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Omega-3 — A Simple Way to Lower Your Risk of Disease

Analysis by Dr. Joseph Mercola | April 28, 2024

STORY AT-A-GLANCE

- The Omega-3 Index test measures the amount of EPA and DHA, the two long-chain omega-3s found in marine sources, in red blood cell membranes, expressed as a percentage of the total fatty acids in the membrane
- Most Americans have an index of 4% to 5% of EPA/DHA in their red blood cell membranes, and the target is between 8% and 12%. To raise your index from 5% to 8%, you need roughly 1,000 mg to 1,200 mg of EPA/DHA per day
- Higher omega-3 index has been linked to better health across the board, and appears to lower the risk of most, if not all, chronic diseases
- Another ratio commonly referred to is the omega-6 to omega-3 ratio, but this ratio is not nearly as useful or important as the omega-3 index
- EPA and DHA help thin the blood, lower the risk of stroke and heart attack, lower serum triglyceride levels, blood pressure and inflammation, add structural stability to the mitochondrial membrane and aid mitochondrial energy processes

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In this video, I interview William (Bill) Harris, Ph.D., an internationally recognized expert on omega-3 fatty acids. He's been studying omega-3s since 1980 and has published more than 300 scientific papers on fatty acids and health.

A few years ago, he founded the Fatty Acid Research Institute (FARI)[1] in South Dakota, which specializes in epidemiological research, where they look at the relationship

between blood omega-3 levels and risk for disease. He's also a faculty member of the University of South Dakota School of Medicine.

> *"We're trying to build a case that omega-3 levels in the blood are as, if not more, important than knowing your cholesterol level when it comes to your health and being able to control it,"* he says.

The Omega-3 Index

What he's referring to is the level of omega-3 in your red blood cell membranes. Two decades ago, his team developed a red blood cell membrane-based omega-3 test called the Omega-3 Index. You can take the **Omega-3 Index test at their website for only $49.95**.

The Index measures the amount of EPA and DHA, the two long-chain omega-3s found in marine sources, in red blood cell membranes, expressed as a percent of the total fatty acids in the membrane.

"We thought that was absolutely the best way to assess your body's omega-3 status, and so we've been using that ever since," he says. Harris has conducted correlation studies showing the Omega-3 Index test reflects the status of the heart in heart transplant patients, for example. Commenting on the usefulness of the index, Harris says:

> *"It responds very well to increased intake of EPA and DHA, like a good biomarker should, and higher levels have been linked to better health across the board of a variety of disease conditions, so I think it really is meaningful."*

Higher Omega-3 Consistently Linked to Better Health

Harris goes on to discuss the relevance of epidemiological, population-based studies, which is where you look at large datasets of people. The Framingham Study is one classic example, where they sought to determine why so many men were dying of heart attacks in a Boston suburb in the 1940s.

Healthy men and women were recruited and data were collected on their lifestyles, diet and bloodwork. Participants were then followed for decades, to see who died of heart attack. The Framingham studies developed the concept of risk factors, which for heart attack include high blood pressure and smoking.

In the mid-1970s, offspring of participants in the original Framingham study were recruited for additional research. This is known as the Framingham Offspring Study, and it included Omega-3 Index testing of stored blood samples.

> *"The people, on average, were about 65 at the time that blood was drawn in the early 2000s. We then asked the question, 'If you have a high (or low) omega-3 index at that age, does that predict any disease outcomes?' Yes, it does. It predicts risk for Alzheimer's disease. It predicts risk for heart disease. It predicts risk for death from any cause.*
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> *With higher levels of omega-3, people live longer. That's a microcosm of the kinds of studies we work on at the Fatty Acid Research Institute because there have been 50 or 60 Framingham-type studies all around the world. [A]lmost all have measured omega-3 levels and disease outcomes. This is our sandbox!"*

What About the Omega-6 to Omega-3 Ratio?

Another ratio commonly referred to is the omega-6 to omega-3 ratio, but Harris doesn't think this ratio is nearly as useful or important as the omega-3 index. For starters, it's not very precise because there are other omega-3 fats besides EPA and DHA, such as DPA and ALA.

There are also seven different types of omega-6 fatty acids, and we don't know a whole lot about them. One exception is **linoleic acid (LA)**, which I've written about on many occasions. I also cowrote a **paper on LA**[2] with Christopher D'Adamo, which was published in the peer-reviewed journal Nutrients in July 2023.

> *"So, when you say omega-6 or omega-3, you don't really know what the denominator is and what the numerator is, and it presumes that all the omega-*

3s behave the same and have the same health benefits, and all the omega-6s have the same health benefits or detriments, which is really not true," Harris explains.

