the incidence of sudden cardiac death. Since 1980 there have been several epidemiological and other studies concerning the benefits of n-3 polyunsaturated fatty acids (n-3 PUFAs) in cardiovascular health and prevention. Results from one of the largest studies, GISSI Prevenzione Trial show that adding the n-3 PUFAs to standard therapy of patients who survived AMI reduces sudden cardiac death (44% risk reduction,  $p=0.0006$ ). In addition, significant decline in all-cause cardiovascular mortality (21% risk reduction,  $p=0.0064$ ) further emphasizes the role of n-3 PUFA in cardiovascular prevention. To date, beneficial effects of n-3 PUFA are attributed to their antiarrhythmic, lipid lowering, antithrombotic and anti-inflammatory properties. To conclude, EPA and DHA improve the prognosis of cardiovascular patients in the secondary prevention of sudden cardiac death without any documented side effects.

PMID: 17604611

[PUBMED]

HISTORICAL OVERVIEW OF N-3 FATTY ACIDS AND CORONARY HEART DISEASE.

LEAF A.

## Source

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## Abstract

The first evidence that fish oil fatty acids might have a beneficial effect on coronary heart disease came from the discovery that Greenland Eskimos, who have a diet high in n-3 fatty acids, have a lower mortality from coronary heart disease than do Danes and Americans. Long-chain polyunsaturated fatty acids are essential in our diets and can be classified in 2 groups: n-6 fatty acids found in plant seeds and n-3 fatty acids found in marine vertebrates. Further evidence of n-3 benefits to human health include a 1989 study demonstrating a 29% reduction in fatal cardiac arrhythmias among subjects with a recent myocardial infarction who had been advised to consume fish oil. The GISSI-Prevenzione Trial found a significant reduction in relative reduction of death, cardiac death, nonfatal myocardial infarction, and stroke in subjects consuming n-3 fatty acids. In a recent study, subjects with implanted cardiac defibrillators (ICDs) at high risk for fatal ventricular arrhythmias were randomly assigned to four 1-g capsules

of either an ethyl ester concentrate of n-3 fatty acids or olive oil daily for 12 mo. Subjects receiving n-3 who thus had significantly higher levels of eicosapentaenoic acid and docosahexaenoic acid in their red blood cell membranes showed a longer time to first ICD events and had a significantly lower relative risk of having an ICD event or probable event ( $P = 0.033$ ). These studies demonstrate that fish oil fatty acids have beneficial effects on coronary heart disease.

PMID: 18541598

[PUBMED - INDEXED FOR MEDLINE]

BIOMED PHARMACOTHER. 2002 OCT;56(8):365-79.

THE IMPORTANCE OF THE RATIO OF OMEGA-6/OMEGA-3 ESSENTIAL FATTY ACIDS.

SIMOPOULOS AP.

#### Source

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#### Abstract

Several sources of information suggest that human beings evolved on a diet with a ratio of omega-6 to omega-3 essential fatty acids (EFA) of approximately 1 whereas in Western diets the ratio is 15/1-6.7/1. Western diets are deficient in omega-3 fatty acids, and have excessive amounts of omega-6 fatty acids compared with the diet on which human beings evolved and their genetic patterns were established. Excessive amounts of omega-6 polyunsaturated fatty acids (PUFA) and a very high omega-6/omega-3 ratio, as is found in today's Western diets, promote the pathogenesis of many diseases, including cardiovascular disease, cancer, and inflammatory and autoimmune diseases, whereas increased levels of omega-3 PUFA (a low omega-6/omega-3 ratio) exert suppressive effects. In the secondary prevention of cardiovascular disease, a ratio of 4/1 was associated with a 70% decrease in total mortality.

A ratio of 2.5/1 reduced rectal cell proliferation in patients with colorectal cancer, whereas a ratio of 4/1 with the same amount of omega-3 PUFA had no effect. The lower omega-6/omega-3 ratio in women with breast cancer was associated with decreased risk. A ratio of 2-3/1 suppressed inflammation in patients with rheumatoid arthritis, and a ratio of 5/1 had a beneficial effect on patients with asthma, whereas a ratio of 10/1 had adverse consequences. These studies indicate that the optimal ratio may vary with the disease under consideration. This is consistent with the fact that chronic diseases are multigenic and multifactorial. Therefore, it is quite possible that the therapeutic dose of omega-3 fatty acids will depend on the degree of severity of disease resulting from the genetic predisposition. A lower ratio of omega-6/omega-3 fatty acids is more desirable in reducing the risk of many of the chronic

diseases of high prevalence in Western societies, as well as in the developing countries, that are being exported to the rest of the world.

ENDOCR METAB IMMUNE DISORD DRUG TARGETS. 2011 JUN 8. [EPUB AHEAD OF PRINT]  
ROLE OF  $\Omega$ 3 LONGCHAIN POLYUNSATURATED FATTY  
ACIDS IN REDUCING CARDIO-METABOLIC RISK FACTORS.  
ABEYWARDENA MY, PATTEN GS.

