

Harnessing the Power of Omega-3s to Lower Your Risk of Disease

A Special Interview With Bill Harris, Ph.D.

By Dr. Joseph Mercola

Dr. Joseph Mercola:

Welcome, everyone. Dr. Mercola helping you take control of your health, and today we're going to dive deep into omega-3 fats with one of the leading experts, Dr. Bill Harris. So, welcome and thank you for joining us today.

Bill Harris:

Thank you, Joe. Great to be with you.

Dr. Joseph Mercola:

I suspect many people know who you are, but there's probably more who don't, so I think you would be best qualified to provide us with your long-standing history in this area and what you've done in your journey to achieve the level of prominence you have in this field.

Bill Harris:

Well, that's kind of you. I just happen to get on the right horse at the right time. I think that's the way it worked out. Yeah, my background is in nutrition, a Ph.D. in Nutrition from University of Minnesota. And then around 1980, I got involved with omega-3 research when I did my postdoctoral fellowship with Dr. Bill Connor in Portland, Oregon. That's when we started studying the effects of salmon oil on blood cholesterol levels. That was really our primary interest at the time.

It turned out that that's just about the time that the Eskimo studies had been reported from the Greenland physicians, Drs. Dyerberg and Bang, and they found omega-3s were really helpful for cardiovascular disease. And we were just getting into it from a lipid, lipoprotein area and platelet studies, so blood clotting studies. It turned out to be a very, very productive field, and I've been blessed to be part of it ever since.

Dr. Joseph Mercola:

Where are you at now? What are you doing?

Bill Harris:

Now, I'm at the University of South Dakota School of Medicine and that's where I'm on faculty, but I'm primarily a researcher at what we formed about three years ago called The Fatty Acid Research Institute, where we collect a variety of specialists [who] work together primarily in epidemiological studies. Studies looking at the relationship between blood omega-3 levels and

risk for certain disease outcomes, whether it's death or cancer or heart disease or kidney disease or whatever. 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, at least as important when it comes to your health and being able to control it.

Dr. Joseph Mercola:

So, when you say "in the blood," I would assume you're meaning not the serum but the red blood cell membranes?

Bill Harris:

Right, yeah. I thought we'd get into that later, but right. In principle, the test that we developed about 20 years ago is a red blood cell membrane-based omega-3 test called the Omega-3 Index. That's the amount of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), the two long-chain omega-3s that are in marine sources. The amount of EPA and DHA in red cell membranes expressed as a percent of the total fatty acids in the membrane. So, that, we thought, was absolutely the best way to assess your body's omega-3 status, and so we've been using that ever since.

Dr. Joseph Mercola:

I'm sure you've done, but I'm not aware of it, and if I was, I forgot it. Have you done correlation studies with this? With tissue analysis like the liver or other organs to see how well that correlates?

Bill Harris:

Yeah, early on we did it with the heart. We were able to get human heart tissue from heart transplant patients, actually, and we were able to show that the omega-3 level in the red blood cell was a good reflection, at least it correlated well with the heart. It's been done in a variety of other tissues since that time. Of course, you could do that in animals more readily than humans because you can't get, at most, solid organs in humans unless you're at autopsy. In all cases, I think the place where it doesn't reflect as well is the brain. The brain is a very highly specialized and protected organ. We do know the DHA levels in the brain are very important for health, but whether you can, as an adult, change your brain omega-3 content by taking supplements or eating more fish, that's still an open question.

Dr. Joseph Mercola:

Yeah, it's an important question because-

Bill Harris:

Yeah.

Dr. Joseph Mercola:

-from all perspectives we all appear to be fatheads because I think, I believe – you would probably know – the concentration of fat in the brain is like 80%.

Bill Harris:

Yeah. If you look at lipids writ large right there, there are so many membranes, and membranes are made up mostly of lipids, so the brain is very much a lot of fat.

Dr. Joseph Mercola:

All right. Well, let's get back to the test you developed because – and then of course we're going to dive deep into omega-3s. I've been really looking forward to this because – not omega-3, but omega-6 has become an absolute passion of mine because I believe it in excess, it is in 99.999% of the public. It leads to devastating impacts on health. Not many people believe that they can balance the omega-6 [to] omega-3 ratio and that would provide benefits. We can certainly dialogue on that, but there are some big question marks, in my mind at least, that's not going to be quite as effective as lowering the linoleic acid (LA) content.

Why don't we go into the ratio and you've discussed that it's a pretty good reflection of what's in your body tissues. We don't know the brain yet. Oh, that's surprising. In all this time, the 50 years you've been working on this, that they haven't been able to do animal studies to come to some conclusion on that.

Bill Harris:

Yeah. Well, they do animal studies, it's just they don't typically do it in fully grown "adult" rats, mice, and do feeding studies that give reasonable amounts. It's so easy in animal studies to give hyper omega-3 doses, huge doses that are physiologically almost irrelevant for humans because you can't eat that much, but experimenters can manipulate the diet like crazy with animals. What's missing is the human data, but we can talk about the Omega-3 Index. Again, that's EPA and DHA. It's a good reflection of most of the other organs and your typical – one nice thing about it, 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 for a variety of disease conditions, so I think it really is meaningful.

Dr. Joseph Mercola:

What are some of the deep meanings you can extract from finding out these results?

Bill Harris:

Well, the way – I guess it's probably easy to back up and say how we do these studies that we're primarily focusing on in The Fatty Acid Research Institute because what we do is we access data, and there are just hundreds and thousands of data sets out there. People who have done studies over the years, who have – The classic study is epidemiologic studies, as you all know the Framingham Study. Framingham is a suburb of Boston and back in the 1940s, men, particularly, were just falling dead from heart attacks at fairly early ages. Nobody knew why.

Thought it was genetic, maybe. They just didn't know what it was. And that was pretty much the impetus for starting this population-based "Let's recruit a bunch of presumably healthy men and women in a town and just measure everything we can in their blood and their diet and their lifestyle, and then just watch them over time and see who develops heart attacks."

