

## Getting Your Omega-3 to Omega-6 Ratio Right Is Essential

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#### STORY AT-A-GLANCE

- > While omega-3s have an anti-inflammatory effect, the omega-6 found in seed oils tend to be proinflammatory. Maintaining a healthy 3:1 ratio of omega-6 to omega-3 is important, as chronic low-grade inflammation is a hallmark of most chronic diseases, including obesity, diabetes and heart disease
- > Omega-3 fats are essential polyunsaturated fats your body needs for a wide variety of functions, including proper cell division and function of cell receptors, muscle activity, cognition and heart health
- > DHA is particularly important for your brain, as about 90% of your brain is made up of DHA, while EPA appears to be of particular importance for heart health
- > Compared to placebo, people taking a daily supplement containing 1 gram of marinebased omega-3 and 2,000 IU's of vitamin D for five years lowered their risk of heart attack by 28%
- > People with the lowest fish intake had a 19% reduction in major cardiovascular events (the primary endpoint) and a 40% reduction in heart attacks (a secondary endpoint) when they supplemented with 1 gram of marine-based omega-3 and 2,000 IU's of vitamin D

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Omega-3 fats are essential polyunsaturated fats (PUFAs) your body needs for a wide variety of functions, including proper cell division and function of cell receptors, muscle activity, cognition and heart health.

Importantly, the marine-based omega-3 fats docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) — two long-chained PUFAs found in fatty fish, fish oil and krill oil — are actually cellular components, which makes them all the more crucial for optimal functioning of cells and mitochondria.

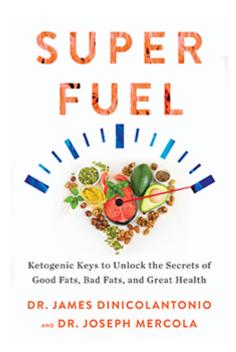
DHA is particularly important for your brain, as about 90% of the fat in your brain is DHA, while EPA appears to be of particular importance for heart health.

## **EPA Lowers Cardiovascular Health Risks**

For example, recent research<sup>1,2,3</sup> involving a proprietary prescription formulation of fish oil called Vascepa — a highly-processed form of EPA — found the drug lowered cardiovascular health risks by 25% compared to placebo containing mineral oil. This included heart attacks, strokes, bypass surgery and chest pain requiring hospitalization.

Participants received 4 grams of EPA per day, which is two to four times more EPA than typically given, which supports the prediction that most people need far more omega-3 than currently recommended.

I discuss this in my latest book, "Superfuel," cowritten with James DiNicolantonio, Pharm. D., who has published a number of papers on omega-3 and the health implications of the ratios between omega-3 and omega-6. Based on his review of the scientific literature, which I'll review further below, 3 to 4 grams of EPA and DHA appear to be ideal.



Meanwhile, you only need 1 to 2 grams of whole food-based omega-6 linoleic acid per day (not to be confused with conjugated linoleic acid found in grass fed animal foods), ideally from plant seeds and tree nuts, not vegetable oils, as the oxidized omega-6 in these oils actually contribute to heart disease.<sup>4</sup>

## **VITAL Study Confirms Heart Healthy Benefits of Fish**

Another recent omega-3 study,<sup>5</sup> funded in part by the National Institutes of Health, followed more than 25,000 individuals aged 50 and older for over five years.

Participants were taking either a daily supplement containing 1 gram of marine-based omega-3 and 2,000 IUs of vitamin D, or a placebo. As reported by The Harvard Gazette:<sup>6</sup>

"For omega-3 fatty acids, the previous randomized trials had largely been in high-risk populations with a history of cardiovascular disease (CVD) or with selected risk factors for CVD. VITAL is the first large-scale randomized trial of marine omega-3s in a general population at 'usual risk' of CVD.

It's also one of the first randomized trials of these supplements in a racially and ethnically diverse study population. Assessing the role of these supplements in a general population free of cardiovascular disease and cancer at baseline fills an important gap in knowledge."

While omega-3 supplementation led to "only a small, statistically nonsignificant 8% reduction" in the primary endpoint of major cardiovascular events (heart disease plus stroke plus total CVD mortality), some of the secondary endpoints showed impressive improvement when viewed separately.

For example, heart attacks alone were reduced by 28% in the overall population. The authors suggest the lack of reductions in stroke or CVD mortality "watered down" the results for the primary endpoint of major cardiovascular events. They also found that:

- Compared to the placebo group, African-Americans who received the supplement had a 77% reduction in heart attacks.
- People with high fish intake also reaped far greater benefits than the population as a whole. Those with the lowest fish intake had a 19% reduction in major cardiovascular events (the primary endpoint) and a 40% reduction in heart attacks (a secondary endpoint).