#### Source

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#### Abstract

Cardiovascular disease is the leading cause of mortality in many economically developed nations, and its incidence is increasing at a rapid rate in emerging economies. Diet and lifestyle issues are closely associated with a myriad of cardiovascular disease risk factors including abnormal plasma lipids, hypertension, insulin resistance, diabetes and obesity, suggesting that diet-based approaches may be of benefit. Omega-3 long chain-polyunsaturated fatty acids ( $\omega$ 3 LC-PUFA) are increasingly being used in the prevention and management of several cardiovascular risk factors.

Both the  $\omega$ 3 and  $\omega$ 6 PUFA families are considered essential, as the human body is itself unable to synthesize them. The conversion of the two precursor fatty acids – linoleic acid (18:2 $\omega$ 6) and  $\alpha$ -linoleic acid ( $\alpha$ 18:3 $\omega$ 3) – of these two pathways to longer ( $\geq$ C(20)) PUFA is inefficient. Although there is an abundance of  $\omega$ 6 PUFA in the food supply; in many populations the relative intake of  $\omega$ 3 LC-PUFA is low with health authorities advocating increased consumption.

Fish oil, rich in eicosapentaenoic (EPA, 20:5 $\omega$ 3) and docosahexaenoic DHA, 22:6 $\omega$ 3) acids, has been found to cause a modest reduction in blood pressure at a dose level of >3g/d both in untreated and treated hypertensives. Whilst a multitude of mechanisms may contribute to the blood pressure lowering action of  $\omega$ 3 LC-PUFA, improved vascular endothelial cell function appears to play a central role. Recent studies which evaluated the potential benefits of fish oil in type-2 diabetes have helped to alleviate concerns raised in some previous studies which used relatively large dose (5-8 g/d) and reported a worsening of glycemic control. Several meta-analyses have confirmed that the most consistent action of  $\omega$ 3 LC-PUFA in insulin resistance and type-2 diabetes is the reduction in triglycerides. In some studies, fish oil has been found to cause a small rise in LDL-cholesterol, but a change in the LDL particle size, from the smaller more atherogenic form to the larger, less damaging particle size, have also been noted.  $\omega$ 3 LC-

PUFA are effective modulators of the inflammation that accompanies several cardio-metabolic abnormalities. Taking into consideration the pleiotropic nature of their actions, it can be concluded that dietary supplementation with  $\omega$ 3 LC-PUFA will lead to improvements in cardio-metabolic health parameters. These fatty acids pose only minor side effects and more importantly, do not interact adversely with the common drug therapies used in the management and treatment of hypertension, dyslipidemia, type-2 diabetes, and obesity/metabolic syndrome, but in some instances work synergistically, thereby providing additional cardiovascular benefits.

PMID: 21651471

CURR OPIN LIPIDOL. 2011 OCT 7. [EPUB AHEAD OF PRINT]

NOVEL DEVELOPMENTS IN OMEGA-3 FATTY ACID-BASED STRATEGIES.

DAVIDSON MH, KLING D, MAKI KC.

#### Source

University of Chicago Pritzker School of Medicine, Chicago, Illinois Omthera Pharmaceuticals, Inc., Bedminster,

New Jersey Provident Clinical Research, Biofortis-North America, Glen Ellyn, Illinois, USA.

#### Abstract

##### PURPOSE OF REVIEW:

Omega-3 polyunsaturated fatty acids (n-3 PUFAs) have been attributed with several health benefits, including triglyceride lowering and cardiovascular disease risk reduction. This review focuses on new prescription omega-3 fatty acid products in development and recently published data regarding omega-3 fatty acid effects on arrhythmias, heart failure, and platelet inactivation.

##### RECENT FINDINGS:

A free fatty acid form of n-3 PUFA was found to produce a four-fold higher area under the plasma n-3 PUFA curve than prescription omega-3-acid ethyl esters in patients on a low-fat diet. Eicosapentaenoic acid ethyl esters reduced triglyceride without significantly elevating LDL cholesterol in patients with severe hypertriglyceridemia and in those with mixed dyslipidemia. Recent investigations of n-3 PUFA effects on ventricular and atrial arrhythmias, including studies in patients with implanted defibrillators, failed to demonstrate a significant benefit. However, increased fatty fish or n-3 PUFA consumption was associated with a lower rate of hospitalization in heart failure patients. A further important finding was potentiation of the antiplatelet response when n-3 PUFAs were added to aspirin + clopidogrel.

## SUMMARY:

Although n-3 PUFA therapy continues to show promise in the prevention and management of cardiovascular diseases, further research is necessary to more fully elucidate its role in specific disorders.