That's the beginning of cardiovascular epidemiology, and what they discovered in that first Framingham group was that it looked like people who had high blood pressure were the guys who were dying of heart attacks. Guys who had high cholesterol were dying of heart attacks. Guys who smoked were having heart attacks. They kind of developed this concept of a risk factor that we are so familiar with now, but that was something that kind of came out of the early Framingham studies. Anyway, that cohort was recruited in the '40s, they're all dead. But in the 1970s, their offspring were recruited into the same kind of study. It's called The Framingham Offspring Study, and it's in that study that we measured the Omega-3 Index in blood samples that had been stored from [inaudible 00:09:16]-

Dr. Joseph Mercola:

What year did that start? What year did that start?

Bill Harris:

That started in the mid-'70s. We see these people about every four years, roughly, to follow up who's developing what diseases, et cetera, et cetera. In the early 2000s was an exam, Framingham Offspring Exam, where they drew blood and they stored red blood cells. It was those red blood cells that we were able to get ahold of and measure the Omega-3 Index in. We have been then doing studies asking the question – And the people on average were about 65 at the time that blood was drawn in the early 2000s. And so we're able to ask 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, predicts risk for death from any cause. 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. Started for different reasons, started by different investigators, but they almost all have saved blood and they've measured omega-3 levels. And so, we have a coalition now. This is actually a group that's organized out of Tufts University. Dr. [Dariush] Mozaffarian started this thing. This is a coalition of studies like the Framingham, like I discussed. We put all this data together from 50,000, 60,000 and 70,000 people, linking omega-3 levels in the blood to different outcomes. We've been publishing with that group for some time and finding, again, that higher omega-3 just across the board is just a signal for better health.

Dr. Joseph Mercola:

Let's get into the details. When you say the Omega-3 Index, is this the percentage of omega-3s which would be – Are the omega-3s just cross-qualified as EPA and DHA? Or are you using other omega-3s in there? And is this [inaudible 00:11:38]-

Bill Harris:

Just EPA and DHA. Yeah.

Dr. Joseph Mercola:

Just EPA and DHA, which are the primary ones, of course, but there are others.

Bill Harris:

There are others.

Dr. Joseph Mercola:

Is that the percentage of the total lipids in the membrane? Or is it – I would assume that's the case.

Bill Harris:

Yeah.

Dr. Joseph Mercola:

Okay. That's pretty straightforward. Okay.

Bill Harris:

Yeah.

Dr. Joseph Mercola:

Then, because there's another compounding index or ratio that's commonly ascribed, which I don't think you're a fan of, but I certainly could be mistaken, which is the Omega-6 to [Omega-3] Ratio.

Bill Harris:

Yeah, I would say I'm less of a fan of that than I am of the Omega-3 Index, and I've got a few reasons, of course. One is [that] it's not very precise. As you alluded to, there are more omega-3 fatty acids than just EPA and DHA. There's DPA (docosapentaenoic acid), there's ALA (alpha-linolenic acid), and when you say omega-3 writ large, you don't know which omega-3s you're talking about, so that's a problem. Plus, you don't know which omega-6 fatty acids. There are about seven of them in the blood. The principal ones are linoleic acid and arachidonic acid, but there's a bunch of other ones. When you say "omega-6," "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, have the same health benefits, and all the omega-6s have the same health benefits or detriments, which is really not true.

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 – that's another reason I don't like it. 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, I think, that's the most important. To me, what we're missing in America, or in the West in general, is we're lacking 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.

Dr. Joseph Mercola:

All right. Well, the counterargument to that would be that there are a set of enzymes, desaturases and elongases, that take the baseline, essential fats essentially, the ALA, typically, or the linoleic acid, and converts them to the longer chains, in EPA and DHA, the 20 and 22 carbons. The argument is that if you're overwhelming the system with these omega-6s, you essentially monopolize those enzyme systems, and the availability to the omega-3 precursors for the higher-order fats is almost eliminated because it's overwhelmed.

Bill Harris:

But if you're talking about actually consuming the preformed long-chain omega-3s, then that [inaudible 00:14:59]-

Dr. Joseph Mercola:

It's not an issue, right.

Bill Harris:

It's not an issue, right.

Dr. Joseph Mercola:

But, but-

Bill Harris:

Right, I know you're going to say there are other enzymes downstream that take the long-chains, [like] arachidonic, and compete with those, and that's true. But there are certain metabolites of even arachidonic acid that are beneficial, anti-inflammatory. Lipoxygenase, for one, is beneficial. There are metabolites of linoleic acid itself that don't go through arachidonic, that have at least beneficial relationships with blood pressure and inflammation, things like that. 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.

Dr. Joseph Mercola:

Yeah. Okay. So, do you report the Omega-6 to Omega-3 ratio in your Omega-3 Index?

Bill Harris:

Yeah, that's one of the reports that's available from OmegaQuant. Yeah.

Dr. Joseph Mercola:

Okay, so [inaudible 00:16:01]-

Bill Harris:

Yeah, so we have [inaudible 00:16:01]. We have a basic test. It's just the Omega-3 Index, and that's what you get. And then the next step up is an Omega-3 Index plus Omega-6/Omega-3 Ratio, because a lot of people like it, you know?

Dr. Joseph Mercola:

Mm-hmm.

Bill Harris:

They don't have to – We'll give them what they want. I don't have to like it.

Dr. Joseph Mercola:

You don't put any disclaimers on the test when you send them the report?

Bill Harris:

Oh, we just say, "Here's what's normal. Here's what we think the evidence would say is a good ratio." I still like the – The way to fix a bad ratio, I think we say this in the report, the primary way to improve a bad omega-6 to omega-3 ratio is to increase your EPA and DHA intake. That's what I think. That's the action that follows. That will fix any ratio if you do that.

Dr. Joseph Mercola:

All right, and we'll get into [the] details of that because that's where it's important, but before we do, why don't you provide the supposition as to why omega-3s are so beneficial for health?