# **Vitamin D Supplementation May Lower Tumor Risk**

As for vitamin D, the study was not long enough to really identify the impact of supplementation on cancer risk, but after accounting for a latency period, the researchers found a 25% reduction in cancer deaths, which clearly would have been greater had the study been longer.

"Laboratory and clinical studies suggest that vitamin D may affect tumor biology, making tumors less invasive, less aggressive and less likely to metastasize.

And if that's the effect, once there's already a tumor — diagnosed or not, clinically detected or not — you might see a reduction in cancer death over the course of a five-year trial," lead author, JoAnn Manson, a Michael and Lee Bell professor of Women's Health at Harvard Medical School and a professor of epidemiology at the Harvard Chan School, said.<sup>7</sup>

### **Processed Seed Oils Contribute to Low-Grade Inflammation**

Papers written by DiNicolantonio also reveal the importance of omega-3 for health, and the importance of maintaining the right balance between omega-3 and omega-6. In his editorial, "Importance of Maintaining a Low Omega-6/Omega-3 Ratio for Reducing Inflammation," published in the BMJ journal Open Heart, DiNicolantonio notes:

"The consumption of seed oils high in the omega-6 PUFA linoleic acid contributes to low-grade inflammation, oxidative stress, endothelial dysfunction and atherosclerosis. Moreover, dietary linoleic acid significantly increases cyclooxygenase-2 (COX-2) expression in the aorta, converting arachidonic acid to proinflammatory eicosanoids ...

Additionally, there is an arachidonic acid-independent pathway of inflammation promoted by the intake of omega-6 seed oils such as increased production of oxidized linoleic acid metabolites and proinflammatory linoleic acid CYP-eicosanoids.

Oxidized linoleic acid metabolites formed from linoleic acid activate NF-kB and increase proinflammatory cytokines, endothelial adhesion molecules, as well as chemokines, all of which are paramount in the formation of atherosclerosis. Linoleic acid also induces an inflammatory environment in endothelial cells that may increase the risk of coronary heart disease (CHD).

Oxidized linoleic acid metabolites are found at a fiftyfold higher concentration in plasma than arachidonic acid metabolites, suggesting that they are more consequential in CHD and other chronic diseases, and lowering dietary linoleic acid reduces oxidized linoleic acid metabolites in the body."

In short, while omega-3s have an anti-inflammatory effect, the omega-6 found in seed oils tend to be proinflammatory, largely due to the processing the oils undergo, which oxidize the PUFAs. This is important, as chronic low-grade inflammation is a hallmark of most chronic diseases, including obesity, diabetes, heart disease and cancer.

As noted by DiNicolantonio, research shows that as atherosclerotic lesions become more advanced, the ratio between oxidized and unoxidized linoleic acid increases, suggesting the omega-6 in vegetable oils is a driver of coronary heart disease. He addresses these links more directly in his paper, "Omega-6 Vegetable Oils as a Driver of Coronary Heart Disease: The Oxidized Linoleic Acid Hypothesis."

Research has also shown that lowering the omega-6 to omega-3 ratio from 18-to-1 to 3-to-1 reduced the release of a proinflammatory cytokine known as IL-6 when eating a high-saturated-fat diet, suggesting that replacing omega-6 with omega-3 indeed reduces inflammation.

# Balancing Omega-6 to Omega-3 Ratio May Aid Weight Management

In an earlier editorial,<sup>10</sup> published in 2016, DiNicolantonio discusses the importance of balancing your omega-6 to omega-3 ratio for the prevention and management of obesity, as the two PUFAs have very different effects not only on inflammation markers but also on body fat. In short, they're "metabolically and functionally distinct," and produce very different health impacts. He writes:

"[C]alories from vegetable oils high in linoleic acid ... an omega-6 fatty acid, are proinflammatory and thrombogenic, whereas calories from eating fish high in omega-3 fatty acids are anti-inflammatory and antithrombotic ...

Furthermore, calories from omega-6 ... intake from vegetable oils high in linoleic acid (corn oil, sunflower, safflower, cottonseed, soya bean oil) have different effects on fat tissue development and type than calories from omega-3 fatty acid intake high in  $\alpha$ -linolenic acid (ALA) (such as flaxseed oil, canola oil, perilla oil, chia oil) ...

The typical Western diet now provides an omega-6 to omega-3 ratio of around 16-to-1. High dietary intake of omega-6 fatty acids as occurs today leads to

increases in white adipose tissue and chronic inflammation, which are the 'hallmarks of obesity.'

Omega-6 and omega-3 fatty acids specifically metabolize to prostaglandins, thromboxane and leukotrienes. Prostaglandin E2 from arachidonic acid leads to differentiation and proliferation of adipose tissue and prostaglandin  $F2\alpha$ , also from arachidonic acid, prevents the browning of white adipose tissue, which is the good fat tissue as it increases thermogenesis, burning fat through the release of heat."