"That's not very nuanced in my view, because we've seen some studies where some omega-6 fatty acids are apparently good. They're associated with better outcomes, whereas, others are not. So, to pool them into one metric where you don't know how it's made up is another reason I don't like this particular ratio.

I guess the third one is, you can have a high level of omega-6 and a high omega-3, or a low omega-3 and a low omega-6 and have exactly the same ratio. It's really the amount that's there that's the most important. What we're lacking in America, or in the West in general, is the long-chain omega-3s. That's the biggest problem.

I hate to distract from that problem by digging into the omega-6 side of it because some people could say, 'Well, I can fix my ratio just by eating less omega-6 and not increasing my omega-3,' and I don't think that's going to help."

The counterargument to that would be that there are enzymes, desaturases and elongases, that take the baseline essential fats — ALA and LA — and convert these precursors into the long chains products, EPA/DHA and ARA, and if you overwhelm the system with LA, you essentially monopolize those enzyme systems and the omega-3 products are harder to make.

If you consume preformed long-chain omega-3s, then that is not an issue, but if you don't, then excessive omega-6s will prevent the conversion of omega-3. Limiting omega-6 can, in this way, be somewhat helpful, as it allows for the shorter chain omega-3 (ALA) to be converted to the longer chain EPA and DHA. Harris responds:

"That's true, but there are certain metabolites of even arachidonic acid that are beneficial. For example, lipoxygenase A1 is anti-inflammatory, and prostacyclin prevents platelet aggregation.

> *There are metabolites of linoleic acid itself that don't go through arachidonic that have at least beneficial relationships with blood pressure and inflammation. It's a much more complicated system, I think, than just omega-6 is bad, omega-3 is good. It's just much more nuanced than that."*

OmegaQuant does offer an omega-6 to omega-3 ratio test called Omega-3 Index plus Omega-6/Omega-3 Ratio. But when it comes to addressing a bad ratio, Harris still believes the best way to do that is to increase your EPA and DHA intake, as opposed to merely lowering your omega-6 intake.

Why Omega-3s Are So Beneficial to Health

So, what is it about omega-3 EPA and DHA that makes them so important for health? In summary, these fatty acids:

Help thin the blood, which discourages inappropriate clotting that can lead to a stroke or heart attack

Lower serum triglyceride levels

Help lower blood pressure, in part by improving the health of the lining of your blood vessels so that they can relax better

Have several anti-inflammatory effects — For example, provided you have enough EPA and DHA in your membranes, when an inflammatory insult occurs, metabolites of the EPA and DHA — resolvins and protectins — will be synthesized. As their names imply, these metabolites help protect against and resolve inflammation. If you do not have sufficient omega-3, the inflammatory response persists longer and can become chronic

Help the mitochondrial membrane process energy — Improving the fluidity and flexibility of the mitochondrial membrane allows enzymes and the other proteins embedded in the membrane to operate more smoothly

Add structural stability to cell membranes throughout the body — Importantly, if the membrane is loaded with monounsaturated or saturated fats, the omega-3 cannot get in there. The membrane will then be stiffer in that area, which impedes the activity of essential receptors, enzymes, transporters and other proteins that control the flow of nutrients into and waste products out of the cell.

With the proper amount of omega-3, the membranes allow these agents to move freely, making everything work as it should

Why Fish Oil Is Not an Ideal Omega-3 Source

While most reach for fish oil to increase their omega-3 level, this isn't the best choice. In fact, most “fish oils” on the market today are actually synthetic ethyl esters, which are different from the triglyceride and phospholipid forms omega-3 found in sea foods, which are roughly 50/50 triglycerides and phospholipids. Krill oil also delivers omega-3 primarily in the phospholipid form. Harris explains:

> *"Yes, there are two natural forms. The omega-3s are found in triglycerides, which we classically think of as oils. A triglyceride has three fatty acids on each molecule. Typically, in most fish that are rich in omega-3, one of those three will be EPA or DHA, so about 30% of the fish oil will be omega-3. That's the triglyceride.*
>
> *The other natural form that marine omega-3s are found in is phospholipids. Phospholipids are the primary constituents of cell membranes, and it's in the cell membrane where the omega-3s do their primary work.*
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> *There are two spots for fatty acids on a phospholipid, and it depends on the fish, but typically about maybe 20% to 30% of the phospholipids have EPA and DHA. Those two forms are natural. You get both triglycerides and phospholipids when you eat a salmon steak or any other 'oily' fish; these are the highest in omega-3.*

The ethyl ester is a completely synthetic product. It starts out as a raw fish oil. That's where that EPA and DHA molecules come from in the first place, but at the refinery, all the fatty acids get chopped off of the triglyceride backbone. Then they throw away the monounsaturates, the saturates and the small amount of omega-6s, and that leaves the omega-3s by themselves.