Bill Harris:

Well, I mean, we do provide information about the benefits of omega-3.

Dr. Joseph Mercola:

No, no. Just to our audience now, let us know. Summarize what are the primary benefits from your longstanding, multi-decade career in this field.

Bill Harris:

Yeah, so why are omega-3s beneficial? Good question, and it's a multi-pronged answer because omega-3s are so important across multiple systems. The first thing we knew about omega-3s was they – Actually, the first thing we knew about from the Eskimo studies was they made the blood – We call it “thin the blood.” It made your blood less likely to clot in the wrong places.

Obviously, we want our blood to clot at the right times, but when it clots at the wrong time, you've got a heart attack or a stroke, and omega-3s help prevent that inappropriate blood-clotting via a complicated mechanism of how they affect the blood platelets and things like that. Second thing was [that] it lowered triglyceride levels. Serum triglycerides are the second lipid in the blood the doctors typically look at. Cholesterol is the first, then they look at triglycerides, and omega-3s were uniquely effective at lowering blood triglycerides.

Dr. Joseph Mercola:

Does it lower them more effectively than omega-6?

Bill Harris:

Yeah. Oh yeah, yeah. Omega-6 will lower triglycerides – Well, it won't lower triglycerides pretty much at all. Omega-3s are the ones that do that.

Dr. Joseph Mercola:

Okay.

Bill Harris:

Next thing that came along really was, I think, a blood pressure-lowering effect. [Omega-3s] had good effects on the vascular [lining], the blood vessel lining, that made it more healthy so it would relax better, which had an effect on blood pressure, so a little bit of a blood pressure-lowering effect. Then, the big – I think, now, the gorilla in the room – or was it an elephant? – is the primary mechanism most of us think about is anti-inflammatory. Omega-3s have multiple prongs of anti-inflammatory effects. As they reside in the membrane and once they're released from the membrane, they become anti-inflammatory molecules. Those are really the big four, I think, we'd say.

Dr. Joseph Mercola:

Do you think they play any role in membrane physiology, specifically in mitochondrial membranes?

Bill Harris:

Yeah, I think so. They do appear to help the mitochondrial membrane process the energy. Of course, the mitochondria is the energy-producing organelle in the cell and there's some pretty good evidence, although it's not been studied extremely well. It's a fairly new field in the omega-3 story, but changing mitochondrial membranes are the fluidity, flexibility. It allows the enzymes and the other proteins that are embedded in those membranes to operate more smoothly. It's kind of like having the right amount of oil in your car. It just moves more smoothly.

Dr. Joseph Mercola:

Now, one of the researchers that I interviewed recently shared that – obviously most people who study these know that they increased membrane fluidity, but what he shared with me was that they actually form structural stability factors because unlike a saturated fat or a mono, which are mostly long, simple chains and you can compile many in a row, they're not bulky. They really can't form these – like, I guess, rebar and cement, that provides some stability to the membrane.

Bill Harris:

Yeah. There are some sections of the membrane, which researchers have figured out, they call them "lipid rafts," like a raft on the ocean. We think of a membrane as a very homogeneous, boring sheet, like an envelope that a letter is in, but a membrane is much, much more complicated than that. There are sections of the membrane, the lipid or the raft, where a lot of metabolic processes take place. The omega-3s can improve the function of those rafts if they're loaded with monounsaturates or saturated fatty acids.

The fatty acids are tight, they stick, the membrane is stiffer in that area, and the enzymes and the transporters and the other proteins that move through that membrane can't do it as well. They're not as efficient in what they do. But the omega-3s, because they're big and chunky and bulky, they spread it out and that's at least my picture of it. They make more room for the proteins to do their thing.

Dr. Joseph Mercola:

All right, so you've provided the assertions [on] the benefits of omega-3s and you've got a lot of data to support that. Then, the obvious recommendation is, "Well, how do we increase our omega-3s?" This is where, I think, it's vitally important to understand the details, because if you fail to do that, you're going to make yourself much worse, in my view. I'd like to see what your views are. I believe the market for fish oils is like \$3 billion. It's a pretty big market and most of those, in my mind, should not be used for human consumption. They're synthetic. They never existed in nature before. They're ethyl esters, which is absolutely different than the triglyceride form of omega-3. In my mind, a huge question is if the benefits outweigh the risks. So, why don't you give us your perspective on this? Because this is your field.

Bill Harris:

Yeah, sure, and you're right. The natural form of omega-3 in fish – there are really two natural forms. The omega-3s are found in triglycerides, which we classically think of as oils and they're

typically about one – 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%. That's the triglyceride. The other molecule omega-3s that are naturally found in fish is phospholipids. Phospholipid is what really makes up the primary membrane of cells. And the omega-3s – There are two spots for fatty acids on a phospholipid, and it depends on the fish, but typically about maybe 20%, 30% of the phospholipids have EPA and DHA. Those two forms are natural. You picture salmon, you get both triglyceride and phospholipid when you eat a salmon steak or any fish that's oily, high omega-3 fish.

The ethyl ester, which you mentioned, is a completely synthetic product. That's true. It starts as a raw fish oil. That's where that molecule comes from in the first place. But when it gets taken into a factory, the fatty acids get chopped off of the triglycerides. Typically, we're just starting with triglyceride — Chop off the fatty acids, throw away the monounsaturates, throw away the saturates [and] leave the omega-3s by themselves. They have to be hooked to something, typically, and so the favorite thing is to hook, instead of a glycerol, which is what they're naturally hooked to, which is an alcohol, they pick ethanol, an alcohol. Everybody knows that one. And they put an ethyl group on the fatty acid, on the omega-3s, and then they are chemically able to separate all the non-omega-3s and the omega-3s once they're in that form, and they can concentrate them and put them in a pill. So, all the pharmacological products that are omega-3-based are ethyl esters because they can get more, they can cram more molecules into one capsule.