AM J CLIN NUTR. 2008 JUN;87(6):1981S-90S.  
ROLE OF N-3 FATTY ACIDS IN THE TREATMENT OF HYPERTRIGLYCERIDEMIA AND CARDIOVASCULAR DISEASE.  
JACOBSON TA.

## Source

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## Abstract

n-3 Fatty acids (FAs) when used in doses of 3-4 g/d eicosapentaenoic acid and docosahexaenoic acid have profound effects on triacylglycerol (TG) concentrations. The mechanism for their TG reduction relates to their favorable effects on reducing hepatic production and secretion of VLDL and VLDL apolipoprotein B particles, along with favorable effects on plasma lipolytic activity through lipoprotein lipase-mediated clearance, as well as stimulation of beta-oxidation of other FAs in the liver. Their hypotriglyceridemic properties are related to both the dose of n-3 FAs used and the baseline TG concentrations of the population. In patients with TG concentrations >500 mg/dL, 4 g n-3 FAs have been shown to reduce TGs by 45%, VLDL by 42%, and non-HDL by 10.2%. A recent pooled meta-analysis with multiple doses of n-3 FAs ranging from 0.8 to 5.4 g revealed changes in TGs of -27 mg/dL (95% CI: -33, -20), in HDL of +1.6 mg/dL (95% CI: + 0.8, +2.3), and in LDL cholesterol of +6 mg/dL (95% CI: + 3, +8). The clinical uses of n-3 FAs include treatment of severe and moderate hypertriglyceridemia, use in statin-treated patients with elevated TG concentrations or non-HDL cholesterol (mixed hyperlipidemia), and use in the secondary and primary prevention of cardiovascular disease. Existing large-scale clinical trials such as the GISSI-Prevenzione Study and JELIS with low doses of n-3 FAs (1-2 g) show clinical benefit in reducing coronary heart disease without substantial changes in concentrations of TGs or other lipids. Future clinical trials need to determine whether the TG-lowering doses of n-3 FAs (3-4 g/d) result in additional risk reduction.

EFFICACY OF N-3 POLYUNSATURATED FATTY ACIDS ACCORDING TO CLINICAL CHARACTERISTICS OF PATIENTS  
WITH RECENT MYOCARDIAL INFARCTION: INSIGHTS FROM THE GISSI-PREVENZIONE TRIAL.  
MARCHIOLI R, MARFISI RM, BORRELLI G, CHIEFFO C, FRANZOSI MG, LEVANTESI G, MAGGIONI AP, NICOLOSI GL, SCARANO M,  
SILLETTA MG, SCHWEIGER C, TAVAZZI L, TOGNONI G.

#### Source

Consorzio Mario Negri Sud, Santa Maria Imbaro (CH), Italy. marchioli@negrisud.it

#### Abstract

The GISSI-Prevenzione trial established the efficacy of n-3 polyunsaturated fatty acids (PUFAs) for reducing mortality in patients after recent myocardial infarction. The generalisability of such results to clinical practice could vary according to other individual patient characteristics. We analyzed the GISSI-Prevenzione database to assess whether other major risk factors, comorbidities, dietary habits, or medications could interact with the efficacy of n-3 PUFA treatment to reduce total mortality. We found no evidence that concomitant disease states, habits, or interventions altered the therapeutic benefit of n-3 PUFA consumption in survivors of recent myocardial infarction.

PMID: 17876196  
[PUBMED - INDEXED FOR MEDLINE]  
CURR ATHEROSCLER REP. 2007 AUG;9(2):145-53.  
BEYOND LIPIDS: THE ROLE OF OMEGA-3 FATTY ACIDS  
FROM FISH OIL IN THE PREVENTION OF CORONARY HEART DISEASE.  
JACOBSON TA.

#### Source

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#### Abstract

Omega-3 fatty acid therapy shows great promise in the secondary prevention of coronary artery disease. A meta-analysis of recent omega-3 trials shows reductions of coronary heart disease mortality of 36% (95% CI, 20%-50%;  $P < 0.001$ ) and total mortality of 17% (95% CI, 0%-32%;  $P = 0.046$ ). Some of the potential mechanisms for cardiovascular protection include a reduction in cardiac arrhythmias and plaque stabilization. Since the publication of the landmark GISSI-Prevenzione trial, there have been three major intermediate cardiovascular endpoint studies in patients with implantable cardioverter defibrillators (ICDs) and one large trial, the Japan EPA Lipid Interventional Study (JELIS) trial, which involved 18,645 Japanese patients in



primary and secondary prevention. The three studies with ICD patients have been mixed, with favorable trends toward reduction in the incidence of ventricular arrhythmias in some but not all of the studies. Results of the recent JELIS trial in a Japanese population already consuming a high intake of omega-3 fatty acids showed a 19% risk reduction in major coronary events. Most of the reductions were in unstable angina and nonfatal coronary events, but not in sudden death and cardiovascular mortality. The totality of evidence suggests greater benefits with omega-3 fatty acids in secondary prevention than primary prevention and in populations consuming low amounts of omega-3 fatty acids

HERZ. 2006 DEC;31 SUPPL 3:83-95.