The omega-3s have to be hooked to something before encapsulation, and so the favorite thing is to hook them up to ethanol (alcohol) to make 'ethyl esters.' When all they have in the vat is now omega-3 ethyl esters, then they can pack more EPA and DHA into each capsule, so the concentration is higher.

Virtually all of the pharmacologic products that are omega-3-based are ethyl esters, and they have been used since the mid-1990s. But there is nothing 'natural' about an ethyl ester. I guess there's debate on how effective they are. We do know that if you take the ethyl ester on an empty stomach, you're not really going to absorb it. They're very poorly absorbed.

Their absorption can be improved if you take the ethyl ester with a fatty meal, because that will stimulate the digestive juices and allow some of it to be absorbed, but it's not the best form for absorption. Triglycerides and phospholipids are much better forms for absorption."

In November 2023, I spoke to a few hundred people at the Documenting Hope Conference in Orlando and was able to share my latest insights on how to optimize your health and prepare for the next crisis. I was surprised that people fly in from around the world to see me.

Are Ethyl Esters Beneficial?

In the Italian GISSI-Prevenzione Trial,[3] published in 1999, heart attack survivors were given one capsule of Omacor (an ethyl ester form with 840 mg of EPA+DHA per 1 g capsule) a day. After two to three years of follow-up, they reported a tremendous drop in cardiovascular death and all-cause mortality.

However, there was no placebo group. They merely compared it to standard of care. It was also an open-label trial, with no objective assessment of compliance.[4] Moreover, the study was funded by companies that sell the product, so there's a conflict of interest there that may have influenced the results.

Indeed, since then, several studies have used Omacor (or Lovaza, the U.S. version) and have produced mixed results. Some showed no benefit at all, others were positive. An example of the latter is the REDUCE-IT Study, which used an EPA-only ethyl ester called Vascepa, made by Amarin. Patients at high risk for heart disease were given 4 grams a day.

Compared to placebo, at the five-year mark, the treatment group had a 25% lower risk of cardiovascular disease, nonfatal heart attacks and all-cause mortality. That was a very positive outcome. However, the placebo was an indigestible mineral oil, which may have confounded results. Did Vascepa really improve health, or did the “placebo” increase the risk of cardiac events?

> *"That's been hotly debated,"* Harris says. *"Of course, if your placebo really is harmful, even if your drug does nothing, it will look like the latter is doing great because it's doing better than the placebo, which is supposed to be neutral.*
>
> *Well, there is considerable evidence now that at least some of the apparent benefit of the EPA ethyl ester was derived from a worsening of outcomes in the placebo group. Taking 4 grams, almost a teaspoon of mineral oil a day for five years, well, that's just not natural at all."*

How Much Omega-3 Do You Need?

So, in summary, the best sources of omega-3 DHA and EPA are cold-water fatty fish like wild-caught Alaskan salmon (farm-raised salmon has omega-3 but in lower amounts than it used to since farmers have been adding vegetable oils to the salmon feed), mackerel, herring, sardines and krill oil.

The next question is, how much do you need for optimal health and disease prevention? This brings us back to the Omega-3 Index. Most Americans have an index of 4% to 5% of EPA/DHA in their red blood cell membranes, and the target is thought to be between 8% and 12%.

From Harris' studies, raising your index from 5% to 8%, you need roughly 1,000 mg to 1,200 mg of EPA/DHA per day. As for the ratio of EPA to DHA, Harris says the general recommendation is either a 60-to-40 or 40-to-60 mix. "Just don't do a 10-to-90 mix." The ratio is a nonissue if you're getting your omega-3s from fatty fish, which provide these fatty acids in a fairly balanced amount.

> *"Personally, I try to eat fish a couple of times a week,"* Harris says. *"But I don't always succeed, so I do what a lot of people do. I take a supplement. I take about 1,400 mg a day, EPA and DHA."*

The best way to determine the dose you need is to do an Omega-3 Index test, available from **OmegaQuant**. It's a dried blood spot test and the kit is sent to your home. The basic test is about $50, and you get your results about five days after it's received in the lab. After a few months of supplementing, retest to see where you're at, and adjust your dose accordingly. In closing, Harris notes:

> *"Again, my mantra is the Omega-3 index. EPA and DHA [levels] are what need to be improved, need to be increased. It's not a silver bullet, but it's one thing you CAN do something about cheaply, safely, easily, quickly. There's not a disease yet that we've seen that has not benefited from having a higher omega-3."*

Sources and References

- [1] Fatty Acid Research Institute
- [2] Nutrients July 13, 2023; 15(14): 3129
- [3] The Lancet August 7, 1999; 354(9177): 447-455
- [4] The Lancet October 30, 1999; 354(9189): 1554