That was the thought, and that's been used for – Those have been used since Omacor came out probably in the mid-1990s. But you're right, they are not natural. I guess there's debate on how effective – 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, a meal that's got some fat in it because that will stimulate the digestive juices and allow some of it to be absorbed, but it's not the best form for absorption. Triglyceride and phospholipid are much better forms for absorption.

Dr. Joseph Mercola:

What are the relative concentrations of the amount of omega-3 in natural forms? Is it like maybe two-thirds triglyceride and a third phospholipid?

Bill Harris:

In salmon?

Dr. Joseph Mercola:

No, just in general. And I know there's a range, but I'm just curious.

Bill Harris:

Yeah. No, I think it's about – In natural forms in fish, it would be about 50/50, 50% in triglycerides, [inaudible 00:27:05]. Because they don't store a lot of fat – I mean, they store

some, of course. Cod stores all their fat in their liver, not in the muscle. So cod fish, it's a very low-fat fish unless you're eating the liver or extracting oil from the liver. But salmon, mackerel, herring, sardines — those sorts of fish do store their fat in their muscle, and so it's kind of a mixture of roughly 50/50 triglyceride and phospholipid.

Dr. Joseph Mercola:

All right. So, for the last three decades, the industry has developed the capability of providing us with fish oils in ethyl ester form. As you said, it's somewhat controversial. But has anyone in your group or others examined the data out there? I mean, this is a long time and I know it takes a long while to do these studies, but certainly someone's looked at evaluating these ethyl esters with respect to consequences on all-cause mortality and morbidity.

Bill Harris:

Yeah. The first study that set us all on fire was reported right around the year 2000. It was called The GISSI-Prevenzione Study, and GISSI, G-I-S-S-I, is an acronym for a group of Italian cardiology researchers. They have a group and they did a study with what was then known as Omacor. Now, it's Lovaza. But it's an ethyl ester, and they gave one capsule a day of this ethyl ester to people who'd had a heart attack and survived it.

Dr. Joseph Mercola:

How many milligrams of omega-3 was in it?

Bill Harris:

840 milligrams EPA plus DHA.

Dr. Joseph Mercola:

That's a [inaudible 00:28:46].

Bill Harris:

Yeah, so that's one capsule. They reported after — actually, this was — It took probably about two or three years of follow-up. They reported a tremendous drop in not only cardiovascular death, but [also in] all-cause mortality, and that was with this ethyl ester product. Now, there was no placebo. It was usual care versus this one capsule of Lovaza. Okay [inaudible 00:29:22]-

Dr. Joseph Mercola:

And it was funded by the people selling the product.

Bill Harris:

Well-

Dr. Joseph Mercola:

Imagine that.

Bill Harris:

Imagine that, I mean, yeah, I guess-

Dr. Joseph Mercola:

It's a prime conflict of interest.

Bill Harris:

Well, every drug is a conflict of interest, right? Everything.

Dr. Joseph Mercola:

Yeah.

Bill Harris:

Yeah, exactly. But they were trying to get approval for selling this as a pharmaceutical, and the reason they want to do that instead of selling it as a supplement is you get insurance reimbursement for pharmaceuticals. You don't get them for dietary supplement, even if it's the exact same molecule. So, it's driven by a desire to make a profit, and Pronova was the company at the time that was doing that. That's what they did, and that tradition has been continued and unfortunately, there have been several studies where they've used Lovaza or Omacor or other similar ethyl esters that did not show a benefit; didn't show any harm, but just didn't show the benefit that was seen in those early GISSI studies. That's dampened enthusiasm pretty much after 2010, over the last, maybe, 15 years.

Several studies have been reported that were not successful with one exception, which is called the REDUCE-IT Study, [in] which we used an ethyl ester, but it was an ethyl ester [that's] just EPA-only. This is a product that was originally developed in Japan and found its way into a more worldwide distribution. The company, Amarin, an Irish company, picked up this drug and decided to test it in people at high risk for heart disease, and they gave them 4 grams a day of EPA ethyl esters, no DHA, versus a placebo, which has been quite controversial whether it really was a placebo or not. They used a thing called mineral oil, unabsorbable oil that you need a placebo of some kind. You need some kind of a control group to compare.

They found after five years that there was a marked 25% reduction in cardiovascular risk, risk for total mortality, risk for nonfatal heart attacks, fatal – It was a slam dunk. Great outcome. Surprising, I think, to many people. But there it was and it looked very good for the omega-3 space, and the FDA (Food and Drug Administration) has given that company approval for an indication to give it to reduce risk for cardiovascular disease. Previous to that, the only real FDA-approved indication for omega-3 pharmaceuticals was you had to have very high triglyceride

levels. That's what they're for and, of course, doctors can prescribe things off-label if they want to. And so, they could be prescribed for other reasons, but that's the FDA approval.

So, Amarin, for its product Vascepa, the EPA-only ethyl ester, they got an approval for cardiovascular disease reduction. The controversy around that has been: Did the omega-3 product actually lower risk or did the placebo increase risk for events? That's been hotly debated. Of course, if your placebo really is harmful, even if your drug does nothing, it will look like it's doing great because it's doing better than the placebo, which is supposed to be neutral. Well, [with] mineral oil, there is considerable evidence now that at least some of the apparent benefit, and probably not all, but some of the apparent benefit of the EPA ethyl ester was derived from a worsening outcome in the placebo group.

Dr. Joseph Mercola:

Yeah, mineral oil is not a food. It is not a food. It could only do bad things to you.

Bill Harris:

Yeah, well, you're right. Taking 4 grams, almost a teaspoon of this stuff a day for five years, I mean, that's just not natural at all. Nothing close.

Dr. Joseph Mercola:

Yeah, yeah. Most likely, it is going to contribute to some fat-soluble mineral and vitamin deficiencies. It's going to just excrete them out of the body.