DiNicolantonio also notes that by acting directly on your central nervous system, omega-3 and omega-6 fatty acids influence your food intake and your body's sensitivity to insulin and leptin — but again in opposite directions.

While omega-6 has been shown to increase insulin and leptin resistance, diabetes and obesity in both rodent and human models, omega-3 has the converse effect, and can help "reverse the dysregulation of this system, improve insulin sensitivity and control body fat," DiNicolantonio writes, adding "It is therefore essential to return to a balanced dietary omega-6 to omega-3 ratio based on data from evolutionary studies."

His paper also delves into some of the genetic research showing how omega-3 and omega-6 fats affect genetic expression that directly affects fat storage and thermogenesis (the production of body heat, which affects energy expenditure and fat accumulation).

## **Dietary Recommendations Are Seriously Distorted on Omega-6**

While the American Heart Association (AHA) recommends you to consume 5% to 10% of your calories as omega-6 from vegetable oils such as soybean oil, canola, corn, olive, cottonseed, sunflower and peanut oil, research suggests you really need only 1 to 2 grams of linoleic acid per day, and ideally from whole food sources such as whole nuts and seeds.

With the exception of flax, chia and hemp seeds, most other plant seeds have high amounts of omega-6. In a recent interview, DiNicolantonio comments on the discrepancy between conventional recommendations and what nutritional research actually shows:

"Instead of recommending whole foods, [the AHA] recommends refined oils, which makes absolutely no sense. The Lyon Diet Heart Study<sup>11</sup> lowered linoleic acid from over 5% to about 3.5% [and found] a 70% reduction in cardiovascular [problems] and mortality.

There's actually no evidence to support the AHA or the United States dietary guidelines,<sup>12</sup> [which] recommends consuming high amounts of omega-6s from vegetable oils ... [T]hese isolated oils ... don't have the natural vitamins and minerals and antioxidants in the coatings around seeds and nuts that give us omega-6 to protect them from oxidizing in our body.

When you consume these isolated oils, even if it's a cold-pressed omega-6, the acid in your stomach will oxidize those oils and create lipid hydroperoxides and aldehydes. We absorb these and they cause a ton of damage."

# To Protect Your Heart and Brain, Normalize Your Omega-3-to-6

Getting back to the issue of heart disease, it's important to realize that it's not your total cholesterol or cholesterol per se that causes heart disease. Rather, it's that the linoleic acid in omega-6-rich vegetable oils gets integrated into your high-density lipoproteins (HDLs), low-density lipoproteins (LDLs) and very low-density lipoproteins (VLDLs), and when it oxidizes, it then causes atherosclerosis, i.e., hardening and narrowing of your arteries.

Linoleic acid also damages the endothelium — the layer of cells lining your blood vessels — thereby allowing LDLs and VLDLs to penetrate into the subendothelium.

This chain of events is also at play in neurodegenerative diseases. The aldehydes created by linoleic acid crosslink tau proteins and create neurofibrillary tangles. As

noted by DiNicolantonio, "It has been shown in animal studies that these aldehydes can literally create neurofibrillary tangles that you see in Alzheimer's disease."

Between 1959 and 2008, the linoleic acid concentration in subcutaneous adipose tissue in Americans increased by about 250%,<sup>13</sup> from 9.1% to 21.5%. Since the half-life of linoleic acid is about two years in adipose tissue, this is a reliable marker of intake, and this rise in linoleic acid intake parallels the increase in prevalence of both obesity and diabetes, suggesting the advice to eat more vegetable oils is an unwise one.

As mentioned, the American diet is also extremely lopsided in favor of omega-6 over omega-3, which further worsens the situation, as omega-3 can to some degree ameliorate the damaging effects of oxidized linoleic acid. Rather than a ratio of 16-to-1 in favor of omega-6 (the national average), we need to aim for a ratio of 3-1-to-1. Again, ideal amounts appear to be around:

- 1 to 2 grams of omega-6 (linoleic acid) from plant seeds and tree nuts, not vegetable oils.
- 3 to 4 grams of omega-3 (EPA and DHA) in the form of fatty fish, krill oil, or fish oil
  in which the omega-3s are bound to triglycerides and not ethyl esters. (Ethyl esters
  are a synthetic substrate created through the micro distillation process of crude
  fish oil, in which ethanol and/or industrial alcohol is added.

This mix is heat distilled in a vacuum chamber, resulting in a concentrated omega-3 ethyl ester condensate, which are the least bioavailable form of omega-3. This appears to be one of the reasons why many commercial fish oils fail to produce expected health benefits in some studies, so if using fish oil, make sure it's a triglyceride form.)

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