HIGHLY PURIFIED OMEGA-3 POLYUNSATURATED FATTY ACIDS IN CLINICAL DEVELOPMENT.

VIK H.

SOURCE

PRONOVA BIOCARE, LYSAKER, NORWAY.

#### Abstract

Highly purified omega-3 polyunsaturated fatty acids (PUFAs) (Omacor) is the focus of an extensive and ambitious clinical development program that seeks to build on the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione study. Studies currently in progress include very large clinical outcome trials designed to evaluate the impact of omega-3 PUFAs on death and major morbid events in defined patient populations such as individuals with heart failure or diabetes, specialist investigations in very high-risk populations such as patients requiring hemodialysis, and a range of specialized studies concerned with mechanisms of action and effects on biochemical and laboratory indices. The emergence of results from these studies can be expected to define a spectrum of indications for omega-3 PUFAs in the management of cardiovascular and renal disease.

HERZ. 2006 DEC;31 SUPPL 3:74-82.

A MULTI-COUNTRY HEALTH-ECONOMIC EVALUATION OF HIGHLY CONCENTRATED

N-3 POLYUNSATURATED FATTY ACIDS IN THE SECONDARY PREVENTION AFTER MYOCARDIAL INFARCTION.

LAMOTTE M, ANNEMANS L, KAWALEC P, ZOELLNERS Y.

#### Source

HEDM-IMS, Bruxelles, Belgium.

#### Abstract

Patients who survive an acute myocardial infarction (MI) are at increased risk of subsequent major cardiovascular events and cardiac (often sudden) death. The use of highly

concentrated and purified omega-3 polyunsaturated fatty acids (n-3 PUFAs), in addition to standard secondary prevention after MI, results in a significant reduction in the risk of sudden death. This study assessed the cost-effectiveness of adding n-3 PUFAs to the current secondary prevention treatment after acute MI in 5 countries: Australia, Belgium, Canada, Germany, Poland.

Based on the clinical outcomes of GISSI-Prevenzione (MI, stroke, Revascularisation rate and mortality), a decisionmodel was built in DataPROTM. The implications of adding n-3 PUFAs to standard treatment in patients with a recent history of MI were analysed from the health care payer's perspective. The time horizon was 3.5 years (identical to GISSI-Prevenzione). Event costs were based on literature data. Life expectancy data for survivors of cardiac disease were taken from the Saskatchewan database and then country-adjusted. Results are expressed as extra cost (Euro) per life-year gained (LYG). Annual discounting of 5% was applied to health effects and costs. Treatment with highly concentrated n-3 PUFAs yielded between 0.260 (Poland) and 0.284 (Australia) LYG, at an additional cost of Euro 807 (Canada) to Euro 1,451 (Belgium). The incremental cost-effectiveness ratio (ICER) varied between Euro 2,867 (Canada) and Euro 5,154 (Belgium) per LYG. Sensitivity analyses on effectiveness, cost of complications and discounting proved the robustness of the results. A 2nd order Monte Carlo simulation based on the 95% CIs obtained from GISSI showed that highly concentrated n-3 PUFAs are cost-effective in more than 99% of patients (assuming societal willingness to pay threshold of Euro 20,000/LYG). Including health care costs incurred during the remaining life-years considerably increased total costs but had no impact on the ICER-based treatment recommendation. Adding highly concentrated n-3 PUFAs to standard treatment in the secondary prevention after MI appears to be cost-effective in the 5 countries studied.



*A final word from Garey Simmons:*

- *Join us in our quest to prevent a million heart attacks. This year there will be far too many heart attacks in the United States. Half of them, a full 50%, will be fatal. This can be prevented.*
- *Don't let this happen to you or to your loved ones. Let's get people taking Omega-3 fish oil and start whittling away at this number. If we*

*reduce 100,000 heart attacks a year, we could save a million people over a ten-year period. All we have to do is getting folks at risk on a appropriate regimen of Omega-3 and encourage a better nutritional habit.*

*Be well,*

*Garey Simmons*

877.572.3444

443.852.1000

For more information, please visit:

<http://OptimalHealthBridge.com>

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& 240 capsules

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In conclusion, it makes abundant sense to do one thing every day. Take Omega-3s. According to the American Heart Association:

Omega-3s benefit:

»Healthy people

»Those at high risk of heart disease

»Those who have heart disease

So, it really doesn't matter which category you fit into, it's recommended and beneficial to take Omega-3 daily.

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\* Call Garey Simmons at 443.852.1000 and ask any questions you may have regarding health and nutrition.