Bill Harris:

They talked about, also, many of these people are on statins. In fact, I think everybody was on a statin because they were all [at] high risk for cardiovascular [disease], so that would potentially maybe dissolve it, prevent the statin from being absorbed well, too. I mean, there's evidence on both sides. It's a hotly contested issue, but there's a cloud hanging over the REDUCE-IT Study. Unfortunately, yeah, DHA tends to get villainized, vilified by the folks who – yeah, right. But I think DHA is great. I think you need both EPA and DHA.

Dr. Joseph Mercola:

So, you can certainly make a strong argument for that, but I don't know that you can make the argument and extend it to most supplements, especially synthetic supplements. I think there's pretty good [crosstalk 00:34:55]-

Bill Harris:

By that you mean ethyl ester?

Dr. Joseph Mercola:

Ethyl ester. Yes.

Bill Harris:

Yeah, because if we keep running down the different forms of omega-3, of course, krill oil is an important contributor to the omega-3 space and that's a natural product, but mostly-

Dr. Joseph Mercola:

A hundred percent natural. Mostly phospholipids.

Bill Harris:

Mostly phospholipids, right. That's good. And then there are these things called restructured triglycerides or re-esterified triglycerides. They're omega-3 products that are back in the triglyceride form, but they've been put that way by a chemical company that has thrown away the non-omega-3 fatty acids and stuck the omega-3s back on this three-carbon glycerol backbone. You really can't call it natural. The triglyceride is a natural product, but an omega-3 triglyceride is not a natural product.

Is it bad for you? I don't think so. But if you want to be picky, there's only krill oil or phospholipids and triglycerides, natural triglycerides that are unmolested by – Well, I guess you can't even say that because there is certainly the cleaning-up process when you get raw fish oil. Nobody's putting raw fish oil into capsules. They have to be cleaned up a lot.

Dr. Joseph Mercola:

Yeah, they have to be. They're toxins that are in the ocean, so that has to be-

Bill Harris:

Right. Well, and there are some odors that are not very pleasant either that [[crosstalk 00:36:33](#)]-

Dr. Joseph Mercola:

Oh, yeah. And those odors – and actually the human nose is a very sensitive instrument, even probably more sensitive to some of the tests they use to detect them. But these peroxidized lipids, rancid lipids, are very dangerous to health and that's one of the problems with omega-3s and actually any PUFA, polyunsaturated fatty acid, is that these double bonds are highly susceptible to oxidative damage and you have to be absolutely committed to the highest-level quality to protection. Usually vitamin E is a pretty good solution, but it's got to be followed through the whole chain.

Bill Harris:

Yeah, right. And they exclude oxygen, they exclude air from the whole processing chain to do it under nitrogen, which is not reactive. Yeah, the best producers are very careful and it makes the

products more expensive because it just takes more effort and more expensive chemicals to do it, but yeah.

Dr. Joseph Mercola:

Yeah, for sure. It's a little bit easier to do with krill because it's in the phospholipid form, but anyway, that's another rabbit hole I won't go down now. One of the potential variables that contributes to the benefits that you described earlier from the omega-3 supplementation or increase in the diet would be two substances, resolvins and protectins, or group of substances. I am confused as to how those are derived. Are they actually in the oil initially? Or are they derived metabolically from the original fatty acids?

Bill Harris:

It's kind of both. There's a whisper, there's a small amount of some of these metabolites of EPA and DHA that can be found in fish oils, but it's less than 1%, for example. Most of it is made in your body on demand. If you've got the omega-3s EPA [and] DHA in your membranes, in your cells, when you have an inflammatory insult of some kind, these molecules are synthesized, the resolvins [and] protectins. There's a few other classes, but just the general idea is these are molecules that you're designed to actually resolve, hence the name, resolve the inflammation. We used to think that when you have an inflammatory insult, you have the inflammatory response and then somehow it just goes away. It just goes away, which is not a very scientific explanation of anything.

Charles Serhan at Harvard has been the leader in discovering that inflammation doesn't just go away. It actually gets driven down. It gets resolved, it gets pushed, and it's these omega-3 products that are doing that pushing, that are driving those inflammatory processes back into a quiet state. If you haven't got the omega-3s, the inflammatory response stays longer and it becomes a little more chronic, and that's, I think, the problem.

Dr. Joseph Mercola:

Do you think it's the resolvins and protectins that are metabolized that produce this suppression of inflammation? Or is it more the prostaglandins and eicosanoids that are derived from the omega-3s that are responsible for lowering inflammation? Or is it both?

Bill Harris:

I think it's more of the resolvins and protectins. Those are the molecules that are – More so than the cyclooxygenase products, the prostaglandin-type products, which are also important. There are so many different metabolites from EPA and DHA, and then they all – We're learning the dance. It's a concert, it's an orchestra, all these molecules doing different things on demand. Some of them are suppressing even the receptors on the cell that will sense an inflammatory action happening in the body. If you suppress that action, the cell doesn't make an inflammatory [response], so it actually suppresses the inflammatory response, which is good to a point. As well as once inflammation starts, the omega-3s will suppress it to keep it from getting out of hand, but

it's the resolvins and protectins that are doing that latter thing, that actually is actively suppressing or reversing.

Dr. Joseph Mercola:

I wasn't aware of that. That is interesting, and especially in light of the fact of information I learned about linoleic acid. I published a narrative review on LA in July in Nutrients, and one of the reviewers gave me feedback and said, "Listen." Because I purported one of the mechanisms was it actually increases inflammation and that the speculated consensus is that linoleic acid is converted to arachidonic acid, which is pro-inflammatory. Then, he responded with this review that showed that actually conversion from LA to arachidonic acid is pretty minimal contribution to arachidonic. I couldn't dispute. I mean, it was solid evidence.

Then, I just capitulated and said, "Okay, well, that's not the mechanism." And just like you referred to with the resolvins and protectins, it's the metabolites that are so key. In LA, it's the metabolites that destroy your health, which are typically – most of the metabolites, which are referred to as OXLAMs, or oxidative linoleic acid metabolites, like 4-hydroxynonenal, malondialdehyde, glyoxal, methylglyoxal, there are hundreds of these toxic reactive aldehydes that get spun off from LA that make it so perniciously dangerous in excess. In excess.

Bill Harris:

So [crosstalk 00:42:47] people?

Dr. Joseph Mercola:

I'm sorry?

Bill Harris:

Does that happen in people? Does that happen in [inaudible 00:42:50]-

Dr. Joseph Mercola:

Oh yeah, a hundred percent. No, you don't have to have McDonald's French fries to get these things. No, no. They're there if you heat up the oil. But no, this spontaneously happens at biological temperatures, for sure. Unless they're protected well with vitamin E, then that peroxidation is pretty radically reduced.

Bill Harris:

Yeah, yeah. Well, I'm glad you brought this [up]. It's an interesting topic because one of these – this group of researchers, The Force Coalition, we've looked at blood omega-3 levels predicting outcomes, health outcomes. We also looked at the same studies, the same blood samples, the same people, looked at the linoleic acid levels in the blood and we've asked the same question. I mean [inaudible 00:43:40]-

Dr. Joseph Mercola:

By blood you mean the red cell membranes?

Bill Harris:

Well, it can mean plasma, linoleic acid, plasma phospholipids or red blood cells. They're all kind of like the omega-3s. They correlate with each other pretty quickly.

Dr. Joseph Mercola:

Okay, so the serum correlates with membrane fatty acids, too? It would seem to me it would be changed based on your last meal.

Bill Harris:

Well, yeah, and linoleic acid in the blood, of course, can only come from diet, as you know. It's an essential fatty acid. But it's, particularly in the West, as you know, we've had a lot of linoleic acid in our diet for decades.

Dr. Joseph Mercola:

That's a profoundly serious understatement.

Bill Harris:

Fair enough. So what you eat today, it really isn't going to bump your linoleic acid. It's kind of buffered already, so it doesn't really change very much day to day. In fact, you just alluded to the point that the conversion to arachidonic acid is very minimal, like 1%, something like that, when they use radioactive tracers to look and see how much shows up. So, the linoleic acid and arachidonic are – Arachidonic is pretty well-regulated by systems, how much level we should have. But when we've looked at linoleic acid levels in the blood – I mean, the hypothesis would be, if the idea that linoleic [acid] is bad for you, [then] higher levels of linoleic [acid] in the blood should predict long-term adverse health outcomes. That would be a reasonable hypothesis.

When we've looked at that, we've looked at it for two different diseases, for cardiovascular outcomes, whether it's death or events, and we've looked at it for developing Type 2 diabetes. In both cases, the higher levels of linoleic acid, the lower the risk for those two diseases. So it's the opposite of the idea that it's bad for you, as it looks like – if it was omega-3, we'd say they're good for you because higher levels of omega-3 [are] associated with better health outcomes.

Now, we're finding higher linoleic acid levels in the blood are at least associated with better or lower risk for heart disease or diabetes. You've got to think, "Well, okay, how do you explain that? What do you do with that? How do you square that with some of this chemical evidence that you're talking about?" Some of these metabolites-

Dr. Joseph Mercola:

Well, and epidemiological evidence, too. I mean, the incidence of heart disease has increased over 5 million times. Heart attacks were essentially an unknown commodity in the United States. The first report of heart attack in the United States was 1912, and now it's 250,000 people dying a year. Yeah, there's a lot of variables that contributed to it, but for me, the evidence is beyond abundantly clear. It's the industrialized processed seed oils produced in the U.S. Civil War, started being produced then, and then it gradually increased. That study's side is intriguing for sure, but I'd like to dive into details because I'm virtually close to 100% percent convinced that it's wrong, 100% wrong.

Bill Harris:

Okay, okay. [inaudible 00:47:00] I'll send you the papers. You can have a look at them, see what you think is – Yeah, it does require some explanation if we're going to hypothesize that linoleic [acid] is bad for you. I mean, it's certainly possible that seed oils could be bad for you. It doesn't have to be.

Dr. Joseph Mercola:

No, and let me be more precise. Excess linoleic acid. Your body absolutely requires linoleic acid. If you didn't have it, you would have severe health problems, but it's almost impossible not to get enough because it's in every food. It's questionable whether or not to call it "essential." Yes, technically it is because your body cannot make that from scratch, but if you're eating food to stay alive, you're going to have more than enough, so is it really essential?

Bill Harris:

Yeah, yeah. I guess if you're getting the "pure nutrition definition"-

Dr. Joseph Mercola:

Yeah, yeah, it'd have to be-

Bill Harris:

-[inaudible 00:47:51] is essential, right?

Dr. Joseph Mercola:

But pragmatically, it's not.

Bill Harris:

Yeah, it's there everywhere, right.

Dr. Joseph Mercola:

Everywhere.

Bill Harris:

What would you recommend [as] the percent of calories as linoleic?

Dr. Joseph Mercola:

Well, it's not me. I mean, even the conservative, hyper-conservative RDAs (Recommended Dietary Allowances) are 2% of total daily calories. The average person is at 25%. I mean, this is a highly damaging fatty acid that just is taken in excess. Most of the bulk of that is industrial processed seed oils, and I don't think any rational scientist or someone committed to integrity is going to deny that we should be avoiding processed seed oils like the plagues, unlike what the American Heart Association was recommending in the '50s and still to this day. When you increase seed oils, you actually lower cholesterol levels, which they believe is a healthy thing, that's a whole other area we don't have time to go into now, but it's not.

Bill Harris:

It's complicated. It is complicated, for sure. Yeah, yeah. No, I mean, I guess I would push back under 25% of calories as linoleic acid. I think the evidence is more like it's 6% or 7% in America.

Dr. Joseph Mercola:

Oh no, no, no. I mean, tissue biopsies are 12% to 13%.

Bill Harris:

Well, I mean your dietary intake, not necessarily tissue levels, dietary intake. I'm sure you can find tissues where it's that high.

Dr. Joseph Mercola:

Well, 99% of the fat consumed in the United States in the 19th century was from animal sources. That obviously can include fish, seafood. Today, 80% to 90% are from seed oils.

Bill Harris:

Yeah, that's [crosstalk 00:49:38]-

Dr. Joseph Mercola:

It's [crosstalk 00:49:39] totally switched it. We swapped it.

Bill Harris:

-[inaudible 00:49:40] animal fat really isn't, milk, cheese, dairy, beef, pork, chicken-

Dr. Joseph Mercola:

Yeah.

Bill Harris:

-they've all been [inaudible 00:49:47].

Dr. Joseph Mercola:

That was pretty much the only option people had in the 19th century, and now It's been villainized and demonized.

Bill Harris:

Yeah. Yeah. Well, it's great. Saturated fat has been an interesting topic as well as dietary cholesterol.

Dr. Joseph Mercola:

Yeah, for sure, for sure, but that's the simple data. The data is we went from 99% to basically swapping it around all with vegetable oils. I mean, ancestry, historically and just logically, doesn't make any sense that it would have some serious impact, most likely negative on human health.

Bill Harris:

Well, right. Certainly, before you could actually mill grains and press oils out of them, you were just eating the natural oil that was in the kernel corn or a kernel of wheat. There was not much there, and sure.

Dr. Joseph Mercola:

Anyway, we went on a tangent because I'm passionate about this, but what I wanted to go get back to, and [what] we started with, is your affirmation, that you're in agreement with, that synthetic fish oils are probably not the best idea. It's certainly controversial and debated in the field. We get back to the recommendation. What do you do? What is the recommendation? How do you get increases of omega-3s in your tissues?

Bill Harris:

Yeah, and the question we often get is how much EPA and DHA do you need?

Dr. Joseph Mercola:

Yeah, that's another good question for sure.

Bill Harris:

It gets back to the Omega-3 Index as your marker of your omega-3 status, your omega-3 meter in your blood. Most Americans are around 4% or 5% of EPA, DHA and red cell membranes. We think the target ought to be 8% to 12%, somewhere up in there, at least over 8%, so the levels are at least half of what they ought to be in America. How do you do that? How do you get up there? From our studies, it looks like if you want to go from a 5% Omega-3 Index to an 8%, [it] takes roughly 1,000 to 1,200 milligrams a day of EPA/DHA on average [inaudible 00:52:05]-

Dr. Joseph Mercola:

What ratio of the EPA/DHA?

Bill Harris:

It doesn't really make a lot of difference. I think we always advocate both of them together, whether it's kind of a 60/40 mix or 40/60 mix. Just don't do 10-to-90 mix.

Dr. Joseph Mercola:

It becomes less of an issue if you're eating whole seafood.

Bill Harris:

Totally, totally. You get both of them in a fairly even mix in whole seafoods. Roughly, that 1 gram a day is a great target for most people. That's 10 times what the average intake in America is right now, so even a gram a day doesn't seem like a lot, but relative to what we're eating, it's a lot. That's about what it will take. When you look at a Japanese population where their – at least historically, the traditional Japanese diet, not the current one, which is becoming more and more Westernized, sadly – their intake was roughly 1 gram to 1,200 [grams] a day and their average Omega-3 Index is about 9% or 10% in those days.

So, it fits, and the Japanese, it's a great – You can't pin it on the omega-3s, but I like to try – Japanese do live about four years longer on average than we do. They have higher omega-3 indexes, but they smoke more, they have more hypertension, they have more stress, things that should shorten their lives, but in reality, they live longer, [have] very little heart disease. They have strokes because they have a lot of salt in their diet and they have high blood pressure, so you can cause hemorrhagic strokes, but the Japanese experience is certainly one of the pillars of the evidence that higher omega-3 levels are good and safe.

Dr. Joseph Mercola:

Do you think the hemorrhagic strokes might be partially attributed to the increase in the omega-3s because one of the things they do is antiplatelet or antithrombin?

Bill Harris:

That's true. [inaudible 00:54:07]-

Dr. Joseph Mercola:

[inaudible 00:54:07] likely bleeding time.

Bill Harris:

And that's been a concern, but when it's been looked at in clinical trials or in observational studies, there's no increase in clinically significant bleeding. We're about to publish a study in one of our collaborative things with 70,000 people, looking at risk, the relationship between omega-3 levels in the blood and risk for stroke. So, two kinds of strokes. One is the more common stroke where it's an atherosclerotic clot, so you have a brain infarction, a thrombotic stroke. The other kind of stroke is what you're talking about, is a hemorrhagic stroke where you bleed. And we actually found [a] higher omega-3 reduced risk for the first kind of stroke, the thrombotic stroke, and no difference, no effect on hemorrhagic stroke. Whether you're high or low omega-3 did not increase your risk for hemorrhagic stroke.

Dr. Joseph Mercola:

That's good to know because most of the strokes are thrombotic, so overall the [crosstalk 00:55:19]-

Bill Harris:

Yeah, [crosstalk 00:55:18] in the West. But certainly, like heart attacks, right.

Dr. Joseph Mercola:

Yeah. Interesting. So, what do you do personally or would recommend personally? It would seem, from my perspective, the ideal is to get it from seafood. Now, that's not convenient for a lot of people and a supplement might be a wiser choice, so why don't you walk us through your interpretation of the data and conclusions?

Bill Harris:

Yeah, me personally, we try to eat fish. I mean, I live in South Dakota, okay, but you can get fish anywhere.

Dr. Joseph Mercola:

Yeah, of course.

Bill Harris:

We have Costco here. Come on, you [inaudible 00:55:57] salmon whenever you want. So, we try to eat fish a couple times a week. [I] don't always succeed, so I do what a lot of people do. I take a supplement. I take about 1,400 milligrams a day, EPA and DHA, and my Omega-3 Index is about-

Dr. Joseph Mercola:

Is that supplement an ethyl ester?

Bill Harris:

No, it's a restructured triglyceride.

Dr. Joseph Mercola:

Okay, so it's not, as we discussed earlier, not totally natural, but a lot closer than an ethyl ester?

Bill Harris:

Right, right, and it does the job. Take it with food. Always take it after a meal so it's absorbed best.

Dr. Joseph Mercola:

It sounds like your conclusion is that ideally the whole food or the seafood approach – a clean seafood, of course. You don't want to be eating shark or whale or tuna because of its concentration of heavy metals.

Bill Harris:

Yeah, yeah. Well, right, and that is always the recommendation. Go food first if you can, but as you alluded to, just because you think that's the best way to do it. If people don't do it, then you got to give them a plan B.

Dr. Joseph Mercola:

Yeah. It's the same thing with sunshine. I have not swallowed vitamin D supplements for 15 years and my levels very rarely go below 90 and typically in the summer are over a hundred. But I still capitulate and say, "Listen, people don't have the opportunity to live in subtropics like I do and go outside every day around solar noon, so then if they're confined to the indoors and unable to do that, then you probably should take a vitamin D supplement."

Bill Harris:

Yeah, right. It's the same. You got to be practical.

Dr. Joseph Mercola:

Yeah, pragmatic for sure. Where's the best way to get the Omega-3 Index? Not the [Omega-]6 to [Omega-]3 Ratio, the Omega-3 Index. We're really precise here.

Bill Harris:

You can have the ratio if you want it, but we'll give you the index. too. That's the one I think it's actionable. That's fine. OmegaQuant, O-M-E-G-A, OmegaQuant.com. You can order this test directly. If it's a dried blood spot test, the kit is sent to your home. The basic test for the Omega-3 Index is about \$50 I think, and you get a report about five days after it's received in the lab. You should get a report of your omega-3 status, and I always recommend it.

Dr. Joseph Mercola:

That's pretty good.

Bill Harris:

Yeah, I think it's – I love it. It's a test we developed 20 years ago and we'd still love to see it in more clinical medicine. Love to see it as common as a cholesterol test.

Dr. Joseph Mercola:

I agree. I think there's a lot more value to it and it's really convenient because you don't have to get your butt out to a lab to get your blood drawn. You get to draw it yourself. I think is it one spot or two spots around the card?

Bill Harris:

One spot, one drop.

Dr. Joseph Mercola:

One spot? Okay, one drop, so yeah-

Bill Harris:

[inaudible 00:58:54]

Dr. Joseph Mercola:

It has to be a good drop, you got to fill up that circle, but it's pretty easy to do.

Bill Harris:

I mean, I think, we're offering now – I think most cards have three spots and you can fill three spots, and then if you decide you want your vitamin D done or your hemoglobin A1C, then we've already got the blood there and we can do it. You can change your mind, but [inaudible 00:59:18]-

Dr. Joseph Mercola:

What's the charge for the vitamin D [test]?

Bill Harris:

That's also \$50, I believe.

Dr. Joseph Mercola:

Yeah, that's pretty good. Yeah, I mean, because even the wholesale costs for physicians – and that's the 25-hydroxy[vitamin] D I'm assuming, right?

Bill Harris:

Yeah.

Dr. Joseph Mercola:

Yeah, so that's a pretty good deal actually. All right, so if you want your vitamin D – and I think everyone should get their vitamin – Talk about tests that's every bit as important as cholesterol, if not more, would be your vitamin D.

Bill Harris:

Vitamin D, right.

Dr. Joseph Mercola:

Yeah, because just like there's no way you know what your blood pressure is, you don't know what your vitamin D level is or your omega-3 level. You can get some idea because you know what you've been eating, but when it comes to vitamin D – I guess you know what you've been doing with respect to the sun exposure or swallowing your vitamin D, but still you've got to measure it. That's the only way to know.

Bill Harris:

That's the only way to know. Everybody's so different, too.

Dr. Joseph Mercola:

Yeah.

Bill Harris:

Yeah.

Dr. Joseph Mercola:

Wow. Any other insights you'd like to share with us?

Bill Harris:

I guess, how would you wrap it up? Again, I think my mantra is the Omega-3 Index, EPA/DHA, is what needs to be improved, it needs to be increased. There are other factors as well for – It's not a silver bullet, but it's one thing you can do something about cheaply, safely, easily, quickly, and improve your omega-3 status. There's not a disease yet that we've seen that has not benefited from having a higher omega-3 reduced risk, so-

Dr. Joseph Mercola:

I'm wondering if you integrate a vitamin E recommendation while taking omega-3s or a food source?

Bill Harris:

We have not. I certainly understand the logic of it. That's very reasonable. I guess I've not seen the damage that you're talking about. I have not particularly looked for it. That's the other side [inaudible 01:03:06].

Dr. Joseph Mercola:

If you're doing things unnaturally, which certainly taking a synthetic fish oil is, and you're taking it in excess trying to achieve these benefits you as ascribed to omega-3s earlier, I mean, it just seems obvious you're going to get damage because it's totally unnatural and you're pushing the system where it wasn't designed to go.

Bill Harris:

Yeah.

Dr. Joseph Mercola:

And there's biochemical solid evidence that this is a potential risk of increasing oxidative damage. I mean, PUFAs are – I mean, they're essential. You've got to have them, you need them. But in excess, the key is in excess, is where the issue becomes.

Bill Harris:

Right, and then that becomes, obviously, a definition of excess.

Dr. Joseph Mercola:

Right, right,

Bill Harris:

Right, right, and that's-

Dr. Joseph Mercola:

All right. Well, this has been great. I thank you for all your wisdom and sharing it with us and [being] kind enough to do that and help us understand some of the mechanics of it and offering a practical tool to help us assess where we fit on this goal. It's relatively inexpensive and convenient, which it's a pretty good combination.

Bill Harris:

That's what we hope to do. It's been fun talking to you, Joe. Thank you for having me.

Dr. Joseph Mercola:

All right. Well, thanks, Bill. Appreciate it and all the best.

Bill Harris:

Okay, take care.